THE PREVALENCE OF LEUKAEMIA IN THE CHILDREN OF 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, and recent reviews have suggested that there is a range of conditions that veterans (and their children) may suffer from as a result of exposure to herbicides[1,2].

This work arose out of a self-reported questionnaire, in which we asked veterans if their children suffered from certain conditions. We decided to attempt to validate the existence of some of the conditions in the children. The aim of the study was to validate reports of leukaemia and to examine the particular sub-types of leukaemia.

Methods and Materials

As previously described, a postal survey was undertaken of all male Australian Vietnam veterans for whom a current postal address could be found[3]. Each veteran who indicated on the original survey that they had a child who suffered from leukaemia was again approached and asked to provide contact details or other information relating to the affected child. This approach was made about eighteen months after the initial survey. For children below the age of 17, parental consent to obtain medical records that would validate the existence of the condition was sought. The consent of the affected child was sought for those children over 17 and alive.

Veterans were sent up to two reminder letters. The first was sent three weeks after the initial validation study contact and the second about eight weeks later. In some areas of interest, insufficient replies were received, and so telephone reminders followed the postal questionnaires. For the children above the age of 17, there was also an initial mail out, followed by postal reminders, and then telephone reminders.

Once appropriate consent and demographic details had been obtained, we attempted to validate the condition in a number of ways.

A centralised, compulsory, nation-wide register holds all cases of cancer that have occurred in Australia since 1982, withe States having registries operating prior to this time. If the cancer had occurred before 1982 in a State that had a cancer register when the cancer was reported to have developed, an attempt was made to match that cancer at a State cancer registry. If it could not be matched, then it was classified as "not validated", if matched, it was classified as validated. In many cases we had to attempt to validate the condition by finding original medical records. In many cases, these records were unavailable, so the condition was classified as "not able to be validated".

For many veterans who had initially indicated that they fathered a child with leukaemia, we were not able to ascertain the validation status for other reasons. These included the death of the veteran (thus effectively preventing us from finding the details of the child 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). In addition, there were some cases among the children over the age of 17 who were lost to follow-up, and some of the children declined to give consent for validation. All of those were classified as not able to be validated.

The proportion of children who could not be validated was substantial, and there were reasons to believe that many of those who were placed in the "not able to be validated" category did actually have the condition. Further, some of those (either veterans of children) who simply did not respond may have had the condition.

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 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 pro-rated these between the validated and not validated categories, assuming that those who could not be validated would have had 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 pro-rating 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 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 a pro-rata 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.

The response rate averaged about 63 per cent, although for veterans who stated that they had fathered a child with leukaemia, it was slightly better at 65.9 %. There are many reasons why there was no response. It also may include some cases in which the child did not actually have the condition. We are 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 out models we distributed the non-responders to provide an estimate of the number of conditions present within our populations.

In addition, 15.3 % of children with leukaemia could not be validated. 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 children of Vietnam veterans (see above).

This study has important drawbacks. The response rate was low, 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.

The number of conditions of acute myeloid leukaemia (AML) in veterans' children , while higher than might be expected and suggestive of increased risk, is not raised to a statistically significant extent in most of our models.

Similarly, in most of our models the number of cases of acute lymphatic leukaemia (ALL) among veterans' children is significantly lower than the expected number of conditions. Chronic lymphatic leukaemia (CLL) and chronic myeloid leukaemia (CML) in veterans' children show no significant difference from the expected numbers of conditions.

Table 1. Validation results for leukaemia in veterans' children using selected reallocation models

Condition	Model 1	Model 2	Model 3 [(a)]	Model 4	Model 5 [(a)] (confidence interval)	Expected
ALL	18	18	23	27	35	41 (28–54)
CLL	0	0	0	0	0	0
AML	9	9	12	14	18	9 (3–15)
CML	1	1	2	2	3	3 (0–6)
Total leukaemia	28	28	36	43	55	57 (42–72)
ALL	Low	Low	Low	Low	—	
CLL	—	—	—	—	—	
AML	—	—	—	—	High	
CML	—	—	—	—	—	
Total leukaemia	**Low**	**Low**	**Low**	**Low**	—	

(a) The four leukaemia types do not sum to total leukaemia because of rounding differences.

Notes

1. High—The estimated validated conditions are statistically significantly higher than the Morbidity Study derived community standard at the 95 % confidence level.
2. Low—The estimated validated conditions are statistically significantly lower than the Morbidity Study derived community standard at the 95 % confidence level.
3. Dashes indicate no statistically significant differences from the Morbidity Study derived community standards.

The overall level of leukaemia is lower than expected in Model 1 to Model 4. As there is little reason to expect that Vietnam veterans should have children with lower rates of leukaemia, this suggests that our methodology is under-reporting the true level of leukaemia. This may suggest that Model 5 is the most appropriate model to examine the rate of leukaemia, and using this model, AML is elevated. This is similar to a report by Wan-Qing *et al*, who found an increased risk of AML among offspring whose father served in Vietnam[4].

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