Under-ascertainment of multiple myeloma among participants in UK atmospheric atomic and nuclear weapons tests

S R Roff

In June 1999, Roff reported that 54 cases of multiple myeloma had been identified among the approximately 22,000 veterans of the UK’s atmospheric atomic and nuclear weapons tests programmes in response to a postal self administered questionnaire to the approximately 2200 members of the British Nuclear Tests Veterans Association. The study had generated considerable publicity which itself prompted some veterans to report their cases to the researcher. Since this was more than twice the number of cases of multiple myeloma reported in the second study of the veterans that had been conducted by the National Radiological Protection Board (NRPB) under commission from the Ministry of Defence (MoD), the issue was raised whether the data collection strategy used by the NRPB—a linkage between the Office of National Statistics and the Service Records Offices. These findings have implications for the conduct and robustness of follow up studies of long term health effects among participants in nuclear weapons tests.

METHODS
In response to this situation, the Ministry of Defence announced that a third study of the nuclear tests would be undertaken by the NRPB. The study duly commenced in December 1999 and included an inter-comparison of the cases detected by the NRPB and those reported by the present researcher (who had secured consent of the subjects or their relicts to share the information with the NRPB).

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An inter-comparison of cases of multiple myeloma among UK participants in the UK’s atmospheric atomic and nuclear weapons tests ascertainment by direct follow up methods detected at least a third more cases than a strategy relying solely on data linkage between the Office of National Statistics and the Service Records Offices. These findings have implications for the conduct and robustness of follow up studies of long term health effects among participants in nuclear weapons tests.

Criteria for eligibility
The population of the third NRPB study is essentially the same as that in the second analysis. Contemporary records held by the MoD had been searched to identify test participants among servicemen and civilian employees of the Atomic Weapons Establishment (AWE) and Atomic Energy Research Establishment. These men had visited at least one of the test locations (Monte Bello Islands, Emu Field, and Maralinga range in Australia; Malden and Christmas Islands in the Pacific Ocean) at the relevant times, or had sampled radioactive clouds. The analysis in the third study is based on 21,357 test participants, of whom 29% were in the Royal Navy, 27% were in the Army, 40% were in the Royal Air Force, and 4% were civilians. A control group of 22,333 men who did not participate in the tests was also identified from MoD archives. The controls were selected from other servicemen who served in tropical or subtropical areas and other men employed by AWE at the time of the tests. The participants and controls had very similar distributions by service and rank, as well as by year of birth, year of enlistment or employment, and year of discharge or end of employment.

Disease definition
The inter-comparison was conducted on a wide definition of multiple myeloma, namely the 9th revision of the International Classification of Diseases codes 203.0, 203.1, 238.6, 273.1, as derived from a review of up to date haematological information.

Methods of follow up of vital status and death certificate retrieval and coding
In the third NRPB study test participants and controls were followed up to 1 January 1999, using information from the NHS Central Registers for England, Wales, and Scotland, and the Central Services Agency in Northern Ireland. In the third NRPB study any cases not identified by this data linkage but otherwise acknowledged to meet the eligibility criteria as above were not included in the main study but were treated separately as “independent responders”. Causes of death were coded according to the 9th revision of the International Classification of Diseases. In analysing cancer incidence, information on deaths from cancer as underlying cause was
supplemented by cancer registrations and by death certificates where cancer was listed as a contributory cause. Where more than one type of cancer was mentioned, myeloma was selected in preference to other cancers in the incidence analysis.

**Sources of information for ascertainment of incident cases**
At the time that this follow up was conducted, cancer registration data were thought by the NRPB to be complete up to the end of 1994. Registration data up to the end of 1998 were included in the analysis because, although these data are likely to be incomplete, cancer incidence rates in participants have been compared with rates in controls, based on the same follow up mechanisms, rather than with national rates.

**Loss to follow up**
The NRPB analyses reported that as of January 1999, 9% of participants and 8% of controls had emigrated; 23% of both groups had died; 68% of participants and 69% of controls were alive; and 0.1% of both groups were lost to follow up.

**RESULTS**
The NRPB ascertained 35 cases of multiple myeloma among the 21,357 nuclear test veterans included in their study utilising the data linkage between the Office of National Statistics (ONS) and the Service Records Offices (SROs). They reported the same number of cases among the 22,333 controls who were veterans of the armed services who had not served at nuclear weapons test sites. Two thirds (66%) of these 35 cases among the nuclear test veterans had also been ascertained by the present researcher. At the time of the inter-comparison the NRPB indicated that it was aware of five cases not detected by the ONS-SRO data linkage method but which they accepted were confirmed cases of multiple myeloma among confirmed test participants. Three (60%) of these cases were also ascertained by the present researcher. The NRPB termed these five cases “independent responders” and declined to include them in what they termed “the main study”. The explanation for this bias lies largely in the fact that 11 of these “independent responders”—including five (83%) of the six cases accepted by the NRPB from the present researcher and three of the independent responder cases

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**Main messages**

- Ascertainment strategies depending on data linkages between the UK Service Records Office and ONS registries failed to detect at least 30% of verified cases of multiple myeloma among UK participants of UK nuclear weapons tests.
- This under-ascertainment rate is higher than that reported in other studies depending on such data linkage strategies.
- One of the major data sources for the present study—the RAF Service Records—is shown to be particularly deficient.
- These findings confirm the necessity reported in other studies of nuclear test veterans of utilising other standard procedures of verifiable case detection.
- The implications of the under-ascertainment reported for one marker condition, multiple myeloma, should be considered in relation to the other potentially radiogenic conditions.

**Policy implications**

- The UK Nuclear Test Veterans Database should be maintained and made available for ongoing analysis, including that by non-government funded researchers.
- Additional ascertainment strategies should be implemented as used in other veterans’ epidemiology to enhance the reliability of the database.
- The results of the third NRPB study should be reanalysed to include the “independent responders”.

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DISCUSSION
At least 30% of the confirmed cases of multiple myeloma among documented participants in the UK’s atmospheric atomic and nuclear weapons tests have been ascertained among the 15% of participants not included in the NRPB studies. Those studies are therefore unrepresentative since the rate of incidence and mortality from multiple myeloma—an accepted radiogenic marker condition—is twice that of the main study among the excluded cases.
they were already aware of—served in the Royal Air Force at the tests in what is acknowledged by the NRPB and the Ministry of Defence to have been activities particularly vulnerable to radiation exposure. Air crews flew through mushroom clouds to collect fission samples; ground crews worked on known contaminated planes. The NRPB’s second study estimated that only 74% of eligible RAF participants had been included in the main study’s cohort.2 Of the 21 358 test participants included in the second NRPB study, the largest group (39.5%) were from the RAF,2 yet the first NRPB test participants included in the second NRPB study, the cases in their studies:

used multiple ascertainment strategies to include 99% of the US nuclear weapons tests termed Operation Crossroads study estimated that only 74% of eligible RAF participants mushroom clouds to collect fission samples; ground crews vulnerable to radiation exposure. Air crews flew through the tests in what is acknowledged by the NRPB and the they were already aware of—served in the Royal Air Force at

The bias was compounded by the refusal of the NRPB to admit cases where the lack of ascertainment was due to the lag in the ONS data, even though the cases were shown to have been certified in death certificates and verified diagnoses registered during the time frame of the third study. This was despite being aware of the findings of Macdonald and colleagues6 that direct follow up identified 96% of cases and documented 11 cases not reported by the UK’s NHSCR of ovarian cancer in a similar sized cohort of 22 000 women. The NHSCR identified only 78% of the cases. Similarly, Dickinson and colleagues6 concluded that the NHSCR missed at least 10% of all incident cases of malignant diseases. Dickinson et al conclude that “Without additional ascertainment from multiple sources and diagnostic review, it would be incautious to use NHSCR cancer registrations as the sole basis of an epidemiological study”. Macdonald et al conclude that ‘some of these limitations can be overcome by the use of an independent, direct method of follow-up based on postal questionnaire’.

The NRPB contends that it cannot include these “independent responders” in the risk analysis calculations—even though they indicate a major risk to the cohort of radiogenic multiple myeloma—because the cases detected in the control group were ascertained by one strategy only—the ONS/SRO linkage—and to “privilege” the sample with multiple ascertainment strategies creates its own bias. This is despite the fact that the control group contains 976 more subjects than the sample, and itself constitutes not 85% of a given cohort but simply a roughly matching number of subjects. In contrast, the Five Series studies9 of the participants in the US nuclear weapons tests termed Operation Crossroads used multiple ascertainment strategies to include 99% of cases in their studies:

“The assembled information for this epidemiologic study comes from more than 100 distinct sources. Handwritten paper logs, microfilm or microfiche, computer files, medical records, word orders, transport orders, memos, interoffice memoranda, testimony, secondary compilations of primary sources, letters from spouses, death certificates, film badge records, computer programs, and benefits and compensation claims represent a diverse sample.”

The Five Series study also relied on the Nuclear Test Personnel Review database which included a nationwide toll-free call-in program set up by the Defence Nuclear Agency (which became the Defence Special Weapons Agency in 1996) for veterans of the US atmospheric tests to report details of their participation. The Five Series researchers also utilised the National Association of Atomic Veterans Medical Survey of 1784 veterans, advertised in a range of veterans’ journals, and held public meetings. Similar methods had been used earlier by Watanabe and colleagues8 in their study of cancer mortality risk among military participants of a 1958 US atmospheric nuclear weapons test.

The NRPB argues that it would bias the findings to include the cases identified by strategies other than the simple data linkage that was used for the control group. But as we have seen, the SROs were deficient in their record keeping, particularly for the RAF subjects. It was known to the NRPB researchers that a significant lag can occur in ONS registrations. Since the incidence of multiple myeloma among the independent responders is at least 30%—or twice the 15% rate estimated by the NRPB in deciding to settle for an 85% sample cohort—the NRPB studies seriously under-report the incidence of this marker radiogenic condition among veterans of the UK’s atmospheric atomic and nuclear weapons tests.

Although it is accepted that any “healthy soldier effect” would have been present in both the study cohort and the control group because both were drawn from the population of service personnel, and equally that any exposure mis-classification is likely to have impacted both groups, it is clear that failures of ascertainment within both the 85% of the nuclear test participants included in the third NRPB study and the 15% not included resulted in an under-ascertainment of the marker condition, multiple myeloma, and may have also occurred in relation to other potentially radiogenic conditions.

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