Australian participants in British nuclear tests in Australia

Vol 2: Mortality and cancer incidence

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Australian Government
The Repatriation Commission

2 June 2006

Mr Bruce Billson MP
Minister for Veterans' Affairs
Parliament House
CANBERRA ACT 2600

Dear Minister

I have pleasure in submitting the final reports of the *Australian Participants in British Nuclear Tests in Australia, Dosimetry and Mortality and Cancer Incidence Study*, which have been prepared on behalf of the Repatriation Commission by the Department of Public Health at the University of Adelaide and members of the Dosimetry Subcommittee. I would personally like to thank all the researchers for their hard work on this study.

On 16 July 1999, the former Minister for Veterans' Affairs, the Hon Bruce Scott MP, announced that a cancer and mortality study of Australian nuclear test participants in British tests in Australia would be conducted. The aim of the study was to examine whether there is an increased rate of death and cancer among male nuclear test participants compared to the general Australian community.

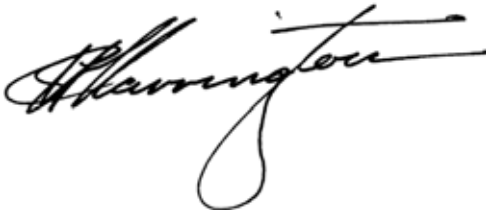
The study has taken a significant time to complete. This was due to the need to develop a nominal roll of Australian participants in the tests, which was required as the starting point for the study, and the complexity of reconstructing radiation dosage estimates received by participants at the test sites.

The Scientific Advisory Committee had the role of reviewing and advising on the methodology of the study, and supervised the report's preparation. The membership of the Committee is set out at Appendix 3 of the Dosimetry Report. In addition, an Exposure Panel was established to reconstruct ionising radiation dose estimates for participants of the tests, and its membership is outlined at Appendix 4 of the Dosimetry Report.

I would like to take this opportunity to thank the members of the Consultative Forum for their contribution during the conduct of the study. Due to the length of time over which the study was conducted, a number of changes in membership took place. A full list of members, and the organisations they represented, can be found at Appendix 2 of the Dosimetry Report.

Finally, I would like to thank all the departmental staff who worked on this study.

Yours sincerely



Simon Harrington
COMMISSIONER

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1 June 2006

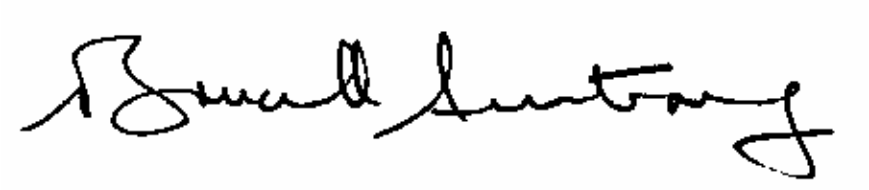
Rear Admiral C S H Harrington AM RAN (Retd)
Repatriation Commissioner
PO Box 21
Woden ACT 2606

Dear Rear Admiral Harrington

I am writing to you as Chair of and representing the Scientific Advisory Committee to the studies of dosimetry and mortality and cancer incidence in Australian participants in the British nuclear tests in Australia. I am pleased to report that the members of the Committee, with one exception, consider that the studies have been conducted and analysed to a high level of scientific quality and that the final reports of them entitled *Australian Participants in British Nuclear Tests in Australia, Dosimetry and Mortality and Cancer Incidence Study,* prepared for the Repatriation Commission by the Department of Public Health at the University of Adelaide and members of the Dosimetry Subcommittee, accurately represent and soundly interpret the studies' findings.

Towards the end of the Committee's consideration of the reports, there was contention over the content and wording of some parts of them; particularly the section entitled *Main Findings*. Most of the Committee members present at the time considered the matters under contention to be matters of presentation not of science. However, the contention was not resolved and Ms Ann Munslow-Davies, the Consultative Forum representative on the Committee, felt, in consequence, that she could not endorse the reports.

Yours sincerely



Bruce Armstrong

cc Mr Barry Telford
Chair
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Main findings

The study to investigate the health effects of participation in the British nuclear tests in Australia is reported in two volumes. Volume 1, the radiation dosimetry study, used data from the tests and modelling to estimate the radiation exposure of participants in the tests. Volume 2 includes: the mortality study, which compared the number of deaths in test participants with that of the general population from the time of the nuclear tests to the end of 2001; and the cancer study, which compared the number of cases of cancer, whether fatal or not, in test participants, with that in the general population from 1982 to the end of 2001, and compared radiation exposure of participants with and without leukaemia.

The overall death rate in test participants was similar to that of the general population. There were 4233 deaths observed in participants, compared with 4150 expected from the general population.

The most common cause of death in test participants was cancer, and death from cancer was 18% greater in test participants than would be expected in the general population. Deaths from causes other than cancer were generally fewer than expected in test participants compared with the general population, with the number of deaths from heart disease, cerebrovascular disease (mostly strokes), and external causes (suicide, accidents, poisonings, etc) fewer than expected. The number of deaths from respiratory diseases in test participants was about the same as expected from the general population.

The cancer incidence study showed an overall increase in the number of cancers in test participants, similar to that found in the mortality study. The number of cancer cases found among participants was 2456, which was 23% higher than expected. A significant increase in both the number of deaths and the number of cases was found for (figures in brackets show increase in mortality and incidence):

- all cancers (18% and 23%)
- cancers of the lip, oral cavity and pharynx (50% and 41%)
- lung cancer (20% and 28%)
- colorectal cancer (24% and 16%)
- prostate cancer (26% and 22%).

The number of cancer cases (but not the number of deaths) was also significantly greater in test participants for the following cancers (figures in brackets show increase in incidence):

- oesophageal cancer (48%)
- melanoma (40%)
- all leukaemias (43%)
- all leukaemias except chronic lymphatic leukaemia (61%).

Other findings included:

- of the 26 mesothelioma cases in test participants, 16 occurred in RAN personnel, which was nearly three times the number expected
- in RAAF personnel, there was nearly double the expected number of deaths from melanoma, and cases of melanoma were increased by two–thirds.

The increases in cancer rates do not appear to have been caused by exposure to radiation. No relationship could be found between overall cancer incidence or mortality and exposure to radiation. None of the above cancers occurring in excess showed any association with radiation exposure in this study. In particular, there was no link between radiation exposure and leukaemia, excluding chronic lymphatic leukaemia (non-CLL leukaemia), which is commonly found to be increased in groups exposed to radiation. These findings are consistent with the low levels of radiation exposure found in this study. Only 4% of the study population had an estimated radiation exposure greater than 20 millisieverts (mSv) from test participation, and 79% had an estimated exposure of less than 1 mSv. The estimated mean radiation exposure of the study population due to participation in the tests was 2.8 mSv, only slightly greater than the background exposure received by every Australian every year.

In the absence of a correlation with radiation exposure, the excess of non-CLL leukaemia is unexplained. Other than radiation, the best established cause of leukaemia is exposure to benzene, but there is no information available about benzene exposure in test participants.

Mesothelioma is a cancer that is nearly always associated with past exposure to asbestos, and the excess mesothelioma in RAN personnel is most likely due to asbestos in naval vessels. The asbestos exposure need not necessarily have occurred at the time of the nuclear tests.

Lung cancer is strongly related to smoking, and the excess could be due to a higher smoking prevalence in test participants. Oesophageal cancer and cancers of the lip, oral cavity and pharynx are also known to be strongly smoking-related. Together, the excesses of these cancers indicate that there was probably a higher smoking prevalence in participants than in the general population.

However, some contribution to the lung cancer excess is also likely from asbestos in RAN personnel, and possibly in civilian participants also. The occurrence of mesothelioma in RAN and civilian subjects is a definite indication of asbestos exposure, and occurrence of other asbestos-related diseases would therefore not be surprising. The occurrence of lung cancer cases is also highest in RAN and civilian subjects. Many of the civilian subjects in the cohort were in the construction industry, where asbestos was commonly used, at a time when less caution was exercised than in recent years. Whether any of these subjects were exposed to asbestos during the nuclear tests is not known.

Asbestos exposure is also a possible contributing factor to the excess of colorectal cancer. The incidence of this cancer was also highest in RAN and civilian personnel.

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Executive summary

Between 1952 and 1957, the United Kingdom conducted 12 major nuclear weapons tests in Australia. The tests were carried out in five major operations: two at Monte Bello Islands, Western Australia (1952 and 1956); one at Emu Field, South Australia (1953); and two at the Maralinga Range, South Australia (1956 and 1957). Scientific studies on weapons components, known as minor trials, were undertaken in parallel between 1953 and 1963 at both Emu Field and the Maralinga Range.

Over 16,000 Australians, both military and civilians, participated in the tests. The range of tasks performed by Australian personnel increased steadily during the various series. The first three series (Hurricane, Totem, Mosaic) had limited Australian involvement. However, by the final two series (Buffalo, Antler), Australian participation was quite extensive, including responsibility for the Maralinga Range between and following the major tests.

The health effects of nuclear weapons tests on the British participants have been investigated, and three reports have been issued. In 1999, the Commonwealth Government resolved that a nominal roll would be compiled of Australian participants in the tests, and that this would form the basis for a mortality and cancer study.

There are two reports from this study:

- Volume 1: a report on radiation exposures received by participants
- Volume 2: a report on mortality and cancer incidence of participants, and a case–control study on the occurrence of leukaemia in relation to radiation exposure.

Study population

The study population was based on the nominal roll of test participants compiled by the Australian Government Department of Veterans' Affairs (DVA). The study population comprised 10 983 male subjects, of whom 7116 were military participants and 3867 were civilians.

Subjects were followed to a cut-off date of 31 December 2001, when 5494 subjects (50%) were confirmed living, and 4427 subjects (40%) were confirmed deceased. A further 23 participants were known by DVA to be deceased, but corroborating evidence for the death could not be found. Less than 1% of participants (105 participants) were known to be living overseas or to have died overseas. The vital status of 934 subjects (8.5%) on the cut-off date was unknown.

Cancer incidence was studied from 1982 to 2001. Because cancer rates in the study population were compared with national rates, which are only available from 1982 onwards, this study excluded test participants who died before 1982. This limitation probably does not greatly affect the study findings, because cancers caused by external factors do not usually develop until many years after initial exposure.

Study methods

Mortality rates and cancer incidence rates in participants were compared with national rates, compiled by the Australian Institute of Health and Welfare.

Because of the substantial number of subjects lost to follow-up, two methods of analysis were used. Results are presented for the method representing the estimate that is likely to be closest to the true rate.

Mortality is expressed as a standardised mortality ratio (SMR), with a confidence interval. The SMR is the ratio of the actual number of deaths in the participants to the number expected if the death rate was the same as in the general Australian population. An SMR greater than 1.0 indicates that the mortality is greater than in the general population, and an SMR less than 1.0 indicates that it is less. However, the SMR calculated using the study data is only an *estimate* of the true SMR. The confidence interval is a statistical estimate of the likely range within which the true SMR lies. If the lower boundary of the confidence interval exceeds 1.0, we can be reasonably confident that the true SMR exceeds 1.0, in which case the SMR is said to be 'significantly increased' — that is, the mortality rate is considered to be higher than in the general population. Conversely, if the *upper* boundary of the confidence interval is less than 1.0, the SMR is said to be 'significantly reduced', and the mortality rate is considered to be lower than in the general population.

Only statistically significant findings are shown in this summary. A 'significant' increase in SMR does not necessarily mean that it is a large increase.

Cancer incidence refers to the rate of occurrence of new cancers, regardless of whether the outcome is fatal. The standardised incidence ratio (SIR) is the ratio of the actual number of cancers in the participants to the number expected if the cancer rate was the same as in the general Australian population. Like the SMR, if the SIR is greater than 1.0, then the test participants have a greater than expected number of cancers.

Radiation dosimetry

A panel of health physicists (the Dosimetry Panel) was convened to develop estimates of the radiation doses received by participants. These estimates were used to investigate any relationship between radiation and health outcomes. The panel drew on extensive, but not complete, sets of historical and primary documents, kept at organisations such as the Australian Radiation Protection and Nuclear Safety Agency and the National Archives of Australia. Documents relating to the tests held by individuals were also reviewed, and some participants were interviewed to obtain an understanding of the tasks undertaken by work groups at the tests.

One of the main sources of information on participants' exposure to external radiation is the record of film badges worn during the tests. Although the records are by no means complete, and it is apparent that not all the badges worn were actually processed, there are sufficient numbers to provide a basis for dose estimation. These film badge records have been supplemented by estimates based on measured radiation levels in contaminated areas and the estimated time that participants spent there. Computer calculations have also been used to estimate the dose rates that would arise from ground contamination, and how these would change with time. For internal exposure, such as that resulting from

inhalation of radioactive dusts, virtually no monitoring data were available and only computer modelling could be used.

Each participant was assigned an estimated accumulated dose for each test series from the dose rate estimates, the work groups they were in (e.g. military formations, ships' companies) and the activities of each work group during that series. On the basis of these estimates, participants were grouped into one of five exposure categories, A to E, which represent effective doses of:

A less than 1 millisievert (mSv)

B 1 to less than 5 mSv

C 5 to less than 20 mSv

D 20 to 50 mSv

E over 50 mSv.

For some individuals, there is insufficient information on which to base an estimate of the dose; these are assigned to category F: 'unknown' exposure. If an individual attended several test series, the doses were combined.

Results

Radiation dosimetry

The radiological hazards that the participants faced arose mainly from nuclear weapons debris, including fallout, when it was distributed throughout their working environment. Those in areas contaminated by radioactive materials could be exposed to external radiation directly or to internal radiation from inhaled or ingested radioactive material, or to both.

The radiation doses received by Australian participants were generally small. Approximately 79% of the participants were assessed as receiving doses less than 1 mSv — that is, approximately half the annual dose received from natural background radiation. Only 4% received more than 20 mSv, the current internationally accepted annual limit for a radiation worker recommended by the International Commission on Radiological Protection. The average accumulated dose to participants was 2.8 mSv, approximately equal to the annual dose from natural background radiation. Although many participants have expressed concerns about the radiation dose they may have received from the actual flash of a detonation, exposures from this source were negligible, except in a group of military 'Indoctrinees' who participated in Operation Buffalo at Maralinga in 1956.

Some groups did receive significant exposures. The main groups who were exposed at the level of category C (5 to less than 20 mSv) or higher were:

- some RAAF aircrew who flew through the contaminated clouds in RAAF or RAF aircraft after nuclear explosions

- crew members from HMAS Hawkesbury who assisted in records recovery and participated in Joint Services Training Unit (JSTU) exercises during Operation Hurricane
- crew and divers from HMAS Koala who recovered a landing craft during Operation Hurricane
- members of the JSTU who undertook radiation monitoring training during Operation Hurricane
- members of the Radiation Hazards group at Operation Totem
- Peace Officers who patrolled contaminated areas
- Indoctrinee Force members at Operation Buffalo
- elements of the Maralinga Range Support Unit who provided a range of engineering and support duties in forward areas from Operation Buffalo through to post Operation Antler activities
- drivers and passengers in contaminated vehicles travelling over contaminated ground
- members of the Australian Health Physics Group (AHPG) who conducted radiation surveillance
- members of the AHPG team who collected Cobalt-60 (^{60}Co) pellets after Operation Antler
- a team that decontaminated and dismantled the DC 12 building in Maralinga Village at the end of the minor trials.

This dosimetry study was made independently of a similar UK study that estimated the doses received by British participants in the tests in Australia. The UK dose estimates are broadly similar to those presented here for the Australian participants.

Death rates

The commonest causes of death in the study group were cancer (1497 deaths) and ischaemic heart disease (coronary artery disease, 1148 deaths). Other leading causes of death were stroke (254); respiratory disease (338); and external causes, including accidents, poisoning and suicide (281).

The overall death rate was not significantly different from that in the general Australian male population. There were 4233 deaths observed in participants, compared with 4150 expected from the general population.

In RAN personnel, mortality was significantly higher than in the general population. In RAAF personnel, mortality was significantly lower than in the general population.

Cancer mortality was 18% higher than in the general male population. Mortality rates for diseases other than cancer were not elevated. Mortality from ischaemic heart disease was significantly lower than in the general population. Mortality from respiratory diseases was close to population rates. The death rate from external causes (suicide, poisonings, injury) was lower than in the general population. The suicide rate was 65% less than the rate in the general population.

SMRs by major cause are shown in Table 1.

Table 1 Standardised Mortality Ratios (SMRs) for main causes of death

Cause of death	SMR
All causes	1.02
All cancers	1.18*
Heart disease	0.90*
Stroke	0.86*
Respiratory disease	1.05
External causes (e.g. accidents, poisoning)	0.88*
Suicide	0.35*

SMR greater than 1 means that mortality rate is greater than in the general male population.
SMR less than 1 means that mortality rate is less than in the general male population.
* means that mortality rate is statistically significantly different from in the general population.

Cancer mortality and incidence

A total of 2456 cancers occurred from 1982 to 2001.

The death rate from cancer was 18% above the population rate, and the cancer incidence rate was 23% above the population rate. Mortality and incidence rates were significantly greater than in the general population for a number of cancers, as shown in Table 2.

Table 2 Standardised Mortality Ratios (SMRs) and Standardised Incidence Ratios (SIRs) for selected cancers

Cancer type	SMR	SIR	Comment
All cancers	1.18*	1.23*	
Lip, oral cavity and pharynx	1.50*	1.41*	
Oesophagus	1.15	1.48*	
Lung	1.20*	1.28*	Highest rate in RAN
Mesothelioma	na	1.46	Significant increase in RAN
Colorectal	1.24*	1.16*	
Melanoma	1.22	1.40*	Highest rate in RAAF
Prostate	1.26*	1.22*	
All leukaemias	1.18	1.43*	
All leukaemias except chronic lymphatic	1.25	1.61*	

SMR/SIR greater than 1 means that mortality/incidence rate is greater than in the general male population.
SMR/SIR less than 1 means that mortality/incidence rate is less than in the general male population.
* means mortality/incidence rate is statistically significantly higher than in the general population.

Cancer mortality and incidence by service category

Of the 26 mesothelioma cases in the cohort, 16 occurred in RAN personnel, and there was a significant 180% mesothelioma excess compared with the general population. Naval personnel showed a significant excess of both deaths from and incidence of all cancers (16% and 31% respectively), and lung cancer (48% and 50%). They also had a significantly raised incidence of cancers of the lip, oral cavity and pharynx (48%); melanoma (32%); prostate cancer (27%); and leukaemias other than chronic lymphatic leukaemia (non-CLL leukaemia, 87%). There was excess mortality from colorectal cancer.

In army personnel, the only incident cancer in significant excess was pancreatic cancer.

In RAAF personnel, both mortality and incidence of melanoma were significantly elevated, with a doubling of the mortality rate. There was a significant excess incidence of prostate cancer (30%), all leukaemias (64%) and non-CLL leukaemia (78%).

In civilian participants, the all-cause mortality and cancer incidence were elevated (21% and 19%). There was an excess of both mortality from and incidence of lung cancer (30% and 36%). There were also excesses of cancers of the lip, oral cavity and pharynx (41%) and colorectal cancer (23%).

Radiation and cancer

For all cancers combined and for specific cancers with a possible association with radiation, the cancer death rates were compared between the different exposure categories. Category A, the lowest exposure category, was used as the baseline group for comparison. If an association with radiation exposure was present in this cohort, a trend to increasing death rates with categories of increasing exposure would be expected.

Neither all cancers combined nor any cancer known to have an association with radiation showed any increase in mortality or incidence with increasing radiation exposure in this cohort.

The lack of association between cancer and radiation is not surprising, given the estimated low radiation exposure of most cohort members, and the relatively small proportion of subjects with any significant exposure. The average exposure in the test participants was only slightly above the background exposure experienced by all people in a single year, and about 100 times less than the dose received by the people who survived the Japanese atomic bombs, in whom excess cancers were found.

The number of excess cancers and cancer deaths to be expected from these exposure levels can be estimated by applying radiation levels to the known risk levels from other studies. It is estimated that up to six of the 2456 total cancers could be expected to have occurred from the exposures incurred in the study cohort.

Specific cancers

Leukaemia

Leukaemia is a cancer of particular interest because of its well-established association with ionising radiation exposure, but no association was found between the level of radiation exposure and death from non-CLL leukaemia. To search further for any such association, a case–control study was carried out, where the radiation exposure of participants with non-CLL leukaemia (cases) was compared with that of a sample of participants who did not have non-CLL leukaemia (controls). For this study, the panel was able to make a more detailed examination of likely radiation exposures of the 54 leukaemia cases and 216 controls included in this study. The panel examined each subject's activities at the test sites, using documents such as service records, radiation film badge readings, and in some cases responses to a questionnaire administered in the

1980s. This study confirmed the findings from the mortality and cancer incidence studies of an absence of an association between leukaemia and radiation exposure.

The lack of association between non-CLL leukaemia and radiation in this cohort is not surprising given the low exposures. The findings are similar to those of the study conducted in the UK of British participants in the nuclear tests, where non-CLL leukaemia incidence was raised relative to comparison subjects. The UK study also found no association between leukaemia and radiation exposure, although it did not include retrospective exposure assessments, such as were made in the current study.

The overall excess of non-CLL leukaemias is unexplained. Other known causes of leukaemia include benzene, but estimating the extent of any exposure to benzene at the nuclear test sites is beyond the scope of this study. Viral infection is associated with one type of leukaemia (adult T-cell leukaemia), but there were no known cases of this type in participants.

Mesothelioma

Of 26 incident cases of mesothelioma, 16 occurred in RAN personnel. This is more than 2½ times the rate in the general population. Mesothelioma is nearly always associated with past exposure to asbestos, and asbestos in naval vessels is the likely source of exposure in most of these cases. It is likely that repeated asbestos exposure occurred, which need not necessarily have occurred at the time of the nuclear tests.

Of the other 10 cases of mesothelioma, 8 occurred in civilians. Because the cases could not be individually linked to other study records (due to privacy laws), the occupations of these civilians is unknown. However, many of the civilian subjects in the cohort were in the construction industry, where asbestos was commonly used, at a time when less caution was exercised than in recent years. Whether any of these subjects were exposed to asbestos during the nuclear tests is not known.

Lung cancer

An excess of lung cancer always suggests a higher smoking prevalence than in the general population.

However, some contribution from asbestos is also likely because lung cancer has a known association with asbestos. The occurrence of mesothelioma in RAN and civilian subjects is a definite indication of asbestos exposure, and occurrence of other asbestos-related diseases would therefore not be surprising. RAN and civilian participants also had the highest rates of lung cancer.

No association was found between lung cancer incidence and radiation exposure in this cohort. Although previous research has shown an association between lung cancer and ionising radiation, this result is not surprising given the generally low average radiation exposure found in this study

Melanoma

A significant excess of melanoma occurred in RAAF personnel. The occurrence of excess melanoma has been noted elsewhere in aircrew, and occupational exposure to cosmic

radiation has been considered as a possible cause. Because of privacy constraints, it was not possible to identify which of the 71 cases in RAAF personnel were aircrew. However, only 4 of the 22 melanoma deaths in RAAF personnel were known to be aircrew. (The occupation of 5 decedents was not known.) It is probable that the excess melanoma incidence in RAAF personnel is not confined to aircrew.

There was no significant trend in melanoma incidence with increasing radiation exposure.

Colorectal cancer

Although colon cancer has been cited as a radiogenic cancer, no association was found between mortality or incidence of colorectal cancer and radiation exposure. Asbestos exposure is a possible contributing factor to the excess of colorectal cancer mortality. Colorectal cancer mortality was significantly elevated in RAN personnel, who also had the highest mortality from lung cancer and most of the cases of mesothelioma, diseases known to be associated with asbestos exposure.

Head and neck cancer (cancers of the lip, oral cavity and pharynx)

Both mortality and incidence of these cancers occurred in significant excess. Head and neck cancers are strongly smoking-related and are also related to alcohol intake. The excess lung cancer rate suggests a higher smoking prevalence in this cohort than in the general population. However, the absence of an excess incidence of liver cancer or of death from cirrhosis of the liver suggests that alcohol consumption is not excessive in this cohort.

Prostate cancer

A possible contributing factor to the excess of prostate cancer in this cohort is increased intensity of diagnosis in the military participants. The reported incidence of prostate cancer has risen in recent years following the introduction of PSA (prostate specific antigen) testing. It is plausible that ex-service personnel would undergo more intensive medical surveillance and care than the general population, so that diagnosis of the cancer would be more likely.

‘Radiogenic’ cancers

‘Radiogenic’ cancers are a group of cancers shown in the Life Span Study of Japanese atomic bomb survivors to be causally associated with radiation. They are cancers of the thyroid, stomach, colon, liver, lung, breast, ovary, bladder; leukaemia (excluding chronic lymphatic leukaemia); and non-melanoma skin cancer. Both mortality and incidence of this combined group of cancers was significantly elevated in the study cohort. However, no association was found with radiation exposures. Of the cancers classified as ‘radiogenic’, more than 75% were lung or colorectal cancers, and it is possible that the excess of this group of cancers is due to other factors associated with these particular cancers.

1 Introduction

1.1 Background

Between 1952 and 1963, the United Kingdom (UK) conducted a program of nuclear weapons development trials in the Monte Bello group of islands off the coast of Western Australia and at Emu Field and Maralinga in the South Australian desert. Servicemen and civilians from the UK and Australia participated in the tests. The health effects of the tests have been investigated in the British participants; however, until now a comprehensive and scientifically rigorous study has not been conducted on the Australian participants.

A Royal Commission into the testing series, headed by Justice McClelland, reported in 1985 (McClelland et al 1985). The role of the commission was to examine:

> The measures taken during the tests to protect against ionising radiation;
>
> If said measures were adequate; and
>
> If the health of Australian participants was adversely affected by exposure to ionising radiation.

The commission heard testimony from some 311 witnesses and examined a massive amount of documentation, including written statements from witnesses and documentation from the UK and Australian governments (McClelland et al 1985). The commission concluded that a register of participants (the nominal roll) should be established and the test sites should be cleaned and made fit for habitation by the traditional Aboriginal owners.

In 1999, the then Minister for Veterans' Affairs, the Hon Bruce Scott, acting on the recommendation of the Royal Commission, announced that a nominal roll would be compiled of Australian participants in the tests (DVA 2001). This nominal roll would form the substrate for a mortality and cancer study. In 2003, the Review of Veterans' Entitlements (known as the Clarke Review) was published, and one of the findings was that the study of participants in the nuclear testing program should be expedited (Clarke et al 2003). Thus, in early 2003, the Department of Public Health at the University of Adelaide was commissioned by the Department of Veterans' Affairs (DVA) to undertake the study of mortality and cancer incidence in Australian nuclear test participants.

The only previous study of Australian test participants was conducted by Donovan and colleagues in 1982 (Donovan et al 1983). This study incorporated a postal survey of nuclear test participants and an analysis of causes of death. The list of potential test participants was compiled by the Department of Resources and Energy, which collated names from all relevant sources (contemporary documents from Australian and UK government agencies, compensation claims, nuclear veterans' associations and other enquiries about the tests). Contact details for this list of participants were then acquired from various sources, such as the electoral roll. Of 15 364 names on the original list, contact details were found for 8255 people and questionnaires were issued to these participants. The questionnaire instructed recipients not to answer the questions about their health if they considered themselves to have been only indirectly involved with the tests; that is, if they '…never actually visited the area of the tests or any area affected by

them (e.g. atomic clouds or fallout)' or if they '… did work in these areas but left before any explosions'. Thus, participants were self-selected into the cohort. Respondents were asked about their work during the tests, if they felt that they had been exposed to ionising radiation, and about a range of other health issues, such as general health perception, smoking habits and time spent in the sun. They were then asked if they had ever had cancer or other major illness, or if they had infertility problems. Respondents were also asked for consent to examine medical records, and for the details of doctors and hospitals where treatment had been received.

The response rate to the survey was around 80%. A total of 3870 respondents out of the 8255 who were sent questionnaires stated that they had not been involved in the tests. With other reasons for nonresponse, the final sample comprised 2536 respondents who considered themselves to have been involved in the tests; this was about 30% of the original sample. The study examined the prevalence of the diseases of interest (cataract, malignant melanoma, other skin cancers, and other cancers) with 'radiation indicators', including tasks performed, use of health physics services for radiation protection, proven exposure from a film badge or dosimeter and the respondent's self-belief of exposure to radiation. There was no control or comparison group for this study — groups of people within the cohort were compared to one another according to these 'radiation indicators'. Thus, it is impossible to assess whether the nuclear test participants had an excess of the diseases of interest compared with the general population or to populations of other workers (to account for the healthy worker effect). Numerous comparisons (i.e. comparison of each 'radiation indicator' with the outcomes) also increased the likelihood of finding significant associations by chance. Moreover, the study concentrated on the differences between groups of test participants that had been identified through official records and those who had self-identified. All of these factors make the results difficult to interpret.

There were some additional limitations to the study. Entry into the study itself relied on the participant's perception of whether or not they were 'involved in the tests', which is not necessarily a good indicator of whether or not they were exposed to ionising radiation. For some respondents, the study team made a decision about whether the questionnaire should be reissued because exposure seemed likely. This process was likely to be open to bias because it was based on the limited information given by the respondent. Likewise, respondents who had developed medical conditions that they perceived to be related to radiation exposure may have been more likely to have indicated that they were involved in the tests, and more likely to believe they had been exposed to radiation. The reliance on self-reporting of the conditions of interest is also a weakness. Only a small proportion of the cases could be medically confirmed, although these cases were found to have a high degree of verification, giving the authors confidence in the self-reported diagnoses.

The study found no conclusive associations between radiation indicators and outcomes; even associations found to be significant — for example, between decontamination duties and malignant melanoma — could be explained by other information. Conclusions about other cancers, other health outcomes and radiation exposure could not be drawn due to the lack of appropriate information. The authors concluded that the limitations of the study were such that no conclusions could be drawn about the health effects of participation in the British nuclear testing program.

The mortality and cancer experience of the British participants in the nuclear testing series in Australia and the Pacific has been investigated since the 1980s, with the study reporting first in 1988 and again in 1993 and 2003 (Darby et al 1988, 1993; Muirhead et al 2003). This study compared 21 357 test participants with 22 333 comparison subjects on

mortality rates from particular cancers and from all causes, and on cancer incidence. Test participants were service personnel in the Royal Navy, British Army and Royal Air Force or other military units, and civilians working for the Atomic Weapons Establishment (AWE) or the Atomic Energy Research Establishment. Comparison subjects were servicemen who had served in tropical and subtropical locations but had not taken part in the tests; civilian controls were other employees of the AWE.

All-cause mortality and cause-specific mortality were compared between the study group and the population of the UK as a whole, and between the study and comparison groups. In the overall follow-up, the study found no difference in deaths from all causes between study and comparison groups (relative risk [RR] 1.01; 90% confidence interval [CI], 0.98 to 1.05). Both study and comparison groups had lower standardised mortality ratios (SMRs) than the population as a whole (0.89 for test participants and 0.88 for comparisons). However, deaths from accidents and violence were higher than in the general population for both study (SMR 1.21) and comparison (SMR 1.16) populations, although there was little difference between these two groups (RR 1.07; 90%CI, 0.95 to 1.21). There was no difference between the study and comparison groups in mortality from all cancers (RR 1.01; 90%CI, 0.96 to 1.08), and SMRs for all cancers were again lower than the general population in both groups (0.93 for test participants and 0.92 for comparisons).

The exception was leukaemia, for which mortality was higher among test participants. Mortality rates differed over time, with a statistically significant excess 2–25 years after participation in the tests (RR 3.38; 90%CI, 1.45 to 8.25). Over the whole follow-up period, this difference persisted, but it was not statistically significant (RR 1.45; 90%CI, 0.96 to 2.17). For leukaemia excluding chronic lymphatic leukaemia (non-CLL) — CLL has no association with ionising radiation — the results remained significant over the whole follow-up period. For the first 2–25 years of follow-up, there was a significant excess of non-CLL leukaemia (RR 2.99; 90%CI, 1.26 to 7.41), and for the whole follow-up period the RR was 1.83 (90%CI, 1.15 to 2.93). This finding could reflect the shorter latency period of leukaemia. The authors concluded that the possibility that test participation had caused a small increase in risk of non-CLL leukaemia could not be ruled out, with the evidence suggesting that the risk was greatest in the early years after the tests.

The incidence of all cancers did not differ between the study and comparison groups (RR 0.99; 90%CI, 0.94 to 1.03). The only cancers to show significant overall differences between incidence rates in the test participants and the comparison group were liver cancer (RR 1.99; 90%CI, 1.19 to 3.38) and prostate cancer (RR 1.22; 90%CI, 1.04 to 1.43). The incidence of leukaemia in the period 2–25 years after test participation was significantly higher in test participants (also reflected in the mortality statistics), with the overall RR 3.17 (90%CI, 1.63 to 6.31). This relative risk was less over the whole follow-up period (RR 1.33; 90%CI, 0.97 to 1.84). For non-CLL leukaemia, the first 2–25 years of follow-up showed a statistically significantly higher incidence in test participants (RR 3.97; 90%CI, 1.73 to 9.61), which again did not remain a significant increase in the whole follow-up period (RR 1.41; 90%CI, 0.96 to 2.09). There was no evidence of increased leukaemia risk in subjects with a recorded dose of external radiation (n = 2264), nor of a trend towards increasing risk with increasing dose. Other analyses of subjects identified as liable to exposure to radiation found no clear evidence of raised leukaemia rates.

New Zealand naval personnel were involved in the British nuclear testing program in the Pacific during the 1960s, and a follow-up study similar to that of the British participants has been conducted (Pearce et al 1990, 1997). In the follow-up to 1992, the study found

no significant difference in mortality rates from all causes (RR 1.1; 90%CI, 0.9 to 1.3) or from all cancers (RR 1.2; 90%CI, 0.8 to 1.7) between test participants and the comparison group. Similarly there was no difference in the incidence of cancer (RR 1.0; 90%CI, 0.8 to 1.4). However, there was an increase in haematological cancers, including leukaemia, in the test participants (RR 3.8; 90%CI, 1.4 to 10.8). The authors concluded that there is evidence for a link between haematological cancers and test participation, but no association with other cancers, and noted that the study was based on a small number of participants (528 men) (Pearce et al 1997).

The United States tested nuclear weapons on their home soil in the Nevada desert and in the Pacific between 1945 and 1963. The Five Series Study followed up some 70 000 of the 200 000 US military personnel involved in the tests (Thaul et al 2000). These servicemen participated in at least one of five tests — representing both the Nevada and Pacific sites used for the testing — selected for the study. Test participants were compared with a comparison group of servicemen who were of equivalent military employment in terms of branch of service, time of active military duty, type and general location of assigned unit, age and paygrade (Thaul et al 2000). No exposure assessments were made. The study found no statistically significant difference between the test participants and the comparison group for all-cause mortality rate, cancer mortality rate or leukaemia mortality rate. The rate of leukaemia mortality was elevated in the test participants group, but did not reach statistical significance (hazard ratio [HR] 1.15; 95%CI, 0.93 to 1.43); there was no difference for non-CLL leukaemia (HR 1.14; 95%CI, 0.90 to 1.44). The authors concluded that the study cohort was too small to find the observed risk statistically significant (Thaul et al 2000).

1.2 Description of the testing program in Australia

The testing program took place in Australia between 1952 and 1963, as shown in Table 1.1. Twelve major nuclear explosions were carried out under five separate ‘operations’. In addition, 600 minor trials were conducted. Over 16 000 Australian members of the Defence Force and civilians participated in the tests (DVA 2001). British participants numbered more than 20 000 in this Commonwealth operation (Muirhead et al 2003).

The Monte Bello Islands were the first location used for the British nuclear testing program. Operation Hurricane was the first of the nuclear tests, with a plutonium implosion bomb detonated in the hull of a 1450-ton frigate anchored in a lagoon 400 yards off the western shore of Trimouille Island. Four years later, Operation Mosaic was conducted on Trimouille and Alpha Islands. The Royal Commission into the British atomic tests later found that the Monte Bellos should not have been used for these tests due to the large chance that weather conditions would be unfavourable (McClelland et al 1985).

Table 1.1 The major nuclear explosions in the British nuclear testing in Australia

Operation Hurricane (1 bomb) — Monte Bello Islands	3 October 1952
Operation Totem (2 bombs) — Emu Field	15 October 1953 27 October 1953
Operation Mosaic (2 bombs) — Monte Bello Islands	16 May 1956 19 June 1956
Operation Buffalo (4 bombs) — Maralinga	27 September 1956 4 October 1956 11 October 1956 22 October 1956
Operation Antler (3 bombs) — Maralinga	14 September 1957 25 September 1957 9 October 1957

Meanwhile, it was decided on the use of Emu Field (480 km northwest of Woomera) to test the first land-based weapon, and the two bombs which made up Operation Totem were exploded in October 1953. Before and during the Totem tests, the Kittens minor trials were also conducted at Emu Field; these involved radioactive material but no nuclear explosions. The Totem 1 explosion was responsible for the 'black mist incident', in which many Aboriginal people reported becoming ill from a cloud passing over their settlements near Wallatinna. The Royal Commission found that the evidence given by Aboriginal people, and the scientific modelling, were sufficient to conclude that the black mist did occur and may have made people temporarily ill. However, there was not enough evidence to say whether the black mist caused other illnesses or injuries (McClelland et al 1985).

During this time, a site in the South Australian desert, north of the transcontinental railway line between Cook and Ooldea, was being prepared to be the permanent proving ground for British nuclear weapons. The area was inhabited by Tjarutja people, but named Maralinga by anthropologists working with Aboriginal people in eastern Australia (Keane 2003). Maralinga, meaning 'thunder fields', was developed as a township, with housing for 2000 servicemen and the concomitant services such as repair garages, a hospital and laboratories, as well as facilities such as a swimming pool and cinema (Keane 2003). The site was used for 11 years, hosting major nuclear explosions as well as 600 'minor trials'. Originally, the British planned to close the range between the major tests, but changed their plans to accommodate the extensive program of minor trials (McClelland et al 1985).

The first series of nuclear tests at Maralinga, Operation Buffalo, occurred during September and October 1956. Before this, the minor trials Kittens and Tims had taken place. The conduct of the Buffalo trials was controversial, although they were also shrouded in secrecy, and much of the information about the conduct of the tests was not released until the Royal Commission in 1984. This applied especially to the safety of the Aboriginal population, and the Royal Commission found that the 'attempts to ensure Aboriginal safety during the Buffalo series demonstrate ignorance, incompetence and cynicism on the part of those responsible for that safety' (McClelland et al 1985). In addition, the Royal Commission reported that all four tests in the Buffalo series were conducted under conditions that violated the firing conditions proposed by the safety committee (McClelland et al 1985). However, overall the Royal Commission found that radiological and physical safety arrangements for participants in the Buffalo tests were well planned and sound, although it acknowledged that this did not negate the possibility of unplanned exposures to radiation (McClelland et al 1985).

The second major operation at Maralinga was Operation Antler, which took place during September and October 1957. These tests occurred against a background of increasing public and political concern about nuclear contamination, and were fewer than originally planned (McClelland et al 1985). The Royal Commission found that the extent of fallout from the third Antler explosion, in which the bomb was suspended from balloons, was seriously underestimated (McClelland et al 1985). Again, the Commission found that 'inadequate attention was paid to Aboriginal safety during the Antler series' (McClelland et al 1985). However, it also found that the series was the best planned and organised of all the tests conducted in Australia, although unplanned incidents, such as the dispersal of cobalt-60, would have exposed personnel to radiation (McClelland et al 1985). Throughout and after these test series, numerous minor trials were conducted. A wide range of activities was undertaken under the general umbrella of 'minor trials'. A number of radioactive materials was used, including plutonium, polonium and uranium. The most significant radiologically were the Vixen B trials, which simulated the accidental detonation of a bomb, and spread large quantities of plutonium into the environment. Other trials included the burning of plutonium in air, and explosive tests on uranium and other samples. Further details of the trials, including recommendations and regulations relating to radiation safety, are provided in Volume 1.

Maralinga cleanup activities began in 1963 and were still occurring in the 1990s. As yet, the area is not fit for habitation by the traditional Aboriginal owners.

The British nuclear test series was conducted under stringent security conditions, with the complete cooperation and support of the Australian Government. There is no doubt that the safety and security of the Aboriginal inhabitants were seriously compromised by the tests. Controversy continues about the possible exposures of test participants and other people further afield who claim to have been affected by the tests (James 2003, James and Starick 2003). Numerous authors have made claims about the level of deception of both the Australian Government and the participants regarding the safety of the tests; to this day, aspects of the conduct of the tests remain secret (e.g. Milliken 1986, Cross 2001).

1.3 Role of Australian personnel

1.3.1 Army

The Australian military personnel were involved primarily in service roles, preparing test sites, monitoring and observing the tests, and cleaning up the sites.

1.3.2 Royal Australian Navy

Most naval personnel were involved through their presence on naval vessels in the first major test in Australia, entitled Operation Hurricane, in which one device was exploded on 3 October 1952 in the Monte Bello Archipelago off the northern coast of Western Australia. A smaller number of naval personnel participated in the land-based tests.

1.3.3 Royal Australian Air Force

In addition to working in the test areas, some RAAF personnel carried out tasks at sites remote from the tests that may have led to some ionising radiation exposures. This group

was primarily aircraft maintenance personnel who were involved in the decontamination and servicing of aircraft that had flown through the mushroom clouds.

1.3.4 Civilians

The civilians at the test sites were Australian employees of firms contracted to construct, maintain and/or support the testing facilities. They also included Australian public servants and Australian employees of semi-government organisations involved with the conduct of the testing program, whose work required them to be in the area while the tests were carried out.

1.4 Health effects of ionising radiation

Ionising radiation has been linked with effects on health ever since the discovery of the X-ray in 1895. Firstly, the acute effects of high doses of radiation were discovered. Later, skin cancers, leukaemias and other cancers were found in high numbers in radiation workers (Doll 1995). A review by Sir Richard Doll described the research, spurred on by nuclear testing, into the health effects of low doses of ionising radiation. The evidence shows that four effects are possible from doses less than those required to produce acute effects: mutations in germ cells, congenital defects from irradiation in utero, an increased rate of nonspecific ageing and an increased risk of cancer (Doll 1995). Studies of the epidemiology of cancer are impeded by the large sample sizes needed to detect differences in the rates of diseases that have a low incidence. The study of survivors of the atomic bombs in Japan has shown that exposure to ionising radiation is associated with excess risk for almost all types of cancer, particularly cancer of the stomach, lung, liver, colon, bladder, breast, ovaries, thyroid, and skin, as well as multiple myeloma and leukaemia (Radiation Effects Research Foundation 2003).

Some types of cancer are particularly strongly associated with ionising radiation exposure, namely acute myeloid leukaemia (AML), acute lymphatic leukaemia (ALL) and chronic myelogenous leukaemia (CML) (UNSCEAR 2000). Based on studies of Japanese atomic bomb survivors and patients treated with radiation for medical conditions, dose–response relationships have been demonstrated for AML, CML and ALL (Little et al 1999). On the other hand, there appears to be no such evidence for an association between radiation exposure and chronic lymphatic leukaemia (CLL). Indeed, several studies of patients treated with radiation therapy show a lack of association with CLL (Curtis et al 1994, Boice et al 1987).

There is considerable difficulty associated with measuring the risk associated with exposure to radiation. Notably, cancers due to radiation exposure may appear decades after exposure and do not manifest in any different way from a cancer of spontaneous origin, and thus cannot be differentiated from them (UNSCEAR 2000). Nonetheless, there is evidence that ionising radiation can induce most cancers, and there is a linear dose–response relationship with exposure, with different levels of radiation sensitivity in different parts of the body (Ron 1998, Brenner et al 2003). Exposure at a young age and being female increases cancer risk (Ron 1998).

Much of the epidemiological information about the health effects of ionising radiation has come from studies of Japanese people who survived the atomic explosions in Hiroshima and Nagasaki during World War II. The prospective cohort study of these atomic bomb survivors conducted by the Radiation Effects Research Foundation in Hiroshima shows

that survivors have an excess of cancer mortality, and for leukaemia this excess occurred in the first 15 years after exposure. This is in contrast to the excess for solid cancers, which is represented as a lifelong elevation of the natural age-specific cancer risk (Pierce et al 1996). This study has also shown that noncancer mortality increases in survivors with increasing radiation dose (Shimizu et al 1999). The study also notes that the risk associated with exposure to radiation depends not only on the dose, but also on sex and age at exposure, with younger people faring worse (Pierce et al 1996).

A study of British radiologists found that there was an 'increasing trend in the risk of cancer mortality with time since first registration with a radiological society' (Berrington et al 2001). This was attributed to a long-term effect of exposure to radiation, and to the fact that exposures in the early days were more likely to have been greater than in recent times. There appeared to be no effect of radiation exposure on other causes of mortality (Berrington et al 2001). A similar study of radiologic technologists in the United States found increased risks of cancer for those employed before 1940; the risk decreased with later employment start dates, again probably reflecting higher exposures in the early days (Mohan et al 2003).

Other radiation workers, such as those employed in the nuclear power industry, have also been studied in depth for associations between exposure to ionising radiation and cancer. These studies are aided by accurate dose measurements; personal dosimetry is required in the industry for regulatory purposes. A Japanese study found no difference in mortality rates from cancer for nuclear industry workers compared with the general population, and found no dose–response relationship for most cancers (Iwasaki et al 2003). However, the average follow-up in this study was only 4.5 years, clearly not long enough to detect radiation-induced cancers. A Finnish study of nuclear workers also failed to find evidence for an association between radiation and cancer, or between cumulative radiation dose and cancer (Auvinen et al 2002). Similarly, a study of employees at the Chapelcross plant of British Nuclear Fuels found no evidence for an association between exposure to radiation and cancer (McGeoghegan and Binks 2001). A 1992 study using the United Kingdom's registry of radiation workers found evidence for an association between exposure to radiation and leukaemia that was consistent with dose measurements (Kendall et al 1992). A review using seven published epidemiological studies also found an increased risk of leukaemia in workers exposed to higher doses of radiation compared with those exposed to lower doses (Wilkinson and Dreyer 1991). A further review combining data from the United States, the United Kingdom and Canada analysed 2 124 526 person-years at risk (Cardis et al 1995). This study found associations between radiation dose and risk of leukaemia and multiple myeloma, but no evidence of an association between radiation exposure and all-cause or all-cancer mortality (Cardis et al 1995).

Much research has also been conducted on the children of nuclear workers. Results from these studies vary markedly in their assessment of evidence for an association between parental employment in the nuclear industry and infertility, fetal death, congenital malformations and childhood leukaemia. A study into primary infertility in nuclear workers in the United Kingdom found no evidence for a link between employment in the nuclear industry and male infertility (Doyle et al 2001). There was a difference found in infertility rates between monitored and nonmonitored (i.e. those presumed not to be at risk of radiation exposure) women employees, but it was not statistically significant, and the authors noted that the numbers were too small to draw any firm conclusions (Doyle et al 2001). Another study by the same group of authors found no association between paternal employment in the industry and miscarriage, stillbirth or congenital malformation, although it did find a slightly increased risk of miscarriage and stillbirth if the mother had been monitored for radiation exposure before conception, compared with unmonitored

nuclear workers (Doyle et al 2000). The authors concluded that this evidence was not unequivocal and required further investigation. A study by Parker et al found an increased risk of stillbirth in Sellafield employees that was associated with exposure to ionising radiation before conception (Parker et al 1999).

Purported 'clusters' of leukaemia in the children of nuclear workers or those living in the vicinity of nuclear installations have been investigated. A case–control study by Gardner found an increased incidence of leukaemia and non-Hodgkin's lymphoma in the children of men who worked at the Sellafield nuclear plant and who had a recorded external dose of whole body radiation before the child's conception (Gardner et al 1990). This finding was disputed by Kinlen, who proposed that leukaemia has an infective basis (Kinlen 1993, Kinlen and Stiller 1993). He suggested that population mixing, where an influx of new residents into small, isolated or new geographical locations, such as during the British 'new town' developments in the 1950s, could bring a range of new infections to the existing population. The theory of an infective basis for leukaemia could then explain the raised leukaemia incidence in these areas. This is consistent with Gardner's finding that the increased incidence of leukaemia was concentrated in the children born in the vicinity of the nuclear facility, not those who had moved to the location as children. There is no research providing evidence for an infective basis for leukaemia in adults.

There is also an association between radiation used for medical (diagnostic and treatment) purposes and cancer, particularly for children. Studies have shown increased risks of thyroid and breast cancer and leukaemia in children with increasing numbers of X-rays received for conditions such as scoliosis (Ron 1998). Likewise, there is a strong dose–response relationship between radiotherapy treatment for benign disease and thyroid cancer in children, but this relationship does not persist in adults (Ron 1998, 2002).

The accident at the nuclear power plant at Chernobyl in northern Ukraine in 1986 has led to a considerable amount of research on the effects of radioactive fallout on cancer rates. A review of these studies found evidence that rates of thyroid cancer in children have risen in areas affected by the accident (Moysich et al 2002). The evidence for increased rates of thyroid cancer in adults, however, is far less conclusive (Moysich et al 2002). There is little evidence to support an association between leukaemia and the Chernobyl accident in either children or adults; however, it is too early for most solid cancers given their longer latency (Moysich et al 2002).

Despite the limitations of the epidemiological studies on exposure to ionising radiation and cancer, there is scientific consensus that an association exists. The association is well established for leukaemia. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) in its 2000 Report has assessed the lifetime risk of cancer following exposure to ionising radiation. The estimates vary with the models used, with gender and with country. For males, following an acute dose of 1 Sv, the estimated lifetime risk of mortality from solid cancers is between 6% and 9%, and for leukaemia (other than CLL) it is 0.9%. For a dose of 0.1 Sv, the estimated lifetime risk of death from solid cancers is about 1% and from leukaemia about 0.05%, depending on the models used (UNSCEAR 2000).

Further information about the biological effects of radiation exposure is provided in Volume 1.

1.5 Structure of the study and reports

The study of Australian participants in British nuclear tests in Australia consists of three components: a study of the estimated radiation exposure of the participants; a mortality study of participants; and a cancer incidence study of participants, including a case–control study of leukaemia cases nested within the cohort.

The primary aim of the research is to identify and measure any association between participation in the tests and mortality and cancer incidence, with particular interest in exposure to ionising radiation.

The study is reported in two volumes:

- report of ionising radiation exposure at the test sites
- report of the mortality and cancer incidence study of Australian nuclear test participants.

This volume is the report of the mortality and cancer incidence component of the study.

1.6 Aims of the study

The mortality study aims were:

- to compare the mortality of tests participants with that of males of the same age in the general population
- to identify any association in test participants between the incidence of specific cancers and mortality from specific causes of death, on the one hand, and estimates of their exposure to ionising radiation in the nuclear testing program, on the other.

The cancer incidence study aims were:

- to compare the cancer incidence of test participants with that of males of the same age in the general population
- to identify any association between the incidence of specific cancers and exposure to ionising radiation in test participants
- to identify any association between mortality from, or incidence of, non-CLL leukaemia and ionising radiation in test participants (case–control study).

1.7 Administrative structure

A number of bodies have collaborated in the production of this report.

The Department of Public Health at the University of Adelaide was contracted by DVA to carry out the epidemiological study.

DVA developed the Nominal Roll of Atomic Veterans, from which the cohort was drawn.

Retrospective assessment of radiation exposure of test participants was carried out by an independent scientific panel (the Dosimetry Panel). The panel activities were overseen by a subcommittee, and DVA provided administrative support. Radiation exposure

assessments of the panel were transcribed onto the roll of cohort members, and the data were passed to the University of Adelaide to be merged with the study database.

DVA also provided administrative support for the mortality study. Through DVA, extensive use was made of the DVA client base in tracking cohort members. DVA also undertook the search of death registry records in Western Australia, Victoria and the ACT.

For the mortality component of the study, the Australian Institute of Health and Welfare (AIHW) coordinated the search of the other state death registries, and checked the quality of doubtful matches obtained from all state registries. AIHW also supplied the National Mortality Tables.

For the cancer component of the study, AIHW searched the National Cancer Statistics Clearing House for matches to the study cohort for all states except Victoria. The Victorian Cancer Registry searched its database independently and provided matches to AIHW for amalgamation with the rest of the data before it was passed to the study team at the University of Adelaide.

The National Centre for Classification in Health carried out the coding of death certificates that had not been coded in the National Death Index.

The study team at the University of Adelaide reported to and received advice from a Scientific Advisory Committee, whose members were appointed by DVA.

The study team also had periodic meetings with a Consultative Forum, whose membership was representative of numerous veterans' organisations.

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2 Mortality study design

2.1 Retrospective cohort study

This was a retrospective cohort study of mortality of the Australian personnel who participated in the British nuclear testing program. In cohort studies, a cohort or group of individuals is tracked through time.[1]

The cohort study is a standard method of assessing the association between an exposure and an outcome. In this study, the association of interest was between participation in the tests and mortality in participants. This study is a historical or retrospective cohort study, which is a common method for occupational cohorts. In such a study, the cohort is defined and the exposure is assessed retrospectively, and the cohort members are followed up to a cutoff date to determine outcomes (dos Santos Silva 1999). A disadvantage of retrospective studies is that historical records of subjects' employment and exposures are often incomplete. However, a historical cohort study was the only option for this cohort of test participants, because the cohort was defined by test participation up to 50 years ago. The criterion for membership of the cohort was participation in the British nuclear testing program in Australia. Each member of the cohort was tracked to the end of 2001.

2.2 Choice of comparison population

In a cohort mortality study, the mortality rate of the exposed cohort (in this case the 'exposure' being participation in the nuclear testing program) is compared with the rate in an unexposed cohort or population. It is desirable that the comparison cohort is similar to the exposed cohort in every way except for their exposure, so that if there were no association between the exposure and outcome, the same rates of outcome would be expected in the exposed cohort and the comparison cohort (dos Santos Silva 1999). However, it is often found to be impracticable to form such a comparable group, and the mortality rate must be compared with the rate in the general population, with adjustment being made in the analyses for differences between the groups, such as age distribution.

Consideration was given to forming an external comparison cohort for this study. Obtaining a comparison cohort for the military participants was considered through use of the study of veterans of the Korean War. However, that study produced findings that were unexpected in a veteran cohort, and thus the Korean cohort was considered unsuitable for use as the comparison (Harrex et al 2003). Controls for the civilian participants in the cohort were not readily available, because there are limited records of civilian workers from the 1950s and 1960s with sufficient detail for comparison. It was finally decided that, due to difficulties associated with identifying appropriate comparison subjects at the

[1] The term cohort is derived from the Latin noun *cohors*, meaning enclosure. A cohort originally applied to an ancient Roman military unit, which was enclosed in the sense that no other individual could enter the cohort, and nobody could leave it except through death. Thus, membership of a Roman cohort was fixed from the time of inception and became extinct when the last member died. Similarly, in studies of occupational cohorts, individuals remain in the cohort even if they change jobs or leave the workforce, and their membership of the cohort lasts until their death. For practical reasons, exceptions are made to this rule when individuals cannot be tracked with confidence.

time of the nuclear testing, comparison would be made with the mortality rates in the Australian population.

2.3 Addressing the healthy worker effect

The main concern with having to compare mortality rates with the general population instead of a comparable working population is the 'healthy worker effect'. This is the term used to describe the common finding that rates of mortality in the general population are higher than in the working population, due to exclusion of many ill and disabled people from the workforce. The lower rates in the occupational cohort may then obscure any real increased risk associated with the occupation (Breslow and Day 1987). A detailed analysis of the factors contributing to the healthy worker effect is given in Appendix 4, but the two main contributing factors are variation in mortality with social class and a selection effect.

2.3.1 Social class effect

If the social class distribution in the occupational cohort is different from that in the general population, this will affect the mortality rate ratio for causes of death that vary between social class or socioeconomic status (usually measured by occupational status or income). Unemployed persons are more likely to be in lower socioeconomic categories, so that the working population is likely to have a higher socioeconomic status on average than the general population. Since certain causes of death — for example, heart disease — are more common in people in lower socioeconomic categories, the death rate from heart disease is likely to be lower in an occupational cohort than the national rates.

2.3.2 Selection effect

People with serious illness or disability are likely to be excluded from the workforce, because they may be less likely to seek, obtain or remain in employment. Therefore, mortality from cancer and some other diseases is likely to be less than in the general population for the early years of follow-up.

It is possible that the influence of the healthy worker effect was limited in this study. There is evidence that the healthy worker effect diminishes with time, so that the age-standardised mortality rate of occupational cohorts converges towards that of the general population as cohorts age; this is likely with this cohort, to which there were no entrants after 1965.

Nevertheless, several measures were included in the design of this study to measure the relationship between test participation and death or disease, free of the influence of the healthy worker effect.

To overcome the selection effect, the first 2 years of follow-up time of each subject were excluded from the analyses. As stated above, the selection effect is likely to lessen with time, but the timescale will vary for different causes of death. For leukaemia, which was a cause of death of particular interest in this study, it is likely that the selection effect will not last beyond 2 years; this is because the survival time of leukaemias other than chronic lymphatic leukaemia (non-CLL leukaemia) would rarely exceed 2 years of follow-up.

People with leukaemia would be unlikely to be sent to the nuclear tests, so that the leukaemia death rate in the cohort will reflect only cases of leukaemia that developed after entry into the cohort, whereas the death rate from leukaemia in the general population will reflect leukaemia deaths irrespective of time of onset. The result will be a relative lowering of leukaemia mortality in the cohort. Because of the short survival time from leukaemia in the 1950s and 1960s, any cohort members who died from leukaemia at that time are unlikely to have developed the disease more than 2 years before death. Therefore, the number of subjects dying from leukaemia more than 2 years after entry into the cohort will no longer be artificially lowered by failure to recruit people with leukaemia or to post them to a test site.

Hence, deaths occurring within 2 years of cohort entry, and the first 2 person-years of observation of all subjects, were excluded from the analysis. (This is a separate issue from latency period of cancer, which is discussed in Sections 2.7 and 3.7.2.) However, deaths that occurred in the first 2 years of follow-up were documented, as they may have been caused by acute illnesses related to test participation.

Other measures taken to overcome the absence of a comparable working population were:

- internal comparisons of different categories of cohort members
- a case–control study of leukaemia and ionising radiation exposure.

2.4 Internal comparisons

In these analyses, the mortality rates were compared between groups of cohort members categorised by the estimated radiation exposure received from participation in the nuclear testing.

Radiation exposure was assessed by the Dosimetry Panel, who were blinded to the health status and outcomes of the participants.

As this was an internal analysis within the cohort, it was not subject to a healthy worker effect.

2.5 Veterans of Korean and Vietnam conflicts

The Department of Veterans' Affairs (DVA) has now reported on the Mortality Study and the Cancer Incidence Study of Korean veterans (Harrex et al 2003, AIHW 2003). These studies showed excess mortality from several causes of death and several cancers. The overall mortality was significantly elevated, as were the mortality rates for a number of causes, including deaths from a number of cancers. Likewise, the study of mortality of Vietnam veterans showed excess mortality in veterans from all causes, and from cancer, heart disease and suicide (Crane et al 1997). Since a significant proportion of participants in the nuclear tests were also Korean veterans or went on to serve in Vietnam, it is possible that factors associated with those conflicts could affect the results. Accordingly, an additional analysis was carried out in which Korean and Vietnam War veterans were excluded.

2.6 Outcomes of interest

The study addressed a range of mortality outcomes, including all-cause mortality, deaths from major disease categories and deaths from the major categories of cancer.

Due to the potential exposure of test participants to ionising radiation, cancers that have been found to be associated with radiation in other studies were of interest in this study. These cancers included non-CLL leukaemia. CLL has been shown to have no association with ionising radiation (UNSCEAR 2000). Other solid cancers were selected for analysis based on information from a variety of sources that have suggested an association with ionising radiation, the largest of these studies being the studies of Japanese atomic bomb survivors (Pierce et al 1996). Multiple myeloma was selected as a cause of death of interest because studies conducted on the UK nuclear test participants suggested a possible association (Muirhead et al 2003, Roff 2003). Other causes of death shown by the Japanese studies to be associated with radiation dose were also considered in this study (Preston et al 2003).

The outcomes assessed in this study were:

Deaths

All cancers (excluding non-melanotic skin cancer)
Ischaemic heart disease
Stroke
Respiratory disease (including chronic bronchitis, emphysema and chronic obstructive pulmonary disease)
Diseases of the digestive system (including cirrhosis of liver)
Diseases of the nervous system (including motor neurone disease)
Accidents and violence (including suicide)

Cancer deaths

Lip, oral cavity and pharynx
Oesophagus
Stomach
Colon
Rectum
Liver
Gallbladder
Pancreas
Nasal cavities, middle ear and sinuses
Larynx
Lung
Pleura
Connective tissue
Melanoma
'Radiogenic' cancers
Bladder
Kidney
Eye
Brain and nervous system
Thyroid
Non-Hodgkin's lymphoma

Multiple myeloma
All leukaemias
All leukaemias except chronic lymphatic leukaemia
Chronic lymphatic leukaemia
Prostate
Testis
All other cancers and unspecified sites

2.7 Examination of latency

For leukaemia, analyses were performed to identify any induction latency period; that is, the interval between exposure (to radiation) and disease onset.

There is evidence that the leukaemia risk following radiation exposure declines with time. Based on studies of leukaemia in Japanese atomic bomb survivors and patients treated with radiation for medical conditions, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has observed that the excess relative risk from chronic myeloid leukaemia (CML) and acute myeloid leukaemia (AML) decreases substantially about 10 years after exposure. However, most of the evidence for this decrease related to CML (UNSCEAR 2000).

The design of this study therefore included an examination of any change in the risk of leukaemia with time since exposure to radiation.

2.8 References

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3 Mortality study methods

3.1 The Nominal Roll of Australian Participants in the British Atomic Tests in Australia

3.1.1 Development of the Nominal Roll

The study population was derived from the Nominal Roll of Australian Participants in the British Atomic Tests in Australia. Despite the fact that the Royal Commission into the tests recommended in 1984 that a nominal roll be established, the preliminary roll was only published in 2001 (McClelland et al 1985).

The nominal roll was compiled by the Department of Veterans' Affairs (DVA), using records of the previous study into the atomic tests conducted by Donovan (Donovan et al 1983), Department of Defence records, personnel records of private firms that worked on the tests, the report of the Royal Commission, and records of the issue of Maralinga Security Cards.

During development of the roll, it was checked for completeness against the list of radiation-exposed personnel compiled by JR Moroney in the Australian Radiation Laboratory document, 'Personal monitor records from exposure to beta and gamma radiation during engagement in the program of British nuclear weapons tests in Australia', dated 10 October 1984 (see DVA 2001).

Moroney's document includes lists of participants sourced from the following documents (DVA 2001):

- the British Government's 'Listing of persons at UK overseas defence nuclear experimental programmes, citizens of Australia' (the 'Blue Book')
- Australian Health Physics listing of radiation exposure at Maralinga, prepared by the Department of National Development and Energy during 1981
- 'Radiological health during Operation HURRICANE (Monte Bello Is. October/November 1952) and Operation TOTEM (Emu Claypan, SA October/November 1953)', Minute, 1 December 1953, to Director General Medical Services (RAAF) from Sqn. Ldr. AD Thomas (Scientific Advisor to the Chief of the Air Staff).

Where the name of an armed services member listed in the Australian Radiation Laboratory document was not found on the roll, and it could be verified against Department of Defence records, it was added to the roll. Where a name from the list could be confidently matched with a record already on the roll, additional identifying personal details from the list were included on the roll.

In addition, nuclear veterans' groups provided documents from which additional people were added if they were found to be eligible. Eligibility was checked using service records or other official documentation.

When the nominal roll was initiated, public notices invited people who might be on the roll to opt out of having their name published and, when the original nominal roll was published by DVA, a public notice invited test participants to check that they had not been excluded. DVA received many calls from people making sure that they were on the roll. A small number of individuals advised the DVA that their names had been omitted. Names of these individuals were checked against service records and other documents by DVA, and in some cases their presence at a test site was confirmed and the names were added. In other cases, individuals on the nominal roll advised that they were not present, and their names were deleted.

For the purposes of the roll, the definition of an Australian 'atomic participant' is:

> Someone who was present, either working or as a visitor, in at least one of the testing areas whilst a test or tests were conducted in that area or was there within a 2 year period after the explosion (DVA 2001).

Some people on the nominal roll are not covered by this definition, because their involvement in the tests was at places other than test sites. In particular, this includes RAAF personnel who were at RAAF bases at Amberley, Edinburgh and Pearce in units responsible for decontamination of aircraft that had flown in the test area**.**

Duplications on the nominal roll were removed from the roll on the basis of information reported after the preliminary roll was published (DVA 2001). Some duplications were identified during the vital status search and were also removed.

3.1.2 Limitations of the nominal roll

A group of people, on publication of the preliminary nominal roll, believed themselves to have been wrongly omitted from the roll. These individuals were added if they were found to be eligible by verification of service records and other official documentation. In the study of British nuclear veterans, this group who self-notified were analysed separately from the main cohort, because people are more likely to take an interest in the study and want to be included if they have a medical condition they believe to be related to their exposure. Indeed, a higher rate of the primary disease of interest, leukaemia, was found among self-notifiers in the British study (Darby et al 1988). It was intended in the study protocol (see Appendix 1) that self-notifiers to the roll would also be analysed in a separate group in this study. However, in practice, this was not possible, as these individuals were not identifiable from the nominal roll. DVA believes that the number of subjects who are in the roll as a result of self-notification is less than 100; this number is too small to give meaningful results if analysed separately.

Another source of uncertainty is the RAAF personnel who were in units responsible for decontamination of aircraft that had been in the test area soon after detonation. While these personnel have been retained in the study cohort, it was generally not possible to ascertain which members of these units were actually involved in aircraft decontamination and which were not.

3.2 Defining the study population

From the nominal roll, certain groups of people were declared ineligible for the study, and these subjects were excluded. These included females, pastoralists, rabbiters, indigenous people, and people with insufficient information provided on the roll to facilitate

follow-up. Females (n = 209) were excluded because there were too few to enable meaningful analysis. Aboriginal people were excluded because there were no records of the indigenous people residing or passing through the test areas. The number involved, their location and radiation dose are thus unknown. In addition, at that time, birth certificates and death certificates were not universally issued for the Aboriginal people in the area, so that ascertaining age of individuals at the time of involvement and at death is difficult. Further, neither the death registries nor the cancer registries record aboriginality, and so comparative data for expected rates would be very difficult, and probably impossible, to obtain. Finally, in some Aboriginal cultures, mentioning the names of deceased persons is offensive. For all of these reasons, it was decided that it would be impracticable and unethical to attempt to study the cancer or mortality experience of these individuals with this study design. Pastoralists and rabbiters were excluded because no comprehensive list was made of those who lived or worked near the test sites, and it would now be impossible to construct such a list.

People on the roll who did not have a date of birth recorded were excluded from the study population, as follow-up searching could not be undertaken with appropriate accuracy and certainty.

Some individuals were excluded because a lack of data on the dates of entry and exit to test sites cast doubt on their participation in the tests. These were people on the nominal roll by virtue of the existence of a Maralinga Security Card. However, the existence of this card does not necessarily mean that they actually were present at a test site; anecdotal evidence collected by DVA suggests that, in some cases, security cards were prepared for people expected at the sites who then never arrived. An example of this is some Commonwealth police who had been prepared for duty at the test sites but then were not assigned there. There is no way of knowing which of the people on the roll fall into this category; however, DVA believes that these people are likely to be those without entry and exit dates on the nominal roll. These individuals were excluded from the study.

Inclusion on either the nominal roll or in the study population had no relation to exposure status; people are subjects in the study based on their name appearing on official documents, not on the likelihood of exposure to ionising radiation.

3.2.1 Details of each subject on the study roll

The study roll contained the following information on each participant:

- study ID
- service (or civilian)
- surname
- forenames (up to 3)
- other names
- date of birth
- service number
- for each test service period (not complete for all participants)
  - start date
  - end date

- rank
- unit/employer
- area
- job.

Information about service in the Korean and Vietnam wars was provided at a later stage by DVA. Information on exposure to radiation is discussed in Section 3.5.

Data were incomplete for some participants, although at least one forename, surname and date of birth were included for every participant. Where data were incomplete on day or month for date of entry to the cohort, estimations were made based on other information held on the roll or on the data for other members of the cohort who entered at the same time (in the same month or year). This is discussed in further detail in Section 3.6.

3.3 Data sources for ascertaining vital status

Information on the vital status and, if deceased, date and cause of death, of each member of the cohort was sought from a variety of sources. In some cases, information about vital status on an individual from one source was found to be discordant with information from another source. These cases were assessed individually using all available information and, where necessary, further information was sought. Decisions about the matches were made by consensus between members of the study team.

The initial step to ascertain vital status was to match the study roll with the DVA client base. The cohort roll was also submitted simultaneously to the Australian Institute of Health and Welfare (AIHW) for matching with the National Death Index (NDI), and to the Australian Electoral Commission (AEC) for matching with the Commonwealth electoral roll.

3.3.1 DVA client database

Information about many of the study participants was available from DVA's own database of client information. People are on the DVA client database if they have received or are receiving benefit payments such as income support or a pension from DVA; if they have received compensation from DVA; if they have a health care or gold card (entitling them to care at veterans' health providers); if they died in a war; or if they had applied for DVA financial assistance, even if their request was rejected. Although the client database is not complete, it is accurate with regard to vital status for benefit recipients. Information was available on participants both known to be alive and known to be dead. People receiving payments were considered alive.

Information on participants recorded as dead on the database, and who were not located in the NDI, was treated in one of three ways. Where death certificates were available from the client's file, these were sent to the National Centre for Classification in Health (NCCH) for the cause of death to be coded into the International Classification of Diseases–revision 10 (ICD-10). This is a standard, worldwide system for coding diseases. Where death certificates were not available, the last known address and date of death were used to identify the state of death registration so that the certificate could be obtained from the relevant state or territory registrar, and then sent to NCCH for coding. For some participants, a death certificate was unavailable, but a certified cause of death was recorded and this was coded by NCCH. For others, particularly participants who had

died while still serving in the military, a cause of death was not available because it had never been recorded (it was not required on official records at the time). These individuals were assigned an unknown cause of death. For a small proportion of known deaths, a death certificate or other confirmation of death could not be located. Where such a death could not be confirmed to have occurred in Australia, the participant was considered censored at the recorded date of death. Other deaths recorded by DVA but which could not be confirmed were treated as lost to follow-up. The DVA client file was also used to confirm discordant matches found during other stages of matching.

Cohort members receiving pensions overseas were classified as having emigrated. The date of the last payment made in Australia, if available, was taken as the date of emigration. Other participants known to have emigrated were censored at their last known date in Australia; sometimes this was their date of discharge from the services, and sometimes it was their last known date at the nuclear tests.

3.3.2 National Death Index

The NDI, which is maintained by AIHW, holds a record of every death registered in each state and territory in Australia since 1980. Data on name, date of death and cause of death are held, as well as other demographic information. Not all records contain the date of birth, because it has not always been a required item on death certificates. In 1980, only 16.9% of death certificates included date of birth. Since then, all states have now included this item on death certificates, so that the figure in 2002 was 99.8% (AIHW, personal communication, 2004).

It is likely that the NDI is an almost complete record of deaths occurring in Australia. In one validation study published in 2000, the NDI found 88.8% of people known to be dead (Kelman 2000). A study published later in 2000 found 95% of people known to be dead (Powers et al 2000). The difference between these two studies probably reflects differences in the matching programs used. Indeed, the sensitivity found in these studies is probably not that of the NDI but that of the matching program. Even the best matching program cannot detect people who have changed their name, for example.

AIHW used a probabilistic linking package to match the cohort to the NDI, using multiple passes which assessed different characteristics of the data in each pass, generally with each pass more liberal with matching than the last. In addition, phonetic codes were used to account for variations in spellings of the same surname, while alternative first names (e.g. Bob for Robert) were also incorporated.

As earlier death records do not have a date of birth, the NDI output was presented in two extracts. Extract 1 presented matches with death records containing a date of birth. Extract 2 was based on records with no date of birth; in these records, the year of birth was estimated from date of death and age at death. Matches made on later passes were reviewed by the study team and compared with information from other sources (DVA client database or the electoral roll search). Matches were either accepted or rejected or, where there was still doubt, details were submitted to DVA to see if further information could be accessed to assist with assessing the match. The final decision on the match was made by the study team.

3.3.3 Commonwealth electoral roll

The electoral roll is a common source of follow-up information for health researchers in Australia, and has been used in many studies for the purpose of ascertaining vital status. Information on name and address is publicly available from the roll, but appropriate approval must be gained to access information about date of birth.

As voting is compulsory in Australia, the proportion of eligible people enrolled is very high. The most recent estimate by the AEC is that 95% of eligible persons are enrolled (AEC 2004). Limitations of the electoral roll include the fact that only Australian citizens are eligible to enrol, so that any immigrant subjects who have not taken up Australian citizenship will not be on the electoral roll. In addition, the electoral roll cannot account for name changes, and this can result in failure to match individuals. Changing of name was relatively common in the immigrant population from Eastern Europe, who 'anglicised' their names on settling in Australia around the time the cohort was established. A number of subjects may have not been matched for this reason.

For this study, the electoral roll was matched to the cohort, and only perfect matches on name and date of birth were returned. All matches were accepted, except for those which were also matched to the NDI; these were reviewed by the study team and again a decision to accept, reject or submit for further review by DVA was made, based on information in the nominal roll. In many cases, doubtful matches were referred to DVA for comparison with additional information in departmental records.

3.3.4 Health Insurance Commission (Medicare)

Because Australia has virtually universal health cover provided by the government, comprehensive records are kept of health services used. The Health Insurance Commission (HIC) is responsible for storing this information. Access was granted to the records of general practitioner episodes of care for individuals in the previous five years. For the purposes of this study, information was only obtained on the date of last service, to ascertain whether the individual was alive on the cutoff date. Names of all cohort participants who were not matched through DVA, NDI or AEC were submitted to HIC. Perfect matches on name and date of birth were provided to the study team with a date of last service, if it was available. Participants were then considered to be alive to that date and, in the absence of more recent information, their follow-up time finished at the date given by HIC or the study cutoff date, whichever was earlier.

The HIC database does not include episodes of care received by veterans holding a health care card or gold card; HIC holds a separate database for veterans, and any person using services as a veteran would be identified in the DVA client database.

3.3.5 State death records

Death certificates of people who died before the advent of the NDI are held by the Registrars of Births, Deaths and Marriages in each state and territory. All participants not located through one of the previous search mechanisms were submitted to each registry for searching, with the exception of the Northern Territory registry, which is prohibitively expensive to search. Thus some deaths that occurred in the Northern Territory before the establishment of the NDI will have been missed in this study. The registry for each state has a different structure and different levels of access available to researchers. AIHW

coordinated the search. For all states except Victoria and Western Australia, the search was conducted by state and territory registries; the other two states were searched by DVA or AIHW. This was predominantly a manual procedure, and all potential matches were sent to AIHW for a decision on the quality of the match. Where matches were made, death certificates were requested from the registries and then sent to NCCH for coding.

In addition, records of the Genealogy Society of South Australia were accessed. These include probate records for most states (held to varying years) and South Australian death certificates to the early 1970s. As it is a very time consuming and costly exercise to manually search for death certificates, Genealogy Society records were used to try to locate a state and year of death for participants about whom nothing else was known, so that the appropriate state registry could be searched for the death certificate. However, in practice it proved difficult to ascertain the certainty of a match from probate records, which do not include date of birth, and so this exercise was not particularly fruitful.

3.3.6 Records from the previous study of atomic test personnel

In 1982, the first study of the health of Australia nuclear test participants was conducted by Donovan and colleagues (Donovan et al 1983). The study investigated deaths as part of its design, and collected over 1500 death certificates of trial participants. These came from a variety of sources, including those held by the former Department for Resources and Energy, and the state and territory death registries. These study records were accessed by DVA, and, where a death certificate for a study participant was located within the Donovan records, it was retrieved and sent to NCCH for coding.

3.3.7 Manual search of the electoral roll

Since the first search of the electoral roll only covered perfect matches, it was likely that participants may have been missed due to errors in spelling and date of birth. Names of participants not located in any previous search were searched for again on the electoral roll, this time allowing for variations in spelling and date of birth translocations. The search was conducted manually by DVA and matches were individually assessed for accuracy.

3.3.8 England and Wales death index

Participants lost to follow-up to this stage were also searched on the England and Wales death indices for 1984 to 2000. The follow-up time of any matches was ended at their last known date of contact in Australia; for the majority, this was their last date at the test site recorded in the nominal roll.

3.3.9 Servicemen's associations

Members of several servicemen's associations were approached to see if people not located in any of the previous searches were known to these associations. This was done on an informal basis, with feedback given directly to DVA. Those thought to be alive by the associations were validated elsewhere, usually through the electoral roll. The death certificates of those thought to be dead were requested.

3.3.10 Department of Immigration, Multicultural and Indigenous Affairs

The Movement Alerts and Border Systems Section of the Department of Immigration, Multicultural and Indigenous Affairs (DIMIA) maintains a record of movements in and out of Australia, compiled from forms completed by individuals travelling abroad and arriving back. The list of cohort members not previously located was submitted to DIMIA for matching. Where the most recent match with a subject was a departure record, the subject was deemed to have emigrated. Where the most recent entry for a matched subject was arrival, the subject was deemed to be alive and living in Australia, and the arrival date deemed the date of last contact (in the absence of any other information later than the arrival date). Information was provided back to DVA and checked with other DVA data before being passed on to the study team.

3.3.11 Cancer incidence search

While the follow-up of vital status of the cohort was being completed, the cancer incidence component of the study was also under way. This part of the study involved searching the records of the state and territory cancer registries for cancer registrations for the cohort members. The National Cancer Statistics Clearing House (at AIHW) was searched for matches to the cohort for cancers registered in all states except Victoria, and the Victorian cancer registry was searched separately. The method of the cancer incidence study can be found in Chapter 8. During this process, a number of previously unidentified deaths were found and were included in the mortality study.

3.4 Ascertainment of cause of death

3.4.1 Coding from the National Death Index

The NDI contains all deaths occurring in Australia since 1980. All deaths in the NDI are in the ICD classification used at the time of death. Deaths from 1980 to 1996 have ICD-9 coding, and those from 1997 have ICD-10 coding.

3.4.2 Coding of deaths by NCCH

For deaths occurring before 1980, or after 1980 but not found on the NDI (such as deaths known to DVA), it was necessary to obtain the death certificates and submit them for coding. In many cases, death certificates of deceased service personnel were already held by DVA. For other identified deaths, a death certificate was obtained from the appropriate state death registry. In a minority of cases, certified causes of death were known by DVA from defence personnel files.

All certificates or certified causes were sent to NCCH for coding. NCCH, located in the School of Public Health, Queensland University of Technology, is the primary centre for coding in Australia, providing coding services for research and training for clinical coders around the country. Deaths were coded in ICD-10.

3.4.3 Quality control

Some variation may be expected between the cause of death given on the NDI and the cause given by NCCH after coding of death certificates. This is because deaths on the NDI are coded according to the practice at the time the certificate was coded (approximating when the individual died). In contrast, the certificates sent to NCCH are coded using current practice, regardless of the date of death of the individual. Thus, a validation study was undertaken to assess the degree of concordance on cause of death coding between the NDI and NCCH.

A power calculation determined that, to detect an accuracy of 95% by NCCH, and to estimate this degree of accuracy within 5%, a sample of 75 death certificates would need to be submitted to NCCH for recoding. Seventy-nine deaths found in the NDI were identified, and their death certificates retrieved (either from DVA files or from the NSW Registrar of Births, Deaths and Marriages). Deaths were chosen deliberately from the years close to the beginning of the NDI, as this would maximise the likelihood of detecting differences in coding practice that would result in different causes of death being assigned. As the majority of the coding done by NCCH was for deaths before 1982, when the NDI was established, this approach would estimate the difference that might be expected between the coded causes of death in the cohort and the population rates from the same time (taken from Australian Bureau of Statistics figures, coded in the same manner as the NDI). The validation death certificates were sent to NCCH, which was blind to the purpose of the coding.

The validation study showed 94% agreement on the coding of cause of death. Four certificates were given a completely different code to that on the NDI. One death was coded by NCCH as alcoholic cirrhosis of the liver, while the NDI code was chronic bronchitis; one death was coded as essential primary hypertension by NCCH but as a dissecting aortic aneurysm on the NDI; the third was coded as abnormal reaction from surgery (surgical operation with anastomosis) by NCCH but as coronary atherosclerosis on the NDI; and the fourth was considered congestive heart failure by NCCH but sarcoidosis on the NDI. One death by hanging was considered accidental by NCCH but suicide on the NDI. All other deaths were concordant between NCCH and NDI. The five discordant cases were resubmitted to NCCH and, in each case, the NDI coding was found to be correct. On this basis, it is possible that there is a 6% error rate in the coding of the deaths (26% of all deaths) that occurred before the NDI. Thus the overall error rate from this source was approximately 1.6%. There were no coding errors for deaths from cancer.

3.5 Exposure assessment

Radiation exposure, which is the prime determinant variable of interest in this study, was assessed by a scientific panel with expertise and experience in radiation dosimetry (the Dosimetry Panel), using records of dosimetry, health physics and other information. The exposure assessments were assigned to members of the cohort according to information on the database, such as test site they attended, date of arrival and departure, branch of the services and occupation.

Radiation doses are measured in units of millisieverts (mSv). All subjects were assigned to one of five categories of accumulated dose:

A <1 mSv

B 1 to <5 mSv

C 5 to <20 mSv

D 20 to 50 mSv

E >50 mSv

F unknown

The assessment relates only to the exposure incurred as a result of the nuclear explosions of the testing program, and includes doses from both external sources and internal sources (e.g. arising from inhalation of radioactive dust). No account was taken of background exposure at the test site, medical exposures, or exposure as a member of the general population after leaving the test site. The report of the Dosimetry Panel is presented in Volume 1 of the study findings.

An exposure category was entered into the record of each cohort member by DVA, and then added to the cohort database by the researchers at the University of Adelaide.

3.6 Deriving person-years of follow-up

In this study, each member of the cohort was followed through time to see whether they had died. The amount of time for which individuals were followed (the follow-up time) differed for each person. The beginning of follow-up time depended on when each member of the cohort first participated in the tests, and the end of their follow-up time depended on when they died, or when they could no longer be traced, or the study cutoff date.

3.6.1 Entry date

The date of entry into the cohort was the day of first entry to a test site, or the date of the first atomic detonation at that site, whichever was later. For a number of participants, only a month and year of entry or just a year of entry were available from the nominal roll. In these cases, date of entry was estimated from other information contained in the roll. For some, this meant that their date of entry was the date of detonation. Those whose partial date was after the first detonation were assigned the mean date of entry for other participants who entered the cohort in that year. This was a slight variation on the method given in the protocol for estimating date of entry, which turned out not to apply appropriately to many of the participants with partial dates.

3.6.2 Cutoff date

The choice of cutoff date for the study is important because the estimated mortality rates in the cohort and in the general population need to be comparable. It must be ensured that enumeration of deaths in the national mortality data is complete, and the cutoff date reflects the latest possible date that this is the case. Accordingly, the cutoff date for the study was 31 December 2001.

Follow-up time for cohort members finished as follows:

- Subjects known to be alive on 31 December 2001 were followed up to that date.
- Subjects who died before 31 December 2001 were followed up to the date of death. Subjects who died after 31 December 2001 were considered alive at the cutoff date.
- Subjects who had emigrated before 31 December 2001 were followed up to the day of emigration, if known. This date was taken to be the date of departure from DIMIA Movement Records, or, for subjects receiving pensions from DVA payable overseas, the date of the last pension payment in Australia. For some subjects, follow-up time finished on their last known date of contact in Australia, either their discharge from service or their last known date at the test sites.
- For subjects whose vital status was unknown on 31 December 2001 and who were not known to have emigrated, the cutoff date was the last day of contact.
- Subjects who were still alive on reaching the age of 85 years were followed up to their 85th birthday. This measure, adopted in the study of UK test participants, was considered appropriate for two reasons: (i) there is often some uncertainty over the accuracy of the certified cause of death in the very old, and (ii) the expected death rate rises steeply each year after 85, so that the observed and expected rates will not be comparable if the age distribution within this group differs from that of the general male population.
- Subjects known by DVA to have died, but for whom no confirmation of that death occurring in Australia could be found, were followed up to the date of death, but the death was not counted for mortality estimation.

3.6.3 Follow-up time

In this study, follow-up time in all analyses commenced 2 years after entry into the cohort. The first 2 years have been excluded to reduce the influence of selection in the healthy worker effect. As discussed in Section 2.3, the healthy worker effect is partly due to the reduced participation in the workforce of people with serious or chronic diseases. To the extent that such individuals die younger than people in the workforce, the mortality rates in cohorts of working people (after adjustment for age and year of death) will be lower than in the general population. As cohorts age, this effect of selecting seriously ill people out of the workforce will diminish. Ideally, this selection effect is overcome by omitting the earliest years of the follow-up time from the analysis. However, the rate of decline varies with the cause of death; for deaths from injury, the duration of a selection effect is nil. For diseases such as multiple sclerosis, the duration is decades. In this study, the disease of primary interest was leukaemia, for which the selection effect was unlikely to exceed 2 years because of the relatively short survival time in the 1950s and 1960s. Accordingly, the follow-up time for each subject commenced 2 years after entry into the cohort, and deaths in the first 2 years were excluded from the analysis.

This 2-year period was not optimal for all causes of death, being too long for deaths from injury, and too short for some other causes of death. However, it was likely to be reasonably close to the optimal period for minimising the selection effect for all causes of death.

3.6.4 Treatment of subjects lost to contact

Subjects whose vital status was unknown on the cutoff date were deemed to be lost to contact. There were a number of possible explanations:

- The subject may have emigrated.
- The subject may have died in Australia but the name was not detected in matching with the NDI or state death records. This is particularly likely if the person has had a name change.
- The subject may have been alive and living in Australia but was not on the electoral roll or on Medicare records.
- The subject may have been alive and on the electoral roll and/or Medicare records but not detected in matching. This was likely because the AEC and HIC did not supply information if the match was not exact.

Two methods of dealing with the participants of unknown vital status were applied to the cohort. These were similar to the methods applied in the cohort study of Korean veterans (Harrex et al 2003).

Using Method 1, the follow-up time of subjects lost to contact ceased on the date of last contact; that is, the follow-up time of these subjects from date of last contact to 31 December 2001 was not included. This gives an accurate estimate of mortality of the whole cohort if the participants lost to contact have the same mortality rate as those participants whose vital status on the cut-off date is known. To the extent that this method excluded the follow-up time of subjects who were still alive and living in Australia, the total person-years of follow-up was underestimated, leading to an overestimate of the mortality rate relative to the national rate. However, this overestimate could be offset to the extent that some subjects lost to contact had actually died after the last contact but their names were not found in the search of the NDI or state death registries. The exclusion of these deaths would lead to an underestimation of the mortality rate.

Using Method 2, subjects lost to contact were treated as being alive and living in Australia, so that their follow-up time extended to 31 December 2001. In fact, it is highly unlikely that all participants lost to follow-up were actually alive and living in Australia. Because this method probably includes follow-up time of subjects who are dead or who would never be located in the NDI (e.g. because they have emigrated or had a name change), the total person-years was overestimated, leading to an underestimate of the mortality rate relative to the national rate. There could be a further contribution to the underestimation if subjects lost to contact had died but their names were not found in the search of the NDI or state death registries.

3.7 Analysis

The analysis investigated the mortality of the test participant cohort relative to the general population of males in Australia, and in relation to variables of importance such as exposure. The analysis took account of any possible healthy worker effect.

3.7.1 National mortality data

National mortality data were required for comparing the mortality experience of the cohort with that of the general population. National mortality data were obtained from AIHW. These data comprised tables of numbers of deaths by all causes and each cause of interest, stratified by five-year age group at death and year of death, as well as the population counts for each year and age group. Despite the introduction of several different versions of the ICD during the follow-up period of this study, national mortality data are tabulated according to the ICD code at the time for each cause.

A major limitation of the population data is that some causes of death were not separately identified and coded until the introduction of the ICD-8 coding system in 1968. This limitation applies to the following causes of death:

- chronic bronchitis, emphysema and chronic obstructive pulmonary disease (COPD)
- diseases of the digestive system
- cirrhosis of liver/alcoholic liver disease
- diseases of the nervous system
- motor neurone disease
- the following cancers
  - gallbladder
  - pancreas
  - nasal cavities, middle ear and sinuses
  - larynx
  - pleura
  - connective tissue
  - nonmelanotic skin
  - brain and nervous system
  - multiple myeloma
  - leukaemia subtypes.

With the exception of leukaemia, all these causes of death were analysed from 1968 onwards only.

Differentiation of leukaemia types before 1968

The problem with a lack of information on leukaemia subtype before 1968 is of special concern, since the major outcome of interest in this study is not all leukaemias, but leukaemias excluding chronic lymphatic leukaemia (CLL). The mortality from leukaemia in these early years of the cohort is particularly important because of the likelihood that leukaemia has a shorter latency period following causal exposures such as radiation or benzene, and because the survival time from leukaemia in that era was comparatively short (UNSCEAR 2000).

Data on death from non-CLL leukaemia was available for members of the cohort who died before 1968, because their cause of death was extracted from their death certificate, which generally includes the leukaemia subtype. However, the subtype information was not available for the general population before 1968, because the classification used before that time for coding cause of death classified all leukaemias as one disease. Thus,

it was necessary to estimate the number of non-CLL leukaemias in the general population data that predated 1968, for use in the calculations.

On examining the population mortality rates for the subtypes of leukaemia that were available post-1968, it was found that the rate of CLL varied strongly by age (following a Gompertz distribution) and by calendar year (in a near-linear fashion). Thus a model was constructed taking both of these variables into account. The complementary log-log model estimated the proportion of all leukaemias that would have been CLL before 1968. Extensive testing of the model against the known data showed it to be a good fit, and thus it was used to estimate the number of non-CLL leukaemias in each age and year stratum before 1968.

3.7.2 Measures of mortality

Two measures of mortality were used in the analysis:

- The standardised mortality ratio (SMR) was used to compare mortality rates between the cohort and the general Australian male population.
- The relative mortality ratio (RMR) was used for internal analysis, in which different categories of subjects within the cohort were compared with each other.

Both of these measures are discussed below.

Standardised mortality ratios

The SMR is a measure of the death rate occurring in the cohort population compared with the death rate occurring in the national population. It can be measured for the whole cohort population or any subset (e.g. RAAF), for any particular cause of death, or for all causes combined. The SMR is obtained by dividing the number of deaths 'observed' in the nuclear test participants by the calculated 'expected' number that would arise in a group of the same age and sex at the same time in the Australian national population. The expected number is computed by multiplying the national death rates (by age and year of occurrence) by the number of person-years in each age and calendar year in the cohort.

If the deaths in the nuclear test participants are occurring at the same rate as in the national population, then the SMR will be 1.0. If the SMR is greater than 1.0, then deaths in the cohort are occurring more frequently than would be expected. If the SMR is less than 1.0, then deaths in the cohort are occurring less frequently than expected. Thus, the SMR forms a measure of the risk of death in the test participants compared with Australians as a whole, with age and year of occurrence taken into account.

The SMRs are accompanied by 95% confidence intervals. The SMR as shown is actually a statistical estimate of the true ratio. The true ratio cannot be known exactly, and a spread of estimates of the SMR is calculated within which it is 95% certain that the true figure lies. This spread is called the confidence interval.

The choice of 95% confidence intervals is commonly used in health studies, and simply means that the chance of the true figure lying outside the confidence interval is about 1 in 20.

The importance of this lies in the interpretation of the SMR. Where the SMR is higher than 1.0, then a true increase in mortality may be present, but if the lower end of the

confidence interval extends below 1.0 then it is possible that the real ratio is 1.0 or less and no increase is present. However, when the lower end of a confidence interval is above 1.0, then we can say with some certainty that there is an increase in mortality. This is described as being a statistically significant result.

As described in Section 3.6.4, SMRs were calculated using the number of person-years measured in two different ways, according to whether or not person-time lost to contact was included.

SMRs were generated for the following groups:

- the whole cohort
- Army
- RAN
- RAAF
- civilians
- military participants excluding Korean War veterans
- military participants excluding Korean and Vietnam war veterans.

Relative Mortality Ratios

The RMR was used for comparisons within the cohort. Where a measure or ranking of exposure to a harmful agent can be obtained, the RMR can be calculated by comparing those who have more exposure with those who have less. Generally, it would be expected that if the exposure were causing the effect, then those with more exposure would have worse health outcomes. This is known to apply, for example, for the number of cigarettes smoked and the risk of getting lung cancer. It applies for most exposures that create risks to health.

For the outcome of interest, a 'baseline' exposure level is chosen, and represented as having a risk of 1.0. Risk for all other exposure categories is then compared with the baseline.

The RMR analyses were done using Poisson regression models. As these models depend on 'large sample' theory for statistical validity, 95% confidence intervals were not given if either of the two categories being compared had fewer than four cases. All analyses were adjusted for age and person-time in the cohort.

RMRs were used for internal comparisons for non-CLL leukaemia and other causes of death found to be significant in the SMR analysis.

The following comparisons were made:

- Between categories of radiation exposure.
- According to time since cohort entry. This analysis was performed to examine the influence of latency — that is, the period from exposure to disease onset. Comparisons were made between mortality rate in the period from 2 to 15 years, and 15 years after entry, into the cohort.
- According to rank — that is, commissioned officers vs other ranks.

Unlike analyses based on the SMR, only one method was used for computing follow-up time. This was Method 1: person-time of subjects lost to contact was censored on the date of last contact.

3.8 Confounding

Confounding variables are other factors in the cohort (apart from the exposure of interest) that affect the health outcomes being studied. Where these factors can have large influences on outcomes, such as with smoking and cancer, it is necessary to account for them. For example, even small differences in exposure to tobacco smoke can cause large differences in lung cancer rates. To cause confounding, a variable has to be a cause of the disease in its own right, and must be unequally distributed between the different groups being compared.

Differences in risk between various exposure groups can therefore be masked or falsely elevated if confounding variables are not allowed for.

In the SMR and RMR estimates, adjustment is made for confounding by age and calendar year — that is, to take account of varying death rates by age and year.

Other causes of disease also need to be considered as potential confounders. The most important in this study would be smoking, which is strongly related to many causes of death. Unfortunately, no smoking history was available for members of this cohort. Therefore, indirect measures have been used to estimate the likely confounding effect of smoking. One means is to examine the cancer rate or death rate from diseases almost exclusively due to smoking, such as emphysema and laryngeal cancer. Another method is to estimate what the smoking prevalence would have to be to explain fully an excess of a cancer or cause-specific death by smoking alone. This is discussed in the following section.

Another cause of confounding is asbestos exposure, which has an association with lung cancer. This study did not have information on asbestos exposure in cohort members.

3.8.1 Estimating cancer mortality rates from hypothetical levels of smoking prevalence

Since no smoking data were available for this cohort, it was not possible to compute the proportion of deaths from diseases such as lung cancer caused by smoking. However, an indirect measure was used to compute the level of smoking prevalence in the cohort that would be required to account for any excess mortality. The method adopted was that developed by AIHW for the Korean Veterans Mortality study (Harrex et al 2003). This analysis generated a hypothetical number of expected deaths based on a range of smoking prevalences from 30% to 100%.

Further details about the method for calculating hypothetical smoking prevalences can be found in Appendix 5.

3.9 Software

Data were analysed using Stata version 8.2.

3.10 Ethics approval

Ethical approval was obtained for this study from the Human Research Ethics Committees of the following:

- University of Adelaide
- Australian Institute of Health and Welfare
- Department of Veterans' Affairs
- Department of Defence.

In addition, ethical safeguards were required from the following authorities that assisted with matching:

- Australian Electoral Commission
- Health Insurance Commission
- Department of Immigration, Multicultural and Indigenous Affairs.

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4 Description of the mortality study cohort

As described in Chapter 3, the cohort of Australian nuclear test participants was formed from the nominal roll with some exclusions. In total, 10 983 participants were included in the cohort and they are described in the following sections.

4.1 Study population by service category

Of the 10 983 participants, 7116 were military participants and 3867 were civilian participants. Table 4.1 shows the distribution of subjects by service category.

Table 4.1 The study population by service category

Service category	Number of participants
RAN	3097
Army	1245
RAAF	2774
Civilians	3867
Total	10 983

4.2 Excluded subjects

For reasons given in Chapter 3, women participants, pastoralists, rabbiters and indigenous persons at the test sites were excluded from the study. Since knowledge of the date of birth of all subjects is essential for comparing mortality and cancer rates with the general population, subjects whose date of birth was not known were also excluded from the analysis.

Subjects excluded from this study are shown in Table 4.2. A total of 2227 subjects were excluded, most commonly because the date of birth was not known.

Table 4.2 Excluded subjects

Ineligible group	Number
Women	209
Pastoralists	5
Indigenous	29
Rabbiters	38
No date of birth	1946
Total	2227

4.3 Attendance and frequency of attendance at test sites

The attendance at test sites by participants is described in Table 4.3. RAAF participants were involved mainly at air bases around Australia, not at the test sites. RAAF participants and civilians involved after the Totem tests did not have a test specified, and are thus included in the post-Totem figure.

Table 4.3 First test attendance — numbers at each test, by service

Test	RAN	Army	RAAF	Civilians
Hurricane	2296	30	216	10
Monte Bello Inter Trial	248	0	0	0
Totem	0	211	915	142
Post-Totem	0	0	1643	3715
Mosaic	267	0	*	*
Buffalo	76	281	*	*
Buffalo/Antler	0	147	*	*
Antler	48	114	*	*
Post-Antler	162	462	*	*

* Included in 'Post-Totem' figure

The frequency of attendance at test sites is shown in Table 4.4. Just over 11% of military participants (n = 841) attended 2 or more tests.

Table 4.4 Frequency of test attendance by service

Number of visits	RAN	Army	RAAF	Civilians	Total
1	2890	1168	2254	3231	9543
2 or more	207	77	520	636	1440

4.4 Age of study population

The age of the cohort is shown by the distribution of year of birth in Table 4.5. Over 90% of cohort members were born between 1910 and 1939. The civilian participants as a group were older than service personnel.

Table 4.5 Year of birth distribution

Year of birth	Military	Civilian	Total
Pre-1900	2 (<1%)	11 (<1%)	13 (<1%)
1900–1909	141 (2%)	353 (9%)	494 (4%)
1910–1919	718 (10%)	846 (22%)	1564 (14%)
1920–1929	2967 (42%)	1463 (38%)	4430 (41%)
1930–1939	3064 (43%)	1007 (26%)	4071 (37%)
1940–1948	224 (3%)	187 (5%)	411 (4%)

The civilian participants were also older than the military participants at entry to the cohort. The average age of entry for the whole cohort was 29 years. It was 34 years for

the civilian participants, and the RAN participants were the youngest. The distribution of age of the cohort participants is shown in Table 4.6.

Table 4.6 Age at entry to the cohort

Age group (years)	RAN	Army	RAAF	Civilians	Total
<20	565 (18%)	115 (9%)	261 (9%)	139 (4%)	1080 (10%)
20–29	2143 (69%)	596 (48%)	1562 (56%)	1378 (36%)	5679 (52%)
30–39	327 (11%)	334 (27%)	671 (24%)	1272 (33%)	2604 (24%)
40–49	52 (2%)	172 (14%)	262 (9%)	804 (21%)	1290 (12%)
50+	10 (<1%)	28 (2%)	18 (<1%)	274 (7%)	330 (3%)
Mean age (years)	24.6	30.1	28.4	34.0	29.5

4.5 Rank of the military participants

The military participants in the cohort had a rank recorded on the nominal roll. Over 80% of the participants were at ranks other than officers, as shown in Table 4.7.

Table 4.7 Rank by service category

Service	Other ranks	Officers	Total
RAN	2820 (91%)	277 (9%)	3097
Army	952 (76%)	293 (24%)	1245
RAAF	2161 (78%)	613 (22%)	2774
Total	5933 (83%)	1183 (17%)	7116

4.6 Participation in conflicts in Korea and Vietnam

The nuclear tests in Australia were conducted between the Korean and Vietnam wars, and thus many of the nuclear test participants were involved in these conflicts. As shown in Table 4.8, 2485 military cohort members (35%) and 45 civilian cohort members (1%) were veterans of the Korean War, the Vietnam War or both.

Table 4.8 Participation in conflicts in Korea and Vietnam

Conflict	Military	Civilian	Total
Korea	1675	25	1700
Vietnam	597	19	616
Korea and Vietnam	213	1	214

4.7 Exposure to ionising radiation

Participants in the cohort were allocated an exposure category according to their work group, locations, jobs, etc. This exposure assessment was made by the independent exposure panel, as described in Chapter 3. Results are shown in Table 4.9.

Overall, 6% of the cohort could not be allocated to an exposure category due to a lack of information on their test participation. Only 4% of the study population had an estimated radiation exposure greater than 20 millisievert (mSv) from test participation, and 79% had an estimated exposure of less than 1 mSv. The estimated mean radiation exposure of the study population was 2.8 mSv. For purposes of comparison, the current annual Occupational Exposure Limit to ionising radiation is 20 mSv. According to the United Nations Scientific Committee on the Effects of Atomic Radiation, the mean estimated exposure from natural background radiation is 2.5 mSv worldwide.

Table 4.9 Estimated exposure to ionising radiation

Exposure category	RAN	Army	RAAF	Civilian	Total
A (<1 mSv)	2274 (73%)	747 (60%)	2028 (73%)	3615 (93%)	8664 (79%)
B (1 to <5 mSv)	622 (20%)	45 (4%)	19 (<1%)	12 (<1%)	698 (6%)
C (5 to <20 mSv)	194 (6%)	201 (16%)	71 (3%)	40 (1%)	506 (5%)
D (20 to 50 mSv)	2 (<1%)	232 (19%)	3 (<1%)	164 (4%)	401 (4%)
E (>50 mSv)	0	4 (<1%)	14 (<1%)	1 (<1%)	19 (<1%)
F (unknown exposure)	5 (<1%)	16 (1%)	639 (23%)	35 (<1%)	695 (6%)

4.8 Summary of vital status determination

The vital status of the cohort members, and the primary source from which this was determined, are shown in Table 4.10. At the censor date of 31 December 2001, 5494 subjects (50%) were confirmed living, and 4427 subjects (40%) were confirmed deceased. A further 23 participants were known by the Department of Veterans' Affairs (DVA) to be deceased, but corroborating evidence for the death in the form of a death certificate or National Death Index (NDI) registration could not be found. These participants were followed up to their date of death. One hundred and five participants (<1%) were known to be living overseas or to have died overseas. The vital status of 934 subjects (8.5%) on the cutoff date was unknown. Of these, 72 had been confirmed alive some time between the nuclear testing program and the cutoff date; the remaining 862 (75% of them civilians) were untraced since the nuclear testing.

Table 4.10 Follow-up results

Status	Source	Military	Civilian	Total
Alive at censor date	Electoral roll	3302 (46%)	1243 (32%)	4545 (41%)
	DVA	197 (3%)	8 (<1%)	205 (2%)
	Health Insurance Commission	226 (3%)	166 (4%)	392 (4%)
	Died after censor date	245 (3%)	107 (3%)	352 (3%)
TOTAL ALIVE		3970 (56%)	1524 (39%)	5494 (50%)
Censored before 31 December 2001	Health Insurance Commission	46 (<1%)	26 (<1%)	72 (<1%)
	Overseas (DVA)	69 (<1%)	36 (<1%)	105 (<1%)
	Uncorroborated death(DVA)	14 (<1%)	9 (<1%)	23 (<1%)
TOTAL CENSORED		129 (2%)	71 (2%)	200 (2%)
Dead	Death certificates	819 (12%)	535 (14%)	1354 (12%)
	National Death Index	1971 (28%)	1060 (27%)	3031 (28%)
	Other	15 (<1%)	27 (<1%)	42 (<1%)
TOTAL DEAD		2805 (39%)	1622 (42%)	4427 (40%)
UNMATCHED		212 (3%)	650 (17%)	862 (8%)
TOTAL		7116	3867	10 983

5 Mortality study results

5.1 Interpretation of results

The mortality of the nuclear test participants is mostly expressed as a standardised mortality ratio (SMR), with a confidence interval.

The SMR is the ratio of the observed number of deaths in the participants to the expected number of deaths if the participants had the same mortality rates as the general Australian population. The method of computing the SMR is explained in Section 3.7.2. An SMR greater than 1.0 indicates that the mortality is greater than expected in the general population, and an SMR less than 1.0 indicates that it is less than expected. However, the SMR is only an estimate of the true mortality ratio. The confidence interval (CI) is a statistical estimate of the likely range within which the true mortality ratio lies. If the lower boundary of the CI exceeds 1.0, we can be reasonably confident that the true SMR exceeds 1.0, in which case the SMR is statistically significantly increased — that is, the mortality rate is considered to be higher than expected in the general population. Conversely, if the *upper* boundary of the CI is less than 1.0, the SMR is considered to be statistically significantly lower than expected.

In this report, a 'significant' increase in SMR refers to a statistically significant increase — that is, the true mortality rate is likely to exceed that expected. It does not necessarily mean that it is a large increase.

As discussed in Chapter 3, two different methods were used to treat the individuals lost to follow-up in this study. In Method 1, the person time of individuals lost to follow-up was censored at their date of last contact. In this method, a total of 369 462 person-years were included in the study. In Method 2, where individuals lost to follow-up were considered alive at the censor date of 31 December 2001, a total of 404 545 person-years were contributed. Method 2 assumes that all subjects lost to contact are alive and living in Australia, and is almost certainly a considerable underestimate.

Method 1 is accurate to the extent that the mortality rate in those lost to contact is the same as in the rest of the cohort, and represents the best estimate of mortality rates. Accordingly, only results from Method 1 are shown here. The complete results from both methods are given in Appendix 2.

5.2 All-cause mortality

Mortality from all causes combined is shown in Table 5.1.

The death rate from all causes combined was not significantly different from that in the Australian male population (SMR 1.02; 95%CI, 0.99 to 1.05).

There was no difference in mortality rates between military and civilian participants. Within the military participants, RAN personnel had a statistically significantly higher mortality than expected (SMR 1.14; 95%CI, 1.08 to 1.21). There was a small but not significant excess in Army personnel, the SMR being 1.07 (95%CI, 0.98 to 1.17). In

RAAF personnel, the SMR was significantly less than expected in the general population (0.89; 95%CI, 0.84 to 0.95).

Table 5.1 All causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the cohort and selected groups within the cohort

Group	Observed	Expected	SMR	95%CI
Whole cohort	4233	4150.4	1.02	0.99–1.05
Service category				
Military	2714	2662.3	1.02	0.98–1.06
Civilian	1519	1487.8	1.02	0.97–1.07
Service category, military				
RAN	1173	1026.4	1.14	1.08–1.21
Army	510	477.3	1.07	0.98–1.17
RAAF	1031	1158.6	0.89	0.84–0.95

5.3 Mortality by major cause

Mortality by major disease category is shown in Table 5.2, Table 5.3 and Table 5.4. It can be seen from Table 5.2 that there was an excess of cancer mortality in the test participants (SMR 1.18; 95%CI, 1.12 to 1.24).

The SMR was significantly lowered for ischaemic heart disease and cerebrovascular disease (mainly stroke). Mortality from respiratory diseases, nervous system diseases and digestive diseases was not significantly different from the population rates. There was no difference in mortality from alcoholic liver disease or the more specific definition — cirrhosis of the liver — introduced in 1979. The SMR for external causes (injury, poisoning) was significantly reduced, as was the SMR for suicide.

Table 5.2 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the cohort

Cause of death	Observed	Expected	SMR	95%CI
All cancers	1465	1238.7	1.18	1.12–1.24
Ischaemic heart disease	1107	1229.4	0.90	0.85–0.96
Cerebrovascular disease	243	282.4	0.86	0.76–0.98
Respiratory disease	325	310.6	1.05	0.94–1.17
Chronic obstructive pulmonary disease[a]	198	198.7	1.00	0.86–1.15
Nervous system disease[a]	59	57.8	1.02	0.78–1.32
Motor neurone disease[a]	16	12.9	1.24	0.71–2.02
Digestive diseases[a]	137	144.3	0.95	0.80–1.12
Alcoholic liver disease[a]	42	47.1	0.89	0.64–1.21
Cirrhosis[b]	30	30.1	1.00	0.67–1.42
External causes of injury and poisoning	281	320.5	0.88	0.78–0.99
Suicide	32	90.6	0.35	0.24–0.50

a Data available from 1968 onwards
b Data available from 1979 onwards

As shown in Table 5.3, the findings were very similar for the military personnel analysed separately. Cancer mortality was significantly elevated, and mortality from external

causes and from suicide in particular was significantly reduced. There was no significant finding in relation to deaths from respiratory disease.

In the civilian participants, there was a significant elevation of cancer mortality (SMR 1.21; 95%CI, 1.10 to 1.32), and it was slightly higher than that of the military participants, as shown in Table 5.4. There was also a significant lowering of ischaemic heart disease mortality (SMR 0.83; 95%CI, 0.75 to 0.92) and of suicide (SMR 0.22; 95%CI, 0.08 to 0.49).

Table 5.3 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the military participants

Cause of death	Observed	Expected	SMR	95%CI
All cancers	953	814.4	1.17	1.10–1.25
Ischaemic heart disease	723	766.0	0.94	0.88–1.02
Cerebrovascular disease	145	170.5	0.85	0.72–1.00
Respiratory disease	193	192.2	1.00	0.87–1.16
Chronic obstructive pulmonary disease[a]	125	122.1	1.02	0.85–1.22
Nervous system disease[a]	43	37.2	1.16	0.84–1.56
Motor neurone disease[a]	8	8.6	0.93	0.40–1.84
Digestive diseases[a]	83	96.1	0.86	0.69–1.07
Alcoholic liver disease[a]	28	33.1	0.85	0.56–1.22
Cirrhosis[b]	17	21.2	0.80	0.47–1.28
External causes of injury and poisoning	187	226.5	0.83	0.71–0.95
Suicide	26	63.9	0.41	0.08–0.49

a Data available from 1968 onwards
b Data available from 1979 onwards

Table 5.4 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the civilian participants

Cause of death	Observed	Expected	SMR	95%CI
All cancers	512	424.4	1.21	1.10–1.32
Ischaemic heart disease	384	463.4	0.83	0.75–0.92
Cerebrovascular disease	98	111.9	0.88	0.71–1.07
Respiratory disease	132	118.4	1.12	0.93–1.32
Chronic obstructive pulmonary disease[a]	73	76.6	0.95	0.75–1.20
Nervous system disease[a]	16	20.6	0.78	0.44–1.26
Motor neurone disease[a]	8	4.3	1.87	0.81–3.68
Digestive diseases[a]	54	48.2	1.12	0.84–1.46
Alcoholic liver disease[a]	14	14.0	1.00	0.55–1.68
Cirrhosis[b]	13	8.9	1.46	0.78–2.49
External causes of injury and poisoning	94	94.0	1.00	0.81–1.22
Suicide	6	26.8	0.22	0.08–0.49

a Data available from 1968 onwards
b Data available from 1979 onwards

5.4 Effect of excluding Korean and Vietnam War veterans

As shown in Chapter 4, 2485 of the military participants also served in the Korean and/or Vietnam Wars. Since this service in armed conflict could have influenced the mortality

analysis, the all-cause mortality was analysed excluding Korean War veterans and then excluding veterans of both wars (see Table 5.5). Of the military cohort, 1675 participants had served in Korea, and their exclusion led to a reduction in the all-cause mortality from 1.02 (95%CI, 0.98 to 1.06) to 0.99 (95%CI, 0.94 to 1.03). However, when Vietnam veterans were also excluded, the SMR was very close to that of the whole cohort. This indicates that the Korean War veterans had a higher SMR than the other military members of the cohort.

Table 5.5 Mortality from all causes combined: for military participants excluding veterans of Korean and Vietnam wars

All causes	Observed	Expected	SMR	95%CI
Military participants	2714	2662.3	1.02	0.98–1.06
Excluding Korean war veterans	1948	1975.9	0.99	0.94–1.03
Excluding Korean and Vietnam war veterans	1792	1785.2	1.00	0.96–1.05

5.5 Cancer mortality

Mortality from specific cancers is shown in Table 5.6. The point estimates exceeded unity for nearly all cancers. Mortality rates were significantly higher than in the general population for colorectal cancer (SMR 1.24; 95%CI, 1.08 to 1.42), lung cancer (SMR 1.20; 95%CI, 1.09 to 1.32), cancers of the lip, oral cavity and pharynx (SMR 1.50; 95%CI, 1.13 to 1.94) and prostate cancer (SMR 1.31; 95%CI, 1.10 to 1.55). The excess mortality from melanoma did not attain statistical significance (SMR 1.22; 95%CI, 0.89 to 1.62). Mortality from all leukaemias and from leukaemias excluding chronic lymphatic leukaemia (non-CLL leukaemia) were elevated, but the elevation was not statistically significant in either (SMR 1.18; 95%CI, 0.87 to 1.57; and SMR 1.25; 95%CI, 0.89 to 1.70, respectively).

Table 5.6 Mortality from cancer: observed and expected deaths, SMRs and 95% confidence intervals for the cohort

Cancer death	Observed	Expected	SMR	95%CI
Lip, oral cavity, pharynx	56	37.5	1.50	1.13–1.94
Oesophagus	44	38.2	1.15	0.84–1.55
Stomach	77	61.7	1.25	0.99–1.56
Colorectal	202	162.8	1.24	1.08–1.42
Liver[b]	19	20.5	0.93	0.56–1.45
Gallbladder[b]	8	7.1	1.13	0.49–2.23
Pancreas	57	55.6	1.03	0.78–1.33
Nasal, ear, sinuses[a]	4	2.3	1.74	0.47–4.46
Larynx	20	17.8	1.12	0.69–1.74
Lung	429	357.4	1.20	1.09–1.32
Pleura[b, c]	10	8.2	1.22	0.58–2.23
Connective tissue[a]	6	5.5	1.10	0.40–2.39
Melanoma	46	37.8	1.22	0.89–1.62
Non-melanocytic skin[a]	14	11.9	1.18	0.64–1.98
Prostate	131	103.7	1.26	1.06–1.50
Testis	3	3.2	0.93	0.19–2.71
Bladder	30	30.1	1.00	0.67–1.42
Kidney	30	30.4	0.99	0.67–1.41
Eye	2	1.2	1.68	0.20–6.06
Brain and nervous system	40	39.7	1.00	0.72–1.37
Thyroid	4	2.2	1.83	0.50–4.67
Non-Hodgkin's lymphoma	47	42.1	1.12	0.82–1.48
Multiple myeloma[a]	20	17.7	1.13	0.69–1.75
Unknown primary site	85	65.2	1.30	1.04–1.61
All leukaemias	47	39.9	1.18	0.87–1.57
Non-CLL leukaemia	40	32.0	1.25	0.89–1.70
'Radiogenic' cancers	752	526.1	1.43	1.33–1.54

a Data available from 1968 onwards
b Data available from 1979 onwards
c 'Pleural cancer' is an approximation of deaths from mesothelioma, derived from ICD-10 45 (mesothelioma) and ICD-9 163 (cancers of the pleura).

There was an excess of the total number of cancers considered to be 'radiogenic'. These are cancers shown in the Life Span Study of atomic bomb survivors and reported by the United Nations Scientific Committee on the Effects of Atomic Radiation to be causally associated with ionising radiation (UNSCEAR 2000). The cancers are: thyroid, stomach, colon, liver, lung, bladder, non-CLL leukaemia, and non-melanocytic skin cancer. The SMR for this group of cancers was 1.43 (95%CI, 1.33 to 1.54).

5.6 Cancer mortality by service

Table 5.7, Table 5.8 and Table 5.9 show the mortality rates in military and civilian participants for selected cancers.

In military participants, mortality from all cancers was significantly increased, as was mortality from cancer of the lip, oral cavity and pharynx; colorectal cancer; lung cancer and prostate cancer. There was a marginally significant increase in mortality from

melanoma. Table 5.7 also shows the SMRs in military participants after exclusion of Korean and Vietnam veterans. For all cancers combined and four specific cancers — lip, oral cavity and pharynx; colorectal; lung; and melanoma — mortality was lowered after exclusion of the Korean veterans, reflecting a higher mortality rate in those participants who had served in Korea. In each case, the SMR increased when Vietnam veterans were also excluded.

Table 5.7 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals for all military participants, and all military participants excluding Korean and Vietnam veterans

Cause of cancer death	Observed	Expected	SMR	95%CI
All cancers	953	814.4	1.17	1.10–1.25
Excl Korea	689	597.4	1.15	1.07–1.24
Excl Korea/Vietnam	632	536.1	1.18	1.09–1.27
Lip, oral, pharynx	38	25.5	1.49	1.05–2.04
Excl Korea	26	18.4	1.41	0.92–2.07
Excl Korea/Vietnam	24	16.4	1.47	0.94–2.18
Colorectal	133	107.9	1.23	1.03–1.46
Excl Korea	93	79.0	1.18	0.95–1.44
Excl Korea/Vietnam	85	70.7	1.20	0.96–1.49
Lung	269	234.0	1.15	1.02–1.30
Excl Korea	186	171.1	1.09	0.94–1.25
Excl Korea/Vietnam	177	153.8	1.15	0.99–1.33
Melanoma	36	26.0	1.39	0.97–1.92
Excl Korea	25	18.9	1.33	0.86–1.96
Excl Korea/Vietnam	23	16.7	1.38	0.87–2.06
Prostate	85	64.6	1.32	1.05–1.63
Excl Korea	65	48.5	1.34	1.04–1.71
Excl Korea/Vietnam	55	44.1	1.25	0.94–1.62
All leukaemias	30	26.3	1.14	0.77–1.63
Excl Korea	25	19.4	1.29	0.84–1.91
Excl Korea/Vietnam	20	17.4	1.15	0.70–1.78
Non-CLL leukaemia	26	21.2	1.23	0.80–1.80
Excl Korea	21	15.6	1.35	0.83–2.06
Excl Korea/Vietnam	18	14.0	1.29	0.76–2.04

In RAN personnel, there were significant mortality excesses for all cancers combined; cancers of the lip, oral cavity and pharynx; and lung and colorectal cancers. In army personnel, mortality was elevated from cancers of the lip, oral cavity and pharynx. There was a significant excess of melanoma mortality in RAAF personnel.

Table 5.8 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals, by branch of armed service

Cause of cancer death	Observed	Expected	SMR	95%CI
RAN				
All cancers	418	325.3	1.29	1.16–1.41
Lip, oral, pharynx	13	10.9	1.20	0.64–2.05
Colorectal	61	43.7	1.40	1.07–1.79
Lung	138	93.5	1.48	1.24–1.74
Melanoma	12	11.0	1.09	0.56–1.90
Non-melanocytic skin[a]	3	3.0	0.99	0.21–2.91
Prostate	32	22.8	1.40	0.96–1.98
All leukaemias	10	10.5	0.95	0.46–1.75
Non-CLL leukaemia	10	8.5	1.18	0.56–2.16
Army				
All cancers	163	141.6	1.15	0.98–1.34
Lip, oral, pharynx	10	4.3	2.35	1.13–4.33
Colorectal	18	18.6	0.97	0.57–1.53
Lung	41	40.7	1.00	0.72–1.37
Melanoma	2	4.3	0.46	0.06–1.67
Non-melanocytic skin[a]	2	1.4	1.46	0.18–5.27
Prostate	16	11.9	1.34	0.77–2.18
All leukaemias	4	4.6	0.88	0.24–2.24
Non-CLL leukaemia	3	3.7	0.82	0.17–2.39
RAAF				
All cancers	372	347.5	1.07	0.96–1.18
Lip, oral, pharynx	15	10.4	1.44	0.81–2.38
Colorectal	54	45.6	1.18	0.89–1.54
Lung	90	99.7	0.90	0.73–1.11
Melanoma	22	10.6	2.07	1.30–3.13
Non-melanocytic skin[a]	4	3.4	1.18	0.32–3.03
Prostate	37	29.8	1.24	0.87–1.71
All leukaemias	16	11.2	1.42	0.81–2.31
Non-CLL leukaemia	13	9.0	1.45	0.77–2.47

a Data available from 1968 onwards

In civilian participants, there was a significant excess of mortality from all cancers combined and lung cancer.

Table 5.9 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals for civilian participants

Cause of cancer death	Observed	Expected	SMR	95%CI
All cancers	512	424.4	1.21	1.10–1.32
Lip, oral, pharynx	18	12.0	1.51	0.89–2.38
Colorectal	69	54.9	1.26	0.98–1.59
Lung	160	123.4	1.30	1.10–1.51
Melanoma	10	11.8	0.85	0.41–1.55
Non-melanocytic skin[a]	5	4.1	1.22	0.40–2.84
Prostate	46	39.1	1.18	0.86–1.57
All leukaemias	17	13.6	1.25	0.73–2.00
Non-CLL leukaemia	14	10.8	1.30	0.71–2.18

a Data available from 1968 onwards

5.7 All-cause mortality by rank

Table 5.10 shows all-cause mortality in the military participants analysed by rank. Mortality in officers was compared with that of other ranks, the latter being the baseline. The mortality rate of officers was significantly less than that of other ranks; the Relative Mortality Ratio (RMR) for officers compared with other ranks was 0.73 (95%CI, 0.66 to 0.81). Since officers would usually be in higher socioeconomic strata than other ranks, this result is to be expected. For non-CLL leukaemia, the RMR was much higher for non-officers; however, this was based on a small number of cases and the confidence intervals were therefore large.

Table 5.10 Mortality from all causes combined and from non-CLL leukaemia: comparisons within military participants based on rank

	Deaths	Person-years	Age-and-year adjusted RMR	95%CI
All causes				
Other ranks	2217	222 643	1.0	
Officers	497	41 682	0.73	0.66–0.81
Non-CLL leukaemia				
Other ranks	23	222 643	1.0	
Officers	3	41 682	0.43	0.12–1.48

5.8 All-cause mortality by radiation exposure category

Table 5.11 shows relative mortality from all causes combined according to category of radiation exposure. The baseline category for comparison was the lowest exposure category, which has an RMR of 1.0, by definition. Excluding exposure category F, there was no trend to increasing mortality with increasing exposure ($P = 0.41$).

In a further attempt to identify a dose–response effect, radiation exposures (excluding category F) were combined into 3 categories and compared. No trend was identified ($P = 0.43$). Furthermore, dichotomising exposure did not show an increase in all-cause mortality for those who received an estimated dose of radiation greater than 1 mSv.

Table 5.11 Mortality from all causes combined: comparisons within the cohort based on exposure to ionising radiation

Exposure	Deaths	Person-years	Age-and-year adjusted RMR	95%CI
Category A (<1 mSv)	3331	282 347	1.0	
Category B (1 to <5 mSv)	231	26 464	0.94	0.82–1.07
Category C (5 to <20 mSv)	224	19 231	0.91	0.80–1.04
Category D (20 to 50 mSv)	167	13 240	1.00	0.86–1.17
Category E (>50 mSv)	9	701	1.14	0.59–2.20
Category F (unknown)	271	27 478	0.79	0.70–0.89
Category A	3331	282 347	1.0	
Category B–C	455	45 695	0.92	0.84–1.02
Category D–E	176	13 941	1.01	0.87–1.18
Category A	3331	282 347	1.0	
Categories B to E combined (>1 mSv)	631	59 636	0.95	0.87–1.03

5.9 Cancer mortality by radiation exposure category

Table 5.12 shows a similar analysis for all cancers. No trend was apparent using all exposure categories except category F ($P = 0.24$). Comparing three categories of radiation exposure, again no trend was identified ($P = 0.23$). As for deaths from all causes, no increase in cancer mortality was found in those with an estimated radiation dose of greater than 1 mSv.

Table 5.12 Mortality from cancer: comparisons within the cohort based on exposure

Exposure	Deaths	Person-years	Age-and-year adjusted RMR	95%CI
Category A (<1 mSv)	1152	282 347	1.0	
Category B (1 to <5 mSv)	71	26 464	0.79	0.62–1.00
Category C (5 to <20 mSv)	68	19 231	0.81	0.63–1.04
Category D (20 to 50 mSv)	60	13 240	1.06	0.82–1.38
Category E (>50 mSv)	2	701	0.70	0.18–2.82
Category F (unknown)	112	27 478	0.95	0.78–1.15
Category A	1152	282 347	1.0	
Category B–C	139	45 695	0.80	0.67–0.95
Category D–E	62	13 941	1.05	0.81–1.35
Category A	1178	282 347	1.0	
Categories B to E combined (>1 mSv)	201	59 636	0.86	0.74–1.00

In Table 5.13, due to small numbers of deaths from non-CLL leukaemia, exposure was categorised into three categories (excluding category F). No trend in mortality with increasing category of radiation exposure was found ($P = 0.22$). Again, no increase in

mortality was identified for participants who received an estimated dose of radiation of more than 1 mSv.

Table 5.13 Mortality from non-CLL leukaemia: comparisons within the cohort based on exposure

Exposure	Deaths	Person-years	Age-and-year adjusted RMR	95%CI
Category A (<1 mSv)	34	282 347	1.0	
Category B–C (1 to <20 mSv)	2	45 695	0.38	0.09–1.60
Category D–E (>20 mSv)	1	13 941	0.58	0.08–4.21
Category A	34	282 347	1.0	
Categories B to E combined (>1 mSv)	3	59 636	0.43	0.13–1.41

Table 5.14 shows that, excluding category F, there was no association between increasing radiation exposure and either lung cancer mortality ($P = 0.56$) or mortality from 'radiogenic' cancers ($P = 0.54$) . However, there was an inverse association between radiation exposure and colorectal cancer, with the relationship statistically significant for trend ($P < 0.05$). Of the 762 'radiogenic' cancer deaths in this group, 642 (85%) were lung and colorectal cancer deaths. It is likely that the excess of 'radiogenic cancers' is due to the factors responsible for these individual cancers rather than to radiation.

Table 5.14 Mortality from selected cancers: comparisons within the cohort based on radiation exposure

Exposure	Deaths	Person-years	Age-and-year adjusted RMR	95%CI
Lung cancer				
Category A (<1 mSv)	343	282 347	1.0	
Category B–C (1 to <20 mSv)	47	45 695	0.90	0.67–1.23
Category D–E (>20 mSv)	17	13 941	0.96	0.59–1.56
Colorectal cancer				
Category A (<1 mSv)	170	282 347	1.0	
Category B–C (1 to <20 mSv)	16	45 695	0.61	0.36–1.02
Category D–E (>20 mSv)	2	13 941	0.23	0.06–0.94
'Radiogenic' cancers				
Category A (<1 mSv)	595	282 347	1.0	
Category B–C (1 to <20 mSv)	77	45 695	0.84	0.66–1.06
Category D–E (>20 mSv)	32	13 941	1.07	0.75–1.52

5.10 Cancer mortality by time since entry into the cohort

Analyses were also performed to identify any variation in mortality with time since entry into the cohort, and the results are shown in Table 5.15, Table 5.16 and Table 5.17.

For all causes combined, the RMR was significantly lower in the period following the first 15 years after entry in to the cohort.

Table 5.15 Mortality from all causes combined: comparisons within the cohort based on time since entry to the cohort

Time since entry to cohort	Deaths	Person-years	Age-adjusted RMR	95%CI
2 to 15 years	594	146 168	1.0	
More than 15 years	3639	223 293	0.80	0.72–0.89

For all cancers the reverse was found, with a marginally significant increase in RMR after 15 years.

Table 5.16 Mortality from cancer: comparisons within the cohort based on time since entry to the cohort

Time since entry to cohort	Deaths	Person-years	Age-adjusted RMR	95%CI
2 to 15 years	114	146 168	1.0	
More than 15 years	1351	223 293	1.25	1.00–1.56

In the case of non-CLL leukaemia, nearly all deaths (37 out of 40) occurred more than 15 years after cohort entry. The RMR was slightly raised relative to the deaths before 15 years. However, the confidence intervals were very wide due to the small numbers of deaths in the earlier period.

Table 5.17 Mortality from non-CLL leukaemia: comparisons within the cohort based on time since entry to the cohort

Time since entry to cohort	Deaths	Person-years	Age-adjusted RMR	95%CI
2 to 15 years	3	146 168	1.0	
More than 15 years	37	223 293	1.07	0.33–3.48

5.11 Smoking prevalence and selected cancer mortality

To estimate the likelihood that the excess SMR from lung cancer was due to a higher prevalence of smoking than in the general male population, the expected number of cancers for given levels of smoking prevalence were computed. As shown in Table 5.18, a prevalence of smoking (ever) of between 50% and 60% in the cohort, compared with a population rate of between 40% and 50%, would be sufficient to account for the excess SMR. This increase in smoking prevalence in the cohort is possible. However, for lip, oral cavity and pharynx cancer, a smoking prevalence of 90% in the cohort, compared with a population rate of around 50%, would be required to account for the excess SMR, and this is not as likely. These excess cancers were probably not due to smoking alone.

Table 5.18 Expected number of deaths from selected cancers according to hypothetical smoking prevalence

Cancer	Obs	Expected (using Method 1)	SMR	95%CI	Hypothetical smoking prevalence (%)							
					30	40	50	60	70	80	90	100
					Expected deaths							
Lung	429	357.4	1.21	1.10–1.33	237	307	376	445	514	583	653	722
Lip, oral, pharynx	56	37.5	1.52	1.15–1.97	28	33	37	42	47	52	56	61

5.12 Deaths in the first two years of follow-up

Deaths that occurred during the first two years of entry to the cohort were not included in the main analyses. As shown in Table 5.19, a total of 46 deaths occurred in this time period.

Table 5.19 Deaths that occurred in the first two years after entry to the cohort

Cause and ICD-10 code	Deaths
External causes of injury and poisoning (V01-Y98)	32
Aircraft accidents	6
Suicide	2
Gunshot accidents	3
Vehicle accidents	7
Other accidents	14
Cancer (C00-C97)	7
Stomach	3
Mesothelioma	1
Lung	1
Peritoneum	1
Biliary duct	1
Ischaemic heart disease (I20-I25)	3
Cerebrovascular disease (I60-I69)	2
Digestive system disease (K00-K93)	1
Unknown cause	1

As explained in Chapter 3, these deaths were excluded from the analyses to minimise a healthy worker effect due to the selection effect — that is, people already diagnosed with chronic diseases such as leukaemia are unlikely to be deployed at a test site. This means that in the early years of follow-up there will be a lower death rate from these diseases in the cohort than in the general population. However, the selection effect is not equal for all causes of death. It is clear that a disproportionate number of deaths from external causes occurred in the first two years, and so an analysis was conducted that included the deaths from external causes and the corresponding person-time in the first two years of entry to the cohort. The SMR for the cohort for external causes rose to 0.91 (95%CI, 0.81 to 1.02). The corresponding SMRs for suicide were still very low at 0.36 (95%CI, 0.25 to 0.50).

5.13 References

1. UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) (2000). *Report of UNSCEAR to the General Assembly. Vol II: Effects. Annex 1: Epidemiological Evaluation of Radiation-induced Cancer*, UNSCEAR: Vienna.

6 Mortality study discussion

6.1 Treatment of subjects lost to follow-up

Of the two methods used for treating the follow-up time of subjects lost to contact, it is likely that Method 2 leads to an underestimate of mortality, from overestimating the follow-up time and from underestimating the number of deaths. For the military personnel, who had a much higher follow-up rate than civilians, the estimate from Method 2 was much closer to that of Method 1 (1.02 with Method 1, 0.98 with Method 2) and close to the estimate for civilians using Method 1. This suggests that, as the follow-up rate increases, the standardised mortality ratio (SMR) derived using Method 2 will converge towards that derived from Method 1. Since Method 2 is considered likely to cause substantial underestimates of mortality, only results from use of Method 1 have been presented in the previous chapter.

However, it is possible that even the SMR using Method 1 is an underestimate. After the search of the National Death Index (NDI) had been completed, a further 42 deaths were found in a search of the National Cancer Statistics Clearing House (NCSCH). Nearly all of these deaths were found when the NDI was re-examined, indicating shortcomings in matching.

Because deaths from cancer after 1982 were found in the NCSCH, and because most cancers occurred after this time, it is likely that the undercounting of cancer deaths would be small. However, it is highly probable that other deaths were missed from diseases other than cancer, for which disease registries do not exist. Most of the deaths missed in this way were from subjects otherwise lost to contact, so that there would be a similar underestimate of expected deaths as well as observed deaths. The net effect could be a small underestimate of all SMRs, although an overestimate is also possible. This matter is discussed further in Section 6.7.2.

6.2 Mortality in the cohort

All-cause mortality did not differ significantly between the test participants and the general population. However, there was a significant increase in the cohort in deaths from all cancers. All other major causes of death were significantly lower than or the same as in the general population.

6.3 Leukaemia, excluding chronic lymphatic leukaemia

Leukaemia excluding chronic lymphatic leukaemia (non-CLL leukaemia) was an outcome of primary interest because of the excess deaths from this group of diseases in the Japanese atomic survivors cohort (Pierce et al 1996), and many other studies showing an association with ionising radiation. In this study, the SMR of 1.25 was not statistically significant.

Of the individual service categories, the highest SMR was in RAAF personnel. However, the numbers of cases in each service category are small and the confidence interval very

wide, so it is not possible to draw a conclusion about any service category having a different risk from any other.

It is important to consider whether the SMR could have underestimated the true leukaemia risk because of a healthy worker effect. Unlike the studies of UK test participants and participants in nuclear tests in the United States, there is no occupational cohort for comparison in this study. As discussed in Appendix 4, leukaemia does not exhibit the social class gradient found in diseases such as respiratory disease and heart disease, so that a healthy worker effect is unlikely to occur with leukaemia.

In fact, the study of UK test participants found little evidence of a healthy worker effect for non-CLL leukaemia. Whereas the all-cause SMR was 0.89 (95%CI, 0.86 to 0.91), for non-CLL leukaemia the SMR was 1.06 (95%CI, 0.77 to 1.46).

On the other hand, in the US veterans study, the SMRs for non-CLL leukaemia were only 0.75 for the participants and 0.65 for the controls. Moreover, the difference between this finding and that of the present study cannot be explained by ageing of the cohort, since the US testing program began in 1945 — even sooner than the tests in Australia — and ended in 1963.

The Australian cohort is somewhat different from the US and UK cohorts in that there was a relatively high proportion of civilians — 35%, compared with none in the US study and 4% in the UK study. This does not explain the higher SMR in the Australian cohort, because the SMRs for non-CLL leukaemia were similar for military and civilian personnel (SMRs 1.23 and 1.30, respectively).

The comparison of relative mortality between categories of estimated radiation exposure showed no association between risk of death from non-CLL leukaemia and radiation exposure. Such an outcome is not surprising, given the estimated low radiation exposure of most cohort members, and the relatively small proportion of subjects with any significant exposure. An estimate of the likely contribution of radiation to the burden of leukaemia was made by calculating the average dose to participants, and using standard risk factors to calculate the expected cancer mortality, assuming that the actual exposure in each category was at the mid-point of the range. For the highest exposure category, category E (>50 mSv), an exposure of 100 mSv was assumed. The resultant mean exposure is 2.79 mSv. These exposures have been applied to three estimates of the excess relative risk (ERR) of non-CLL leukaemia mortality per 1 Sv to compute the expected number of leukaemias in this cohort caused by radiation exposure at the test sites, applying linear estimates. Three estimates of ERR per 1 Sv were used, as shown in Table 6.1.

The first estimate is based on the risk factor from the recently published report of a retrospective multicentre study by Cardis et al, sponsored by the International Agency for Research on Cancer (IARC) (Cardis et al 2005). On this basis, the ERR is 0.5%, which would account for less than one single case of the 40 leukaemias in this cohort.

The second estimate is based on the Life Span study of survivors of the atomic bombing of Hiroshima and Nagasaki (Pierce et al 1996). On this basis, the risk factor is 0.9%, which would again account for less than one single case of the leukaemias.

The third estimate is taken from the 2000 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), which summarised the known epidemiological studies of the effects of ionising radiation (UNSCEAR 2000).

Several estimates of ERR/Sv have been made. To obtain a worst-case estimate, the highest estimate (for external radiation) was used, 6.0/Sv, taken from the effects of low-linear energy transfer (LET) radiation on ankylosing spondylitis patients (Weiss et al 1995). On this basis, the risk factor is 0.0167 (1.7%), which would account for less than one single death from leukaemias (i.e. 1.7% of 40 = 0.67 deaths).

Table 6.1 Expected number of non-CLL leukaemia deaths from radiation exposure at test sites

Reference	ERR per Sv	ERR	Number of leukaemia deaths
Cardis et al 2005	1.93	0.0054	0.22
Pierce et al 1996[a] (atomic survivors)	3.15	0.0088	0.35
UNSCEAR 2000 (highest estimate)	6.0	0.0167	0.67

The ERR in column 2 is based on an assumed mean exposure estimate of 2.79 mSv.
a The estimate used here is the IARC estimate quoted in Richardson and Ashmore (2005), but based on the study cited in Weiss et al (1995).

The lack of association with ionising radiation is similar to the findings of the study of UK participants, who were nearly all service personnel. That study showed an SMR for non-CLL leukaemia close to that expected from population rates, but in comparison with a cohort of nonparticipant service personnel, the relative risk was significantly elevated. No increase in risk could be detected for those participants considered a priori to have been potentially exposed to ionising radiation, but the risk estimates were based on very small numbers. It is possible that the excess risk relative to the control group was merely the result of random variation leading to a low SMR in the control group, although the investigators concluded that an absolute increase in the risk of non-CLL leukaemia could not be ruled out.

The Five Series Study of US nuclear test participants is similarly inconclusive. Participants had a nonsignificant increase in deaths from non-CLL leukaemia compared with a referent cohort (relative risk [RR] 1.14; 95%CI, 0.90 to 1.44). No radiation dosimetry was used in the analysis.

In the study of New Zealand naval personnel involved in the British nuclear testing program in the Pacific during the 1960s, the RR for leukaemia was 5.6 (95%CI, 1.0 to 41.7) based on 4 cases in participants and 2 in controls. The authors concluded that there is evidence for a link between haematological cancers and test participation, but no association with other cancers, and noted that the study was based on a small number of participants (528 men). No dosimetry was performed (Pearce et al 1997).

There were relatively few non-CLL leukaemia deaths in this study (3 out of 40) occurring in the first 15 years after entry into the cohort, but no inference can be drawn from this. There is little empirical information on latency periods for leukaemia following radiation exposure. A recent analysis has suggested an effect of radiation on rates beginning promptly after exposure and diminishing after 30 years. However, the authors point out that their time-window specific estimates of association were highly imprecise, and neither model used produced a fit that was better than the null model (Richardson and Ashmore 2005).

In summary:

- there is a nonsignificant increase (25%) in mortality from non-CLL leukaemia

- the lack of significant association between non-CLL leukaemia and test participation is similar to the findings of the study of test participants from the UK, although the SMR in the latter (1.06) was lower than in this study
- there was no association between mortality from non-CLL leukaemia and radiation exposure
- less than one leukaemia death would be expected given the estimated radiation exposure of the cohort, so that absence of a significant increase in non-CLL leukaemia mortality is consistent with expectations.

6.4 Mortality from other cancers

6.4.1 Lung cancer and mesothelioma

The most important factor to consider in the cause of excess lung cancer is smoking. Apart from lung cancer, this cohort also had a statistically significant excess of deaths from cancers of the lip, mouth and pharynx, cancers strongly associated with smoking. However, the cohort did not have the excess deaths found in the cohort of Korean War veterans from oesophageal or laryngeal cancers, which are also strongly smoking-related. (The only smoking-associated cancer death rate not in excess in the Korean cohort was for bladder cancer.) The SMR for chronic obstructive pulmonary disease (COPD) was 1.00 (95%CI, 0.86 to 1.15), which is less than would be expected in a population with a high smoking prevalence. However, a small true excess of deaths from this smoking-related condition is possible, given the known incomplete identification of deaths from diseases other than cancer. The SMRs both for cancers of the lip, oral cavity and pharynx, and for lung cancer, although significantly elevated, were lower than in the Korean cohort. It is therefore likely that the cumulative tobacco use of the nuclear test participants as a group has been less than that of the Korean veterans cohort, but more than in the general male population.

Smoking is thus a possible contributory cause of the raised SMR from lung cancer. Smoking is such a powerful cause of lung cancer that a relatively small excess in smoking prevalence, compared with the general male population, could increase the SMR appreciably. As shown in Table 5.18 in the previous chapter, a prevalence of having ever smoked of 50%–60% in test participants would be sufficient to account for the excess, compared with a 40%–50% prevalence in the general population (estimated from the prevalence required to produce the expected number of lung cancers).

Relative mortality analysis showed that there was no trend of increasing lung cancer mortality with increased radiation exposure. This is in conformity with the low level of radiation exposure incurred on average by cohort members, which would not be sufficient to account for the observed excess. To take a worst-case estimate, the highest ERR/Sv for lung cancer mortality for males from exposure to low-LET radiation in the UNSCEAR 2000 Report is 0.45 (UNSCEAR 2000). This would account for only 0.13% of lung cancer deaths; in other words, it is likely that, at most, one of the 432 lung cancer deaths is attributable to radiation exposure. (The number would be higher if the radiation dose was mainly by inhalation, but the findings of the exposure panel indicate that the inhaled dose is a small fraction of the total dose for most participants.) Further evidence against radiation as a cause of the excess is seen from exclusion of Korean War veterans from the analysis, which causes a lowering of the SMR for lung cancer; that is, the SMR is higher

in participants who also served in Korea, where radiation exposure was not a likely risk factor.

Asbestos is a well-recognised cause of lung cancer. Asbestos was used extensively in naval vessels at the time, and RAN personnel may thus have been exposed during their service (not only during the nuclear tests). Similarly, asbestos was widely used in the construction industry during this period. If asbestos exposure were to account for the excess lung cancer mortality in this cohort, some cases of mesothelioma would be expected also. There were 10 mesothelioma deaths, compared with an expected 8.2 deaths, a nonsignificant excess SMR of 1.22.[2] Six of the 10 deaths were in RAN personnel and the other 4 in civilians. It is therefore of interest that the highest rates of lung cancer were also found in the RAN and civilian cohorts, which are the groups most likely to have incurred asbestos exposure. Asbestos exposure could well have occurred in naval personnel, and some of the civilians were in the construction industry where asbestos was in widespread use in Australia, with fewer precautions taken to prevent inhalation than is the case today.

In summary, the most likely explanations for the excess of lung cancers are a small excess of smoking prevalence compared with the general male population, and asbestos exposure (probably mostly other than at the test sites), probably in combination in many cases.

Lung cancer shows the most striking difference between this study and the study of UK test participants: the SMR is significantly elevated in the Australian participants and significantly reduced in the UK participants. This difference may be due to differences in the population rates. Lung cancer rates vary widely between countries. Table 6.2 shows age-standardised lung cancer rates for the UK and Australia from the IARC CI5 Publication on Cancer Incidence in Five Continents (IARC 2005). They show UK population lung cancer rates greater than in Australia. Therefore, the absolute lung cancer death rate in Australian test participants is not necessarily different from that of their UK counterparts.

Table 6.2 Age-standardised lung cancer rates (cases per 100 000 person-years, for successive editions of the IARC CI5 project: UK and Australia)[a]

Period	UK	Australia
mid-1970s	77.7–98.0	51.4
1979–82	68.8–92.2	51.9–55.6
1983–87	59.6–87.6	47.8–56.1
1988–92	46.9–79.0	46.6–49.8
1993–97	44.3–71.8	42.0–47.8

a Range lowest to highest rate based on figures from different jurisdictions

There may be a similar situation in the case of the all-cancer SMR, which was significantly elevated in this study but not in the UK participants. Background all-cancer incidence was higher in the UK for much of the study period, although the rates are now similar.

[2] In Table 5.6, mesotheliomas are classified under pleural cancers. Although deaths coded as pleural cancers are nearly always mesotheliomas, it is not certain that all 10 pleural cancers in Table 5.6 were mesotheliomas.

6.4.2 Cancer of the lip, oral cavity and pharynx

These cancers are associated with tobacco and alcohol use. As discussed in the section on lung cancer, there is likely to be some excess prevalence of smoking in the cohort compared with the general male population. As seen in Table 5.18, a smoking prevalence of 90% would be required to explain the excess on the basis of smoking alone. These upper digestive tract cancers have also been shown in other studies to be alcohol-related. However, there is no excess mortality from alcoholic liver disease in this cohort, which would be expected if the level of alcohol use was greater than in the general population.

6.4.3 Melanoma

There was a nonsignificant excess of melanoma mortality (SMR 1.22; 95%CI, 0.89 to 1.62). However, in RAAF personnel, there was a two-fold excess, which was statistically significant (SMR 2.07; 95%CI, 1.30 to 3.13).

Several studies have shown melanoma excess in airline pilots, although it is not clear that these excesses are work-related, since melanoma has a strong association with social class, increasing with higher social class categories (Band et al 1990, 1996; Irvine and Davies 1999; Reynolds et al 2002). One explanation considered for the excess of melanoma in airline pilots is cosmic radiation. In a study of 458 commercial pilots by the Icelandic Cancer Registry, a significant 10-fold incidence of melanoma was observed, with the melanomas occurring in pilots estimated to have had higher exposure to cosmic radiation. The authors discuss the possibility of an effect of social class, possibly from sunbathing associated with high socioeconomic status (Rafnsson et al 2000).

These findings would only be of significance for a minority of the melanoma deaths in this cohort. Of the 22 RAAF personnel with melanoma, only 4 were known to be aircrew. (The occupation was not given for 5 of the decedents). The 1983 questionnaire study by the Commonwealth Department of Health on the health of atomic test personnel noted an increased prevalence of melanoma in respondents who reported having worked on decontamination of aircraft, suggesting that the increased melanoma mortality in RAAF personnel is not confined to aircrew (Donovan et al 1983).

It should also be noted that observed melanoma mortality data may not be representative of all cases of melanoma, as this cancer has a high cure rate.

The nonsignificant SMR of 1.22 contrasts with the finding of a significant excess mortality of 1.65 in the study of UK participants. However, the background melanoma incidence in the two countries is so different (seven times greater in Australia) that comparison between the observed mortality in the two studies is unlikely to be meaningful.

6.4.4 Colorectal cancer

Colorectal cancer mortality occurred in significant excess. The highest SMR, using Method 1, was in RAN personnel (SMR 1.40; 95%CI, 1.07 to 1.79).

Although colonic cancer is cited as radiogenic by UNSCEAR, relative mortality analysis showed that, in this cohort, there was no trend of increasing colorectal cancer mortality with increased radiation exposure. Other than some dietary influences, there are no well-identified environmental risk factors for colorectal cancer. Although some studies have

suggested an association with alcohol consumption, the IARC states in its most recent review (1998) that the evidence of a causal link between alcohol and colonic or rectal cancer is not conclusive (IARC 1998). There is no evidence of increased alcohol use in the cohort, as there is no excess mortality from alcoholic liver disease or from cancer of the oesophagus.

Some contribution from asbestos exposure should not be excluded. Some epidemiological evidence suggests that asbestos exposure can cause colonic cancer. Although a review of 30 cohort studies up to 1993 found that there was no consistent elevation of relative risk, a more recent study has suggested up to a 4-fold increase in risk in highly exposed workers (Weiss 1995, Berry et al 2000). Colorectal cancer mortality was significantly elevated in RAN personnel, who also had the highest mortality from lung cancer and most of the cases of mesothelioma, diseases known to be associated with asbestos exposure.

No excess mortality from colorectal cancer was found in the study of UK test participants.

6.5 Other causes of death

For deaths from external causes (suicide, poisonings, injury), there was a lowering of SMR of borderline significance, possibly due to the exclusion of deaths and follow-up time for the first two years of each subject. This was done to overcome the selection effect component of the healthy worker effect. With all deaths and all person-years included in the analysis, the SMR was 0.91 (95%CI, 0.81 to 1.02).

This finding was unexpected because excesses of deaths from external causes were noted in the UK participants study and the Korean War Veterans study.

Again, in contrast to the Korean War veterans study, there was a large and statistically significant lowering of the SMR from suicide (32 cases vs 90.6 expected; SMR 0.35; 95%CI, 0.24 to 0.50). A possible explanation is that this cohort is not based on subjects with combat experience (although a significant proportion did serve in Korea and/or Vietnam, and possibly World War II). Another factor may be a selection effect. It is likely that subjects with significant psychiatric disorders — a major risk factor for suicide — would not have been deployed to nuclear test sites.

The SMRs for ischaemic heart disease and cerebrovascular disease were statistically significantly lowered. The SMRs for digestive diseases, respiratory diseases and nervous system diseases were not significantly different from expected.

The SMR for chronic obstructive pulmonary disease (COPD) was 1.00 (95%CI, 0.86 to 1.15). This is the only major category of noncancer mortality that may be affected by the known underidentification of deaths in the search of the NDI. Whereas the SMRs for other major noncancer causes of death were well below unity, the known underenumeration of noncancer deaths suggests that a small excess in COPD mortality is possible. An excess from this condition would be expected with the excess SMRs from other smoking-related conditions such as lung cancer and cancer of the lip, oral cavity and pharynx.

6.6 Comparison with other studies

Whereas the mortality from all causes combined in this study was similar to that of the general population, the study of the UK nuclear test participants found all-cause mortality to be significantly lowered (0.89; 95%CI, 0.86 to 0.91) (Muirhead et al 2003b). In the cohort of participants in the study of US nuclear testing participants, the all-cause SMR was 0.71 (Thaul et al 2000).

In this study, there was a significant lowering of mortality from ischaemic heart disease and cerebrovascular disease. The corresponding SMRs in the study of UK nuclear test veterans are not stated in the most recent report, but the SMR of 0.80 for all diseases other than cancer is comparable with the findings of the present study (Muirhead et al 2003b). On the other hand, in the study of US test participants, the SMR for all diseases of the circulatory system was 0.62 (Thaul et al 2000).

There was also a significant lowering compared with population rates in deaths from external causes (i.e. accidents, poisonings, suicide), in contrast with the study of UK participants, where there was a significant excess.

Why the results should be different from the UK and US studies is not clear. In this study, the first two years of follow-up were excluded from the analysis, but it is unlikely that this would account for the difference from the US and UK studies.

Table 6.3 shows the cancer mortality in Australian test participants, UK test participants, and Australian veterans of the Korean War. The Australian and Korean figures are derived from Method 1 and are thus comparable. The UK figures show both the SMRs (mortality compared with the population) and relative risk (mortality compared with comparison cohort).

The most salient differences between the findings of the present study and that of the mortality study of UK participants are:

- for all-cancer mortality, and lung cancer and colorectal cancer mortality — where there are significant elevations in the Australian study but not in the UK study
- for melanoma — where there was an excess mortality in the UK study but not in the present study.

On the other hand, cancer mortality in the present study follows a similar pattern to the cohort of Korean War veterans, with excess mortality from cancers of the lip, oral cavity and pharynx; colorectal and lung cancers; prostate cancer; and all cancers combined.

Table 6.3 Cancer SMRs from the Australian and UK studies of nuclear test participants and the study of Australian veterans of the Korean War

	Australian study		UK study (Muirhead et al 2003b)		Korean veterans (Harrex et al 2003)	
Cancer death	SMR	95%CI	SMR	RR to comparison group	SMR	95%CI
All cancers	1.18	1.12–1.24	0.93	1.01	1.31	1.26–1.36
Lip, oral, pharynx	1.50	1.13–1.94	1.18	0.88	1.96	1.60–2.32
Oesophagus	1.15	0.84–1.55	1.01	0.93	1.59	1.27–1.91
Stomach	0.97	0.74–1.25	0.78	1.08	1.08	0.87–1.30
Colorectal	1.24	1.08–1.42	0.93	1.03	1.18	1.05–1.32
Liver	0.93	0.56–1.45	1.13	1.54	1.30	0.98–1.62
Gallbladder	1.13	0.49–2.23	0.29	0.38		
Pancreas	1.03	0.78–1.33	1.02	1.02	1.13	0.90–1.35
Larynx	1.12	0.69–1.74	1.16	0.87	1.95	1.43–2.46
Lung	1.20	1.09–1.32	0.85	0.97	1.47	1.37–1.58
Pleura	1.22	0.58–2.23	Not available		0.51	0.01–1.00
Connective tissue	1.10	0.40–2.39	0.67	1.36	0.62	0.08–1.15
Melanoma	1.22	0.89–1.62	1.65	1.14	1.28	0.99–1.56
Non-melanocytic skin cancer	1.18	0.64–1.98	0.51	n/a	Not available	
Prostate	1.26	1.06–1.50	1.15	1.20	1.29	1.10–1.48
Testis	0.93	0.19–2.71	1.14	1.15	1.18	0.34–2.03
Bladder	1.00	0.67–1.42	0.95	1.69	0.97	0.67–1.27
Kidney	0.99	0.67–1.41	1.06	1.06	0.74	0.96–1.61
Brain and nervous system	1.00	0.72–1.37	1.02	1.04	Not available	
Thyroid	1.83	0.50–4.67	0.38	1.00	0.90	0–1.89
Non-Hodgkin's lymphoma	1.12	0.82–1.48	0.96	0.84	0.86	0.63–1.09
Multiple myeloma	1.13	0.69–1.75	0.96	1.43	Not available	
Unknown primary site	1.30	1.04–1.61	0.92	0.85	1.51	1.27–1.75
All leukaemias	1.18	0.87–1.57	0.98	1.45	0.99	0.74–1.24
Non-CLL leukaemia	1.25	0.89–1.70	1.06	1.83	Not available	

6.7 Methodological issues

6.7.1 Defining the study population

There was difficulty in the design stage of this study in determining who should and who should not be included in the study population. The difficulty lay mainly in defining what is meant by 'participation' in the testing program.

For the purposes of the nominal roll, from which the study population is derived, the definition of an Australian 'atomic participant' is:

> Someone who was present, either working or as a visitor, in at least one of the testing areas whilst a test or tests were conducted in that area or were there within a 2 year period after the explosion (DVA 2001).

This definition had to be expanded to allow admission of RAAF personnel who did not visit test sites but who serviced aircraft that had become contaminated in the tests. It is not clear from RAAF records which personnel at RAAF bases were involved in these activities, and it is therefore likely that the study population includes some who were not.

Consideration was given to which ships' crews should be included from the Monte Bello tests, because some (e.g. HMAS Sydney) were relatively remote from the test sites. Crews of most ships in the area were included in the study population. This could dilute any excess radiation-related mortality in RAN personnel. However, crews of these ships were all assigned to the lowest radiation exposure category (<1 mSv) so that this would not affect the analysis of relative risk between categories of radiation exposure.

6.7.2 Ascertainment of deaths

For reasons discussed in Section 6.1, only results based on Method 1 for treating the follow-up time of subjects lost to contact are presented in Chapter 5, since Method 2 is likely to have led to substantial underestimates of mortality. However, even Method 1, where subjects lost to follow-up are excluded from the study from the date of last contact, may underestimate SMRs. Method 1 will give an underestimate if the SMR of subjects lost to follow-up is higher than in the rest of the cohort. This in turn depends on how many of the subjects lost to follow-up have died, and when they died. The discovery of 42 cancer deaths in the NCSCH that had been missed in the search of the NDI is an indication that a considerable number have died. Finding these deaths in the NCSCH has probably minimised the underestimation of cancer deaths but not noncancer deaths. Unlike cancer, there are no morbidity registers for these conditions, so that a similar quality control check could not be carried out. Therefore, a significant number of subjects have probably been classified as lost to contact only because their deaths, although registered in the NDI, were not found. Since about one-third of the population experiences cancer during their lives, it is likely that at least double the number of noncancer deaths ($2 \times 42 = 84$) were missed in the NDI search. This would mean that noncancer deaths could be underestimated by as much as 3%. In addition, some deaths may have been missed in the search of state death registries for deaths before 1981.

There is also some indication that there are relatively few subjects lost to contact who are living and will appear on the NDI when they die. As part of the cancer incidence study (see Chapter 8), the NCSCH was scanned for cancers in subjects identified in this mortality study as lost to contact. Only 15 such cases were found. If a large number of the 934 subjects lost to contact were in fact alive and living in Australia, many more cancers would be expected.

The foregoing discussion is about subjects who have not changed their names, and who were on the NDI but not found in the search, or who will be in the NDI when they die. A further potential cause of missed deaths is from subjects who have changed their names, and who were therefore not found and never will be under their original name in the NDI or state death registry.

Thus, although it is theoretically possible that Method 1 could lead to an overestimate of true SMRs, the overall effect of these factors could result in an underestimate of as much as 6%, with the underestimate greatest for noncancer deaths. This does not mean that excesses of noncancer deaths have escaped detection, because for most major categories of noncancer deaths the SMRs are well below unity. For example, the SMR for ischaemic

heart disease is 0.90 (95%CI, 0.85 to 0.96). An important exception could be COPD; the implications of this have been discussed in Section 6.5.

This study does not include deaths of participants who have emigrated. The mortality rates of participants must be computed in the same way as the population statistics with which they are being compared. Deaths that occur outside Australia are not included in national mortality statistics, so deaths in the cohort known to have occurred outside Australia were not included in the observed deaths.

6.7.3 Classification of causes of death

Some variation may be expected between the cause of death given on the NDI and the cause given by the National Centre for Classification in Health (NCCH) after coding of death certificates. As explained in Section 3.4.3, a validation study was undertaken to assess the degree of concordance on cause of death coding between the NDI and NCCH, which coded deaths occurring before the NDI was established. Of 79 death certificates submitted, four were coded differently by NCCH. A fifth had been correctly classified as death from external causes, but had been coded as suicide instead of accidental death. The coding was concordant for the other 74 death certificates. The five discordant cases were resubmitted to NCCH and, in each case, the NDI coding was found to be correct. On this basis, it is possible that there is a 6% error rate in the coding of the deaths (26% of all deaths) that occurred before the NDI. Thus, the overall error rate from this source was approximately 1.6%. There were, however, no coding errors for deaths from cancer.

6.7.4 Evaluation of healthy worker effect

A significant concern has been the possibility of a healthy worker effect (HWE). Since there was no comparable occupational cohort, comparison with the general population was performed, with the resulting risk of underestimation of the true SMR. In the study of UK test participants, where a comparison cohort was used, both participants and controls had a significantly lower SMR for all-cause mortality (SMR 0.89 and 0.88, respectively), suggesting an HWE. Some HWE should therefore be expected in the Australian cohort.

The all-cancer SMR of 1.18 in this cohort suggests that there is little influence of an HWE for cancer mortality. However, the HWE varies between diseases and diminishes with time since inception of the cohort. Thus, there is a likelihood that an HWE has contributed to the low death rate from ischaemic heart disease, where the SMR was 0.90 (95%CI, 0.85 to 0.96).

There is little, if any, evidence of an HWE in the cohort study of Australian veterans of the Korean War. This cohort is a useful comparison, since the Korean War was contemporary with the early years of the nuclear testing program, and a significant fraction of the military component of this cohort also served in Korea. In the Korean veterans' cohort, the SMR from all causes was 1.21 (95%CI, 1.18 to 1.24) using Method 1 and 1.11 (95%CI, 1.09 to 1.14) using Method 2.

Irrespective of the extent of an HWE on other causes of death, it is improbable that the estimated mortality from non-CLL leukaemia has been influenced by an HWE, for the following reasons:

- there is little, if any, variation between leukaemia mortality and social class, which is an important determinant of the HWE
- the effect of selection bias, another component of the HWE, has been minimised by excluding the first two years of follow-up of all subjects (and any death occurring in that time)
- an internal analysis of the association between non-CLL leukaemia and radiation exposure is not subject to an HWE.

The analysis of the association between other cancers and radiation exposure is similarly not subject to an HWE.

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7 Cancer incidence study design

7.1 Components of the study of cancer incidence

This phase of the study had two components:

- a retrospective cohort study of cancer incidence
- a case–control study, nested within the cohort, of the association between leukaemia and exposure to ionising radiation from the nuclear testing in Australia.

7.2 Retrospective cohort study

This was a retrospective cohort study of cancer incidence in the Australian participants in the British nuclear testing program. Information about cohort studies can be found in Section 2.1.

7.2.1 Choice of comparison population

In a cohort study, the health outcome of interest in the exposed cohort is compared with the rate in an unexposed cohort or population. For reasons set out in Section 2.2, the comparison was made with the general population: that is, the cancer incidence in the cohort of nuclear veterans was compared with that in the Australian male population.

A significant concern with having to compare rates with the general population instead of a comparable working population is the 'healthy worker effect' (HWE). This is described in Section 2.3, and a detailed analysis of the factors contributing to the HWE is given in Appendix 4.

An important aspect of the HWE that has received little attention is whether it is confined to mortality analyses or whether it is found in studies of disease incidence as well. It is generally only possible to address this question in the case of cancer, since other diseases are not subject to mandatory registration and therefore cannot be enumerated to the extent required for valid follow-up of a cohort.

In their textbook, *Statistical Methods in Cancer Research*, Breslow and Day state that the HWE appears to be smaller for cancer incidence than for cancer mortality (Breslow and Day 1987). The only explanation they offer is that those with cancer are more likely to have left their job; however, this would not explain disparity between cancer incidence and cancer mortality in a single cohort.

This observation is supported by a recent update in the study of mortality and cancer incidence in the Australian petroleum industry conducted in the Department of Public Health at the University of Adelaide. In this study, cancer mortality and cancer incidence were studied concurrently (Gun et al 2004). The all-cancer standardised mortality ratio (SMR) was 0.84, significantly below unity, whereas the all-cancer standardised incidence ratio (SIR) was 1.04, not significantly different from unity. The HWE was discovered and analysed in an era when only cancer mortality could be examined. The concurrent finding of a low SMR and an SIR close to unity in the Australian petroleum study shows that a

low SMR does not necessarily portend low incidence, and that an HWE found in a mortality estimate does not necessarily mean that the HWE effect exists at all for cancer incidence.

A further reason for an HWE being less likely in the present study is that cancer incidence in the cohort was followed only from 1982. The HWE is believed to be partly due to a selection effect, whereby people with serious illness or disability are likely to be excluded from the workforce. For example, people with cancer may be less likely to seek or to obtain employment. Therefore, the rates of some cancers may be less than in the general population for the early years of follow-up. However, the influence of the HWE is likely to diminish with time, so that the age-standardised cancer rate of occupational cohorts is likely to converge towards that of the general population as cohorts age; this is likely with the current cohort, which had no entrants after 1965 (Monson 1990).

Nevertheless, measures were included in the design of this study to examine the relationship between ionising radiation and cancer, free of the influence of any HWE:

- Internal comparisons were made between cohort members, grouped according to categories of assessed radiation exposure.
- The case–control study of leukaemia and ionising radiation is free from influence by the HWE.

7.3 Outcomes of interest

Rates of all major cancer subtypes in the cohort were compared with rates in the general male population using SIRs. SIRs for each service category were also generated.

Internal comparisons between categories of radiation exposure were made for cancers found to be in excess in the SIR analyses.

7.4 Internal comparisons between categories of radiation exposure

In these analyses, cancer rates were compared between groups of cohort members categorised by the estimated radiation exposure received from participation in the nuclear testing. For more information on the exposure assessment, see Section 3.5.

Relative incidence rates were generated for the various categories of exposure, with the lowest exposure category (<1 mSv) as the baseline category.

As this was an internal analysis within the cohort, it was not subject to an HWE.

7.5 Case–control study of leukaemia

Due to the well-established association between ionising radiation and leukaemia, a major research question in the present study was to identify and measure any association between exposure to ionising radiation and the incidence of leukaemia in test participants.

The case–control study was similar to the comparison of leukaemia rates between radiation exposure categories in the cohort study. However, in that study it was not practicable to make detailed estimates of the radiation exposure of every individual

participant. Instead, the category of radiation exposure relied mainly on information contained in official documents and variables in the nominal roll, such as dates of entry and exit from test sites and occupation, which were applied to work groups as a whole.

Individual exposure estimates were feasible for the limited number of cohort members included in the case–control study. In this study, the subjects were limited to those with leukaemia, and a *sample* of subjects who did not have the disease. With this limited number of subjects, it was practicable to examine information on each individual (e.g. from service records) to obtain the best estimate of radiation exposure.

In the case–control study, each case of non-CLL leukaemia was matched with four subjects without leukaemia (controls). Individual radiation exposures were estimated by the Dosimetry Panel, which was blinded to the case–control status of each subject. The radiation exposure of cases was then compared with those of controls to generate an estimate of the risk of leukaemia due to ionising radiation exposure incurred at the nuclear test sites.

7.6 References

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8 Cancer incidence study methods

8.1 Retrospective cohort study of cancer incidence

The methodology for this study was very similar to that of the cohort mortality study, described in Chapter 3. The outcomes of interest were site-specific cancers, obtained from the cancers registered by the state and territory cancer registries. An important difference from the mortality study is that the study period began on 1 January 1982, when national cancer data were first generated, whereas the study period for the mortality study dated from subjects' initial entry into the cohort (i.e. when they first entered a test site). For both studies, the study period terminated on 31 December 2001.

8.1.1 Defining the study population

As in the cohort mortality study, the study population was derived from the Nominal Roll of Australian Participants in the British Atomic Tests in Australia (DVA 2001). The method of compiling the nominal roll is described in Sections 3.1 and 3.2, together with the reasons for exclusions of certain subjects.

As in the mortality study, only male participants were included in the cancer analysis.

The follow-up period of this study commenced on 1 January 1982, which is when the cancer registry data from all states and territories were consolidated and used to generate national cancer incidence data. For this reason, the study population excluded cohort members who died before 1 January 1982.

8.1.2 Radiation exposure assessment

Exposure assessment for the cohort is described in Section 3.5.

8.1.3 Search for incident cancers

Incident cancers were identified by matching the roll of the study population with official registers of cancer. All state and territory cancer registry data, except for Victoria, are consolidated into the National Cancer Statistics Clearing House (NCSCH), located in the Australian Institute of Health and Welfare (AIHW).

The list of cohort members, containing their name, date of birth and exposure category, was submitted to AIHW and to the Victorian Cancer Registry, which required that cancers in Victoria be searched for separately. The records from the two sources were consolidated by AIHW. Cases of each site-specific cancer were categorised by service category and by radiation exposure. Certain cancers were also categorised by age, year of diagnosis and exposure category, to facilitate the relative incidence ratio analyses. The aggregated data were then supplied to the study team. The data did not include any personal information that could enable individuals to be identified.

8.1.4 Privacy constraints

Initially, an application was made to the AIHW Human Research Ethics Committee to obtain information about cancer diagnosis for each member of the cohort who was identified with cancer in the NCSCH. This application was rejected on the grounds that information identifying individuals cannot be released without the consent of the individual concerned. Obtaining the consent of every individual in this study was clearly impracticable, given that, for many members of the cohort, the only contact details available were from their time at the tests. Thus, the proposal for such a search had to be abandoned. Instead, de-identified cancer incidence information, aggregated by age, year of diagnosis and exposure category, was obtained.

While the information received enabled standardised incidence ratios to be generated, lack of identifiable information is a serious barrier to quality control. For example, anonymous data obtained from AIHW cannot be cross-checked against data from the state cancer registries. It also prevents checking known living cancer cases identified from other sources (in this case records of the Department of Veterans' Affairs, DVA) to ensure that they have been located in the NCSCH.

The blanket ban on obtaining identifiable information without consent has serious implications for the conduct of other retrospective studies — for example, among occupational cohorts. This concern has been addressed in a submission to the review of the private sector provisions of the Privacy Act, conducted by the Commonwealth Privacy Commissioner (Gun 2005).

8.1.5 Coding of cancers

Cancer incidence data provided to the study were coded according to ICD-10.

8.1.6 Deriving person-years of follow-up

National cancer data are only available back to 1 January 1982, and accordingly the follow-up period for each subject commenced on that date.

The cancer analysis covered the period 1 January 1982 to 31 December 2001. Each subject's follow-up time ceased according to the same rules as in the mortality study; see Section 3.6.2.

8.1.7 Computation of follow-up time

The same methodology for treating the person-time of subjects lost to contact was used in the mortality and cancer incidence study. The methodology is described in Section 3.6.4. Only the results using Method 1 are presented in Chapter 9; the results including Method 2 can be found in Appendix 3.

8.1.8 National cancer incidence data

National cancer incidence data, which were required for comparing the cancer rates of the cohort with the general population, were obtained from the AIHW website. The data were stratified by 5-year age group and year of occurrence.

8.1.9 Measures of incidence

Cancer incidence in the test participant cohort was compared with that in the general population of males in Australia. Internal analyses were also carried out in relation to exposure to ionising radiation.

Two measures of incidence were used in the analysis:

- The standardised incidence ratio (SIR) was used to compare incidence rates in the cohort with rates in the general Australian male population.
- The relative incidence ratio (RIR) was used for internal analyses, in which different categories of subjects within the cohort were compared with each other.

Standardised incidence ratio

The SIR is the ratio of the cancer incidence rate in the cohort to the rate in the general population, adjusting for the variation in incidence with age and over time. The SIR was calculated by dividing the observed number of cancers by the number expected from national rates — that is, the number of cancers that would be expected in the cohort if the rate in each 5-year age group and each year of follow-up were the same as the corresponding rate in the general population. The expected number of cancers was computed by the following means: for each subject, the total follow-up time was allocated according to the number of days spent in each age-group and calendar-year stratum. Thus, for each year from 1982 to 2001, there was a stratum for each age group up to the group 81–84 years. The follow-up time of all subjects in each age-calendar year stratum was added to give the total follow-up time (in person-years) for each stratum. The number of person-years in each stratum was multiplied by the national cancer incidence rate for that stratum (measured in cancers per person-year) to obtain the expected number of cancers in that stratum. The expected cancers in each stratum were then summed to obtain the total expected number. The SIR is the number of observed cancers divided by the total expected number.

As described in Section 8.1.7, SIRs were computed using the number of person-years estimated in two different ways, according to the way in which subjects lost to contact were treated.

Relative incidence ratio

The RIR was used for comparisons between categories of radiation exposure.

For the outcome of interest, a ‘baseline’ exposure level was chosen, and represented as having a risk of 1.0. In these analyses, the baseline was the category with the lowest estimated radiation exposure (i.e. <1 mSv). Risk for all other exposure categories was then compared with the baseline. The measure of these comparisons is the RIR.

The RIR analyses were done using Poisson regression models. As these models depend on ‘large sample’ theory for statistical validity, 95% confidence intervals were not given if either of the two categories being compared had fewer than four cases. All analyses were adjusted for age and person-time in the cohort.

RIRs were used for internal comparisons for all incident cancers combined, non-CLL leukaemia and other cancers found to be significant in the SIR analysis.

Unlike analyses based on the SIR, only one method was used for computing follow-up time — that is, Method 1: person-time of subjects lost to contact was censored on the date of last contact.

8.1.10 Confounding

Confounding variables are other factors in the cohort (apart from the exposure of interest) that affect the health outcomes being studied. Where these factors can have large influences on outcomes, such as with smoking and cancer, it is necessary to account for them. For example, when comparing lung cancer rates between two groups with different radiation exposure, even small differences in smoking rates between the two groups can cause large differences in lung cancer rates. To cause confounding, a variable has to be a cause of the disease in its own right, and must be unequally distributed between the different groups being compared.

Differences in risk between various exposure groups could therefore be masked or falsely calculated if confounding variables are not allowed for.

In the SIR and RIR estimates, adjustment was made for confounding by age and calendar year as described in previous sections.

Other causes of cancer also need to be considered as potential confounders. The most important in this study would be smoking, which is strongly related to many causes of death. Unfortunately, no smoking history was available for members of this cohort. Therefore, indirect measures have been used to estimate the likely confounding effect of smoking. One means is to examine the cancer rate or death rate from diseases almost exclusively due to smoking, such as emphysema and laryngeal cancer. Another method is to estimate what the smoking prevalence would have to be to explain fully an excess of a cancer or cause-specific death by smoking alone. This is discussed in the following section.

Another potential cause of confounding is asbestos exposure, which has an association with lung cancer. Asbestos may be particularly relevant for RAN personnel in view of asbestos in ships. Unfortunately, there are no data on asbestos exposure in cohort members; however, some indication may be obtained from the incidence of mesothelioma, a cancer strongly related to asbestos exposure.

8.1.11 Estimating cancer rates from hypothetical levels of smoking prevalence

Since no smoking data were available for this cohort, it was not possible to compute the proportion of cancers such as lung cancer caused by smoking. However, an indirect measure was used to compute the level of smoking prevalence in the cohort that would fully account for any excess risk. The method adopted here was that developed by AIHW for the Korean Veterans Mortality study (Harrex et al 2003). As for the mortality study, this analysis provided for a range of smoking prevalences, from 30%–100%, and generated a hypothetical number of expected deaths, based on these prevalence rates and estimates of attributable risk of cancer death due to smoking. For more information on the calculation of hypothetical smoking prevalence, see Appendix 5.

8.2 Case–control study

The case–control study addressed the specific issue of identifying and, if necessary, quantifying any association between non-CLL leukaemia and exposure to ionising radiation in the nuclear testing program.

The design was a matched case–control study, with four controls per case, matched for age and the number of years since entry into the study period.

8.2.1 Privacy considerations

Approval for the case–control study was sought from the Human Research Ethics Committees of The University of Adelaide, AIHW, DVA and the Department of Defence.

Approval was sought to obtain the names of individual leukaemia cases from the NCSCH. Approval was not given to obtain the names of living leukaemia cases in the absence of consent of the subjects. Accordingly, written application was made to the ethics committees of all state cancer registries. All states gave consent subject to receiving the written consent of all living leukaemia cases. The procedure for obtaining consent varied between states; in general, the treating doctor must first be approached to obtain permission to contact the subject, after which the subject is asked to provide written consent to his inclusion in the study.

State cancer registries were also asked to supply pathology reports of leukaemia cases for independent verification.

Names of cases and control subjects were combined into a single file that was sent to DVA with the case/control status of the subject removed. Data from service records and other information available on subjects was then submitted to the Dosimetry Panel for estimation of radiation exposure. Thus, the panel was aware that some of the subjects were leukaemia cases, but did not know which were cases and which were controls.

8.2.2 Case identification

All non-CLL leukaemia cases, whether identified from a death record or a cancer registry, were included as cases.

For deceased subjects who had developed leukaemia since the establishment of the NCSCH, state cancer registries provided information on date of diagnosis and leukaemia subtype, indicated by ICD-10 and the morphology coding. Most states also provided histology reports of each case where available. (No reports were obtained from NSW, where the privacy provisions extend to deceased subjects).

For deceased cases who developed leukaemia before establishment of NCSCH, no further information was available, and it was assumed that the cause of death on the death certificate (coded in ICD-10 by the National Centre for Classification in Health) was correct.

8.2.3 Case verification

Where pathology reports were available, they were submitted to an independent haematologist to confirm that they were cases of non-CLL leukaemia.

8.2.4 Control selection

A program for control selection was designed, based on the recommendations of Professor Neil Pearce (Pearce and Checkoway 1987).

Four matched controls per case were used in the analysis. Controls were selected by matching according to age and the number of years since entry into the cohort. Controls were required to be alive and not known to have leukaemia at the time of disease onset of the corresponding case. Because some of the leukaemia cases were identified from death records, the date of onset was deemed to be two years before death.

Controls lost to contact at the date of disease onset of the case were ineligible. Where an ineligible civilian control was selected, the next randomly selected eligible civilian was used as a replacement. Similarly, an ineligible military participant was replaced by an eligible military participant.

8.2.5 Radiation exposure estimation

Each individual's radiation exposure status was estimated by the Dosimetry Panel. The panel was blinded to the case/control status of each subject.

The panel was supplied with all available relevant information, including service records, nominal roll data, and the answers of any subjects who had responded to the questionnaire administered in the Donovan Inquiry.

The categories of exposure level were the same as for the mortality study (Section 3.5).

8.2.6 Reliability estimation

The reliability (replicability) of the panel estimates was tested by resubmitting 32 subjects' records to the panel for repeat estimation. The separate estimates for each subject were compared.

8.2.7 Validity testing

Fifteen control subjects were interviewed on their experience as test participants. Each subject was sent a questionnaire, identical to that used in the Donovan study. This was followed up by a telephone call, during which the questionnaire was administered. Interviewees were also given the opportunity to describe their recollections in their own words.

The interview responses were submitted to the Dosimetry Panel, and exposure estimates were made on the basis of this information, again by placing each of the 15 subjects into one of the exposure categories. The results were compared with the original estimates for these subjects.

8.2.8 Analysis

Odds ratios for non-CLL leukaemia by category of radiation exposure were generated by conditional logistic regression.

8.3 Software

Data were analysed using Stata version 8.2.

8.4 References

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9 Description of the cancer incidence study cohort

The study of cancer incidence is reliant, for the purposes of comparison, on Australian population cancer incidence rates, which are only available from the beginning of 1982. Thus, only the follow-up time from 1982 was included in the cancer incidence analysis, and subjects who died before then were not included. Subjects lost to follow-up were treated in two different ways, described in the previous chapter as Methods 1 and 2. Using Method 1, 8728 members of the cohort were still alive on 1 January 1982. Using Method 2, 9588 members of the cohort were still alive on 1 January 1982. This difference arose because, using Method 1, many of those lost to follow up were censored before 1 January 1982 and were thus not included in the population to be analysed, whereas, using Method 2, they were presumed alive at the cutoff date. In total, there were 144 995 person-years of follow-up time using Method 1, and 160 970 person-years of follow-up using Method 2.

9.1 Study population by service category

Military participants comprised 6109 (70%) of the cohort using Method 1, and 6321 (66%) using Method 2. Table 9.1 shows the distribution of subjects by service category for each method.

Table 9.1 The study population by service category

	Method 1	Method 2
RAN	2613 (30%)	2724 (28%)
Army	1037 (12%)	1079 (11%)
RAAF	2459 (28%)	2518 (26%)
Civilians	2619 (30%)	3267 (34%)
Total subjects	8728	9588
Years of follow-up	144 995	160 790

9.2 Age of study population

The age of the cohort used in the cancer incidence study is shown by the distribution of year of birth in Table 9.2. The civilian participants as a group were older than service personnel.

Table 9.2 Year of birth distribution

Year of birth	Method 1		Method 2	
	Military (%)	Civilian (%)	Military (%)	Civilian (%)
Pre-1900	0	1 (<1%)	1 (<1%)	1 (<1%)
1900–1909	79 (1%)	118 (5%)	84 (1%)	193 (6%)
1910–1919	535 (9%)	473 (18%)	555 (9%)	625 (19%)
1920–1929	2541 (42%)	1068 (41%)	2614 (41%)	1303 (40%)
1930–1939	2745 (45%)	801 (31%)	2853 (45%)	966 (30%)
1940–1948	209 (3%)	158 (6%)	214 (3%)	179 (5%)

The civilian participants were also slightly older than the military participants at entry to the cohort on 1 January 1982. The average age at the entry date for the whole cohort was 53 years; it was 55 years for the civilian participants and around 52 years for the military participants. The distribution of age of the cohort participants is shown in Table 9.3.

Table 9.3 Age at entry to the cohort (1 January 1982)

Age group (years)	RAN	Army	RAAF	Civilians	Total
Method 1					
30–39	9 (<1%)	17 (2%)	65 (3%)	70 (3%)	161 (2%)
40–49	818 (31%)	408 (39%)	795 (32%)	718 (27%)	2739 (31%)
50–59	1608 (62%)	378 (36%)	1124 (46%)	1068 (41%)	4178 (48%)
60–69	157 (6%)	193 (19%)	391 (16%)	591 (23%)	1332 (15%)
70–79	21 (<1%)	41 (4%)	83 (3%)	163 (6%)	308 (4%)
80+	0	0	1 (<1%)	9 (<1%)	10 (<1%)
Mean age	52.0	52.9	52.9	55.0	53.3
Method 2					
30–39	9 (<1%)	18 (2%)	65 (3%)	79 (2%)	171 (2%)
40–49	858 (31%)	426 (39%)	823 (33%)	845 (26%)	2952 (31%)
50–59	1666 (61%)	388 (36%)	1144 (45%)	1324 (41%)	4522 (47%)
60–69	169 (6%)	202 (19%)	399 (16%)	746 (23%)	1516 (16%)
70–79	22 (<1%)	43 (4%)	86 (3%)	256 (8%)	407 (4%)
80+	0	2 (<1%)	1 (<1%)	17 (<1%)	20 (<1%)
Mean age	52.0	52.9	52.9	55.6	53.6

9.3 Rank of the military participants

The military participants in the cohort had a rank recorded on the nominal roll. Over 80% of the participants were ranks other than officers, as shown in Table 9.4.

Table 9.4 Rank by service category

Service	Method 1		Method 2	
	Other ranks	Officers	Other ranks	Officers
RAN	2401 (92%)	212 (8%)	2507 (92%)	217 (8%)
Army	792 (76%)	245 (24%)	828 (77%)	251 (23%)
RAAF	1920 (78%)	539 (22%)	1970 (78%)	548 (22%)
Total	5113 (84%)	996 (16%)	5305 (84%)	1016 (16%)

9.4 Exposure to ionising radiation

Participants in the cohort were allocated an exposure category by the Dosimetry Panel, as described in Chapter 3. Table 9.5 shows that the majority of the cohort was estimated to have received a dose of less than 1 mSv, and more military participants than civilians received an estimated dose greater than 1 mSv. Overall, 7% of the cohort could not be allocated to an exposure category due to a lack of information on their test participation.

Table 9.5 Estimated exposure to ionising radiation

Exposure category	RAN	Army	RAAF	Civilian	Total
Method 1					
A (<1 mSv)	1917 (73%)	620 (60%)	1767 (72%)	2436 (93%)	6740 (77%)
B (1 to <5 mSv)	521 (20%)	40 (4%)	16 (<1%)	10 (<1%)	587 (7%)
C (5 to <20 mSv)	168 (6%)	167 (16%)	66 (3%)	33 (1%)	434 (5%)
D (20–50 mSv)	2 (<1%)	199 (19%)	3 (<1%)	120 (5%)	324 (4%)
E (>50 mSv)	0	3 (<1%)	13 (<1%)	1 (<1%)	17 (<1%)
F (unknown exposure)	5 (<1%)	8 (<1%)	594 (24%)	19 (<1%)	626 (7%)
Method 2					
A (<1 mSv)	1995 (73%)	648 (60%)	1819 (72%)	3052 (93%)	7514 (78%)
B (1 to <5 mSv)	551 (20%)	41 (4%)	16 (<1%)	12 (<1%)	620 (6%)
C (5 to <20 mSv)	171 (6%)	172 (16%)	66 (3%)	36 (1%)	445 (5%)
D (20–50 mSv)	2 (<1%)	205 (19%)	3 (<1%)	134 (4%)	344 (4%)
E (>50 mSv)	0	3 (<1%)	13 (<1%)	1 (<1%)	17 (<1%)
F (unknown exposure)	5 (<1%)	10 (<1%)	601 (24%)	32 (<1%)	648 (7%)

10 Cancer incidence study results

10.1 Interpretation of results

Cancer incidence of the nuclear test participants is mostly expressed as a standardised incidence ratio (SIR), with a confidence interval.

The SIR is the ratio of the observed number of cancers in the participants to the expected number of cancers if the participants had the same cancer incidence rates as the general Australian population of the same age and sex. The method of computing the SIR is explained in Section 8.1.9. An SIR greater than 1.0 indicates that the incidence rate is greater than in the general population, and an SIR less than 1.0 indicates that it is less. However, the SIR is only an estimate of the true incidence ratio. The confidence interval (CI) is a statistical estimate of the likely range within which the true incidence ratio lies. If the lower boundary of the CI exceeds 1.0, we can be reasonably confident that the true SIR exceeds 1.0, in which case the SIR is said to be significantly increased — that is, the incidence rate in participants is considered to be higher than in the general population. Conversely, if the *upper* boundary of the CI is less than 1.0, the SIR is considered to be significantly lowered.

In this report, a 'significant' increase in SIR refers to a statistically significant increase — that is, the true incidence rate probably exceeds that of the general population. It does not necessarily mean that it is a large increase.

Two methods were used for computing SIRs, the difference being in the method of treating subjects lost to contact (that is subjects for whom it is not known if they are alive or dead). In Method 1, these subjects were excluded from the analysis, and the resulting SIRs are valid to the extent that subjects lost to contact have the same incidence rates as those whose vital status is known. Method 2 assumes that all subjects lost to contact are alive and living in Australia, and is almost certainly a considerable underestimate. Method 1 is accurate to the extent that the mortality rate in those lost to contact is the same as the rest of the cohort, and represents the best estimate of cancer incidence rates. Accordingly, only results from Method 1 are shown here. The complete results from both methods are given in Appendix 3. The follow-up time using Method 1 was 139 540 person-years.

10.2 All-cancer incidence

As shown in Table 10.1, the incidence of all cancers combined was significantly raised, the SIR being 1.23 (95%CI, 1.18 to 1.28).

10.3 Incidence of specific cancers

The incidence of cancers by site is also shown in Table 10.1. Eight site-specific cancers occurred in significant excess:

- cancers of the lip, oral cavity and pharynx — SIR 1.41; 95%CI, 1.18 to 1.67
- lung cancer — SIR 1.28; 95%CI, 1.16 to1.41

- oesophageal cancer — SIR 1.48; 95%CI, 1.09 to 1.97
- colorectal cancer — SIR 1.16; 95%CI, 1.04 to 1.28
- melanoma — SIR 1.40; 95%CI, 1.21 to 1.60
- prostate cancer — SIR 1.22; 95%CI, 1.12 to 1.32
- leukaemia excluding chronic lymphatic leukaemia (non-CLL leukaemia) — SIR 1.61; 95%CI, 1.18 to 2.14
- all leukaemias combined (i.e. including CLL) — SIR 1.43; 95%CI, 1.12 to 1.80.

Table 10.1 Incident cancers: observed cases, expected cases, standardised incidence ratios and 95% confidence intervals for the cohort, by type of cancer

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	2456	2000.3	1.23	1.18–1.28
Oral cavity (C00-C14)	133	94.1	1.41	1.18–1.67
Oesophagus (C15)	47	31.8	1.48	1.09–1.97
Stomach (C16)	73	65.1	1.12	0.88–1.41
Colorectal (C18-C21)	353	305.0	1.16	1.04–1.28
Liver (C22)	20	19.2	1.04	0.64–1.61
Gallbladder (C23-C24)	15	12.2	1.23	0.69–2.02
Pancreas (C25)	50	43.0	1.16	0.86–1.53
Nasal cavity (C30-C31)	6	4.0	1.50	0.55–3.27
Larynx (C32)	42	34.2	1.23	0.89–1.66
Lung (C33-C34)	406	316.7	1.28	1.16–1.41
Pleura (C38.4)	1	0.6	1.63	0.04–9.06
Melanoma (C43)	209	149.8	1.40	1.21–1.60
Mesothelioma (C45)	26	17.8	1.46	0.95–2.14
Prostate (C61)	548	450.9	1.22	1.12–1.32
Testis (C62)	3	3.4	0.90	0.18–2.62
Kidney (C64)	49	46.5	1.05	0.78–1.39
Renal pelvis (C65)	4	5.4	0.74	0.20–1.89
Bladder (C67)	98	100.7	0.97	0.79–1.19
Eye (C69)	4	5.15	0.78	0.21–1.99
Brain (C70-C72)	38	28.0	1.36	0.96–1.86
Thyroid (C73)	9	6.3	1.43	0.65–2.71
Lymphomas (C81-C85, C96)	78	67.3	1.16	0.92–1.45
Multiple myeloma (C90)	29	23.8	1.22	0.82–1.75
Leukaemia (C91-C95)	73	51.0	1.43	1.12–1.80
CLL (C91.1)	26	20.4	1.28	0.83–1.87
Leukaemia excluding CLL	47	29.1	1.61	1.18–2.14
'Radiogenic' cancers	1006	842.2	1.19	1.12–1.27

There was an excess of the total number of cancers considered to be 'radiogenic'. These are cancers shown in the Life Span Study of atomic bomb survivors and reported by the United Nations Scientific Committee on the Effects of Atomic Radiation to be causally associated with ionising radiation. The cancers are: thyroid, stomach, colon, liver, lung, bladder, non-CLL leukaemia, and non-melanoma skin cancer. Data for non-melanoma skin cancer were not available as it is not a registrable cancer in Australia. All the other

named cancers were combined to form the group ‘radiogenic’ cancers. The SIR for this group of cancers was 1.19 (95%CI, 1.12 to 1.27).

10.4 Cancer by service

Separate SIRs for military and civilian subjects are shown in Table 10.2 and Table 10.3. Results are not shown where the number of observed cases was less than 5. The pattern for military subjects was similar to that for the cohort as a whole.

Table 10.2 Military participants — SIR for selected cancers

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	1720	1380.1	1.25	1.19–1.31
Oral cavity (C00-C14)	94	66.5	1.41	1.14–1.73
Oesophagus (C15)	34	22.0	1.55	1.07–2.16
Stomach (C16)	56	44.3	1.27	0.96–1.64
Colorectal (C18-C21)	238	211.7	1.12	0.99–1.28
Liver (C22)	17	13.5	1.26	0.73–2.01
Pancreas (C25)	39	29.4	1.33	0.94–1.81
Larynx (C32)	36	24.1	1.49	1.05–2.07
Lung (C33-C34)	271	217.8	1.24	1.10–1.40
Melanoma (C43)	156	105.5	1.48	1.26–1.73
Mesothelioma (C45)	18	12.8	1.40	0.83–2.22
Prostate (C61)	388	307.7	1.26	1.14–1.39
Kidney (C64)	33	32.7	1.01	0.70–1.42
Bladder (C67)	80	68.4	1.17	0.93–1.46
Brain (C70-C72)	28	19.7	1.42	0.94–2.05
Thyroid (C73)	8	4.5	1.80	0.78–3.54
Lymphomas (C81-C85, C96)	48	46.8	1.03	0.76–1.36
Multiple myeloma (C90)	14	16.3	0.86	0.47–1.44
Leukaemia (C91-C95)	50	34.8	1.44	1.07–1.90
CLL (C91.1)	18	14.1	1.28	0.76–2.02
Leukaemia excluding CLL	32	19.8	1.62	1.11–2.28

In the civilian members of the cohort, there were significant excess incidences of cancers of the oral cavity, colorectal cancer, cancers of the lung and prostate, and multiple myeloma.

Table 10.3 Civilian participants: SIR for selected cancers

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	736	620.1	1.19	1.10–1.28
Oral cavity (C00-C14)	39	27.6	1.41	1.00–1.93
Oesophagus (C15)	13	9.8	1.33	0.71–2.28
Stomach (C16)	17	20.9	0.81	0.47–1.30
Colorectal (C18-C21)	115	93.3	1.23	1.02–1.48
Pancreas (C25)	11	13.7	0.81	0.40–1.44
Lung (C33-C34)	135	99.0	1.36	1.14–1.61
Melanoma (C43)	53	44.3	1.20	0.90–1.56
Mesothelioma (C45)	8	5.0	1.60	0.69–3.15
Prostate (C61)	160	143.3	1.12	0.95–1.30
Kidney (C64)	16	13.9	1.15	0.66–1.87
Bladder (C67)	18	32.3	0.56	0.33–0.88
Brain (C70-C72)	10	8.3	1.20	0.58–2.21
Lymphomas (C81-C85, C96)	30	20.5	1.46	0.99–2.09
Multiple myeloma (C90)	15	7.5	2.01	1.13–3.32
Leukaemia (C91-C95)	23	16.2	1.42	0.90–2.13
CLL (C91.1)	8	6.3	1.27	0.55–2.50
Leukaemia excluding CLL	15	9.4	1.60	0.90–2.64

Table 10.4 shows cancer incidence in RAN personnel. There were significant excess incidences in cancers of the oral cavity, lung and prostate, and of mesothelioma. Sixteen of the 18 mesotheliomas in the military personnel occurred in RAN members. Mesothelioma showed the highest SIR of 2.79 (95%CI, 1.59 to 4.52). Naval personnel also had significant excesses of colorectal cancer, melanoma and non-CLL leukaemia.

Table 10.4 RAN participants: SIR for selected cancers

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	759	581.3	1.31	1.21–1.40
Oral cavity (C00-C14)	43	29.0	1.48	1.07–2.00
Oesophagus (C15)	16	9.4	1.71	0.98–2.78
Stomach (C16)	23	18.2	1.26	0.80–1.90
Colorectal (C18-C21)	109	90.1	1.21	0.99–1.46
Liver (C22)	9	5.9	1.53	0.70–2.90
Pancreas (C25)	16	12.2	1.31	0.75–2.13
Larynx (C32)	16	10.6	1.51	0.86–2.45
Lung (C33-C34)	138	91.9	1.50	1.26–1.77
Melanoma (C43)	60	45.4	1.32	1.01–1.70
Mesothelioma (C45)	16	5.8	2.79	1.59–4.52
Prostate (C61)	162	127.4	1.27	1.08–1.48
Kidney (C64)	14	14.1	1.00	0.54–1.67
Bladder (C67)	30	28.2	1.07	0.72–1.52
Brain (C70-C72)	9	8.5	1.06	0.48–2.01
Lymphomas (C81-C85, C96)	18	19.7	0.91	0.54–1.44
Multiple myeloma (C90)	2	6.8	0.29	0.04–1.06
Leukaemia (C91-C95)	18	14.3	1.26	0.75–1.99
CLL (C91.1)	3	2.3	1.29	0.27–3.78
Leukaemia excluding CLL	15	8.0	1.87	1.04–3.08

Table 10.5 shows cancer incidence in Army subjects. Pancreatic cancer showed an excess SIR.

Table 10.5 Army participants: SIR for selected cancers

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	278	227.4	1.22	1.08–1.37
Oral cavity (C00-C14)	16	10.8	1.49	0.85–2.42
Oesophagus (C15)	4	3.6	1.11	0.30–2.85
Stomach (C16)	12	7.4	1.62	0.83–2.82
Colorectal (C18-C21)	35	34.7	1.01	0.70–1.40
Liver (C22)	5	2.2	2.31	0.75–5.40
Pancreas (C25)	11	4.9	2.24	1.12–4.02
Larynx (C32)	7	3.8	1.82	0.73–3.75
Lung (C33-C34)	39	35.7	1.09	0.78–1.49
Melanoma (C43)	25	17.3	1.45	0.94–2.14
Mesothelioma (C45)	2	2.0	0.98	0.12–3.54
Prostate (C61)	58	51.0	1.14	0.86–1.47
Kidney (C64)	8	5.3	1.51	0.65–2.97
Bladder (C67)	13	11.4	1.14	0.61–1.95
Brain (C70-C72)	6	3.2	1.86	0.68–4.05
Lymphomas (C81-C85, C96)	6	7.8	0.77	0.28–1.68
Multiple myeloma (C90)	3	2.7	1.11	0.23–3.23
Leukaemia (C91-C95)	8	5.8	1.37	0.59–2.70
CLL (C91.1)	6	5.9	1.01	0.37–2.20
Leukaemia excluding CLL	2	3.4	0.60	0.07–2.15

Table 10.6 shows the results in RAAF personnel. There was a significant excess incidence of melanoma, prostate cancer, all leukaemias and non-CLL leukaemia. There were 71 melanoma cases in RAAF personnel. Due to privacy laws (or their current interpretation), individual matching of cancer cases was not possible, so it is not known how many of these personnel were aircrew.

Table 10.6 RAAF participants: SIR for selected cancers

Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI
All cancers	683	571.4	1.20	1.11–1.29
Oral cavity (C00-C14)	35	26.7	1.31	0.92–1.82
Oesophagus (C15)	14	9.1	1.55	0.85–2.60
Stomach (C16)	21	18.6	1.13	0.70–1.72
Colorectal (C18-C21)	94	86.9	1.08	0.87–1.32
Liver (C22)	3	5.5	0.55	0.11–1.60
Pancreas (C25)	12	12.3	0.98	0.50–1.70
Larynx (C32)	13	9.6	1.35	0.72–2.31
Lung (C33-C34)	94	90.1	1.04	0.84–1.28
Melanoma (C43)	71	42.9	1.66	1.29–2.09
Mesothelioma (C45)	0	5.1	-	-
Prostate (C61)	168	129.3	1.30	1.11–1.51
Kidney (C64)	11	13.3	0.83	0.41–1.48
Bladder (C67)	37	28.8	1.29	0.90–1.77
Brain (C70-C72)	13	8.0	1.63	0.87–2.78
Lymphomas (C81-C85, C96)	24	19.3	1.24	0.80–1.85
Multiple myeloma (C90)	9	6.8	1.32	0.60–2.50
Leukaemia (C91-C95)	24	14.6	1.64	1.05–2.44
CLL (C91.1)	9	5.8	1.55	0.71–2.94
Leukaemia excluding CLL	15	8.4	1.78	1.00–2.94

10.5 Cancer by radiation exposure

Table 10.7 shows the distribution of all cancers combined by estimated radiation exposure. For these analyses, the incidence rate of each category of radiation exposure was compared with the lowest exposure category. As shown in Table 9.5 in the previous chapter, the panel was unable to assign 7% of the subjects to an exposure category. These subjects were not included in analyses of trend.

There was no trend of increasing cancer incidence with increasing radiation exposure ($P = 0.90$). Because of small numbers in some exposure categories, the analysis was repeated with exposure categories combined. Using three exposure categories, again no trend with radiation exposure was present ($P = 0.68$); nor was any trend evident when all categories above 1 mSv were combined.

Table 10.7 The incidence of all cancers combined: comparisons within the cohort based on exposure to ionising radiation

Exposure	Cases	Person-years	Age-and-year adjusted RIR	95%CI
Category A (<1 mSv)	1874	111 564	1.0	
Category B (1 to <5 mSv)	126	10 284	0.79	0.66–0.94
Category C (5 to <20 mSv)	141	7113	1.04	0.88–1.24
Category D (20 to 50 mSv)	96	5310	1.08	0.88–1.32
Category E (>50 mSv)	5	269	1.04	0.43–2.49
Category F (unknown)	214	10 455	1.10	0.96–1.27
Category A	1874	11 564	1.0	
Category B/C	267	17 397	0.90	0.80–1.03
Category D/E	101	5579	1.07	0.88–1.31
Category A	1874	11 564	1.0	
Category B–E	368	22 976	0.94	0.84–1.06

Table 10.8 compares the cancer incidence between exposure categories for those cancers found in excess in the SIR analysis, including 'radiogenic' cancers (see description following Table 10.1). Melanoma showed increasing incidence with increasing radiation exposure, but the trend was not statistically significant.

Table 10.8 The incidence of selected cancers: comparisons within the cohort based on exposure to ionising radiation

Cancer	Exposure	Cases	Person-years	Age-and-year adjusted RIR	95%CI
Oesophagus	Category A	38	111 564	1.0	
	Category B/C	6	17 397	0.96	0.40–2.27
	Category D/E	1	5579	0.55	0.07–3.98
	Category B–E	7	22 976	0.86	0.39–1.94
Colorectal	Category A	287	111 564	1.0	
	Category B/C	31	17 397	0.68	0.47–0.98
	Category D/E	9	5579	0.63	0.33–1.23
	Category B–E	40	22 976	0.67	0.48–0.93
Lung	Category A	312	11 564	1.0	
	Category B/C	44	17 397	0.87	0.64–1.20
	Category D/E	15	5579	0.96	0.57–1.62
	Category B–E	59	22 976	0.89	0.68–1.18
Melanoma	Category A	149	111 564	1.0	
	Category B/C	25	17 397	1.05	0.69–1.61
	Category D/E	10	5579	1.35	0.71–2.57
	Category B–E	35	22 976	1.12	0.78–1.62
Oral cavity	Category A	110	111 564	1.0	
	Category B/C	15	17 397	0.81	0.47–1.39
	Category D/E	1	5579	0.19	0.03–1.36
	Category B–E	16	22 976	0.67	0.40–1.14
Prostate	Category A	417	111 564	1.0	
	Category B/C	62	17 397	0.94	0.72–1.22
	Category D/E	15	5579	0.73	0.44–1.22
	Category B–E	77	22 976	0.89	0.69–1.13
All leukaemias	Category A	54	111 564	1.0	
	Category B/C	6	17 397	0.68	0.29–1.59
	Category D/E	5	5579	1.84	0.74–4.61
	Category B–E	11	22 976	0.96	0.50–1.83
Leukaemia excluding CLL	Category A	39	111 564	1.0	
	Category B/C	2	17 397	0.31	0.08–1.29
	Category D/E	2	5579	1.02	0.25–4.24
	Category B–E	4	22 976	0.48	0.17–1.34
CLL	Category A	15	111 564	1.0	
	Category B/C	4	17 397	1.66	0.55–5.02
	Category D/E	3	5579	3.91	1.13–13.5
	Category B–E	7	22 976	2.21	0.90–5.42
'Radiogenic' cancers	Category A	777	111 564	1.0	
	Category B/C	98	17 397	0.77	0.63–0.95
	Category D/E	40	5579	1.05	0.76–1.45
	Category B–E	138	22 976	0.84	0.70–1.00

The only significant trend found was for chronic lymphatic leukaemias. Conditional logistic regression over categories A to E separately showed a significant trend ($P = 0.02$). As shown in Table 10.8, the RIRs for categories B and C combined and

categories D and E combined were elevated compared with category A, with the elevations for D/E statistically significant.

There was no significant trend for all leukaemias (i.e. with or without inclusion of CLL).

10.6 Smoking prevalence and predicted cancer incidence

Some of the cancers found in excess are known to be smoking-related. To estimate the likelihood that the excess SIRs from these cancers were due to a higher prevalence of smoking than in the general male population, the expected number of cancers for a given level of smoking prevalence was computed.

As shown in Table 10.9, a prevalence of smoking (ever) of between 60% and 70% in the cohort, compared with a population rate (based on expected numbers) of between 40% and 50%, would be sufficient to account for the excess SIR for lung cancer. This increased prevalence is possible. For cancer of the oral cavity, the prevalence in the cohort required to account for the observed number of cancers is between 70% and 80%, compared with a population prevalence of 40%–50%. For cancer of the oesophagus, the prevalence in the cohort to account for the observed number of cancers is between 80% and 90%, compared with a population prevalence of 40%–50%. Due to the large increase in smoking prevalence required to account for the increased number of oral cavity and oesophagus cancers, these cancers are probably not due to smoking alone.

Table 10.9 Expected numbers of incident cancers given hypothetical smoking prevalences

					Hypothetical smoking prevalence (%)							
					30	40	50	60	70	80	90	100
Cancer	Obs	Exp	SIR	95%CI	Expected incident cases							
Lung	406	316.7	1.30	1.18–1.44	225	283	342	401	459	518	577	635
Oral cavity	133	94.1	1.41	1.18–1.67	73	85	98	110	123	135	148	160
Oesophagus	47	31.8	1.51	1.11–2.00	25	29	33	37	41	45	49	53

10.7 Conclusion

Raised cancer incidence rates in the cohort were found for all cancers combined and for several specific cancers. Although there were raised SIRs for leukaemias and other cancers known from other studies to be associated with ionising radiation, no relationship was found between rates of cancer incidence and level of radiation exposure in this study population.

11 Case–control study results

This chapter addresses the relationship between leukaemia other than chronic lymphatic leukaemia (non-CLL leukaemia) and exposure to ionising radiation.

Radiation exposures were compared between all cases of non-CLL leukaemia and a sample of control subjects without non-CLL leukaemia. Radiation exposure was estimated by the Dosimetry Panel, using available documents including the nominal roll, service records and responses to the questionnaire used in the Donovan study.

11.1 Number of cases and controls

All known cases of non-CLL leukaemia were included, whether obtained from cancer registrations or from death certificates. The study included 54 non-CLL leukaemia cases and 4 matched controls for each case ($n = 216$).

Twenty-four cases of non-CLL leukaemia were identified through both mortality and cancer incidence databases, whereas 17 were identified from incidence data only and 13 were identified through mortality data only. Two cases identified through the incidence search were found not to be matches and were not included. Four living subjects with leukaemia were identified through the cancer incidence search; however, consent for their inclusion could not be gained and they were not included in the study. Cases identified through the mortality study only were assumed to have a diagnosis date of two years before their death date; diagnosis date was available for all other cases from the cancer registry. Only subjects not lost to follow-up at the time of diagnosis of the case were eligible as controls.

11.2 Leukaemia subtypes

Where pathology reports were obtained from state registries, they were reviewed by a consultant haematologist. Only 21 reports were obtained. Thus the basis of the case ascertainment was as follows:

Death certificate coding	13
Coding from cancer registry or National Cancer Statistics Clearing House (NCSCH)	17
Cancer registry coding reviewed by consultant haematologist	21
Living cases, coded by consultant haematologist	3

Of the 21 cases reviewed by the haematologist, 4 were assigned a different code. However, all were still non-CLL leukaemias and thus eligible for inclusion in the study.

Although hairy cell leukaemia is a nonacute leukaemia and classified as a lymphoid leukaemia, the 3 hairy cell leukaemia cases were retained in the analysis on the basis of the original decision rule that all leukaemias except those explicitly coded as CLL (ICD-9 204.1, ICD-10 91.1) would be included. There is further justification for inclusion of these two cases in the case–control study. Although the subject receives little attention in the literature, a 1980 study concluded that radiation exposure may be an important

contributor to the development of some cases of hairy cell leukaemia (Stewart and Keating 1980).

The leukaemia subtypes are shown in Table 11.1. The middle column shows the numbers of each leukaemia type based on cancer registry data or death certificate diagnosis, and the right-hand column shows the classifications by the consultant haematologist of those cases where pathology reports were available.

Table 11.1 Leukaemia types in the case–control study

Cancer type	Number (cancer registry or death record)	Number (haematologist or registry or death code)
Chronic myeloid leukaemia	15	14
Acute myeloid leukaemia	24	23
Myeloid leukaemia, unspecified	1	0
Chronic monocytic leukaemia	0	3
Acute lymphocytic leukaemia	2	2
Hairy cell leukaemia	2	3
Acute myelomonocytic leukaemia	1	2
Acute monocytic leukaemia	0	1
Acute myelofibrosis	1	1
Acute leukaemia unspecified	1	1
Acute promyelocytic leukaemia	1	1
Acute megakaryocytic leukaemia	1	1
Lymphoid leukaemia, unspecified	1	1
Leukaemia, unspecified	1	1
Code not provided (living cases)	3	0

11.3 Differences in exposure assessment for the case–control study

The exposure of the 270 subjects in the case–control study was assessed in more detail than in the cohort study. This enabled all but one of the 25 subjects originally assigned to the unknown exposure category (category F) to be reassigned to another category. Three subjects were recategorised into category F for the case–control study. Of the other 242 subjects in the case–control study, 212 received the same exposure category as in the cohort study, and a further 20 were recategorised in the next category up or down. Only in 10 subjects did the exposure change by more than one category. Table 11.2 shows the comparison.

Table 11.2 Differences in exposure assessment between the cohort and case–control study

Cohort assessment	Case–control assessment					
	A	B	C	D	E	F
A	190	8	2		1	1
B	4	12				1
C	1	4	8			1
D	4	2	3	2	1	0
E						
F	19	5				1

Analysis for concordance resulted in a weighted kappa statistic, with scores for categories A to E of 1, 2, 3, 4, 5 (i.e. excluding the unknown category) of 0.63 (95% CI, 0.54 to 0.73). Landis and Koch provide benchmarks for strength of agreement for kappa, and 0.63 is considered substantial agreement on their scale (Landis and Koch 1977).

Additional information obtained for three subjects in the case–control study led to their exposure being reassigned from category B to category A and would have changed the categorisation of the entire work group to which they belonged, had the additional information been available for the cohort study. Because the additional information would not have become available but for the more detailed assessments in the case–control study, assessments of this work group for the cohort study were not revised. An assessment was made, however, of the likely impact on the study findings if the cohort assessments had been revised. There were 166 subjects in the work group, and it is estimated that, if all had been changed from exposure category B to category A, about 6000 person-years would have been transferred from category B to category A in the mortality analyses (Tables 5.11 to 5.14) and about 2500 person-years transferred in the cancer incidence analysis (Tables 10.7 and 10.8). Any of the deaths or cancers among these 166 subjects would also be transferred from exposure category B to category A, but irrespective of the number transferred, the changes would not be sufficient to alter the conclusions.

11.4 Test for replicability of radiation assessments in the case–control study

Thirty-two subjects were selected to test the reliability (replicability) of the panel assessments in the case–control study. As shown in Table 9.5, nearly 80% of the cohort had been assigned to category A, the minimal exposure category (<1 mSv). Therefore, to ensure that a reasonable number of subjects in this test were from the other exposure categories, the latter were deliberately oversampled, so that 12 of the 32 subjects (37.5%) were from categories other than A. Table 11.3 shows the comparison of the first and second assessments.

Table 11.3 Comparison of exposure assessments in 32 subjects between first and second case–control assessments

	Second assessment					
First assessment	A	B	C	D	E	F
A	19					1
B	4					
C	1	3	2			
D						
E						
F	1	1				

In the repeat assessment, two subjects originally categorised as unknown exposure (category F) were assigned a known category, and one subject initially assigned category A was reassigned to the unknown category. Of the other 29, all except one were assigned the same category or an adjacent category. Analysis for concordance, using scores for categories A to E of 1, 2, 3, 4, 5 (i.e. excluding unknown category), gave a weighted kappa statistic of 0.52. This represents moderate agreement (Landis and Koch 1977). This level of agreement is probably less than if a random sample had been selected; subjects in category A were deliberately under-represented in the sample, and there was a much higher level of agreement in this category.

The first assessment was used in the case–control analysis.

11.5 Correlation with assessments from subject interviews

Fifteen controls were randomly selected from the study, and their contact details were obtained from the electoral roll. They were then sent a letter requesting their participation in a questionnaire survey. The subjects were then contacted by telephone and administered a questionnaire concerning their employment during the tests, time spent at test sites, duties undertaken and their perception of exposure to radiation. The questionnaire was the same as that used in the 1983 study on the health of atomic test personnel (the Donovan study, Donovan et al 1983).

The responses to the interviews were then submitted to the Dosimetry Panel for exposure assessment, and the exposure categories were compared with the categories previously assigned to these subjects using the standard methodology for the case–control study.

Compared with the previous assessment, the exposure category of 12 of the 15 subjects was unchanged. One subject was changed to a lower exposure, from category D to category B, and two were changed to a higher exposure — one from category A to category C, and one from category A to category B.

The original panel assessments were used in the analysis.

11.6 Result of analysis

The distribution of non-CLL leukaemia cases and controls by radiation exposure category is shown in Table 11.4. The panel was unable to assign an exposure to 4 subjects. Of the other subjects, 44 of the 53 cases (83%), and 174 of the 213 controls (82%) were assigned

to the minimal exposure category of less than 1 mSv. None of the cases were in categories D or E, whereas there were 2 controls in each of these categories.

Statistical testing showed no trend to increasing risk with increased radiation exposure. Excluding category F, the test for trend using five categories of exposure was not significant ($P = 0.46$). The finding was similar combining exposure into three categories ($P = 0.61$). After combining all exposure categories other than the lowest, the odds ratio (OR) for non-CLL leukaemia for exposure above category A was 0.90 (95%CI, 0.41 to 1.98).

No non-CLL leukaemia cases occurred in subjects in the two highest exposure categories, D and E; that is, none of the cases received more than the current occupational exposure limit for a single year, and the assessments were for total accumulated exposure for the test period.

Thus the analysis shows no association between non-CLL leukaemia and radiation exposure.

Table 11.4 Comparison of non-CLL leukaemia cases and controls by category of radiation exposure

Exposure category	Cases	Controls	OR	95%CI
Category A (<1 mSv)	44	174	1.0	
Category B (1 to <5 mSv)	7	24	1.15	0.47–2.84
Category C (5 to <20 mSv)	2	11	0.71	0.15–3.30
Category D (20 to 50 mSv)	0	2	0	
Category E (>50 mSv)	0	2	0	
Category F (unknown)	1	3	1.35	0.14–12.95
Category A	44	174	1.0	
Category B/C	9	35	1.0	0.45–2.20
Category D/E	0	4	0	
Category A	44	174	1.0	
Category B–E	9	39	0.90	0.41–1.98

11.7 Sensitivity testing

To test for the effect of misclassifying exposure on the result of this analysis, a computerised simulation model was used, assuming a true OR of 2. The model assumed only two categories of exposure (exposed vs non-exposed, equivalent to category A vs categories B–E) and also assumed a range of nondifferential exposure errors — that is, that the panel could have misclassified exposed cases as non-exposed or vice versa. The model assumed a range of error rates from 10% to 70%. For each rate, 1000 simulations were performed, and the OR was computed each time. The average OR was then computed for each rate. (For the sake of simplicity, an unconditional model was used — that is, cases and controls were not matched. However, it can be shown that for these data the conditional and unconditional models yield very similar ORs.)

Then assuming the true OR is 2, the average observed ORs according to the rate of nondifferential misclassification (NDM) were:

NDM rate	OR
10%	1.574
15%	1.488
20%	1.375
25%	1.306
30%	1.220
35%	1.180
40%	1.124
45%	1.100
50%	1.062
55%	1.003
60%	0.976
65%	0.952
70%	0.880

Thus *on average*, about a 55% misclassification rate would be required to degrade an OR of 2 down to 1, given data such as in this case–control study.

For an assumed true OR of 1.5, the average observed ORs were:

NDM rate	OR
10%	1.355
15%	1.303
20%	1.235
25%	1.208
30%	1.158
35%	1.141
40%	1.119
45%	1.077
50%	1.045
55%	1.011
60%	0.991
65%	0.946
70%	0.949

Again, *on average*, about a 55% misclassification rate would be required to degrade an OR of 1.5 down to 1, given data such as in this case–control study.

11.8 References

Donovan J, Stevenson C and Ariotti D (1983). *Health of Atomic Test Personnel*, Commonwealth Department of Health, Canberra.

Landis JR and Koch GG (1977). The measurement of observer agreement for categorical data. *Biometrics* 33(1):159–174.

Stewart DJ and Keating MJ (1980). Radiation exposure as a possible etiologic factor in hairy cell leukemia (leukemic reticuloendotheliosis). *Cancer* 46(7):1577–1580.

12 Cancer incidence study discussion

12.1 Treatment of subjects lost to follow-up

Of the two methods for treating the person-time of subjects lost to follow-up, standardised incidence ratio (SIR) estimates based on Method 2 are probably underestimates, so that Method 1 is the best indicator of increased cancer incidence. Only the results based on this method are given in Chapter 5. Even Method 1 could lead to underestimation, but only if there was sufficient under-ascertainment of *observed* cancers to offset any underestimation of *expected* cancers. The latter will occur to the extent that any subjects lost to follow-up are alive and living in Australia.

A recently published study showed under-ascertainment of cancer cases from linkage with the National Cancer Statistics Clearing House (NCSCH) compared with linkage with state cancer registries (Hoving et al 2005). The authors point to the effects of changes to privacy laws, making cancer registries unwilling to provide uncertain matches. At present, the NCSCH is not permitted by certain state registries to provide external researchers with uncertain matches; instead, they must be referred to states for review and confirmation. In the present study, the Australian Institute of Health and Welfare (AIHW, which administers the NCSCH) was a part of the administrative structure of this study, and only aggregated de-identified information was provided. Thus, AIHW was able to carry out clerical matches in-house of all possible matches, and significant underestimation from this source is unlikely.

Thus, unlike the mortality study of nuclear veterans, under-ascertainment is not a significant problem, and Method 1 is likely to be a close estimate of the true SIRs. On this basis, there is an excess incidence of several cancers in this cohort: cancers of the lip, oral cavity, pharynx, lung and oesophagus; colorectal cancer; melanoma; prostate cancer; non-CLL leukaemia and all leukaemias combined.

Of the cancers occurring in excess, three are commonly associated with smoking — cancers of the oral cavity, oesophagus and lung. The excess incidence of these cancers could be plausibly explained by a higher smoking prevalence in the cohort than in the general male population. However, the mortality study of nuclear test participants has shown no excess mortality from chronic obstructive pulmonary disease (COPD), a finding that would be unexpected in a population with a high smoking prevalence. Nevertheless, as discussed in Chapter 6, there was some under-ascertainment of deaths, particularly for causes other than cancer, so that a small true excess mortality from COPD is possible.

The group of cancers defined as ‘radiogenic’ also occurred in excess, but they showed no tendency to increased incidence with increasing radiation exposure, either as a group or individually. As described in the report of the Dosimetry Panel, radiation exposures were low in this cohort. Therefore, the lack of association between these cancers and radiation exposure in this cohort is to be expected. Of the cancers classified as ‘radiogenic’, over 75% were lung or colorectal cancers, and it is likely that the excess of this group of cancers is due to other factors associated with these particular cancers.

12.2 Comparison with other studies

Table 12.1 shows a comparison of the main cancer incidence findings in the present study with those of the study of UK participants conducted by the UK National Radiological Protection Board, and the study of cancer incidence in Australian veterans of the Korean War conducted by AIHW (Muirhead et al 2003, Harrex et al 2003).

There is an important difference between the UK study and the Australian study. Whereas the Australian study compares cancer incidence in the cohort with the Australian male population, the UK study compares cancer incidence of UK personnel (nearly all military) with a cohort of UK service personnel contemporary with the study cohort but who did not participate in nuclear tests. A more valid comparison with the UK study is probably obtained from the mortality findings, in which comparisons were made with the general population in both the Australian and UK studies.

In contrast with the study of Australian nuclear test participants, the UK cohort shows no overall cancer excess. The only cancers showing a significant excess compared with the control cohort were prostate and liver cancers. Thus, the only excess common to the two studies is prostate cancer, a disease not known to be associated with radiation exposure. However, the UK study shows a marginally significant excess of non-CLL leukaemia (relative risk 1.41; 90%CI, 0.94 to 2.09).

There are, however, a number of similarities between the study of the Korean War veterans and this study. Both studies show significant excesses of cancers of the oral cavity, oesophagus, lung and prostate, and of melanoma. Like the nuclear veterans study, there is an elevated incidence of colorectal cancer in the Korean veterans study, but data on confidence intervals are not published in the latter. There is overlap between the two cohorts, about 18% of the test participants having served in Korea. Separate estimates of cancer incidence in the cohort members who did and did not serve in Korea could not be calculated, as identifiable cancer data could not be obtained because of privacy restrictions.

As the Korean War cohort had no significant exposure to ionising radiation, this cannot be a common factor in the two studies.

Table 12.1 Cancer incidence in the Australian and UK studies of nuclear test participants and the study of Australian veterans of the Korean War

	Australian nuclear test veterans		UK nuclear test veterans (Muirhead et al 2003)		Korean War veterans (Harrex et al 2003)	
Cancer	SIR[a]	95% CI[a]	RR to controls	90%CI	SMR	95%CI[a]
Oral cavity	1.41	1.18–1.67	0.86	0.64–1.16	1.90	1.63–2.17
Oesophagus	1.48	1.09–1.97	0.90	0.69–1.19	1.54	1.18–1.89
Stomach	1.12	0.88–1.41	1.04	0.83–1.29	1.05	0.84–1.25
Colorectal	1.16	1.04–1.28	1.01	0.88–1.15	1.19	⊕
Liver	1.04	0.64–1.61	2.03	1.21–3.43	1.35	0.91–1.78
Pancreas	1.16	0.86–1.53	0.92	0.65–1.28	0.99	0.74–1.24
Larynx	1.23	0.89–1.66	0.95	0.86–1.04	1.72	1.38–2.07
Lung	1.28	1.16–1.41	0.95	0.86–1.04	1.42	1.31–1.52
Mesothelioma	1.46	0.95–2.14	⊕	⊕	0.98	0.60–1.37
Melanoma	1.40	1.21–1.60	1.09	0.78–1.51	1.18	1.03–1.32
Prostate	1.22	1.12–1.32	1.22	1.04–1.44	1.18	1.09–1.27
Multiple myeloma	1.22	0.82–1.75	1.14	0.74–1.74	⊕	⊕
Non-CLL leukaemia	1.61	1.18–2.14	1.41	0.96–2.09	1.07	⊕
All cancers	1.23	1.18–1.28	0.99	0.94–1.03	1.13	1.10–1.17

a SIRs computed using Method 1

⊕ Figures not available from published data

12.3 Reconciliation with the mortality study

The findings of the cancer mortality and cancer incidence studies of test participants are shown in Table 12.2.

Table 12.2 Cancer incidence and cancer mortality

	Cancer incidence[a]				Cancer mortality[a]			
Cancer (ICD-10 code)	Observed	Expected	SIR	95%CI	Observed	Expected	SMR	95%CI
All cancers	2456	2000.3	1.23	1.18–1.28	1465	1238.7	1.18	1.12–1.24
Oral cavity (C00-C14)	133	94.1	1.41	1.18–1.67	56	37.5	1.50	1.13–1.94
Oesophagus (C15)	47	31.8	1.48	1.09–1.97	44	38.2	1.15	0.84–1.55
Stomach (C16)	73	65.1	1.12	0.88–1.41	77	61.7	1.25	0.99–1.56
Colorectal (C18-C21)	353	305.0	1.16	1.04–1.28	202	162.8	1.24	1.08–1.42
Liver (C22)	20	19.2	1.04	0.64–1.61	19	20.5	0.93	0.56–1.45
Gallbladder (C23-C24)	15	12.2	1.23	0.69–2.02	8	7.1	1.13	0.49–2.23
Pancreas (C25)	50	43.0	1.16	0.86–1.53	57	55.6	1.03	0.78–1.33
Larynx (C32)	42	34.2	1.23	0.89–1.66	20	17.8	1.12	0.69–1.74
Lung (C33-C34)	406	316.7	1.28	1.16–1.41	429	357.4	1.20	1.09–1.32
Melanoma (C43)	209	149.8	1.40	1.21–1.60	46	37.8	1.22	0.89–1.62
Mesothelioma (C45)[b]	26	17.8	1.46	0.95–2.14	10	8.2	1.22	0.58–2.23
Prostate (C61)	548	450.9	1.22	1.12–1.32	131	103.7	1.26	1.06–1.50
Thyroid (C73)	9	6.3	1.43	0.65–2.71	4	2.2	1.83	0.50–4.67
Multiple myeloma (C90)	29	23.8	1.22	0.82–1.75	20	17.7	1.13	0.69–1.75
Leukaemia (C91-C95)	73	51.0	1.43	1.12–1.80	47	39.9	1.18	0.87–1.57
Leukaemia excluding CLL	47	29.1	1.61	1.18–2.14	40	32.0	1.25	0.89–1.70

a Both sets of estimates are based on Method 1.

b Mesothelioma deaths are derived indirectly from ICD-10 45 (mesothelioma) and ICD-9 163 (cancers of the pleura).

The table shows a high level of agreement on which cancers and cancer deaths are significantly elevated and which are not.

12.4 Individual cancer types

12.4.1 Non-CLL leukaemia

This is the cancer type most strongly associated with radiation exposure in previous studies. Although a significant excess has been found of both incidence and mortality in this group of leukaemias, radiation exposure was not associated with either. These findings were confirmed in the case–control study, in which radiation exposure of the 270 subjects could be assessed in greater detail (Section 8.2.5).

The consistent finding of a lack of association between non-CLL leukaemia and radiation exposure in this study is not surprising given the low radiation levels experienced from test participation — on average 2.9 mSv, only slightly above the background level incurred every year in the general population.[3] These levels are well below those of other studies in which an association between cancer and radiation has been clearly demonstrated. For example, in the Life Span study of Japanese atomic bomb survivors, the average radiation exposure per subject was approximately 250 mSv, nearly 100 times the computed mean exposure in this cohort of 2.9 mSv (Thompson et al 1994). In a study of leukaemia risk in patients treated with radiotherapy for cervical cancer, the mean exposure was even higher at 7.2 Sv (Boice et al 1987).

An estimate of the likely contribution of radiation to the burden of leukaemia can be made by applying the average dose to participants to risk factors estimated from previous studies, to calculate the expected leukaemia rate. To make a worst-case estimate, the highest estimate of excess relative risk (ERR) was selected from epidemiological studies cited by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). For external low-level linear energy transfer (LET) radiation, the highest ERR for non-CLL leukaemia was from the Japanese Life Span study of atomic bomb survivors. The ERR was 4.37 per Sv, and this was applied to the estimated average exposure in this cohort of 2.91 mSv (Preston et al 1994). On this basis, the proportion of non-CLL leukaemias attributable to radiation is 0.0126, or 1.3% — that is, less than 1 of the 47 non-CLL leukaemias.

The findings are somewhat similar to that of the UK study, where non-CLL leukaemia incidence was raised relative to controls (relative risk 1.41; 90%CI, 0.96 to 2.09). The UK study also found no association with radiation exposure, although the numbers presumed exposed were very small in the UK study, and no retrospective exposure assessment, such as used in this study, was made.

The validity of these findings depends, of course, on the validity of the radiation exposure estimates. In the cohort study, it was not possible to examine the personal records of every participant, so that exposure assessments were made on a group basis, according to the branch of the services, timing of presence at a test site and occupation, as given in the nominal roll. However, more detailed consideration was possible for the 270 subjects in

[3] The average exposure in the cancer incidence study is slightly different from that of the mortality study, because the cancer study excludes participants who died before 1982.

the case–control study, and the good correlation between individual exposure estimates in the two studies suggests that the estimates made in the cohort study are realistic.

There was only moderate agreement between the two sets of estimates in the case–control study (Table 11.3), with a kappa statistic of 0.52. However, this is a likely underestimate because the sample of subjects in the reliability study was not randomly selected; subjects in category A were deliberately under-represented in the sample, and there was a much higher level of agreement in this category. Differentiating between the exposure categories A, B and C is a challenging task because of the very low levels of radiation of the dividing line between categories: 1 mSv between categories A and B and 5 mSv between B and C.

Importantly, there were no leukaemia cases in exposure categories D or E; that is, no case received more than 20 mSv, which is the *annual* permissible occupational exposure limit, so that it can be confidently concluded that there is no association between non-CLL leukaemia and radiation exposure arising from the nuclear tests.

There is limited evidence that leukaemia incidence increases with increased socioeconomic status. The United Kingdom publication *Occupational Mortality — Decennial Supplement 1970-72* shows a trend for increasing leukaemia mortality in higher socioeconomic groups such as professional and executive occupations (Office of Population Censuses and Statistics 1978). On the other hand, Australian data tend to indicate little trend in either direction (Smith et al 1996, Yu et al 2003). No data on the social status of the Australian population are available for comparison with this cohort, so this cannot be investigated in this study.

Alternative explanations for the non-CLL leukaemia excess are not easily found. Other known causes of leukaemia include benzene exposure, viral infection, and possibly population mixing. No data are available on benzene exposures in the nuclear testing program. The only known viral cause of leukaemia is the HTLV-1 virus in adult T-cell leukaemia, of which there were no known cases in the cohort. Mixing of rural and urban populations has been suggested as a possible cause of leukaemia clusters in children, the suggested cause being exposure to a virus by an immunologically naive population. However, this hypothesis has not been cited as a likely factor in adult leukaemia (Kinlen and Balkwill 2001).

12.4.2 Chronic lymphatic leukaemia and all leukaemias combined

There was a significant excess of all leukaemias combined (i.e. including CLL). As with non-CLL leukaemias, there was no significant trend to increasing risk with increasing radiation exposure. However, analysis of CLL alone using conditional logistic regression showed a significant trend with increasing radiation exposure. Previous research has not established a clear link between CLL and ionising radiation, and there are a number of studies of patients treated with radiation therapy showing a lack of association with CLL (Boice et al 1987, Curtis et al 1994, UNSCEAR 2000). For this reason, many studies, including the recent multinational study of nuclear workers, exclude CLL from the analysis (Cardis et al 2005). For the same reason, CLL was excluded from the case–control study. However, a weak association between CLL and radiation is possible, and a recent review concludes that the evidence is not persuasive that CLL is not radiogenic (Richardson et al 2005). A true association with radiation exposure therefore cannot be ruled out, but the lack of any trend with non-CLL leukaemia (which has been shown to be radiogenic), the very low exposures experienced by most subjects, and the finding of no

significant excess of CLL would suggest that the association is a chance effect as can be found in studies where multiple comparisons are performed.

12.4.3 Mesothelioma

Of 26 incident cases of mesothelioma, 16 occurred in RAN personnel, a more than 2.5-fold excess compared with the general population. This cancer is nearly always associated with past exposure to asbestos. Asbestos in naval vessels is the likely source of exposure in most of these cases. The exposure need not necessarily have occurred at the time of the nuclear tests, although some personnel were issued with respirators fitted with asbestos filters.

Of the other 8 cases, 6 occurred in civilians. Because the cases could not be individually matched (due to privacy laws), the occupation of these civilians is unknown, but many of the civilian subjects in the study were in the construction industry, where asbestos was commonly used, with less caution than has been the case in recent years. Whether any of these subjects were exposed to asbestos during the nuclear tests is not known.

12.4.4 Lung cancer

An excess of lung cancer always suggests a higher smoking prevalence than in the general population. As shown in Table 5.18 in Chapter 5, a prevalence of between 60% and 70% of smokers (i.e. having ever smoked) would be sufficient to account for the excess lung cancer incidence.

The lack of association with radiation exposure is not unexpected. Of previous studies of radiation (external LET) and lung cancer, the highest excess relative risk is approximately 1.4 per Sv (Lundell and Holm 1995). With an estimated mean exposure of 2.91 mSv, the estimated excess is 0.004 or 0.4%. Thus this estimate of the radiation exposure would account for fewer than 2 of the 406 lung cancers. (The number would be higher if the radiation dose was mainly by inhalation, but the findings of the exposure panel indicate that the inhaled dose is a small fraction of the total dose for most participants.)

It is likely that some of the lung cancer excess is due to asbestos exposure. As already discussed, the occurrence of mesothelioma in RAN and civilian subjects is a definite indication of asbestos exposure, and occurrence of other asbestos-related diseases would therefore not be surprising. The distribution of lung cancer cases is also skewed towards RAN and civilian subjects, with excesses of 51% and 42% respectively, whereas in Army and RAAF personnel the incidence was not significantly elevated.

Another potential cause of excess lung cancer is beryllium, which is used in atomic and thermonuclear weapons. Some studies of beryllium-exposed workers have shown excess lung cancer mortality, and beryllium is categorised as a human carcinogen by the International Agency for Research on Cancer. Evidence presented to the McClelland Royal Commission suggests that this metal was deployed in significant quantities in the British tests as a neutron moderator and reflector.[4] Although there was an awareness of recommended maximum permissible beryllium exposures, it is not known whether any actual measures of airborne beryllium exist, so it has not been possible to evaluate the possible health effects of any exposures. However, a study of beryllium contamination at

[4] Documentation indicating the intended use of beryllium and awareness of health effects has been provided by Major Alan Batchelor.

Maralinga and Emu Field has been undertaken by the Australian Radiation Laboratory (Williams 1985). Of 104 surface soil samples, only 4, from one small area at the TM50 site, showed significant levels of beryllium. The author stated that the results suggested that beryllium was dispersed in the trials as small metal fragments, which would not constitute an inhalation hazard, rather than in a finely divided form. The mortality analysis in this study showed no deaths from beryllium disease.

12.4.5 Melanoma

Melanoma incidence was significantly raised, the rate being 40% greater than in the general population. The most important environmental cause of this cancer is solar radiation, but it is not clear whether work-related exposure is the cause of the excess in test participants. While service personnel may have, on average, a higher exposure to solar radiation than the general population, intuitively it appears unlikely that the difference is big enough to account for such an excess. Indeed, epidemiological evidence indicates a significantly lower risk of melanoma in people with heavy occupational exposure to solar radiation than in people who have little occupational exposure but substantial recreational exposure (Elwood and Jopson 1997).

A possible factor is the ethnic composition of the test participants, at least of the service personnel. The highest risk of melanoma is in white Anglo-Saxons, and it is likely that the service personnel were overwhelmingly in this ethnic group (Armstrong and Kricker 2001). In these analyses, the participants are being compared with the general Australian population in the 1980s and 1990s, in whom the proportion of people of Mediterranean and Asian descent, who have a lower risk of melanoma, is much higher.

There is considerable variation in melanoma incidence between service categories in this study, with the highest being in RAAF personnel (a significant excess of 68%). There is little evidence in the literature of an association between ionising radiation and melanoma, but data are limited. The strongest indication of an association is an increase in melanoma in air pilots and cabin crew. This may be due to confounders such as a social class effect, but one study has shown an increasing incidence with increasing estimated exposure to cosmic radiation (Rafnsson et al 2000). This may be relevant to RAAF personnel who were aircrew. There was also an excess of melanoma mortality in RAAF personnel in the mortality study, but only a minority of melanoma deaths were found to be in aircrew. Privacy laws prevented identification of individuals in the cancer study, so that it was not possible to determine which and how many of the 72 melanoma cases in RAAF personnel were aircrew. The 1983 questionnaire study by the Commonwealth Department of Health on the health of atomic test personnel noted an increased prevalence of melanoma in respondents who reported having worked on decontamination of aircraft, suggesting that the increased melanoma incidence in RAAF personnel is not confined to aircrew (Donovan et al 1983).

12.4.6 Colorectal cancer

Colorectal cancer incidence occurred in significant excess.

Although colonic cancer is cited as a radiogenic cancer by UNSCEAR, no trend of increasing colorectal cancer incidence with increased radiation exposure was found.

Other than some dietary influences, there are no well-identified environmental risk factors for colorectal cancer. However, some contribution from asbestos exposure should not be excluded, because some epidemiological evidence suggests that asbestos exposure can cause colonic cancer. Although a review of 30 cohort studies up to 1993 found that there was no consistent elevation of relative risk, a more recent study has suggested up to a 4-fold increase in risk in highly exposed workers (Weiss 1995, Berry et al 2000). Colorectal cancer incidence was marginally significantly elevated in RAN personnel, who also had the highest incidence of lung cancer and of mesothelioma, diseases known to be associated with asbestos exposure. There was a similar pattern in civilian participants.

12.4.7 Oral cancer

These cancers are strongly smoking-related. As shown in Table 5.18 in Chapter 5, a smoking prevalence of close to 80% would be required to explain the excess of these cancers. Alcohol use is a possible contributing factor, but the lack of an excess SIR for liver cancer suggests that alcohol consumption is not excessive in this cohort.

12.4.8 Prostate cancer

No environmental factor is known to contribute to the occurrence of this cancer. A possible reason for the excess in this cohort is increased intensity of surveillance for prostate cancer in the military participants. The reported incidence of prostate cancer has risen in recent years following the introduction of PSA (prostate specific antigen) testing. It is plausible that ex-service personnel would undergo more intensive medical surveillance and care than the general population, so that diagnosis of the cancer from PSA testing is more likely, especially in those whose condition is not causing symptoms. This possibility is suggested by the higher incidence of prostate cancer in military members of the cohort than in civilians.

12.5 Overview of the effect of radiation exposure

As discussed in Section 12.4.1, the absence of an association between radiation exposure and non-CLL leukaemia or lung cancer is not surprising. These cancers have been shown to be radiogenic, but in studies where exposures were considerably higher than in the nuclear tests. By extrapolating from such studies, it was estimated that the radiation exposures from the nuclear testing would account for less than 1 of the non-CLL leukaemias and less than 2 of the lung cancers.

Non-CLL leukaemia and lung cancers contribute almost one-half of the total number of ‘radiogenic’ cancers in this study, so it may be expected that the radiation exposures incurred by this population could have caused about 4–6 of the radiogenic cancers in total. Assuming that none of the ‘nonradiogenic’ cancers are actually caused by radiation, it is estimated that 4–6 of the 2456 total cancers could have been caused by the radiation exposures incurred in this cohort.

These estimates are based on the methodology of excess relative risk. An alternative approach to estimating the number of cancers that might be expected to arise as the result of radiation exposure is based on the recommendations of the International Commission on Radiological Protection (ICRP), which proposes a ‘lifetime fatality probability coefficient’ of 4×10^{-2} per Sv (ICRP 1991). With a study population (using Method 1) of

8728 and an average dose to the cohort of 2.9 mSv, the total (collective) dose was approximately 25 Sv; applying the above risk factor to this dose results in an estimate of one fatal cancer arising from the radiation exposure.

These small numbers of cancers or deaths from cancer that might be attributable to nuclear test radiation exposure are consistent with the lack of a trend to increasing risk of the 'radiogenic cancers' with increasing radiation exposure, despite the finding that mortality from and incidence of this combined group of cancers was significantly elevated.

Over 75% of the cancers classified as 'radiogenic' were lung or colorectal cancers, and it is possible that the excess of this group of cancers in test participants is due to factors other than radiation.

Careful consideration has been given to whether the lack of any significant association between cancer and radiation exposure may be due to underestimation of radiation doses. There are several indications that this is unlikely. As shown in Tables 10.7 and 10.8, the estimated cancer incidence in all exposed subjects (i.e. exposure categories B–E) is less than that of the minimally exposed (category A) both for all cancers combined and all 'radiogenic cancers'. This finding is independent of the *magnitude* of the doses received, and so would not change even if the doses in Categories B–E had been underestimated.

The exposure estimates used in the cohort study are broadly confirmed by the individual assessments on the sample of 270 subjects included in the case–control study. All but one of the 25 subjects originally assigned to the unknown exposure category (category F), were reassigned to another category. Three subjects were recategorised into category F for the case–control study. Of the other 242 subjects in the case–control study, 212 received the same exposure category as in the cohort study, and a further 20 were recategorised in the next category up or down. Only in 10 subjects did the exposure change by more than one category.

There are other indications that radiation is an unlikely cause of the excess cancer incidence:

- As shown in Table 10.1, the SIR for radiogenic cancers is less than for all cancers. Therefore, the SIR for all *nonradiogenic* cancers combined is greater than that for radiogenic cancers. It is thus very unlikely that the excess of cancers could be due to radiation.
- Table 12.1 shows that the excess incidence rates of individual cancers in test participants are very similar to those in the Korean veterans study, in which there is no information to suggest that radiation exposure is a significant factor. Some service personnel were in both cohorts, and it is likely that the findings of both studies reflect the cancer experience of service personnel who served at that time. In particular, the excess of most smoking-related cancers in both studies is strong evidence of an excess smoking prevalence.
- The only radiogenic cancer with a significant difference in incidence from the Korean study was non-CLL leukaemia. In this case the lack of association with radiation was confirmed in the case–control study, in which the panel scrutinised individual service records in making their estimates.
- In calculating the average radiation exposure of the cohort, the average dose in each exposure category has been assumed to be at the midpoint of the range. As the

number of people in each category declines with increasing dose, taking the midpoint of each category as the estimate of the mean is likely to cause overestimation. There are no doubt individual participants whose exposure would have been underestimated, and others overestimated, but a large underestimate in many subjects would be required to alter the estimated radiation burden in the cohort sufficiently to affect the total number of predicted cancers.

12.6 Methodological issues

Compared with mortality studies, cancer incidence studies are a better source of knowledge on cancer causation. Many cancers have high cure rates and survival rates, whereas mortality studies address only those cancers that have been fatal. This is seen in the present study, where there were 2456 incident cancers and only 1497 cancer deaths. Reliance on mortality studies therefore involves loss of statistical power.

Another strength of cancer incidence studies is the validity of diagnosis. Mortality statistics are dependent on the doctor's judgement of cause of death, as recorded on the death certificate. Moreover, many people with cancer die from another cause, so that the existence of cancer is not recorded in the death statistics. In contrast, incident cancers are registered and classified on the basis of histological evidence.

A potential disadvantage of the cancer incidence study is that it is based only on cancers registered from 1982, when the National Cancer Statistics Clearing House was established. Consequently, this study excludes any cancers that were diagnosed in the years immediately after the nuclear testing. Most cancers have a long lead time — that is, the cancer does not develop for twenty or more years after exposure — so that relatively few cancers caused by test participation would be missed. Moreover, the general agreement between the findings of the mortality and cancer incidence studies (Section 12.3) indicates that the validity of the cancer incidence findings is not compromised by lack of data before 1982.

There is evidence from other studies that leukaemia, a disease of interest because of its association with radiation, may have a relatively short lead time, but in the mortality component of the study, most leukaemia cases were shown to occur more than 15 years after test participation. Most leukaemia cases in the cohort will therefore have been detected in the cancer incidence study. However, to ensure that all leukaemia cases were considered, the case–control study of leukaemia included not only all incident leukaemias found in the cancer incidence study, but also all cases identified solely through death certificates.

A further difficulty has been securing the inclusion of living subjects with leukaemia. There were 7 such subjects, and their details could only be obtained with their written consent. This was obtained for only 3 of these subjects. One subject from Queensland could not be traced, in spite of the efforts of the Queensland Cancer Registry. Although ethical approval was obtained to search for the 3 living cases from NSW, the information was not supplied by the NSW registry.

The manner in which privacy laws are being interpreted has made this study difficult and time-consuming. Obtaining identifiable information from state cancer registries is no longer possible without the consent of every subject. This is clearly impracticable for a large study such as this, involving nearly 12 000 subjects. This problem has been overcome, with some difficulty, for the study of leukaemia, but information for other

cancers could not be obtained. For example, it was not possible to find out the occupations of subjects with mesothelioma, or to find out how many of the RAAF personnel with melanoma were aircrew.

Large-scale retrospective cohort studies such as this will continue to experience major difficulties until agencies holding health information are willing to accept that epidemiological researchers themselves are highly motivated to maintain confidentiality of medical records and to ensure that they are not misused. Privacy laws themselves do not necessarily prevent access to health data, but in practice they can be interpreted by agencies to prevent access. No change in the approach of agencies and their ethics committees is likely unless the laws are changed.

12.7 References

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Appendix 1 The study protocol

Mortality and Cancer Incidence of Australian Nuclear Test Participants

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in conjunction with the Department of Veterans' Affairs

Background

The British tests of nuclear weapons in Australia 1952–1963

Between 1952 and 1963, the United Kingdom conducted a program of nuclear weapons development trials in the Monte Bello group of islands off the coast of Western Australia and at Emu Field and Maralinga in the South Australian desert. Twelve major nuclear explosions were carried out under five separate 'operations'. In addition, 600 minor trials were conducted between 1953 and 1963. Over 16 000 Australian members of the Defence Force and civilians participated in the tests (DVA 2001). British participants numbered more than 20 000 in this Commonwealth initiative (Muirhead et al 2003).

The Monte Bello Islands were the first location used for the British nuclear testing program. Operation Hurricane was the first of the nuclear tests, with a plutonium implosion bomb detonated in the hull of a 1450-ton frigate anchored in a lagoon 400 yards off the western shore of Trimouille Island. Four years later, Operation Mosaic was conducted on Trimouille and Alpha Islands. The Royal Commission into the British atomic tests later found that the Monte Bellos should not have been used for these tests due to the large chance that weather conditions would be unfavourable (McClelland et al 1985).

Meanwhile, the British decided on the use of Emu Field (480 km northwest of Woomera) to test their first land-based weapon, and the two bombs which made up Operation Totem were exploded in October 1953. Before and during the Totem tests, the Kittens minor trials were also conducted at Emu Field, but these involved no nuclear explosions. The Totem 1 explosion was responsible for the 'black mist incident', in which many Aboriginal people reported becoming ill from a cloud passing over their settlements near Wallatinna. The Royal Commission found that the evidence given by Aboriginal people, and the scientific modelling, were sufficient to conclude that the black mist did occur and may have made people temporarily ill. However, there was not enough evidence to say whether the black mist caused other illnesses or injuries (McClelland et al 1985).

During this time, a site in the South Australian desert, north of the transcontinental railway line between Cook and Ooldea, was being prepared to be the permanent proving ground for British nuclear weapons. The area was inhabited by Tjarutja people, but named Maralinga by anthropologists working with Aboriginal people in eastern Australia (Keane 2003). Maralinga, meaning 'thunder fields', was developed as a township, with housing for 2000 servicemen and concomitant services such as repair garages, a hospital and laboratories, as well as facilities such as a swimming pool and cinema (Keane 2003). The site was used for eleven years, hosting major nuclear explosions as well as 600 'minor trials'. Originally, the British planned to close the range between the major tests,

but changed their plans to accommodate the extensive program of minor trials (McClelland et al 1985).

The first series of nuclear tests at Maralinga, Operation Buffalo, occurred during September and October 1956. Before this, the minor trials Kittens and Tims had taken place. The conduct of the Buffalo trials was controversial, although they were also shrouded in secrecy, and much of the information about the conduct of the tests was not released until the Royal Commission in 1984. This was especially so regarding the safety of the Aboriginal population, and the Royal Commission found that the 'attempts to ensure Aboriginal safety during the Buffalo series demonstrate ignorance, incompetence and cynicism on the part of those responsible for that safety' (McClelland et al 1985). In addition, the Royal Commission reported that all four tests in the Buffalo series were conducted under conditions that violated the firing conditions proposed by the safety committee (McClelland et al 1985). However, overall the Royal Commission found that radiological and physical safety arrangements for participants in the Buffalo tests were well planned and sound, although acknowledged that this did not negate the possibility of unplanned exposures to radiation (McClelland et al 1985).

The second major operation at Maralinga was Operation Antler, which took place during September and October 1957. These tests occurred against a background of increasing public and political concern about nuclear contamination, and were fewer than originally planned (McClelland et al 1985). The Royal Commission found that the extent of fallout from the third Antler explosion, in which the bomb was suspended from balloons, was seriously underestimated (McClelland et al 1985). Again, the Commission found that 'inadequate attention was paid to Aboriginal safety during the Antler series' (McClelland et al 1985). However, it also found that the series was the best planned and organised of all the tests conducted in Australia, although unplanned incidents, such as the dispersal of cobalt-60, would have exposed personnel to radiation (McClelland et al 1985). Throughout and after these test series, numerous minor trials were conducted.

Maralinga clean-up activities began in 1963 and were still occurring in the 1990s. As yet, the area is not fit for habitation by the traditional Aboriginal owners.

The British nuclear test series was conducted under stringent security conditions, with the complete cooperation and support of the Australian Government. There is no doubt that the safety and security of the Aboriginal inhabitants were seriously compromised by the tests. Controversy continues surrounding the possible exposures to test participants and to other people further afield who claim to have been affected by the tests (James 2003, James and Starick 2003). Numerous authors have made claims about the level of deception of both the Australian Government and the participants regarding the safety of the tests; to this day, aspects of the conduct of the tests remain secret.

Ionising radiation

There are two general types of radiation exposure:

- External exposure. External exposure is exposure from sources outside the body. Examples are exposure from an X-ray examination or from standing near a gamma-emitting radionuclide. External exposures are generally fairly predictable — exposures can be estimated from a simple measurement of the general area, using, for example, a Geiger counter, or from personal dosimeters (film badges and the like).
- Internal exposure. Internal exposure is exposure from radioactive material that is inside the body. Such material would usually enter by inhalation of airborne material,

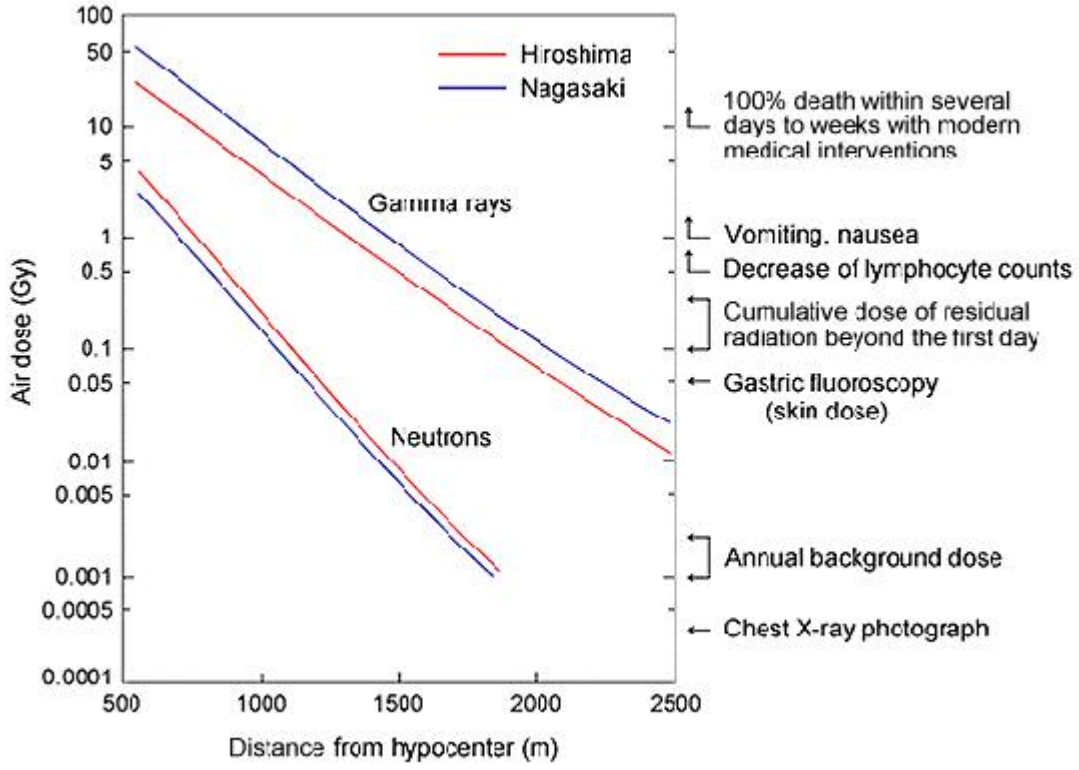
ingestion of contaminated food or water, or more rarely through contamination of wounds. Internal exposure is more difficult to estimate than external. For example, in considering inhalation, account must be taken of the activities being undertaken — in this case, the extent to which dust may be generated — as well as the level of contamination in the local environment. In addition, because the metabolism of different radioactive species can vary considerably, account must be taken of the particular radionuclides present. Monitoring is relatively difficult, requiring (for inhalation) air sampling (preferably personal) and subsequent radiological analysis of the filter.

Detonation of nuclear weapons can result in both internal and external exposures, and can be further subdivided into prompt and delayed exposure.

Prompt exposure

Prompt exposure is from the immediate flash of radiation at the instant of detonation. The nuclear explosion produces a burst of gamma rays and neutrons, which will result in an external exposure to those in the vicinity. Typically, the dose from neutrons is an order of magnitude or more less than that from the gamma rays, and can be neglected. The dose drops off fairly rapidly with distance from the point of detonation, due to the combined effects of the inverse square law, and shielding by the atmosphere. Figure A1.1 shows the dose as a function of distance for the weapons used in Japan. All weapons tested in Australia were of this general size or smaller, with the exception of one Monte Bello bomb, which was around 4 times larger.

Figure A1.1 Prompt exposure from atomic weapons used in Japan (Source: Radiation Effects Research Foundation, 2003)



As can be seen in Figure A1.1, at 2.5 km, the dose from prompt exposure is down to around 20 mGy (approx 20 mSv). At a distance of, say, 3.5 km, it is down to around 1 mSv (i.e. less than annual natural background), and beyond 5 km it is effectively zero. There are unlikely to be any 'special circumstances' that could result in prompt doses beyond this distance.

Delayed exposure

Delayed exposure can be either internal or external. It arises from activation products and fission products:

- Activation products result from neutrons produced in the explosion being absorbed by stable atoms on the ground (and also the bomb casing, the atmosphere, etc), which then become radioactive. The activation products are generally beta and gamma emitters. For the Japanese bombs, significant doses were only found within a few kilometres of the centre. These bombs were exploded at relatively high altitude; for explosions closer to the ground, as in most Australian tests, neutron activation products will be more concentrated at ground zero.

  The activation products have a wide range of half-lives, ranging from seconds to tens of years. Overall, the decay is rapid at least over the first few days or weeks. Of the total dose from activation products received by remaining on the site indefinitely, 80% would be received on the first day, a further 10% on days 2 to 5, and the remaining 10% over the remaining period (i.e. years).

With the exception of the fraction of activation products produced from the bomb casing (considered as 'fallout' below), the activation products are fixed in place around the ground zero.

- Fission products are the radionuclides produced when atoms of the nuclear explosive (plutonium or uranium) split into two in the initial nuclear reaction. Scores of different radionuclides are produced in the fission process; most of them are beta and gamma emitters. They are all created at the heart of the nuclear explosion, and rise with the mushroom cloud, from where they can be dispersed. As with activation products, there is a wide range of half-lives, from seconds to tens of years. A good approximation to the overall decay is the 'rule of seven' — after the first hour, every seven-fold increase in time results in a ten-fold decrease in activity. This will be discussed further under 'fallout'.

Fallout

Radioactive material from a nuclear explosion may rise high into the air before eventually falling to earth as 'fallout'. Fallout may include fission products, activation products (from the bomb casing, etc) and residual plutonium and uranium not consumed in the explosion. Generally, the fission products dominate, at least in the short term. The height to which the fallout rises in the atmosphere depends largely on the size of the explosion — the more energy, the higher they will rise. The subsequent dispersion depends on wind velocities at the various levels of the atmosphere affected. The pattern of dispersion and deposition can be complex and can have unexpected features due to wind changes at various heights. Rainfall can be important in 'washing' the radioactive material out of the atmosphere and onto the ground. The pattern of local fallout from the Maralinga and Emu tests was determined by airborne surveys in conjunction with the clean-up activities.

The fallout radionuclides are initially vaporised in the explosion and subsequently condense into solid particles. When a nuclear explosion takes place high in the air, there

is little other material to condense (only the bomb components), and so the particles formed are very small — aerosols. These will tend to remain aloft, and be widely dispersed. In contrast, when an explosion takes place on or near the ground, so that the fireball touches the ground, very large quantities of soil will be sucked into the mushroom cloud, and some will vaporise. This large quantity of material means that the condensed particles that form will be large and heavy, and will fall to earth rapidly. The fallout will thus be relatively localised, and relatively heavy.

Fallout can contribute to an external dose either as the cloud passes overhead or, usually much more importantly, after falling to the ground in an occupied area. Internal doses can arise from inhalation, either directly or after resuspension of material from the ground, or from consumption of contaminated food or water. Fallout, at least initially, will be as a 'dust' on the surface, and thus would be expected to readily become airborne if disturbed.

As noted above, fission products decay by a 'seven-fold' rule; as these dominate the fallout, this rule can be applied to fallout generally. So, starting 1 hour after production, the activity will fall to one-tenth after 7 hours, one-hundredth after 2 days (49 hours) and one-thousandth after a fortnight. Decay continues, but the rule rather overestimates the amount remaining beyond 6 months.

Evaporative distillation

There were unexpected high radiation levels in the salt water reticulation systems in some RAN vessels at Monte Bello. The source of the contamination is uncertain, and it is not clear if this would translate into significant levels in the drinking water produced by distillation.

Minor trials

A wide range of activities took place under the general umbrella of 'minor trials'. The most significant radiologically were the Vixen B trials, which simulated the accidental detonation of a bomb, and spread large quantities of plutonium into the environment. Other trials included the burning of plutonium in air, and explosive tests on uranium and other samples. It is almost impossible to estimate the doses from these trials without specific monitoring results.

These considerations have implications in retrospective dose assessment. This matter is discussed under 'Dosimetry' and 'Case–control study — Estimation of exposure'.

Health effects of ionising radiation

Ionising radiation has been linked with effects on health ever since the discovery of the X-ray in 1895. Firstly, the acute effects of high doses of radiation were discovered. Later, skin cancers, leukaemias and other cancers were found in high numbers in radiation workers (Doll 1995). A review by Sir Richard Doll described research, spurred on by nuclear testing, into the health effects of low doses of ionising radiation. The evidence shows that four effects are likely from doses less than those required to produce acute effects: mutations in germ cells, congenital defects from irradiation in utero, an increased rate of nonspecific ageing and an increased risk of cancer (Doll 1995). Studies of the epidemiology of cancer are impeded by the large sample sizes needed to detect differences in the rates of diseases that have a low incidence. The study of survivors of the atomic bombs in Japan has shown that exposure to ionising radiation is associated with excess risk for almost all types of cancer, particularly stomach, lung, liver, colon, bladder, breast, ovaries, thyroid, and skin cancer, as well as multiple myeloma and

leukaemia (Radiation Effects Research Foundation). Some types of cancer are particularly strongly associated with ionising radiation exposure, namely the acute leukaemias and chronic myelogenous leukaemia; no such association has been found with chronic lymphatic leukaemia (UNSCEAR 2000).

There is considerable difficulty associated with measuring the risk associated with exposure to radiation; notably, cancers may appear decades after exposure and do not manifest in any different way to cancers of spontaneous origin, so that they cannot be differentiated from them (UNSCEAR 2000). Nonetheless, there is evidence that ionising radiation can induce most cancers. For solid cancers, there is a linear dose–response relationship with exposure, with different levels of radiation sensitivity in different parts of the body (Ron 1998). Exposure at a young age and being female increase cancer risk (Ron 1998).

Much of the epidemiological information about the health effects of ionising radiation has come from studies of Japanese people who survived the atomic explosions in Hiroshima and Nagasaki during World War II. The prospective cohort study of these atomic bomb survivors conducted by the Radiation Effects Research Foundation in Hiroshima shows that survivors have an excess of cancer mortality; for leukaemia, this excess occurred in the first 15 years after exposure. This is in contrast to the excess for solid cancers, which is represented as a life-long elevation of the natural age-specific cancer risk (Pierce et al 1996). This study has also shown that noncancer mortality increases in survivors with increasing radiation dose (Shimizu et al 1999). The study also notes that the risk associated with exposure to radiation depends not only on the dose, but also on sex and age at exposure, with younger people faring worse (Pierce et al 1996).

A study of British radiologists found that there was an 'increasing trend in the risk of cancer mortality with time since first registration with a radiological society' (Berrington et al 2001). This was attributed to a long-term effect of exposure to radiation, and to the fact that exposures in the early days were more likely to have been greater than in recent times. There appeared to be no effect of radiation exposure on other causes of mortality (Berrington et al 2001). A similar study of radiologic technologists in the United States found increased risks of cancer for those employed before 1940; the risk decreased with later employment start dates, again probably reflecting higher exposures in the early days (Mohan et al 2003).

Other radiation workers, such as those employed in the nuclear power industry, have also been studied in depth for associations between exposure to ionising radiation and cancer. These studies are aided by accurate dose measurements because personal dosimetry is required in the industry for regulatory purposes. A Japanese study found no difference in mortality rates from cancer for nuclear industry workers compared with the general population, and found no dose–response relationship for most cancers. However, the average follow-up in this study was only 4.5 years, clearly not long enough to detect radiation-induced cancers (Iwasaki et al 2003). A Finnish study of nuclear workers also failed to find evidence for an association between radiation and cancer, or between cumulative radiation dose and cancer (Auvinen et al 2002). Similarly, a study of employees at the Chapelcross plant of British Nuclear Fuels found no evidence for an association between exposure to radiation and cancer (McGeoghehan and Binks 2001). A 1992 study using the United Kingdom's registry of radiation workers found evidence for an association between exposure to radiation and leukaemia that was consistent with dose measurements (Kendall et al 1992). A review using seven published epidemiological studies also found an increased risk of leukaemia in workers exposed to higher doses of radiation compared with those exposed to lower doses (Wilkinson and Dreyer 1991). A

further review combining data from the United States, the United Kingdom and Canada analysed 2 124 526 person-years at risk (Cardis et al 1995). This study found associations between radiation dose and risk of leukaemia and multiple myeloma, but no evidence of an association between radiation exposure and all-cause or all-cancer mortality (Cardis et al 1995).

Much research has also been conducted on the children of nuclear workers. Results from these studies vary markedly in their assessment of evidence for an association between parental employment in the nuclear industry and infertility, fetal death, congenital malformations and childhood leukaemia. A study into primary infertility in nuclear workers in the UK found no evidence for a link between employment in the nuclear industry and male infertility (Doyle et al 2001). A difference was found in infertility rates between monitored and nonmonitored (i.e. those presumed not to be at risk of radiation exposure) women employees, but it was not statistically significant, and the authors noted that the numbers were too small to draw any firm conclusions (Doyle et al 2001). Another study by the same group of authors found no association between paternal employment in the industry and miscarriage, stillbirth or congenital malformation, although it did find a slightly increased risk of miscarriage and stillbirth if the mother had been monitored for radiation exposure before conception, compared with unmonitored nuclear workers (Doyle et al 2000). The authors concluded that this evidence was not unequivocal and required further investigation. A study by Parker et al found an increased risk of stillbirth in Sellafield employees that was associated with exposure to ionising radiation before conception (Parker et al 1999).

Purported 'clusters' of leukaemia in the children of nuclear workers or those living in the vicinity of nuclear installations have been investigated. A case–control study by Gardner (Gardner et al 1990) found an association between increased incidence of leukaemia and non-Hodgkin's lymphoma in the children of men who worked at the Sellafield nuclear plant and who had a recorded external dose of whole body radiation before the child's conception. This finding was disputed by Kinlen, who proposed that leukaemia had an infective basis (Kinlen 1993, Kinlen and Stiller 1993). He suggested that population mixing, where there is an influx of new residents into small, isolated or new geographical locations, such as during the British 'new town' developments in the 1950s, could bring a range of new infections to the existing population. The theory of an infective basis for leukaemia could then explain the raised leukaemia incidence in these areas. This is consistent with Gardner's finding that the increased incidence of leukaemia was concentrated in the children born in the vicinity of the nuclear facility, not those who had moved to the location as children. There is no research providing evidence for an infective basis for leukaemia in adults.

There is also an association between radiation used for medical (diagnostic and treatment) purposes and cancer, particularly for children. Studies have shown increased risks of thyroid and breast cancer and leukaemia in children with increasing numbers of X-rays received for conditions such as scoliosis (Ron 1998). Likewise, there is a strong dose–response relationship between radiotherapy treatment for benign disease and thyroid cancer in children, but this relationship does not persist in adults (Ron 1998, 2002).

The accident at the nuclear power plants at Chernobyl in northern Ukraine in 1986 has led to a considerable amount of research about the effects of radioactive fallout on cancer rates. A review of these studies found evidence that rates of thyroid cancer in children have risen in areas affected by the accident (Moysich et al 2002). The evidence for increased rates of thyroid cancer in adults, however, is far less conclusive (Moysich et al

2002). There is little evidence to support an association between leukaemia and the Chernobyl accident in either children or adults (Moysich et al 2002).

Despite the limitations of the epidemiological studies on exposure to ionising radiation and cancer, there is scientific consensus that an association exists.

Investigations into the consequences of the nuclear weapons tests in Australia

The first Australian study into the health of nuclear test participants

In 1982, the first study of the health of Australia nuclear test participants was conducted by Donovan and colleagues (Donovan et al 1983). This study incorporated a postal survey of nuclear test participants and an analysis of cause of death.

The list of potential test participants was compiled by the Department of Resources and Energy, which collated names from all relevant sources (contemporary documents from Australian and UK government agencies, compensation claims, nuclear veterans' associations and other enquiries about the tests). Contact details for this list of participants were then acquired from various sources such as the electoral roll. Of 15 364 names on the original list, contact details were found for, and questionnaires issued to, 8255 participants. The questionnaire instructed recipients not to answer the questions about their health if they considered themselves to have been only indirectly involved with the tests; that is, if they '…never actually visited the area of the tests or any area affected by them (e.g. atomic clouds or fallout)' or they '… did work in these areas but left before any explosions'. Thus, participants were self-selected into the cohort. Respondents were asked about their work during the tests, if they felt they had been exposed to ionising radiation, and about a range of other health issues, such as general health perception, smoking habits and time spent in the sun. They were then asked if they had ever had cancer or other major illness, or if they had infertility problems. Respondents were also asked for consent to examine medical records, and for the details of doctors and hospitals where treatment had been received.

The response rate to the survey was around 80%. A total of 3870 respondents out of the 8255 who were sent questionnaires stated that they had not been involved in the tests. With other reasons for nonresponse, the final sample comprised 2536 respondents (about 30% of the original sample) who considered themselves to have been involved in the tests. The study examined the prevalence of the diseases of interest (cataract, malignant melanoma, other skin cancers, and other cancers) with 'radiation indicators', including tasks performed, use of health physics services for radiation protection, proven exposure from a film badge or dosimeter and the respondent's self-belief of exposure to radiation. There was no control or comparison group for this study — groups of people within the cohort were compared with one another according to the radiation indicators. Thus, it is impossible to assess whether the nuclear test participants had an excess of the diseases of interest compared with the general population or populations of other workers (to account for the healthy worker effect). Numerous comparisons (i.e. comparison of each radiation indicator with the outcomes) also increased the likelihood of finding significant associations by chance. Moreover, the study concentrated on the differences between groups of test participants that had been identified through official records and those who had self-identified. All of these factors make the results difficult to interpret.

There were some additional limitations to the study. Entry into the study itself relied on the participant's perception of whether or not they were 'involved in the tests', which is not necessarily a good indicator of whether or not they were exposed to ionising

radiation. For some respondents, the study team made a decision on whether the questionnaire should be reissued because exposure seemed likely. This process was likely to be open to bias because it was based on the limited information given by the respondent. Likewise, respondents who had developed conditions that they perceived to be related to radiation exposure may have been more likely to have indicated that they were involved in the tests, and more likely to believe they had been exposed to radiation. The reliance on self-report of the conditions of interest is also a weakness. Only a small proportion of the cases could be medically confirmed, although these cases were found to have a high degree of verification, giving the authors confidence in the self-reported diagnoses.

The study found no conclusive associations between radiation indicators and outcomes; even associations found to be significant — for example, between decontamination duties and malignant melanoma — could be explained by other information. Conclusions about other cancers, other health outcomes and radiation exposure could not be drawn due to the lack of appropriate information. The authors concluded that the limitations of the study were such that no conclusions could be drawn about the health effects of participation in the British nuclear testing program.

The Royal Commission into British nuclear tests in Australia

In 1984, The Honourable James McClelland was charged with leading the Royal Commission into the British nuclear tests in Australia (McClelland et al 1985). The role of the commission was to examine:

> The measures taken during the tests to protect against ionising radiation;
>
> If said measures were adequate; and
>
> If the health of Australian participants was adversely affected by exposure to ionising radiation.

The commission heard testimony from some 311 witnesses and examined a massive amount of documentation, including written statements from witnesses and documentation from the UK and Australian governments(McClelland et al 1985). The process took just over a year, an amazing feat for a project of this size, and is reported in three volumes published in 1985.

The commission examined each operation individually and found many instances of improper practice (see the description of the British nuclear testing program above). In particular, it highlighted the insufficient measures and the cynical and chaotic approach taken to protecting the Aboriginal inhabitants of the area from exposure to radiation (McClelland et al 1985). It also brings into question the relationship between the British and Australian governments, as it appears that the Australian Government was excluded from knowledge of important aspects of the tests.

The commission concluded that a register of participants (the nominal roll) should be established and that the test sites should be cleaned and made fit for habitation by the traditional Aboriginal owners.

The study of mortality and cancer incidence in British test participants

The first follow-up study of the British participants in the Australian (and Pacific Islands) nuclear testing program was published in 1988 by the UK National Radiological

Protection Board, with follow-up to 1983 (Darby et al 1988). The study was reported with follow-up to 1990 (Darby et al 1993) and again with follow up to 1998 (Muirhead et al 2003). This study compared 21 357 test participants with 22 333 comparison subjects on mortality rates from particular cancers and from all causes, and on cancer incidence. Test participants were service personnel in the Royal Navy, Royal Air Force and Royal Army or other military units, and civilians working for the Atomic Weapons Establishment (AWE) or the Atomic Energy Research Establishment. Comparison subjects were servicemen who had served in tropical and subtropical locations but had not taken part in the tests; civilian controls were other employees of the AWE.

All-cause mortality and cause-specific mortality were compared with the population as a whole and between the study and comparison groups. In the overall follow-up, the study found no difference in deaths from all causes between study and comparison groups (relative risk [RR] 1.01; 90% confidence intervals [CI], 0.98 to 1.05). Both study and comparison groups had lower standardised mortality ratios than the population as a whole (89 for test participants and 88 for comparisons). However, deaths from accidents and violence were higher than in the general population for both study (SMR 121) and comparison (SMR 116) populations, although there was little difference between these two groups (RR 1.07; 90%CI, 0.95 to 1.21). There was no difference between the study and comparison groups for mortality from all cancers (RR 1.01; 90%CI, 0.96 to 1.08), and SMRs for all cancers were again lower in both groups (93 for test participants and 92 for comparisons). The exception was leukaemia excluding chronic lymphatic leukaemia (CLL appears to have no association with ionising radiation, see above), for which mortality was higher among test participants (RR 1.83; 95%CI, 1.15 to 2.93). Mortality rates differed over time; there was a statistically significant excess of leukaemia and bladder cancer in the participants compared with the comparison group followed up until 1990, but those differences did not exist in the follow-up from 1991–98. In fact, most differences found between the study and comparison groups in the earlier follow-up were not found in the follow-up from 1991–98.

The incidence of all cancers did not differ between the study and comparison groups (RR 0.99; 90%CI, 0.94 to 1.03). The only cancers to show significant overall differences in incidence rates between the test participants and controls were liver cancer (RR 1.99; 90%CI, 1.19 to 3.38) and prostate cancer (RR 1.22; 90%CI, 1.04 to 1.43). The incidence of non-CLL leukaemia in the period 2–25 years after test participation was significantly higher in test participants (also reflected in the mortality statistics), with the overall RR 3.17 (90%CI, 1.73 to 9.61). This relative risk was less over the subsequent follow-up period (RR 1.33; 90%CI, 0.97 to 1.84). For the entire follow-up period, the relative risk for non-CLL leukaemia was not significant (RR 1.33; 90%CI, 0.97 to 1.84). There was no evidence of increased cancer risk in subjects with a recorded dose of external radiation (n = 2264), or of a trend towards increasing risk with increasing gamma dose. Other analyses of subjects identified as liable to exposure to radiation found no clear evidence of raised leukaemia rates.

The authors concluded that the possibility that test participation had caused a small increase in risk of non-CLL leukaemia couldn't be ruled out, with the evidence suggesting that the risk was greatest in the early years after the tests.

The study of New Zealand participants in the British nuclear tests

New Zealand naval personnel were involved in the British nuclear testing program in the Pacific during the 1960s, and a follow-up study similar to that of the British participants has been conducted (Pearce et al 1990, 1997). In the follow-up to 1992, the study found

no significant difference in mortality rates from all causes (RR 1.1; 90%CI, 0.9 to 1.3) or from all cancers (RR 1.2; 90%CI, 0.8 to 1.7) between test participants and controls. Similarly, there was no difference in the incidence of cancer (RR 1.0; 90%CI, 0.8 to 1.4). However, there was an increase in haematological cancers, including leukaemia, in the test participants (RR 3.8; 90%CI, 1.4 to 10.8). The authors concluded that there is evidence for a link between haematological cancers and test participation, but no association with other cancers, and noted that the study was based on a small number of participants (528 men) (Pearce et al 1997).

The study of US servicemen involved in nuclear testing

The United States also tested nuclear weapons, on their home soil in the Nevada desert and in the Pacific, between 1945 and 1963. The Five Series Study followed up some 70 000 of the 200 000 US military personnel involved in the tests (Thaul et al 2000). These 70 000 servicemen participated in at least one of five tests selected for the study; the tests represented both the Nevada and Pacific sites used for the testing. Test participants were compared with controls who were of equivalent military employment, in terms of branch of service, time of active military duty, type and general location of assigned unit, age and paygrade (Thaul et al 2000). No exposure assessments were made. The study found no statistically significant difference between the test participants and the comparison group for all-cause mortality rate, cancer mortality rate or leukaemia mortality rate. The rate of leukaemia mortality was elevated in the test participants group, but the difference did not reach statistical significance; the authors noted that the study cohort was too small to find the observed risk statistically significant (Thaul et al 2000).

Aims

The study aims are to:

- compare the mortality of test participants with that of males of the same age in the general population
- compare the cancer incidence of test participants with that of males of the same age in the general population
- identify any association in test participants between the incidence of specific cancers and mortality from specific causes of death and estimates of their exposure to ionising radiation in the nuclear testing program.

Study design

(i) Retrospective cohort study, comparing mortality and cancer incidence of test participants with that of the Australian male population.

(ii) Within the cohort of participants, comparing mortality and cancer incidence in those considered likely to have been exposed to ionising radiation with that in those considered unlikely to have been exposed.

(iii) A case–control study nested within the cohort of participants, to measure the association between the incidence of and mortality from leukaemia (other than chronic lymphocytic leukaemia) and exposure to ionising radiation, using more detailed dosimetry measures than those used in the cohort study.

Consideration was given to analysis of a comparison cohort of servicemen and civilians employed at the same time as the period covered by the testing program. The benefit perceived from such a comparison group would be the avoidance of a 'healthy worker effect', which can occur when comparing mortality of a cohort of working persons with the mortality of the general population. The latter includes many people unfit for employment, and this has been suggested as a cause of a higher overall death rate in the total population than in the working population.

However, there are a number of reasons why the additional time and cost of assembling a comparison cohort would be unlikely to enhance the proposed cohort study:

- The cohort analysis will include internal comparisons of subgroups with different categories of estimated radiation exposure. Such comparisons will not be influenced by any healthy worker effect.
- The proposed nested case–control study will also be devoid of any healthy worker effect.
- There is evidence that the healthy worker effect diminishes with time, so that the age-standardised mortality rate of occupational cohorts converges towards that of the general population as cohorts age; this is likely with this cohort, which closed in 1965.
- While there is good evidence of a healthy worker effect for all causes of death combined and for major categories of cause of death, the evidence for such an effect for leukaemia is limited.

In addition, after careful consideration of the options for selecting such a comparison group, it was felt that it would be very difficult to identify and study a group that could be considered to replicate the test participants in all respects except for test participation. Therefore, it was decided to restrict the study to the cohort of test participants, and where external comparisons are made, to make them with the general population of the time.

Study population

The nominal roll

The nominal roll of Australian participants in the British Nuclear Test Program in Australia is the source population for this study. It was initially compiled by the Department of Veterans' Affairs (DVA), from the following sources (DVA 2001):

- Department of Defence records
- records of private firms engaged for the purposes of supporting and conducting the tests
- Maralinga Security Cards issued by the Commonwealth Police
- documents supplied by the organisations of nuclear veterans
- the report of the 1985 Royal Commission into Atomic Testing.

The listing of a name in these documents does not necessarily guarantee that the individual was in fact present at the nuclear tests; rather, it is an indication that they either were there or had plans to go, or that provision had been made for them to go if it was

deemed necessary (for example, in the case of military police). There is no feasible way that actual presence at the tests could be verified for all people identified by these lists.

In addition, while the nominal roll was being compiled, individual members of the public could telephone an 'Atomic hotline' and identify as participants. As a result of these calls, certain additions and deletions to the nominal roll were made. Generally, if participation could be confirmed in the service records of the individual, they were added to the nominal roll.

Names on the roll were checked against the list of radiation-exposed personnel compiled by JR Moroney in the Australian Radiation Laboratory document, 'Personal monitor records from exposure to beta and gamma radiation during engagement in the program of British nuclear weapons tests in Australia', dated 10 December 1984. Where the name of an Australian Defence Forces member from the list in the Australian Radiation Laboratory document was not found on the roll, and it could be verified against Department of Defence records, it was added to the roll. Where a name from that list could be confidently matched with a record already on the roll, additional identifying personal details from that list were included on the roll.

The Australian Radiation Laboratory document's list includes the lists of participants contained in the following documents:

- the British Government's 'Listing of persons at UK overseas defence nuclear experimental programmes, citizens of Australia' (the 'Blue Book')
- Australian Health Physics listing of radiation exposure at Maralinga, prepared by the Department of National Development and Energy during 1981
- 'Radiological health during Operation HURRICANE (Monte Bello Is. October/November 1952) and Operation TOTEM (Emu Claypan, SA October/November 1953)', Minute, 1 December 1953 to Director General Medical Services (RAAF) from Sqn. Ldr. AD Thomas (Scientific Advisor to the Chief of the Air Staff).

Validation of the nominal roll

Experience from the UK study suggests that the nominal roll may not have identified all subjects eligible for inclusion. Information obtained from sources such as veterans' organisations has identified some participants who were not included on the initial roll. To estimate the completeness of information obtained from official documents, where possible, the information from the nuclear veterans' organisations will be reviewed, to obtain a count of:

(i) veterans who were already on the nominal roll derived from service records

(ii) those not on the list who were not on the nominal roll but who were subsequently found from service records to have been a participant as defined.

The proportion of (i) to (i)+(ii) gives an indication of the completeness of information from service records. The experience of the UK study was that identification was complete for the Navy but only about 80% for the Army and Air Force.

Compiling the study population

The nominal roll will be the starting point for the compilation of the study population. Certain groups from the source population are not eligible to take part in this study; the exclusion of these groups is not based on radiation exposure or outcome (see flow chart at Figure A1.2).

The ineligible groups are:

- those outside the study domain — pastoralists, indigenous people, and females
- those for whom information is inadequate for follow-up (e.g. no date of birth, gender or not enough detail in the name)
- certain contract employees from Kwinana who left test sites before the first explosion, except for any who may have returned later
- RAAF ground crew known not to have been involved in aircraft decontamination or maintenance.

Some people on the nominal roll were added to the roll after self-reporting or as a result of advice from nuclear veterans' associations. These subjects fall into three categories:

(i) those who at the time of notification were found to be on the nominal roll already (i.e. they had already been included from the search of official documents)

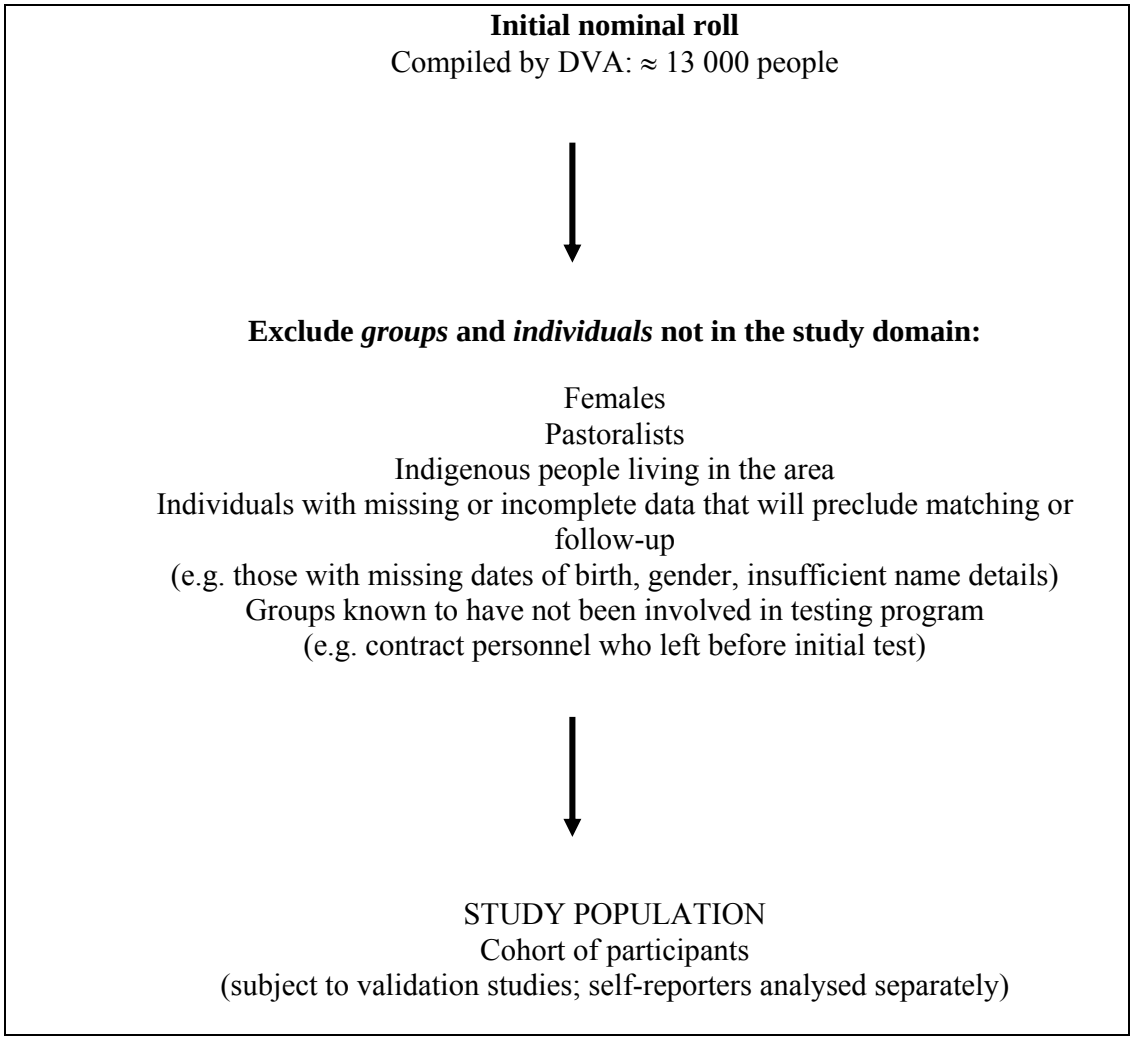
(ii) those who were found not to be on the roll, but whose presence at a test site was found, *after notification*, to be officially documented (these subjects' names were then added to the roll)

(iii) those who were not on the roll, and whose presence at a test site could not be verified from service or other records.

Inclusion in the study population must not be related to the outcomes of interest to the study, and there is a chance people in group (ii) may have self-reported because they have illnesses they believe to be associated with ionising radiation. Thus, their inclusion could be related to an outcome. The UK study indicated that self-reporters have a higher SMR for cancer than the test participants as a whole, suggestive of a voluntary reporting effect (Muirhead et al 2003). Thus, as in the UK study, participants from group (ii) will be included in the study, but analysed as a separate group.

Although a large number of sources have been searched for nominal roll membership, it is quite possible that some more participants not already on the roll will be identified as the study proceeds (for example, if lists of participants become available through searches of exposure documentation). If it can be assured that the circumstances leading to the inclusion of participants are not related to outcome they will be included in the study population. However, any new additions to the study population may only be made before follow-up begins; that is, before the cohort is submitted to the National Death Index (NDI).

Figure A1.2 Formation of the study population



Dosimetry

There are limitations on the capacity to make valid estimates of radiation exposure:

- Only a minority of personnel were issued with film badges, and it is believed that some were not processed or the results are missing.
- Film badges were not as sensitive as they are now.
- Records of exposures are situated at a number of different locations, and some have not been examined or cannot be obtained, such as records in the UK.
- No estimates of internal exposure have been attempted, and it seems unlikely that sufficient monitoring and other information will be available for these to be made, particularly on an individual basis.

Accordingly, it is proposed that exposure categorisation be limited to *likelihood* of radiation exposure. This still does not avoid the need to define a lower limit, since it is possible that much of the population of Australia received some exposure from the tests. Exposure of less than 1 mSv from the testing program is suggested as constituting

negligible exposure. This level is comparable with the annual background exposure in the population.

'Radiation exposure' will thus be defined as follows:

> Any exposure to ionising radiation, either internal or external, estimated to be of a level of 1mSv or greater, from involvement in the testing program.

Estimates of radiation exposure will be made by a scientific panel with expertise and experience in radiation dosimetry, using records of dosimetry, health physics and meteorology.

Estimates will not be made for individuals, since, in most cases, the quality of the data would not justify the level of effort required to generate individual estimates, if it is possible at all. Instead, categorisation will be made according to groups defined by variables, or combinations of variables, in the nominal roll.

Within the constraints of the available data, the panel will assign the cohort algorithmically into the following exposure categories:

> Unlikely to have been exposed or received negligible radiation exposure
> Likely to have been exposed
> Unknown

The panel will also consider the feasibility of classifying the category 'likely to have been exposed' into high and low exposure categories.

The cohort will also be divided into the following categories:

> Participants with a recorded dose of radiation
> Participants with no recorded dose of radiation

The variables of interest in the nominal roll for assigning a probability of exposure are:

> Service
> Start date
> End date
> Rank
> Unit
> Area
> Job

In assigning category of likelihood of exposure to any combination of these variables, consideration will be given to whether:

(i) personnel were close enough to a detonation to receive a prompt dose of external radiation

(ii) personnel entered a zone contaminated by fallout or activation products after the blast or handled contaminated materials or were involved in decontamination and therefore potentially exposed to external and/or internal radiation

(iii) neither of the above applied.

Follow-up

Ascertainment of vital status

Follow-up will be undertaken to the cut-off date 31 December 2001, or the latest date that the National Death Index is complete at the time of matching (if later than 31 December 2001). This will proceed as set out in Table A1.1. Consideration should be given to whether Stages 4 and 5 should be reversed. Stage 4 should be undertaken first, provided that it can be completed reasonably quickly.

In each case, the cohort data file will be submitted to the relevant authority and matched according to its matching routine. Where there is a high degree of confidence in matches, they will be entered electronically. Where matches are less certain, the Australian Institute of Health and Welfare (AIHW) will be asked to re-run these using their own matching routines. AIHW has more experience in this field and its routine may be able to detect matches with greater certainty than that of the Australian Electoral Commission (AEC), for example.

Where there is still doubt over matches, further details will be sought on a case-by-case basis. Methods used will include:

- seeking corroborative information from other files, e.g. a death recorded by the NDI will be checked against the DVA record if the subject is a service pensioner, or searched in the output of the electoral roll search
- seeking further information from subjects' service records
- obtaining the death certificate
- contact with next-of-kin.

Final decisions on such matches will be made by consensus of members of the study team.

Coding of cause of death

Causes of death obtained from the NDI are coded in ICD-9 up to 1996 and in ICD-10 thereafter.

Death registrations before establishment of the NDI will be obtained from state registries. Causes of death for each year will have to be coded in the same ICD version as the coding used by the Australian Bureau of Statistics for national death tables for the corresponding year. The appropriate codes are:

ICD-6	1950–1957
ICD-7	1958–1967
ICD-8	1968–1978
ICD-9	1979–1996

The coding will be done by the National Centre for Classification in Health, in Brisbane.

Table A1.1 Ascertaining vital status

	Match	To	Classify
Stage 1	Study population	Department of Veterans' Affairs database	ALIVE if last contact post 31/12/01. DEAD if death recorded, subject to confirmation in NDI or state death registry. EXCLUDE if found to be receiving a Service Pension or Disability Pension overseas.
Stage 2	Study population	National Death Index	DEAD if found on NDI.
Stage 3	Study population minus those classified as DEAD or ALIVE in stages 1 and 2 but retaining uncertain matches	Australian Electoral Roll	ALIVE if found on roll.
Stage 4	Study population minus those classified as DEAD or ALIVE in stages 1–3	Health Insurance Commission (depending on logistics, time constraints, etc)	ALIVE if have used health services since 31/12/2001.
Stage 5	Study population minus those classified as DEAD or ALIVE in stages 1–4	Data on payment of pensions by Centrelink. Movement records of DIMIA. Commonwealth and state superannuation funds. Overseas (UK and NZ) databases, including death registries, census, electoral rolls and the NHS in UK.	EXCLUDE if overseas (dead or not). ALIVE if still receiving pension or superannuation.
Stage 6	Study population minus those classified as DEAD or ALIVE in stages 1–5	State death registries	DEAD if found on registries.
Stage 7	All as yet unclassified	National Death Index and Australian Electoral roll	Classify if possible; otherwise lost to follow-up.

Ascertainment of cancer incidence

The cut-off date for incident cancers will be 31 December 2000, or, if the National Cancer Statistics Clearing House (NCSCH) is complete in time, 31 December 2001. Incident cancers will be obtained from the NCSCH by AIHW in an aggregated format without identifying individuals. Information on radiation exposure, as estimated by the exposure panel, will have been merged with the cohort data file by the Department of Public Health for the purpose of the mortality analysis. The radiation exposure information fields will be used by AIHW to supply aggregated, de-identified data on cancer by site, 5-year age group, year of cancer registration, and estimated radiation exposure. This will negate the need for individual consent from subjects with cancer who are still alive. Expected cancer rates will be derived from publicly available data on site-specific cancer rates by age, gender and year of diagnosis, and from person-years of follow-up. Thus standardised incidence ratios can be generated without the need to obtain identifiable cancer registrations.

The NCSCH will provide aggregated data on all cancers excluding non-melanocytic skin cancer, back to 1983. All cancers will be coded in ICD-10.

Analysis — cohort study

Enumeration of follow-up time

Person-time for each participant will commence on the day of the first detonation attended after arrival at the test site, which is given in the nominal roll. If a participant first attended a test site after a detonation, his person-time of observation will commence on the day of arrival. If the date of entry to the cohort is unknown, an estimate will be made based on information in the nominal roll or, if there is too little information to estimate date of entry, the median date of entry to the cohort will be assigned.

For RAAF ground crew involved in aircraft decontamination and maintenance, person-time will begin on the first day of performing the task. If this cannot be ascertained, commencement date will be the date of the relevant detonation.

The censoring of person-time will be as follows:

> If person died in Australia before 31 December 2001, censor at date of death
> OR
> If vital status unknown, or if known to have moved or died overseas, censor at date of emigration (if known) or the date of last known contact in Australia
> OR
> If alive and in Australia at or after 31 December 2001, censor at 31 December 2001
> OR
> Censor at 85th birthday.

Cutoff dates for person-time will be the same for the mortality and cancer incidence studies. Subjects' person-time in the cancer incidence study will not be censored from the date of cancer registration because a second or even a third cancer may occur later.

Mortality

National mortality data, stratified by 5-year age group, for each year since the first detonation at Monte Bello, will be obtained from AIHW.

Standardised mortality ratios (SMRs), adjusted by age and calendar year of occurrence by 5-year groupings, will be generated by comparison of mortality with national rates. Observed numbers of deaths by major cause are compared with the expected number derived from applying national rates to the person-years at risk. Exact 95% confidence intervals will be calculated; these do not rely on large numbers for validity. Tests for constant SMR across several categories will be carried out using Poisson regression.

In addition, internal comparisons will be made within the cohort between categories of exposure to ionising radiation. The comparisons will be made by generating relative mortality ratios (RMRs) for selected causes of death considered to be of interest. Mortality rates for each exposure category will be compared with the unexposed category, adjusting for age and calendar year of follow-up

Internal comparison will also be undertaken between participants with a recorded non-zero dose of external radiation, participants issued with a film badge but with a recorded dose of zero or whose exposure was unknown, and participants not issued with a film badge.

To allow for uncertainties in latency, estimates will be made of variation in mortality rates with time since first exposure. Person-years of follow-up for each subject will be categorised and aggregated in the categories 0–10, 10–20 and 20+ years since date of admission to the cohort. The number of cause-specific deaths occurring in each category will be used to derive RMRs for each category, adjusting for age and calendar period of follow-up. The RMRs will be relative to the 0–10 year category, which will be assigned an RMR of 1.0. (Thus this computation does not involve use of an external population for comparison.)

Cancer incidence

The same methodology will be used to study cancer incidence, generating standardised incidence ratios (SIRs) for all cancers combined and for all major cancer types. SIRs will be generated for both the complete cohort of participants and the exposed subset. Data on incident cancers will be provided to the study team in an aggregated format. The data will give number of cancers by site, year of birth, year of diagnosis and category of estimated radiation exposure.

Relative incidence rates will be computed in similar manner to relative mortality rates. Incidence rates for each exposure category will be compared with that of the unexposed category, adjusting for age and calendar period of follow-up. The number of cancers in each stratum will be obtained from the de-identified, aggregated cancer registry data.

Confounding

Potential confounders for the cancer incidence study include smoking and service in other theatres of war — World War II, Korea, Malaysia and Vietnam.

The effect of smoking cannot be obtained because smoking data for the cohort are not available, nor are smoking data for the comparison Australian population. If an excess of a smoking-related cancer is observed, it may be possible to estimate the contribution of smoking from other smoking-related cancers or causes of death (e.g. laryngeal cancer, chronic respiratory disease).

Available information suggests that there is an excess of some cancers in Korean veterans. If an excess of any such cancers is found in this cohort, and if the excess cancers in the Korean veterans are believed to be related to war service, a sensitivity study will be made to to determine whether confounding by service in Korea could be responsible for the excess. However, a cohort analysis stratified by service in Korea will not be possible, because cancer registrations linked to such war service will not be made available (due to the decision of the ethics committee of AIHW).

Service in Vietnam could possibly cause excess cancer from exposure to Agent Orange. This mixture consisted of phenoxyacetic acid herbicides, which are suspected to cause soft tissue sarcoma and non-Hodgkin's lymphoma. Again, this possible confounder will need to be considered if these cancers occur in excess, but a stratified analysis will not be possible. The same considerations apply to dioxin exposure. Dioxin was a contaminant in Agent Orange, and has the potential to cause excess of all malignancies in total.

The question of service in World War II is considered below in relation to the case–control study.

Case–control study

The cohort study is limited, in that accurate exposure measurements, in the form of individual dosimetry, are not possible. However, a case–control study nested within the cohort could be done, as there would be fewer subjects to which an exposure estimation would be assigned. Thus, it is practical to invest time and resources in attempting individual dosimetry within a case–control study.

Scope

Since leukaemia is the primary disease of interest in radiation-exposed persons, it will be the primary outcome of the case–control study. The disease rubric of interest is likely to be the grouping of all leukaemias excluding chronic lymphocytic leukaemia (CLL), which is believed to be unassociated with radiation.

It is uncertain, at present, which other cancers or causes of death, if any, will be the subject of a case–control study.

If there is evidence of a possible association between radiation exposure and other types of cancer (i.e. a statistically significant difference in mortality or incidence of disease between exposed and unexposed groups), a decision will be made on a case–control study of those cancers also, using the same controls.

A case–control study of leukaemia deaths, by definition, excludes not only those leukaemia cases where the subject has not died at the cut-off date, but also those in which the subject died of an unrelated disease, and hence leukaemia was not recorded as the primary underlying cause of death. Moreover, the diagnosis is subject to the knowledge of the certifying doctor of the history of the deceased, which is often imperfect, so that the diagnosis is prone to inaccuracy, especially as to the type of leukaemia.

A case–control study of incident cases of leukaemia would be based on cancer registrations, which usually have all the required detail to enable coding. It will avoid all the disadvantages of a mortality study, but has the great disadvantage of only including cancers registered since the establishment of cancer registries, mostly in the late 1970s or early 1980s. This has a particular disadvantage when leukaemia is the disease under consideration, since radiation-induced leukaemia is considered to have a short induction-latency period in many cases; leukaemias occurring in the participants' cohort before the late 1970s will therefore be missed.

It is therefore proposed that the cases will include all leukaemias, whether identified from cancer registrations or from death registrations. It is likely that incident leukaemia cases identified from cancer registrations will include all those dying since the establishment of the cancer registries whose cause of death was certified as leukaemia. Although data on incident cases of leukaemia before establishment of the cancer registries will not be available, in practice most cases will be identified from death registrations, since leukaemia was usually a fatal disease in the 1950s and 1960s.

Design

The study will be an incidence-based case–control study of leukaemias excluding CLL, with death from leukaemias excluding CLL as a surrogate for incident cases before the establishment of state and territory cancer registries.

The study will be nested within the cohort of participants, and the exposure of interest will be ionising radiation from any source.

Identification and coding of cases

Cases will be all registered cases of leukaemia except CLL. Details of the pathology reports of all leukaemia cases will be sought from the state and territory cancer registries. Death certificates will be obtained for all deaths before the establishment of cancer registries, and all subjects with leukaemia recorded will be included, irrespective of whether it is recorded as the underlying cause of death.

Controls

Four controls will be selected per case by incidence-density sampling, i.e. each participant will have a relative probability of being selected in proportion to his relative contribution to the total person-time of observation of the cohort. Controls will also be matched by age (within 3 years) to cases.

Each case and its age-matched controls will form a risk set. The controls will be selected from all cohort members who were eligible to become cases at the time of diagnosis of the corresponding case. The date of diagnosis will be taken as:

- For incident leukaemia cases in the NCSCH — the date of registration
- For cases based on leukaemia reported in death certificates (whether or not it is cited as an underlying cause of death) — an estimate of the date of onset from the death certificate entry on the duration of the disease. Where duration is not given, the date of diagnosis will be taken as one year before death of the subject.

All cohort members eligible to be controls, after age-matching, on the date of diagnosis of the corresponding subject will be identified, and 4 controls will be randomly selected. Cohort members who have already developed leukaemia, or who have died or been lost to follow-up on the date of diagnosis of the case, will be ineligible as controls. A subject selected as a control who subsequently develops leukaemia will be retained as a control (i.e. he will be a case and a control). A subject randomly selected more than once can be retained as a control more than once.

Estimation of exposure

The considerations discussed above have implications for dose reconstruction.

Those who were not within approximately 5 km of a detonation, and who did not subsequently go into an area contaminated by fallout or neutron activation, would not have received any significant dose. It is likely that there were very few personnel within this sort of range at detonation, and that any who were would almost certainly:

- be under cover — at least to provide protection from blast, etc — and this would have reduced doses
- be monitored; even if only a few of a particular group were monitored, this would give an excellent guide to the external doses of all concerned.

To estimate the external doses to those in fallout or activation product zones, information would need to be known on:

- location in relation to those zones
- time spent in location
- the time that had elapsed since the explosion.

To estimate the internal doses in fallout or activation product zones, the above information would be required, and in addition:

- the type of activities undertaken and their potential for dust generation
- the particular radionuclides involved; this can probably be estimated from the time since detonation.

These doses could only be realistically estimated if adequate monitoring data exists.

Estimates of radiation exposure will be undertaken by the same scientific panel as for the first round of estimates made for the cohort study. Exposure estimates will be made for each individual case and control. The panel will be blinded as to the case or non-case status of each subject, and nobody with knowledge of the identity of any cases may be a member of the panel. Information provided to the panel about each subject must have all information deleted that might indicate whether the subject is a case or a non-case.

The panel will attempt an estimate of cumulative exposure from all tests and test sites for each subject. The estimate will include both internal and external irradiation. It is unlikely that the panel will be able to estimate the total exposure of many subjects, and the estimates may therefore need to be made in categories for both probability of exposure and cumulative exposure; for example, 'probably exposed', 'possibly exposed' and 'unlikely to have been exposed', and <5 mSv, 5–20 mSv, and >20 mSv.

The panel will make estimates by consensus, and document the basis for estimates in each case. Within-panel reliability will be measured by resubmitting a sample of subjects to the panel for a repeat exposure estimate, and measuring concordance.

Statistical analysis

Log odds ratios will be generated by conditional logistic regression. Analyses will be undertaken with varying assumptions of induction latency periods.

For controls, only exposure occurring up to the time of diagnosis of the corresponding case will be deemed as exposure.

Confounding

Participants who served in Japan after the end of World War II could have incurred exposure to ionising radiation. It may be possible to measure the effect of confounding from this source; when the cases and controls names are sent for assessment by the exposure panel, DVA will be requested to identify any individuals who served in Japan and who may have been exposed to fallout from the two atomic bombs.

Statistical power

If there are 40 cases, with 4 age-matched referents per case, α-value = 0.05, using one-sided testing, $\beta = 0.2$, and 25% of referents exposed to radiation, the minimum detectable true relative risk of leukaemia (other than CLL) due to ionising radiation would be 2.5.

Confidentiality

DVA will provide the Department of Public Health (DPH) with the list of study participants, based on the exclusions outlined under 'Compiling the study population'. This file will contain the names, date of birth, branch of armed services, rank, occupation, test site, and date of entry to test site. This file will then be submitted to AIHW for matching against the NDI, and to the other agencies outlined in Table A1.1.

DVA, through the exposure panel, will supply information on the probability of radiation exposure (as described under 'Dosimetry') of participants and DPH will add this information to the study participant file. The file of participants will then be forwarded to AIHW for a search of the NCSCH. AIHW will then supply aggregated data for analysis. The aggregated data will include the year of birth, exposure probability, type of cancer, year of cancer diagnosis, state or territory where the cancer was registered, and, where relevant, date and cause of death. As the data will be in an aggregated format, from which individuals cannot be identified, consent need not be sought from individuals for use of their cancer registration data.

For the case–control study, we will compile a list of leukaemia cases and 4 age-matched controls per case from the original dataset that they hold (before it was aggregated for use in the cohort analysis). We will remove information relating to case–control status, and submit the file to DVA for detailed estimation of radiation exposure, which will be undertaken by an expert panel of health physicists. DVA will require names and dates of birth so that the service record of each military subject can be searched. DVA and the exposure panel will therefore know that 20% of these subjects will have leukaemia, but they will not know which ones they are.

Information about living individuals cannot be released from the cancer registry without their consent. Thus all living cases (expected to total <10 people) will be approached for permission to access the information contained in the cancer registry. Before subjects are approached, the treating doctor will be consulted. Consent is not required from the case subjects who are dead, or the control subjects for whom the cancer registry does not need to be searched. Any subject who refuses permission to access their cancer registration data will be excluded from the case–control study.

The panel will assign and enter the exposure estimate for each subject, and DVA will submit the estimates to the study team. We will restore the record, indicating which subjects are cases and which are controls, and the analysis will proceed.

Ethics approval for these procedures has been granted by AIHW, the University of Adelaide, DVA and the Department of Defence. If it becomes necessary, further ethics approval will be sought from the other Commonwealth agencies providing information to the study.

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Appendix 2 Mortality results including Method 2

Table A2.1 All causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the cohort and selected groups within the cohort

		Method 1			Method 2		
Group	Observed	Expected	SMR	95%CI	Expected	SMR	95%CI
Whole cohort	4233	4150.4	1.02	0.99–1.05	4802.8	0.88	0.86–0.91
Service category							
Military	2714	2662.3	1.02	0.98–1.06	2778.3	0.98	0.94–1.01
Civilian	1519	1487.8	1.02	0.97–1.07	2024.6	0.75	0.71–0.79
Service category, military							
RAN	1173	1026.4	1.14	1.08–1.21	1083.7	1.08	1.02–1.15
Army	510	477.3	1.07	0.98–1.17	504.1	1.01	0.93–1.10
RAAF	1031	1158.6	0.89	0.84–0.95	1190.5	0.87	0.81–0.92

Table A2.2 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the cohort

		Method 1			Method 2		
Cause of death	Observed	Expected	SMR	95%CI	Expected	SMR	95%CI
All cancers	1465	1238.7	1.18	1.12–1.24	1422.7	1.03	0.98–1.08
Ischaemic heart disease	1107	1229.4	0.90	0.85–0.96	1428.5	0.78	0.73–0.82
Cerebrovascular disease	243	282.4	0.86	0.76–0.98	336.4	0.72	0.63–0.82
Respiratory disease	325	310.6	1.05	0.94–1.17	367.5	0.88	0.79–0.99
Chronic obstructive pulmonary disease[a]	198	198.7	1.00	0.86–1.15	236.8	0.84	0.72–0.96
Nervous system disease[a]	59	57.8	1.02	0.78–1.32	68.1	0.87	0.66–1.12
Motor neurone disease[a]	16	12.9	1.24	0.71–2.02	14.7	1.09	0.62–1.77
Digestive diseases[a]	137	144.3	0.95	0.80–1.12	164.5	0.83	0.70–0.98
Alcoholic liver disease[a]	42	47.1	0.89	0.64–1.21	51.9	0.81	0.58–1.09
Cirrhosis[b]	30	30.1	1.00	0.67–1.42	33.5	0.90	0.60–1.28
External causes of injury and poisoning	281	320.5	0.88	0.78–0.99	352.9	0.80	0.71–0.90
Suicide	32	90.6	0.35	0.24–0.50	99.6	0.32	0.22–0.45

a Data available from 1968 onwards
b Data available from 1979 onwards

Table A2.3 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the military participants

		Method 1			Method 2		
Cause of death	Observed	Expected	SMR	95%CI	Expected	SMR	95%CI
All cancers	953	814.4	1.17	1.10–1.25	849.6	1.12	1.05–1.20
Ischaemic heart disease	723	766.0	0.94	0.88–1.02	799.2	0.91	0.84–0.97
Cerebrovascular disease	145	170.5	0.85	0.72–1.00	178.7	0.81	0.68–0.95
Respiratory disease	193	192.2	1.00	0.87–1.16	201.4	0.96	0.83–1.10
Chronic obstructive pulmonary disease[a]	125	122.1	1.02	0.85–1.22	128.0	0.98	0.81–1.16
Nervous system disease[a]	43	37.2	1.16	0.84–1.56	39.0	1.10	0.80–1.48
Motor neurone disease[a]	8	8.6	0.93	0.40–1.84	9.0	0.89	0.39–1.76
Digestive diseases[a]	83	96.1	0.86	0.69–1.07	100.0	0.83	0.66–1.03
Alcoholic liver disease[a]	28	33.1	0.85	0.56–1.22	34.3	0.82	0.54–1.18
Cirrhosis[b]	17	21.2	0.80	0.47–1.28	22.0	0.77	0.45–1.24
External causes of injury and poisoning	187	226.5	0.83	0.71–0.95	234.6	0.80	0.69–0.92
Suicide	26	63.9	0.41	0.08–0.49	66.1	0.39	0.26–0.58

a Data available from 1968 onwards
b Data available from 1979 onwards

Table A2.4 Major causes of mortality: observed and expected deaths, SMRs and 95% confidence intervals for the civilian participants

		Method 1			Method 2		
Cause of death	Observed	Expected	SMR	95%CI	Expected	SMR	95%CI
All cancers	512	424.4	1.21	1.10–1.32	573.1	0.89	0.82–0.97
Ischaemic heart disease	384	463.4	0.83	0.75–0.92	629.3	0.61	0.55–0.67
Cerebrovascular disease	98	111.9	0.88	0.71–1.07	157.7	0.62	0.50–0.76
Respiratory disease	132	118.4	1.12	0.93–1.32	166.1	0.79	0.66–0.94
Chronic obstructive pulmonary disease[a]	73	76.6	0.95	0.75–1.20	108.7	0.67	0.53–0.85
Nervous system disease[a]	16	20.6	0.78	0.44–1.26	29.1	0.55	0.31–0.89
Motor neurone disease[a]	8	4.3	1.87	0.81–3.68	5.7	1.40	0.61–2.76
Digestive diseases[a]	54	48.2	1.12	0.84–1.46	64.5	0.84	0.63–1.09
Alcoholic liver disease[a]	14	14.0	1.00	0.55–1.68	17.6	0.79	0.43–1.33
Cirrhosis[b]	13	8.9	1.46	0.78–2.49	11.5	1.13	0.60–1.94
External causes of injury and poisoning	94	94.0	1.00	0.81–1.22	118.3	0.79	0.64–0.97
Suicide	6	26.8	0.22	0.08–0.49	33.5	0.18	0.07–0.39

a Data available from 1968 onwards
b Data available from 1979 onwards

Table A2.5 Mortality from all causes combined: for military participants excluding veterans of Korean and Vietnam wars

All causes	Observed	Method 1			Method 2		
		Expected	SMR	95%CI	Expected	SMR	95%CI
Military participants	2714	2662.3	1.02	0.98–1.06	2778.3	0.98	0.94–1.01
Excluding Korean war veterans	1948	1975.9	0.99	0.94–1.03	2061.1	0.95	0.90–0.99
Excluding Korean and Vietnam war veterans	1792	1785.2	1.00	0.96–1.05	1867.1	0.96	0.92–1.01
Radiogenic cancers							
Military participants	479	354.7	1.35	1.23–1.48	370.1	1.29	1.18–1.42
Excluding Korean war veterans	340	257.9	1.32	1.18–1.47	269.24	1.26	1.13–1.40
Excluding Korean and Vietnam war veterans	316	230.2	1.37	1.23–1.53	241.1	1.31	1.17–1.46

Table A2.6 Mortality from cancer: observed and expected deaths, SMRs and 95% confidence intervals for the cohort

		Method 1			Method 2		
Cancer death	Observed	Expected	SMR	95%CI	Expected	SMR	95%CI
Lip, oral cavity, pharynx	56	37.5	1.50	1.13–1.94	42.1	1.33	1.01–1.73
Oesophagus	44	38.2	1.15	0.84–1.55	43.6	1.01	0.73–1.36
Stomach	77	61.7	1.25	0.99–1.56	71.2	1.08	0.85–1.35
Colorectal	202	162.8	1.24	1.08–1.42	186.4	1.08	0.94–1.24
Liver[b]	19	20.5	0.93	0.56–1.45	23.3	0.82	0.49–1.27
Gallbladder[b]	8	7.1	1.13	0.49–2.23	8.2	0.98	0.42–1.93
Pancreas	57	55.6	1.03	0.78–1.33	63.7	0.89	0.68–1.16
Nasal, ear, sinuses[a]	4	2.3	1.74	0.47–4.46	2.6	1.54	0.42–3.94
Larynx	20	17.8	1.12	0.69–1.74	20.1	1.00	0.61–1.54
Lung	429	357.4	1.20	1.09–1.32	409.0	1.05	0.95–1.15
Pleura[b]	10	8.2	1.22	0.58–2.23	9.4	1.07	0.51–1.97
Connective tissue[a]	6	5.5	1.10	0.40–2.39	6.2	0.97	0.35–2.10
Melanoma	46	37.8	1.22	0.89–1.62	42.6	1.08	0.79–1.44
Non-melanocytic skin[a]	14	11.9	1.18	0.64–1.98	13.8	1.01	0.56–1.70
Prostate	131	103.7	1.26	1.06–1.50	124.5	1.05	0.88–1.25
Testis	3	3.2	0.93	0.19–2.71	3.5	0.85	0.18–2.49
Bladder	30	30.1	1.00	0.67–1.42	35.5	0.85	0.57–1.21
Kidney	30	30.4	0.99	0.67–1.41	34.7	0.86	0.58–1.23
Eye	2	1.2	1.68	0.20–6.06	1.4	1.47	0.18–5.33
Brain and nervous system	40	39.7	1.00	0.72–1.37	44.4	0.90	0.64–1.23
Thyroid	4	2.2	1.83	0.50–4.67	2.5	1.60	0.44–4.10
Non-Hodgkin's lymphoma	47	42.1	1.12	0.82–1.48	48.2	0.98	0.72–1.30
Multiple myeloma[a]	20	17.7	1.13	0.69–1.75	20.4	0.98	0.60–1.51
Unknown primary site	85	65.2	1.30	1.04–1.61	75.1	1.13	0.90–1.40
All leukaemias	47	39.9	1.18	0.87–1.57	45.9	1.03	0.75–1.36
Non-CLL leukaemia	40	32.0	1.25	0.89–1.70	36.6	1.09	0.78–1.49
Radiogenic cancers	752	526.1	1.43	1.33–1.54	603.7	1.25	1.16–1.34

a Data available from 1968 onwards
b Data available from 1979 onwards

Table A2.7 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals for all military participants, and all military participants excluding Korean and Vietnam veterans

Cause of cancer death	Observed	Method 1			Method 2		
		Expected	SMR	95%CI	Expected	SMR	95%CI
Lip, oral, pharynx	38	25.5	1.49	1.05–2.04	26.5	1.43	1.01–1.97
Excl Korea	26	18.4	1.41	0.92–2.07	19.2	1.36	0.89–1.99
Excl Korea/Viet	24	16.4	1.47	0.94–2.18	17.1	1.40	0.90–2.09
Colorectal	133	107.9	1.23	1.03–1.46	112.5	1.18	0.99–1.40
Excl Korea	93	79.0	1.18	0.95–1.44	82.4	1.13	0.91–1.38
Excl Korea/Viet	85	70.7	1.20	0.96–1.49	74.0	1.15	0.92–1.42
Lung	269	234.0	1.15	1.02–1.30	243.8	1.10	0.98–1.24
Excl Korea	186	171.1	1.09	0.94–1.25	178.4	1.04	0.90–1.20
Excl Korea/Viet	177	153.8	1.15	0.99–1.33	160.8	1.10	0.94–1.28
Melanoma	36	26.0	1.39	0.97–1.92	27.0	1.33	0.93–1.84
Excl Korea	25	18.9	1.33	0.86–1.96	19.6	1.27	0.82–1.88
Excl Korea/Viet	23	16.7	1.38	0.87–2.06	17.5	1.32	0.83–1.97
Prostate	85	64.6	1.32	1.05–1.63	67.9	1.25	1.00–1.55
Excl Korea	65	48.5	1.34	1.04–1.71	50.9	1.28	0.99–1.63
Excl Korea/Viet	55	44.1	1.25	0.94–1.62	46.5	1.18	0.89–1.54
All leukaemias	30	26.3	1.14	0.77–1.63	27.4	1.09	0.73–1.56
Excl Korea	25	19.4	1.29	0.84–1.91	20.2	1.24	0.80–1.83
Excl Korea/Viet	20	17.4	1.15	0.70–1.78	18.2	1.10	0.67–1.70
Non-CLL leukaemia	26	21.2	1.23	0.80–1.80	22.1	1.18	0.77–1.73
Excl Korea	21	15.6	1.35	0.83–2.06	16.3	1.29	0.80–1.97
Excl Korea/Viet	18	14.0	1.29	0.76–2.04	14.6	1.23	0.73–1.95

Table A2.8 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals, by branch of armed service

Cause of cancer death	Observed	Method 1			Method 2		
		Expected	SMR	95%CI	Expected	SMR	95%CI
RAN							
All cancers	418	325.3	1.29	1.16–1.41	343.4	1.22	1.10–1.34
Lip, oral, pharynx	13	10.9	1.20	0.64–2.05	11.4	1.14	0.61–1.95
Colorectal	61	43.7	1.40	1.07–1.79	46.1	1.33	1.01–1.70
Lung	138	93.5	1.48	1.24–1.74	98.6	1.40	1.18–1.65
Melanoma	12	11.0	1.09	0.56–1.90	11.6	1.03	0.53–1.81
Non-melanocytic skin[a]	3	3.0	0.99	0.21–2.91	3.2	0.94	0.19–2.74
Prostate	32	22.8	1.40	0.96–1.98	24.4	1.31	0.90–1.85
All leukaemias	10	10.5	0.95	0.46–1.75	11.1	0.90	0.43–1.66
Non-CLL leukaemia	10	8.5	1.18	0.56–2.16	9.0	1.12	0.54–2.05
Army							
All cancers	163	141.6	1.15	0.98–1.34	149.1	1.09	0.93–1.27
Lip, oral, pharynx	10	4.3	2.35	1.13–4.33	4.4	2.25	1.08–4.14
Colorectal	18	18.6	0.97	0.57–1.53	19.6	0.92	0.54–1.45
Lung	41	40.7	1.00	0.72–1.37	42.8	0.96	0.69–1.30
Melanoma	2	4.3	0.46	0.06–1.67	4.5	0.44	0.05–1.60
Non-melanocytic skin[a]	2	1.4	1.46	0.18–5.27	1.5	1.38	0.17–4.98
Prostate	16	11.9	1.34	0.77–2.18	12.8	1.25	0.72–2.04
All leukaemias	4	4.6	0.88	0.24–2.24	4.8	0.83	0.27–2.13
Non-CLL leukaemia	3	3.7	0.82	0.17–2.39	3.9	0.78	0.16–2.27
RAAF							
All cancers	372	347.5	1.07	0.96–1.18	357.0	1.04	0.94–1.15
Lip, oral, pharynx	15	10.4	1.44	0.81–2.38	10.7	1.41	0.79–2.32
Colorectal	54	45.6	1.18	0.89–1.54	46.9	1.15	0.87–1.50
Lung	90	99.7	0.90	0.73–1.11	102.4	0.88	0.71–1.08
Melanoma	22	10.6	2.07	1.30–3.13	10.9	2.02	1.26–3.05
Non-melanocytic skin[a]	4	3.4	1.18	0.32–3.03	3.5	1.15	0.31–2.94
Prostate	37	29.8	1.24	0.87–1.71	30.7	1.20	0.85–1.66
All leukaemias	16	11.2	1.42	0.81–2.31	11.5	1.39	0.79–2.25
Non-CLL leukaemia	13	9.0	1.45	0.77–2.47	9.2	1.41	0.75–2.41

a Data available from 1968 onwards

Table A2.9 Selected causes of cancer mortality: observed and expected deaths, SMRs and 95% confidence intervals for civilian participants

Cause of cancer death	Observed	Method 1			Method 2		
		Expected	SMR	95%CI	Expected	SMR	95%CI
Radiogenic cancers	273	171.5	1.59	1.41–1.79	233.5	1.17	1.03–1.32
Lip, oral, pharynx	18	12.0	1.51	0.89–2.38	15.6	1.16	0.69–1.83
Colorectal	69	54.9	1.26	0.98–1.59	73.9	0.93	0.73–1.18
Lung	160	123.4	1.30	1.10–1.51	165.2	0.97	0.82–1.13
Melanoma	10	11.8	0.85	0.41–1.55	15.6	0.64	0.31–1.18
Non-melanocytic skin[a]	5	4.1	1.22	0.40–2.84	5.7	0.88	0.29–2.06
Prostate	46	39.1	1.18	0.86–1.57	56.6	0.81	0.60–1.08
All leukaemias	17	13.6	1.25	0.73–2.00	18.4	0.92	0.54–1.48
Non-CLL leukaemia	14	10.8	1.30	0.71–2.18	14.5	0.96	0.53–1.62

a Data available from 1968 onwards

Appendix 3 Cancer incidence results including Method 2

Table A3.1 Incident cancers: observed cases, expected cases, standardised incidence ratios and 95% confidence intervals for the cohort, by type of cancer

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	2456	2000.3	1.23	1.18–1.28	2280.3	1.08	1.03–1.12
Oral cavity (C00-C14)	133	94.1	1.41	1.18–1.67	105.4	1.26	1.06–1.50
Oesophagus (C15)	47	31.8	1.48	1.09–1.97	36.1	1.30	0.96–1.73
Stomach (C16)	73	65.1	1.12	0.88–1.41	74.7	0.98	0.77–1.23
Colorectal (C18-C21)	353	305.0	1.16	1.04–1.28	346.6	1.02	0.92–1.13
Liver (C22)	20	19.2	1.04	0.64–1.61	21.7	0.92	0.56–1.42
Gallbladder (C23-C24)	15	12.2	1.23	0.69–2.02	14.0	1.07	0.60–1.77
Pancreas (C25)	50	43.0	1.16	0.86–1.53	49.3	1.02	0.75–1.34
Nasal cavity (C30-C31)	6	4.0	1.50	0.55–3.27	4.5	1.33	0.49–2.89
Larynx (C32)	42	34.2	1.23	0.89–1.66	38.2	1.10	0.79–1.48
Lung (C33-C34)	406	316.7	1.28	1.16–1.41	360.4	1.13	1.02–1.24
Pleura (C38.4)	1	0.6	1.63	0.04–9.06	0.7	1.41	0.04–7.84
Melanoma (C43)	209	149.8	1.40	1.21–1.60	168.7	1.24	1.08–1.42
Mesothelioma (C45)	26	17.8	1.46	0.95–2.14	19.9	1.31	0.85–1.91
Prostate (C61)	548	450.9	1.22	1.12–1.32	520.0	1.05	0.97–1.15
Testis (C62)	3	3.4	0.90	0.18–2.62	3.7	0.82	0.17–2.38
Kidney (C64)	49	46.5	1.05	0.78–1.39	52.6	0.93	0.69–1.23
Renal pelvis (C65)	4	5.4	0.74	0.20–1.89	6.2	0.65	0.18–1.66
Bladder (C67)	98	100.7	0.97	0.79–1.19	115.7	0.85	0.69–1.03
Eye (C69)	4	5.15	0.78	0.21–1.99	5.8	0.69	0.19–1.76
Brain (C70-C72)	38	28.0	1.36	0.96–1.86	31.5	1.21	0.85–1.66
Thyroid (C73)	9	6.3	1.43	0.65–2.71	7.1	1.28	0.58–2.42
Lymphomas (C81-C85, C96)	78	67.3	1.16	0.92–1.45	76.5	1.02	0.81–1.27
Multiple myeloma (C90)	29	23.8	1.22	0.82–1.75	27.2	1.07	0.71–1.53
Leukaemia (C91-C95)	73	51.0	1.43	1.12–1.80	58.4	1.25	0.98–1.57
CLL (C91.1)	26	20.4	1.28	0.83–1.87	23.2	1.12	0.73–1.64
Leukaemia excluding CLL	47	29.1	1.61	1.18–2.14	33.6	1.40	1.03–1.86

Table A3.2 Military participants — SIRs of selected cancers

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	1720	1380.1	1.25	1.19–1.31	1440.8	1.19	1.14–1.25
Oral cavity (C00-C14)	94	66.5	1.41	1.14–1.73	69.2	1.36	1.10–1.66
Oesophagus (C15)	34	22.0	1.55	1.07–2.16	23.0	1.48	1.03–2.07
Stomach (C16)	56	44.3	1.27	0.96–1.64	46.2	1.21	0.92–1.57
Colorectal (C18-C21)	238	211.7	1.12	0.99–1.28	220.9	1.08	0.94–1.22
Liver (C22)	17	13.5	1.26	0.73–2.01	14.1	1.21	0.70–1.93
Pancreas (C25)	39	29.4	1.33	0.94–1.81	30.7	1.27	0.90–1.74
Larynx (C32)	36	24.1	1.49	1.05–2.07	25.1	1.44	1.01–1.99
Lung (C33-C34)	271	217.8	1.24	1.10–1.40	227.1	1.19	1.06–1.34
Melanoma (C43)	156	105.5	1.48	1.26–1.73	110.0	1.42	1.20–1.66
Mesothelioma (C45)	18	12.8	1.40	0.83–2.22	13.4	1.35	0.80–2.13
Prostate (C61)	388	307.7	1.26	1.14–1.39	322.0	1.21	1.09–1.33
Kidney (C64)	33	32.7	1.01	0.70–1.42	34.1	0.97	0.67–1.36
Bladder (C67)	80	68.4	1.17	0.93–1.46	71.5	1.12	0.89–1.39
Brain (C70-C72)	28	19.7	1.42	0.94–2.05	20.5	1.36	0.91–1.97
Thyroid (C73)	8	4.5	1.80	0.78–3.54	4.6	1.72	0.74–3.40
Lymphomas (C81-C85, C96)	48	46.8	1.03	0.76–1.36	48.9	0.98	0.72–1.30
Multiple myeloma (C90)	14	16.3	0.86	0.47–1.44	17.1	0.82	0.45–1.38
Leukaemia (C91-C95)	50	34.8	1.44	1.07–1.90	36.3	1.38	1.02–1.82
CLL (C91.1)	18	14.1	1.28	0.76–2.02	14.7	1.23	0.73–1.94
Leukaemia excluding CLL	32	19.8	1.62	1.11–2.28	20.7	1.55	1.06–2.18

Table A3.3 Civilian participants: SIRs of selected cancers

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	736	620.1	1.19	1.10–1.28	839.5	0.88	0.81–0.94
Oral cavity (C00-C14)	39	27.6	1.41	1.00–1.93	36.2	1.08	0.77–1.47
Oesophagus (C15)	13	9.8	1.33	0.71–2.28	13.2	0.99	0.53–1.69
Stomach (C16)	17	20.9	0.81	0.47–1.30	28.5	0.60	0.35–0.95
Colorectal (C18-C21)	115	93.3	1.23	1.02–1.48	125.7	0.92	0.76–1.10
Pancreas (C25)	11	13.7	0.81	0.40–1.44	18.6	0.59	0.30–1.06
Lung (C33-C34)	135	99.0	1.36	1.14–1.61	133.3	1.01	0.85–1.20
Melanoma (C43)	53	44.3	1.20	0.90–1.56	58.7	0.90	0.68–1.18
Mesothelioma (C45)	8	5.0	1.60	0.69–3.15	6.5	1.23	0.53–2.41
Prostate (C61)	160	143.3	1.12	0.95–1.30	198.0	0.81	0.69–0.94
Kidney (C64)	16	13.9	1.15	0.66–1.87	18.5	0.87	0.49–1.40
Bladder (C67)	18	32.3	0.56	0.33–0.88	44.2	0.41	0.24–0.64
Brain (C70-C72)	10	8.3	1.20	0.58–2.21	10.9	0.92	0.44–1.68
Lymphomas (C81-C85, C96)	30	20.5	1.46	0.99–2.09	27.6	1.09	0.73–1.55
Multiple myeloma (C90)	15	7.5	2.01	1.13–3.32	10.2	1.48	0.83–2.44
Leukaemia (C91-C95)	23	16.2	1.42	0.90–2.13	22.1	1.04	0.66–1.56
CLL (C91.1)	8	6.3	1.27	0.55–2.50	8.5	0.94	0.40–1.85
Leukaemia excluding CLL	15	9.4	1.60	0.90–2.64	12.9	1.17	0.65–1.92

Table A3.4 RAN participants: SIRs of selected cancers

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	759	581.3	1.31	1.21–1.40	614.1	1.24	1.15–1.33
Oral cavity (C00-C14)	43	29.0	1.48	1.07–2.00	30.5	1.41	1.02–1.90
Oesophagus (C15)	16	9.4	1.71	0.98–2.78	9.9	1.62	0.93–2.63
Stomach (C16)	23	18.2	1.26	0.80–1.90	19.2	1.20	0.76–1.79
Colorectal (C18-C21)	109	90.1	1.21	0.99–1.46	95.1	1.15	0.94–1.38
Liver (C22)	9	5.9	1.53	0.70–2.90	6.2	1.45	0.66–2.75
Pancreas (C25)	16	12.2	1.31	0.75–2.13	12.9	1.24	0.71–2.02
Larynx (C32)	16	10.6	1.51	0.86–2.45	11.2	1.44	0.82–2.33
Lung (C33-C34)	138	91.9	1.50	1.26–1.77	97.0	1.42	1.19–1.68
Melanoma (C43)	60	45.4	1.32	1.01–1.70	47.8	1.26	0.96–1.62
Mesothelioma (C45)	16	5.8	2.79	1.59–4.52	5.1	2.65	1.51–4.30
Prostate (C61)	162	127.4	1.27	1.08–1.48	135.1	1.20	1.02–1.40
Kidney (C64)	14	14.1	1.00	0.54–1.67	14.9	0.94	0.52–1.58
Bladder (C67)	30	28.2	1.07	0.72–1.52	29.8	1.01	0.68–1.44
Brain (C70-C72)	9	8.5	1.06	0.48–2.01	8.9	1.01	0.46–1.91
Lymphomas (C81-C85, C96)	18	19.7	0.91	0.54–1.44	20.8	0.86	0.51–1.37
Multiple myeloma (C90)	2	6.8	0.29	0.04–1.06	7.2	0.28	0.03–1.00
Leukaemia (C91-C95)	18	14.3	1.26	0.75–1.99	15.1	1.19	0.71–1.88
CLL (C91.1)	3	2.3	1.29	0.27–3.78	2.4	1.23	0.25–3.60
Leukaemia excluding CLL	15	8.0	1.87	1.04–3.08	8.5	1.76	0.99–2.91

Table A3.5 Army participants: SIRs of selected cancers

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	278	227.4	1.22	1.08–1.37	239.1	1.16	1.03–1.31
Oral cavity (C00-C14)	16	10.8	1.49	0.85–2.42	11.3	1.42	0.81–2.31
Oesophagus (C15)	4	3.6	1.11	0.30–2.85	3.8	1.06	0.29–2.71
Stomach (C16)	12	7.4	1.62	0.83–2.82	7.8	1.54	0.79–2.68
Colorectal (C18-C21)	35	34.7	1.01	0.70–1.40	36.4	0.96	0.67–1.34
Liver (C22)	5	2.2	2.31	0.75–5.40	2.3	2.20	0.72–5.14
Pancreas (C25)	11	4.9	2.24	1.12–4.02	5.2	2.13	1.06–3.82
Larynx (C32)	7	3.8	1.82	0.73–3.75	4.0	1.74	0.70–3.59
Lung (C33-C34)	39	35.7	1.09	0.78–1.49	37.5	1.04	0.74–1.42
Melanoma (C43)	25	17.3	1.45	0.94–2.14	18.1	1.38	0.89–2.04
Mesothelioma (C45)	2	2.0	0.98	0.12–3.54	2.1	0.94	0.11–3.38
Prostate (C61)	58	51.0	1.14	0.86–1.47	53.8	1.08	0.82–1.39
Kidney (C64)	8	5.3	1.51	0.65–2.97	5.6	1.44	0.62–2.83
Bladder (C67)	13	11.4	1.14	0.61–1.95	12.0	1.08	0.57–1.85
Brain (C70-C72)	6	3.2	1.86	0.68–4.05	3.4	1.78	0.65–3.87
Lymphomas (C81-C85, C96)	6	7.8	0.77	0.28–1.68	8.2	0.74	0.27–1.60
Multiple myeloma (C90)	3	2.7	1.11	0.23–3.23	2.9	1.05	0.22–3.07
Leukaemia (C91-C95)	8	5.8	1.37	0.59–2.70	6.2	1.30	0.56–2.56
CLL (C91.1)	6	5.9	1.01	0.37–2.20	6.3	0.96	0.35–2.08
Leukaemia excluding CLL	2	3.4	0.60	0.07–2.15	3.5	0.57	0.07–2.04

Table A3.6 RAAF participants: SIRs of selected cancers

Cancer (ICD-10 code)	Observed	Method 1			Method 2		
		Expected	SIR	95%CI	Expected	SIR	95%CI
All cancers	683	571.4	1.20	1.11–1.29	587.6	1.16	1.08–1.25
Oral cavity (C00-C14)	35	26.7	1.31	0.92–1.82	27.4	1.28	0.89–1.77
Oesophagus (C15)	14	9.1	1.55	0.85–2.60	9.3	1.51	0.82–2.53
Stomach (C16)	21	18.6	1.13	0.70–1.72	19.2	1.10	0.68–1.68
Colorectal (C18-C21)	94	86.9	1.08	0.87–1.32	89.4	1.05	0.85–1.29
Liver (C22)	3	5.5	0.55	0.11–1.60	5.6	0.53	0.11–1.56
Pancreas (C25)	12	12.3	0.98	0.50–1.70	12.7	0.95	0.49–1.66
Larynx (C32)	13	9.6	1.35	0.72–2.31	9.9	1.31	0.70–2.25
Lung (C33-C34)	94	90.1	1.04	0.84–1.28	92.6	1.02	0.82–1.24
Melanoma (C43)	71	42.9	1.66	1.29–2.09	44.1	1.61	1.26–2.03
Mesothelioma (C45)	0	5.1	-	-	5.2	-	-
Prostate (C61)	168	129.3	1.30	1.11–1.51	133.1	1.26	1.08–1.47
Kidney (C64)	11	13.3	0.83	0.41–1.48	13.7	0.81	0.40–1.44
Bladder (C67)	37	28.8	1.29	0.90–1.77	29.6	1.25	0.88–1.72
Brain (C70-C72)	13	8.0	1.63	0.87–2.78	8.2	1.58	0.84–2.70
Lymphomas (C81-C85, C96)	24	19.3	1.24	0.80–1.85	19.9	1.21	0.77–1.80
Multiple myeloma (C90)	9	6.8	1.32	0.60–2.50	7.0	1.28	0.59–2.43
Leukaemia (C91-C95)	24	14.6	1.64	1.05–2.44	15.0	1.60	1.02–2.37
CLL (C91.1)	9	5.8	1.55	0.71–2.94	6.0	1.51	0.69–2.86
Leukaemia excluding CLL	15	8.4	1.78	1.00–2.94	8.7	1.73	0.97–2.86

Appendix 4 The healthy worker effect

Analysis of causes, and evaluation of strategies for addressing the problem in the cohort study of nuclear test participants

Summary

The healthy worker effect (HWE) is used to describe two different phenomena. In this discussion, use of the term HWE is limited to the low mortality rates observed in occupational cohorts compared with those of the general population.

The HWE has two main contributory causes: a selection effect, whereby those with serious illness or disability are excluded from employment, and a social class effect, whereby the social class composition of the workforce is higher than that of the general population. The latter is the more important cause. To address means of overcoming bias from the HWE, the two factors need to be considered separately.

To overcome the bias from a social class effect, four strategies are possible.

- Comparison with another cohort not subject to the exposure of interest (Muirhead et al 2003). This is the method used in the UK study of nuclear test participants. It has the advantage of avoiding the HWE that would occur from comparison with the general population. However, as the comparison population is much smaller than the general population, the confidence intervals of relative risk estimates are likely to be wide. There is further loss of validity if both the participants group and the comparison group have a significant loss to follow-up. The experience of the UK study indicates that the extra time and expense of assembling and following up a comparison cohort is not justified by any important information.
- Internal comparison between exposure groups within the cohort. This is the preferred method, provided that valid exposure estimates can be made. Even if this should prove to be a limiting factor, a nested case–control study should enable a valid estimate to be made of the association between radiation exposure and leukaemia by focusing on a limited number of subjects.
- Proportionate mortality ratio (PMR) study. Empirically, the PMR has been found to be relatively free of an HWE bias compared with the standardised mortality ratio (SMR). The difficulty with this measure is that an elevation of the PMR can be interpreted in two ways. If an exposure is associated with a raised PMR, it may be because it causes death from the disease of interest or because it reduces the all-cause death rate.
- Mortality odds ratio (MOR). This is similar to the PMR, except that the number of deaths from the cause of interest is expressed as a proportion of the number of deaths from a specific reference cause of death, rather than of all deaths. If the exposure of interest is unrelated to death from the reference cause of death, then the PMR is equivalent to the SMR. However, this measure will be subject to bias from an HWE unless both the disease of interest and the reference cause of death are subject to social class gradients that are the same in both magnitude and direction. Available

evidence suggests that leukaemia has a small reverse social class gradient, and is therefore vulnerable to a small reverse HWE.

The HWE from a selection effect becomes attenuated with time, so that it is overcome by excluding from the analysis deaths and person-years of follow-up in the early years after hire.

Recommendations

1 No comparison cohort will be assembled. However, comparison will be made with the findings of the Korean veterans study. This is a contemporary cohort in which there was no significant radiation exposure.

2 Comparisons will be made between groups with differing exposure estimates within the cohort. More detailed analysis will be made in a case–control study nested within the cohort.

3 Analyses will be carried out using a range of lag periods between presence at test sites and death or cancer.

Description of the healthy worker effect

The term healthy worker effect is applied in two quite different ways. The term was initially used by McMichael in 1976 to describe the low mortality rates observed in occupational cohorts compared with those of the general population (McMichael 1976). Since then, the term has also been used commonly in cross-sectional studies to describe relatively low prevalence of disease or disease markers in occupational groups. This latter use is due to diseased or adversely affected subjects leaving the workforce or transferring to lower-risk jobs, thereby reducing the proportion of affected subjects in higher-risk groups.

The term cohort is derived from the Latin noun *cohors*, meaning enclosure. A cohort originally applied to an ancient Roman military unit, and was enclosed in the sense that no other individual could enter the cohort, and nobody could leave it except through death. Thus membership of a Roman cohort was fixed from the time of inception and became extinct when the last member died. Similarly, in studies of occupational cohorts, individuals remain in the cohort even if they change jobs or leave the workforce, and their membership of the cohort lasts until their death. (For practical reasons, exceptions are made to this rule when individuals cannot be tracked with confidence.)

The present discussion is limited to the HWE as applied to cohort studies.

The term healthy worker effect was used because of the likelihood that people with chronic illness or disability are less likely to gain or retain secure employment. Last, in the dictionary of epidemiology, defines the HWE as ‘a phenomenon observed initially in studies of occupational diseases: workers usually exhibit lower overall death rates than the general population, because the severely ill and chronically disabled are ordinarily excluded from employment’ (Last 2001). It is important to note that Last refers to the HWE as an observed phenomenon. There is no demonstrated theoretical mechanism that can be used to predict the occurrence or extent of an HWE, nor is the HWE in itself an explanation for a low SMR. McMichael pointed out that allowance must be made for variation in the HWE with age, work status, time-period of observation and different

causes of death. Such variation cannot be predicted: estimation of the magnitude of such an effect can only be attempted after the SMR has been computed.

Selection factors as a source of the HWE

Implicit in Last's definition is that the chronically ill and disabled have a reduced life expectancy. However, it is not self-evident that this factor is powerful enough to affect significantly the mortality rates of occupational cohorts. The HWE has been observed to occur mainly in the early years of follow-up of occupational cohorts. While progressive diseases (e.g. cancer, motor neurone disease) are likely to result in both exclusion from the workforce and early mortality, it is not clear that such conditions are so common that their exclusion will greatly affect the all-cause SMR of an occupational cohort. Interpretation in individual studies would depend on the range of exclusions and the particular cause of death being considered. For some causes of death, the effect may be large. A likely example is the effect of excluding those with psychiatric illness such as schizophrenia and severe depression. Such individuals, who until recent decades were institutionalised, tend to be chronically unemployed, and their exclusion is likely to result in low SMRs for suicide in occupational cohorts. Choi has examined the effect of exclusion of diabetics from firefighting on the occurrence of mortality from ischaemic heart disease, and estimated that this leads to a 3–9% reduction in SMR (Choi 2000). This led to reassessment of 23 studies of the association between firefighting and heart disease; whereas only 7 studies had previously shown a positive association, a further 4 showed positive evidence after readjustment for the exclusion of diabetics (Choi 2000). There are other chronic conditions with quantified increases in death rates (e.g. rheumatoid arthritis) (Guedes et al 1999). Overall, however, the effect of exclusion of sick and disabled people on SMRs will depend on the mix of conditions leading to exclusion and their association with different causes of death. For some diseases, it is likely that such exclusion of the sick and disabled will affect SMR estimates, but the extent of any such effect needs to be considered in individual studies.

Social class as a source of HWE

Another likely contributing factor to the HWE is selection of individuals from higher categories of socioeconomic status. Wilcosky and Wing have proposed that the HWE may reflect the selection, for epidemiological study, of subjects relatively advantaged in terms of socioeconomic status and health (Wilcosky and Wing 1987). There is abundant evidence of increasing socioeconomic status associated with lowering of SMR. The Black Report (Black 1980), commissioned by the UK government in the late 1970s, showed such gradients for a variety of cause-specific SMRs, including cancer, respiratory disease and heart disease. Social class was categorised on the basis of occupation into one of the following:

I professional etc occupations

II intermediate occupations

IIIN skilled occupations (nonmanual)

IIIM skilled occupations (manual)

IV partly skilled occupations

V unskilled occupations

It is likely that the unskilled category includes most people who are chronically unemployed, as well as many who find difficulty in obtaining secure employment and are therefore unlikely to participate in occupational cohort studies. Socioeconomic status has been shown to have a strong negative association with smoking, and it is likely that the exclusion of members of the category with high smoking prevalence makes an important contribution to smoking-related diseases such as lung cancer and heart disease. Other social class factors are also likely to contribute directly or indirectly to the HWE, such as area of residence, dietary factors, education and income.

Another factor contributing to the HWE may be improvement in socioeconomic status as a result of being employed (Wen et al 1983). There is some evidence that loss of employment is associated with an increased risk of mortality. Morris et al demonstrated this effect after excluding men who said that their unemployment or retirement was wholly or partly due to ill health; men who became unemployed or retired for reasons other than illness had a significantly raised risk of dying compared with continuously employed men, suggesting that non-employment even in apparently healthy men was associated with increased mortality (Morris et al 1994).

The better health of workers who remain employed compared with those who leave employment has led to a concept of a 'healthy worker survivor effect'. It is claimed that the healthy worker survivor effect can attenuate any tendency for mortality rates to increase with increasing duration of exposure — for example, increased cancer mortality with longer exposure to a carcinogen (Stayner et al 2003). This may be a partial explanation for the finding in some cohort studies of relatively high mortality rates in subjects with a short duration of exposure. The difficulties in interpreting such findings would not occur if exposure could be measured in cumulative exposure (mean concentration × duration) rather than sole reliance on duration of exposure. While the healthy worker survivor effect may affect internal comparisons within a cohort, it should not produce an HWE in comparisons of a cohort with the general population.

Attrition of HWE with time

The tendency for the HWE to decrease over follow-up time has been extensively reported. Many occupational cohorts have shown low SMRs initially, with subsequent convergence towards unity, both with increasing time since hire and increasing age of the cohort.

A detailed analysis of the HWE was published in 1991 by Goldblatt et al, based on a 1% sample of the population of England and Wales at the time of the 1971 census. The cohort was followed to 1981. The all-cause HWE increased with increasing age at the time of inception of the cohort, probably because the proportion of people excluded from the workforce on health grounds increases with age. The HWE effect diminished over the 10-year follow-up period, and the increase in SMR was greater in older age groups, so that the SMR for all age groups converged to a common value (about 0.90) by the end of the follow-up period. The HWE was greatest for respiratory disease, probably because chronic illnesses such as asthma, emphysema and chronic bronchitis have a greater impact on employability than diseases with short survival such as cancer. Over the 10-year period, the SMR for cancer in men rose from 0.91 to 0.97. The authors estimated that a socioeconomic class effect and a selection effect each contributed about one-half to the HWE (Goldblatt et al 1991).

These findings do not necessarily apply to studies of occupational cohorts. Park has pointed out that the cross-section of the workforce in the sample studies by Goldblatt et al

would include people on the margin of the workforce with less ability to obtain secure employment. Such people may be less likely to be included in cohort studies, which may therefore have a greater proportion of workers in higher socioeconomic groups. As Park has pointed out, an all-cause SMR reaching 0.90 after only 10 years of follow-up is not typical of an occupational cohort study, so that the greater and longer-lasting HWE found in occupational cohorts is likely to be predominantly due to over-representation of workers of higher socioeconomic status rather than to selection (Park 1992).

Although the decrease in the HWE with increasing follow-up time has been observed consistently in occupational cohorts, the cause is not clear. Goldblatt et al state that the increase in SMR over time, which they observed for employed men aged over 35 years, is consistent with a major effect of health selection. Thus, it is argued that individuals with chronic disease have a higher risk of early death, so that if they are excluded from employment, SMR of cohorts of employed people will be higher than the general population. On the other hand, exclusionary employment policies will be less successful in detecting diseases that develop after the person has been employed, so that the selection effect, and hence the HWE, will diminish over time. While this reasoning may be sound in the case of chronic respiratory disease, as discussed above, it is not self-evident that the prevalence of diseases detectable at the pre-employment medical examination that also portend a higher death rate is enough to account for the magnitude of observed HWEs; nor does it explain the fact that the HWE does not decrease in occupational cohorts as quickly as observed in the Goldblatt study.

This reasoning indicates that the HWE in occupational cohorts has two components: (i) job selection (i.e. people with diseases that reduce life expectancy tend to be excluded from employment, either because they do not apply, or because of exclusionary employment policies of employers) and (ii) occupational cohorts tend to have a greater proportion of workers in higher socioeconomic groups than the general population. Of these factors, the second is likely to be the more important, although there is some correlation between the two (people in poor health tend to belong to lower socioeconomic groups).

Archer has argued that the HWE must diminish and even go into reverse with increasing time of follow-up. He has reasoned that, since the maximum life span is biologically determined, an early HWE must be compensated by extra deaths at advanced ages. Since it is improbable that selection into an occupational cohort is *per se* unlikely to increase the life expectancy and life span of cohort members, the increase in death numbers will also cause an increase in death rates in later years of follow-up. Archer has tested the hypothesis on data from a study of lung cancer in workers exposed to beryllium, and concluded that reversal of the HWE may cause a spurious increase in SMR (Archer 1995).

Differences between diseases

The foregoing discussion suggests that the main cause of the HWE in occupational cohorts is the relatively high proportion of people of higher socioeconomic status than in the general population. Since death rates for most major categories of cause of death are greatest in the low socioeconomic groups, occupational cohorts will have lower standardised death rates than the general population, not only for each of the causes, but for all causes combined. Another smaller contributing factor is the exclusion of people with diseases affecting life expectancy.

Thus the magnitude of the HWE for a particular disease will depend on four factors:

- the social class gradient of mortality due to the disease — that is, the gradient of standardised mortality from the highest to the lowest social class
- the prevalence of the disease in the population from which the workforce is derived
- the extent to which the disease reduces life expectancy
- the extent to which people with the disease are excluded from the workforce.

A comprehensive analysis of disease-specific mortality by social class in the UK is presented in the publication *Occupational Mortality — Decennial Supplement 1970-72* (Office of Population Censuses and Statistics 1978). For all major categories — diseases of the circulatory system; all cancers combined, as well as many individual cancers, including lung cancer; respiratory diseases; digestive diseases; and accidents, poisonings and violence — there was an increase in mortality rates from Social Class I to Social Class V. On this basis, an HWE effect is to be expected for these causes of death. This expectation was realised in a 1991 review of 95 cohort studies by Park et al (1991). The authors focused on cohort studies considered to be largely free of work-related mortality. The mean SMRs were:

All causes	0.832
All cancers	0.898
Lung cancer	0.926
All non-cancer	0.813

Not all diseases in the UK analysis showed the same social class gradient. Lymphohaemopoietic cancers (ICD-9 200-209), which includes leukaemias, showed a reversal of the usual gradient. Some other causes of death, including some cancers, showed differing patterns of association with social class.

Within the overall category of lymphohaemopoietic cancers, there were some variations. For lymphatic leukaemia, the SMR in Social Class I was 115%, based on 27 deaths; in Social Class V, it was 89%, based on 41 deaths. For myeloid leukaemia, the SMR in Social Class I was 126, based on 65 deaths; for Social Class V, it was 89, based on 78 deaths.

On this basis, no HWE effect is to be expected for leukaemia; if anything, a reverse effect would be expected (Office of Population Censuses and Statistics 1978).

Moreover, any selection effect for leukaemia would be minimal. Although individuals with known leukaemia are quite likely to be excluded from employment, the prevalence of these diseases is low compared with many other chronic diseases. Other factors being equal, the lower the prevalence, the lesser the HWE.

Empirical support similar to that of the Park et al analysis for other diseases is scant in the case of leukaemia. However, some support for a reverse HWE for leukaemia is found in a meta-analysis of 461 cohorts in the chemical industry by Greenberg et al (2001). Overall, there were 10% fewer deaths observed than expected. There were fewer deaths than expected from all causes, cardiovascular disease, noncancer respiratory disease, cirrhosis of the liver, and external causes — which the authors considered possibly due to an HWE — but a 10–15% increase in lymphatic and hematopoietic cancers. (There were also small excesses of lung and bladder cancers, considered likely due to occupational exposure to known carcinogens.)

Differences between mortality and morbidity

An important aspect of the HWE that has received little attention is whether it is confined to mortality analyses or whether it is found in studies of disease incidence as well. It is only possible to address this question in the case of cancer, since other diseases are not subject to mandatory registration and therefore cannot be enumerated to the extent required for valid follow-up of a cohort.

In their textbook *Statistical Methods in Cancer Research*, Breslow and Day state that the HWE appears to be smaller for cancer incidence than for cancer mortality. The only explanation they offer is that those with cancer are more likely to have left their job; however, this would not explain disparity between cancer incidence and cancer mortality in a single cohort (Breslow and Day 1987).

In a recent update of mortality and cancer incidence in the Australian petroleum industry, the all-cancer SMR was 0.84, significantly below unity, whereas the all-cancer standardised incidence ratio (SIR) was 1.04, not significantly different from unity. This suggests that, at least in the case of cancer, the HWE is not due to a low disease incidence in occupational cohorts, but to prolonged survival. The HWE was discovered and analysed in an era when only cancer mortality could be examined. It therefore appears that cancer mortality is an imperfect measure of the occurrence of cancer, being a function not only of cancer incidence, but also of cancer survival and the frequency of death from competing causes. The concurrent finding of a low SMR and an SIR close to unity in the Australian study shows that a low SMR does not necessarily portend low incidence, and that an HWE found in a mortality estimate does not necessarily mean that an HWE effect exists at all for cancer incidence (Gun et al 2004).

A census-based study on Swedish women has similarly failed to find an HWE for cancer incidence. However, the authors did not present any comparison of SMRs and SIRs (Gridley et al 1999).

Suggested means of avoiding error due to HWE

The preceding discussion indicates that the HWE has two main causes — a selection effect, whereby those with serious illness or disability are excluded from employment, and a social class effect, whereby the social class composition of the workforce is higher than that of the general population. To address means of overcoming bias from the HWE, the two factors need to be considered separately.

1 HWE from a social class effect

The social class effect is probably the more important contributor to the HWE in occupational cohorts. Methods to overcome it include comparison with another occupational cohort not subject to the exposure of interest, comparison of subgroups of varying exposures within the cohort, or estimating the proportional mortality ratio (PMR) or mortality odds ratio (MOR).

(i) Comparison with another cohort not subject to the exposure of interest

This is the ideal means of avoiding the HWE. If a comparison cohort is used, it is important that the social class composition is the same as that of the cohort with which it is being compared.

A potential difficulty with such a cohort is that the confidence intervals of mortality rates are wider than general population rates, so that the estimate of rate ratio (cohort of interest to comparison cohort) is less stable than with a SMR.

Another significant drawback of a comparison cohort is that the cost of the study is almost doubled.

An example of the low cost-effectiveness of a comparison cohort is to be seen in the study of UK participants in the nuclear testing program in Australia. In this study, leukaemia and leukaemia mortality were the primary outcomes of interest because of their association with ionising radiation. The comparison cohort was drawn from contemporary service personnel who did not serve in the Australian tests. It was found to have a very low SMR and SIR for leukaemia. The explanation favoured by the researchers was random occurrence of low leukaemia mortality and incidence. Thus the additional expense and effort of assembling and analysing a comparison cohort provided very little additional information.

(ii) Internal comparison between exposure groups within the cohort

This is a much more cost-effective means of assessing the effect of exposure. However, its utility depends on the quality of exposure information. It also requires reasonably high numbers of cohort members within each exposure stratum. Even if there is a relatively even distribution of subjects between strata, there are likely to be relatively wide confidence intervals in the stratum-specific relative mortality ratios.

(iii) Proportionate mortality ratio (PMR) study

The PMR is an estimate of the proportion of all deaths from the cause of interest to deaths from all causes, relative to the proportion in the general population. As with estimates of SMR, the PMR is usually age standardised and stratified by sex. If the HWE of deaths from the disease of interest in the cohort is of the same magnitude as for all deaths, the PMR should be free of the HWE. Empirically, the PMR has been found to be relatively free of an HWE bias compared with the SMR (Waxweiler et al 1981, Park et al 1991).

The likely reason for the relative freedom from HWE is that both the number of deaths from the cause of interest and the number of deaths from all causes are similarly subject to an HWE. That is, the two biases cancel each other out! Thus, if the disease of interest is lung cancer, this shows a strong HWE due to the social class gradient of deaths from this cause. Similarly, deaths from all causes combined show a marked HWE, probably because the main categories of cause of death (i.e. heart disease, all cancers combined, respiratory deaths) are similarly subject to an HWE.

The difficulty with this measure is that an elevation of the PMR can be interpreted in two ways. If an exposure is associated with a raised PMR, it may either be because it causes death from the disease of interest or because it reduces the all-cause death rate (Rothman et al 1998).

(iv) Mortality odds ratio (MOR)

To overcome this difficulty, Miettinen and Wang have proposed the use of the MOR (Miettinen and Wang 1981). This is similar to the PMR, except that the number of deaths from the cause of interest is expressed as a proportion of the number of deaths from a specific reference cause of death rather than all deaths. If the exposure of interest is

unrelated to death from the reference cause of death, then the PMR is equivalent to the SMR.

MOR = (a/c)/(b/d)

Where a = number of exposed subjects who died from disease of interest

b = number of unexposed subjects who died from disease of interest

c = number of exposed subjects who died from a selected disease unrelated to exposure

d = number of unexposed subjects who died from the selected disease unrelated to exposure

Since the comparison disease is unrelated to exposure, the SMR in the unexposed is equal to that for the unexposed, i.e.

Standardised mortality rate in exposed = standardised mortality rate in unexposed

$c/N_1 = d/N_0$

where N_1 = person-years of follow-up of exposed subjects in the study population

and N_0 = person-years of follow-up of unexposed subjects in the study population

so that

$c/d = N_1/N_0$

Therefore MOR = $(a/b)/(c/d) = (a/b)/(N_1/N_0) = (a/N_1)/(b/N_0)$

And since expected number of deaths from disease of interest = $N_1(b/N_0)$

And observed number of deaths from disease of interest = a

MOR = $(a/N_1)/(b/N_0)$ = Obs/Exp = SMR

i.e. provided that the comparison disease is truly unrelated to exposure, the MOR is equivalent to the SMR.

However, the MOR, like the PMR and the SMR, is also potentially vulnerable to confounding, and the HWE itself can be a confounder if its direction and/or magnitude in the cause of death of interest differs from that of the reference cause of death.

Consider the MOR in a case of lung cancer in workers exposed to a respiratory carcinogen. If the reference cause of death is heart disease, the MOR is derived as follows:

(Deaths from lung cancer in exposed workers/deaths from heart disease in exposed workers)/(deaths from lung cancer in general population/deaths from heart disease in general population).

If the HWE effect is similar in direction and magnitude for smoking and heart disease, bias from an HWE will be minimal, and, since the social class gradient is likely to be similar for both causes of death, this is likely to be so. Therefore, provided that death from heart disease is unrelated to the exposure, the MOR will give an unbiased estimate of the effect of the exposure on death from lung cancer. (This assumes that adjustment has been made for smoking, and that there is some residual HWE after allowing for the effect of smoking.)

Bias is still possible if the reference cause of death shows no social class gradient. Consider the above example where the reference cause of death is pancreatic cancer instead of heart disease. This was the only cause of death in the UK analysis that showed no social class gradient. In this case, the numerator (number of lung cancer deaths) is subject to an HWE, but the denominator (number of pancreatic cancer deaths) is not. Therefore, the MOR will *underestimate* the effect of the exposure on the lung cancer death rate, because of an HWE.

Consider now an MOR for leukaemia deaths in a group exposed to an agent causing leukaemia. As described above, leukaemia has a slight reverse social class gradient, so that a reverse HWE is expected, and there is some empirical evidence to support this. Therefore, an MOR for a group exposed to a leukaemia-causing agent, with pancreatic cancer as the reference cause of death, could be expected to produce a slight overestimate of the effect of the agent on the leukaemia death rate.

2 HWE from selection effect

The selection effect is likely to be attenuated with time since enrolment in the cohort. This can therefore be overcome by excluding from the analysis deaths of interest and person-time occurring in the early years of follow-up.

It has been shown that internal comparisons of risk within a cohort will show a bias away from the null of any increase in risk with increasing cumulative exposure, due to an HWE (Flanders et al 1993). The authors demonstrated that controlling for time since hire eliminates the bias.

Conclusion

The experience of the UK study suggests that the additional cost and effort of compiling and analysing a comparison cohort might not be worthwhile. On present indications (March 2004), it is likely that the follow-up rate of the cohort may be less than 90%. If the loss to follow-up of a comparison cohort were comparable, there would be a substantial degree of uncertainty in any estimate of relative risk. Alternative means of avoiding or countering an HWE are preferred.

Nevertheless, comparison with the findings of the study on Korean veterans may be useful, since that cohort was approximately contemporary, and there is no a priori reason to expect a leukaemia-causing exposure from service in Korea. It may be necessary to adjust for personnel who are in both cohorts, who number about 1500.

Internal comparisons of different categories of radiation exposure will be made, both using exposure estimated by the exposure panel, and from exposures recorded on film badges. For leukaemias, the primary outcome of interest, the case–control study should provide evidence of any effect of radiation exposure free of bias. The likelihood of bias

away from the null with any trend with increasing cumulative exposure will be small, since cumulative exposure is dependent on exposure concentration rather than on time. Nevertheless, it would be desirable to include analyses that allow for varying lag periods between potential exposure and death or cancer.

An estimate using MOR was proposed in this study. However, because of a possible absent or reverse social class gradient for leukaemia, it was not possible to find a suitable referent cause of death.

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Appendix 5 Hypothetical smoking prevalence

The prevalence of smoking in the Australian male population was estimated for each 5-year age group for each year from 1952 to 2000. These estimates were calculated by Ridolfo and Stevenson, using a method proposed by Peto et al, and subsequently used in the Australian Burden of Disease Study (Peto et al 1992, Mathers et al 1999, Ridolfo and Stevenson 2001). Peto's method is based on the absolute rate of lung cancer in current smokers and never smokers in the American Cancer Society CPS-II study of one million US subjects. This large study was required to develop stable estimates of lung cancer rates in nonsmokers, in whom lung cancer is an uncommon disease. The lung cancer rates for smokers and nonsmokers in the CPS-II study were used to compute the proportion of smokers and nonsmokers required to produce the actual lung cancer rate in each age–calendar year stratum in the Australian lung cancer mortality data. This provided an estimate of smoking prevalence in each stratum.

The relative risk of the cause of death (e.g. lung cancer or bladder cancer) was taken from a summary estimate by English et al, based on meta-analyses of all epidemiological studies judged adequate for this purpose (English et al 1995).

From these estimates of smoking prevalence in each age–calendar year stratum and relative risk for the particular cause of death, the fraction of the cause of death caused by smoking (the attributable fraction) was calculated from the formula:

$$F = P*(RR-1)/(P*(RR-1)+1)$$

where

F is the aetiological fraction

P is the actual smoking prevalence for the age–calendar year stratum

RR is the ratio of the mortality rate of the cancer among those exposed to smoking to the mortality rate of those not exposed, or the relative risk of the cancer due to smoking.

From these computed levels of F and P, the absolute mortality rate due to smoking and the rate in nonsmokers were then calculated for each stratum.

The mortality rate due to smoking, SR, is given by

$$SR = R*F/P$$

where

R is the actual stratum-specific mortality rate.

The mortality rate for nonsmokers is:

$$NR = R*(1-F)$$

The mortality rate in each stratum was then calculated based on a given *hypothetical* smoking prevalence. This was calculated by weighting the rate attributable to smoking according to the hypothetical smoking prevalence in the population. The formula is therefore:

$DR_h = SR*h + NR$

where

DR_h = derived mortality rate, assuming the hypothetical prevalence h applies
SR = mortality rate due to smoking

NR = mortality rate not due to smoking

h = the hypothetical smoking prevalence

The derived mortality rate in each stratum was then multiplied by the number of person-years in each stratum in the cohort, and the product is the number of deaths expected in that stratum at the hypothetical smoking prevalence. The expected numbers for each stratum were then summed to give the total number of deaths expected at the hypothetical smoking prevalence.

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Appendix 6 Abbreviations used in this report

AEC	Australian Electoral Commission
AIHW	Australian Institute of Health and Welfare
ALL	acute lymphatic leukaemia
AML	acute myeloid leukaemia
AWE	Atomic Weapons Establishment
CI	confidence interval
CLL	chronic lymphatic leukaemia
CML	chronic myelogenous leukaemia
COPD	chronic obstructive pulmonary disease
DIMIA	Department of Immigration, Multicultural and Indigenous Affairs
DVA	Department of Veterans' Affairs
ERR	excess relative risk
HIC	Health Insurance Commission
HR	hazard ratio
HWE	healthy worker effect
IARC	International Agency for Research on Cancer
ICD	International Classification of Diseases
ICRP	International Commission for Radiological Protection
LET	linear energy transfer
MOR	mortality odds ratio
mSv	millisieverts
NCCH	National Centre for Classification in Health
NCSCH	National Cancer Statistics Clearing House
NDI	National Death Index

non-CLL leukaemia	all leukaemias other than chronic lymphatic leukaemia
OR	odds ratio
PMR	proportionate mortality ratio
PSA	prostate specific antigen
RAAF	Royal Australian Air Force
RAN	Royal Australian Navy
RIR	relative incidence ratio
RMR	relative mortality ratio
RR	relative risk
SIR	standardised incidence ratio
SMR	standardised mortality ratio
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation