THE VALIDATED PREVALENCE OF SELECTED CANCERS IN AUSTRALIAN VIETNAM VETERANS

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Introduction

Vietnam veterans comprise a group with possible exposure to 2,3,7,8-tetrachlorodibenzodioxin (TCDD) and phenoxy herbicides. As reported previously, Australian Vietnam veterans show evidence of elevation in overall mortality. An increase in mortality for some diseases associated with prior exposure to these chemicals, such as lung cancer is noted, but not for others, such as non-Hodgkin's lymphoma[1,2]. This cohort also self-reports very high levels of certain disease, and of diseases and mortality in their children[3,4].

Methods and Materials

As previously described, we undertook a postal survey of all male Australian Vietnam veterans for whom a current postal address could be found[3]. We decided to attempt to validate the existence of some of the conditions in both the children (described elsewhere), and the veterans themselves.[5]

Veterans were sent up to two reminder letters. The first was sent three weeks after the initial recontact, and the second about a further eight weeks later. In some areas of interest, insufficient replies were received, and so telephone reminders followed the postal questionnaires.

Once appropriate consent had been obtained, we attempted to validate the condition. For malignancies, there exists a centralised, compulsory, nation-wide register of cancers, which contains data on all cases of cancer registered since 1982. Prior to this time, some States had registries. If the cancer occurred after 1982 or in State that had a register when the cancer was reported to have developed, an attempt was made to match that cancer. If it could not be matched, then it was classified as "not validated"; if matched, it was classified as validated. Death records were also searched, and if a veteran was found to have died, and was certified to have died from the condition that they reported having in the first survey, the condition was classified as validated.

If the malignancy was reported to have developed prior to the establishment of an appropriate cancer registry, an attempt was made to validate the condition by locating the original clinical records. Unfortunately, in Australia hospitals now routinely destroy records after a set period of time (usually seven years), and in many cases the individual's treating doctor had retired, died, or otherwise lost the ability to confirm the records. In these cases, the condition was classified as "not able to be validated".

There were other reasons why the condition could not be validated. These included the death of the veteran (thus effectively preventing us from finding the details that would enable validation). It also included the veteran becoming too unwell or incapacitated to provide the details, and the loss of the veteran to follow-up (such as veteran moving, but not leaving a forwarding address, and not being otherwise traceable), or the veteran emigrating.

The number of veterans whose condition could not be validated was not insignificant. We therefore developed a number of models that allocated both the non-responders and the not able to be validated group to provide us with an estimate of the number of individuals with each disease. These five models descended in their level of strictness for validation.

In Model One, we estimated the validated response by counting only those we had positively validated. In Model Two, we estimated the validated response by counting those we had positively validated, and those who could not be validated because the clinician did not respond or indicated that records were insufficient to provide validation. We prorated these between the validated and not validated group, assuming that those who could not be validated would have the same validation rate as those where the clinician responded with a decision. In Model Three, we estimated the validated response by counting the positively validated, and by prorating the not able to be validated between the validated and not validated group. In Model Four, we estimated the validated response by counting the positively validated and those who could not be validated because the clinician did not respond or indicated that records were insufficient to provide validation. The non-responders were distributed between the validated, not validated and not able to be validated. In Model Five, we estimated the validated response by counting the positively validated responses. Those that could not be validated were distributed on pro-rated basis between the validated and not validated. The non-responders were distributed on a pro-rata basis between validated and not validated.

Results and Discussion

Of the 40 030 males who responded to the original questionnaire, 6 842 letters were sent to veterans seeking validation of conditions in the veteran, their child, or both.

Table 1 below gives the response rate. There are many reasons why there was no response. These include the veteran moving between the initial survey and the subsequent validation survey, the veteran becoming too incapacitated or ill to participate in the validation, and the veteran not believing that the validation process was needed. It also may include some in which the veteran did not actually have the condition. We were unable to ascertain which of these reasons were relevant in any individual case. However, as the non-response rate was not insignificant, in some of our models we distributed the non-responders to provide an estimate of the number of conditions present within our populations.

The rate that the conditions could not be validated was also calculated, and is also given in Table 1. As with the non-responders, there was reason to believe that in some of these cases the condition was present, and in some of our models that attempt to estimate the prevalence of the conditions, the cases were validation could not be undertaken were redistributed among the

validated and not-validated categories. Our models assumed that the rate would be no greater than the rest of the group undergoing validation.

Table 1. The Response Rate by Disease and Rate "not able to Be Validated".

Condition	Total Number	Number Responding	Response Rate %	Number not able to be Validated	Rate %
Lung Cancer	121	79	**65.3**	4	**3.3**
Colorectal Cancer	460	344	**74.8**	12	**2.6**
Soft Tissue Sarcoma	379	266	**71.0**	71	**18.6**
Melanoma	2 618	1 875	**71.6**	236	**9.0**
Prostate Cancer	422	316	**74.9**	17	**4.0**
Breast Cancer	49	34	**69.4**	6	**12.2**
Testis Cancer	148	104	**70.3**	0	**0**
Eye Cancer	95	63	**66.3**	9	**9.5**
Non-Hodgkin's Lymphoma	130	99	**76.2**	9	**6.6**
Leukaemia	67	48	**71.6**	3	**4.3**

Given that both the non-response rate and the rate of conditions being unable to be validated, we developed a number of models for estimating the likely prevalence of the conditions in this population of Vietnam veterans (see above).

Table 2. Number of Estimated Conditions According to Different Models

Condition	Model 1	Model 2	Model 3	Model 4	Model 5	Expected Number
Lung Cancer	44	46	46	64	64	65 (49-61)
Colorectal Cancer	182	185	188	241	245	221 (191-251)
Soft Tissue Sarcoma	10	13	14	37	19	27 (17-37)
Melanoma	***423***	***460***	***483***	***678***	***669***	380 (342-418)
Prostate Cancer	***201***	***210***	***212***	***276***	***279***	147 (123-171)
Breast Cancer	2	2	2	6	4	3 (0-6)
Testis Cancer	59	63	59	71	83	110 (89-139)
Eye Cancer	13	14	15	***24***	***23***	11 (4-18)
Non-Hodgin's Lymphoma	61	***65***	***66***	***82***	***84***	48 (34-62)
Leukaemia	21	22	23	31	33	26 (16-36)

Note: In Table 2, the numbers that are **bold** and in *italics* are above the upper 95 % Confidence Interval of the Expected Rate.

This study has important drawbacks. The response rate, while satisfactory, was not very high, and a proportion of those who responded could not be validated. This required a variety of

models to produce an estimated validated rate. Against this, the study has the advantage of size. In addition, in those cases that could be validated were confirmed by original clinical records or reference to a cancer registry. It should also be noted that when we were able to contact the veteran, a substantial majority gave permission for validation, providing evidence of general support for the study.

This study provided good evidence that this population suffers from an increase in prevalence of melanoma and prostate cancer. The prevalence rate of these malignancies was elevated in all statistical models used. The elevation in prostate cancer was consistent with previous mortality studies on the same population. It is perhaps coherent with other studies of populations of men who have been exposed to phenoxy herbicides and TCDD.

There was evidence of an elevation in the prevalence of Non-Hodgkin's Lymphoma, which was significantly elevated in four models. To a lessor degree eye cancer had evidence of an elevated prevalence.

This study provided good evidence that this population has a lower than expected rate of testicular cancer, which was decreased in all of the statistical models used. It is unclear why this is the case.

In this study, the lung cancer prevalence was significantly lower than the Australian community standard. This is not consistent with previous mortality studies on this cohort. The lower than expected lung cancer prevalence in this study may reflect the severity of the disease and the high possibility that many of these veterans may be unable to respond. It would appear that the prevalence of this condition has been under-reported in this study.

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