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

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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 ascertained 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 finding have implications for the conduct and robustness of follow up studies of long term health effects among participants in nuclear weapons tests.

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 registries of cancer incidence and mortality with records of participants in the weapons tests drawn from the Service Records Office—was adequate. The NRPB maintained that it had captured 85% of the cohort, although it acknowledged that figure might have fallen to around 74% for Royal Air Force (RAF) veterans. The NRPB accepted that if more than 15% of the multiple myeloma cases were ascertained among veterans not included in the 85% reported in their studies, their results could not be considered representative of the full cohort.

If the level of under-ascertainment proved to be equal in both the study cohort (potentially exposed to ionising radiation) and controls (probably unexposed group) the validity of the methodology would have been reasonable, but as the following data indicate, the under-ascertainment rate in the 15% of the study population was probably at least 30% or twice the rate in the 85% for whom data were analysed.

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 analysts 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 term the “main study”. The NRPB also accepted six further cases ascertained by the present researcher as valid cases of multiple myeloma among confirmed participants according to the eligibility and diagnostic criteria reported above, but also refused to include them in the main study. There were thus 11 “accepted” cases that were not included in the main study—that is, 24% of the 45 confirmed cases were excluded because they had not been ascertained by the data linkage method. At least half of these 11 cases had received pensions for their multiple myeloma from the War Pensions Agency (now the Veterans Agency), an agency of the Ministry of Defence which commissioned the studies from the NRPB. Eight of these 11 cases were veterans of the RAF.

There were an additional three cases identified by the present researcher which the NRPB acknowledged were confirmed but whose data had not appeared in the cancer registries in due time for the study although their diagnoses were made within the study’s time frame. While it is accepted that the ONS data can “lag” by five years, it seems inappropriate to exclude cases that all within the time frame of the NRPB’s study; that is, to use the lag as an “excuse” for exclusion in itself—from both the “main study” and the list of “independent responders”. All three of these cases had been active before the War Pensions Agency throughout the time frame of the study. This meant that 14 of the 49 known cases of multiple myeloma (29%) were not included in the NRPB study.

Another two cases were of men who had also been active before the WPA, both receiving pensions for multiple myeloma during the time frame of the study. Despite this they had not been ascertained as nuclear test veterans by the Service Records Office.

This brought the number of confirmed cases of multiple myeloma among documented test participants who were not included in the third NRPB study to 16—which is to say that nearly a third (31%) of the 51 confirmed cases are not included in the results of the third NRPB study. An additional case was excluded from the study because the individual served in the Merchant Navy at the tests and the NRPB stated that it could not track Merchant Navy participants. Another was excluded because he was considered a civilian, even though he had been seconded to the RAF during his service at the tests as a meteorologist. Civilian members of the Atomic Weapons Establishment and the Atomic Weapons Research Establishment are included in the study.

**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.

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...
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. Of the 21 358 test participants included in the second NRPB study, the largest group (39.5%) were from the RAF, yet the first NRPB test participants included in the second NRPB study, the used multiple ascertainment strategies to include 99% of the US nuclear weapons tests termed Operation Crossroads had been included in the main study's cohort. Of the 21 358 study estimated that only 74% of eligible RAF participants worked on known contaminated planes. The NRPB's second mushroom clouds to collect fission samples; ground crews vulnerable to radiation exposure. Air crews flew through Ministry of Defence to have been activities particularly they were already aware of—served in the Royal Air Force at electronic paper 3o f3

Similarly, Dickinson and colleagues concluded that the 22 000 women. The NHSCR identified only 78% of the cases. 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 17 844 veterans, advertised in a range of veterans' journals, and held public meetings. Similar methods had been used earlier by Watanabe and colleagues in their study of cancer mortality rate 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 underreport 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 misclassification 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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