Suicide in Australian pesticide-exposed workers

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Background  Epidemiological research has observed that workers with exposure to anticholinesterase pesticides, and particularly those with a history of acute overexposure, may be at increased risk of depression. However, there is little published research about the risk of suicide in relation to pesticide exposure.

Aims  To investigate risk of suicide in relation to metrics of pesticide exposure and type of work.

Methods  A nested case–control study was performed within a retrospective cohort study of pesticide-exposed workers from various industries. Ninety male suicide deaths and 270 male controls were matched by age bands, state of residence and live status. Cholinesterase inhibition was determined using subject-specific biomonitoring records collected at the time of exposure.

Results  Suicide risk was not significantly elevated in relation to exposure to any particular pesticide classes nor in relation to pesticide overexposure, confirmed by blood test. While the risk of suicide associated with a history of cholinesterase inhibition was raised, this was not significant (odds ratio = 1.90, 95% confidence interval = 0.73–4.93).

Conclusions  This study did not find an elevated suicide risk associated with use of any major class of pesticide and there was little evidence that overexposure was associated with increased risk of suicide. A non-significant association between overexposure to anticholinesterase pesticides may be consistent with previous research showing increased depression in workers with a history of cholinesterase inhibition and warrants further investigation.

Key words  Cholinesterase; nested case-control studies; occupational epidemiology; pesticide exposure; suicide.

Introduction
Suicide is a recognized problem in the farming community both in Australia and elsewhere [1–5] and evidence suggests that farm workers have a higher risk of suicide than workers in almost any other major industry [6,7]. Although evidence of excess suicide risk in farmers is extensive, it is not universal [3,8,9]. The farm suicide phenomenon is complex and likely to be multifactorial [10] and evidence suggests that a wide range of factors such as age, remoteness, social support, lethal vector availability and farm job type are likely to be involved [3,8–11].

The problem is likely to be under-represented in mortality statistics since coroners may be reluctant to assign a finding of suicide to deaths where intentionality is not completely clear [12,13] and in farming families [7]. There is evidence that farmers are less likely than others to leave definitive proof of intentionality in the form of a suicide note [11].

Much of the research on mental illness and suicide in the farming population has focused on stress, resilience and coping mechanisms in farmers, as well as family and social dynamics in farming communities and access to care [2,7]. Because agricultural workers are less likely than others to acknowledge mental health problems, less likely to seek help and tend to select the most lethal suicide vectors, to which the farm workplace provides ready access, suicidal behaviour in this population is characterized by a high ratio of completed suicides [14].

Epidemiological research has observed that workers with a history of overexposure to anticholinesterase insecticides such as organophosphates (OPs) may be subject to long-term neuropsychological changes, including depression and depressive symptoms [15–17]. Steenland et al. [18] and Savage et al. [19] reported significant changes in mood among subjects who had experienced OP poisoning from 3 to >10 years prior to evaluation. In a study of farm pesticide users, Stallones and Beseler [20] found that overexposure events serious enough to cause symptoms of toxicity were associated with a high incidence of depressive symptoms independent of other...
known risk factors for depression. In a study of farm workers with a history of documented cholinesterase inhibition, Reidy et al. [21] found depression and anxiety symptoms were more commonly reported by cases compared with unexposed controls. A cross-sectional study of farmers exposed to OP insecticides through dipping sheep showed increased vulnerability to psychiatric disorder than controls, although no dose–response relationship was evident [22]. A study of female glasshouse workers also found increased tension, depression and fatigue among OP-exposed workers than controls [23]. A recent case–control study of agricultural pesticide applicators diagnosed with clinical depression reported that a history of diagnosed pesticide poisoning was significantly associated with depression. In this study, long-term OP exposure without diagnosed acute poisoning was also associated with depression [24]. This finding demonstrates the possibility that long-term exposed workers without a history of acute cholinesterase inhibition, or possibly with cholinesterase inhibition sufficiently mild to escape detection, may also be at risk [22,25,26].

Although there have been several published studies reporting depression in OP-exposed workers, there are few published studies of suicide among these occupations and this is an important gap, given the widespread concern over suicide in the agricultural community. In a retrospective study of 251 suicide cases in a region of Spain with particularly intensive agricultural activity and high OP use, the suicide rate was significantly higher than that in surrounding regions [27]. They also observed higher suicide mortality in farmers compared with other occupations. A Canadian case–control study found no specific association between OP exposure and suicide, but this study lacked individual-level exposure assessment, relying on farm-level census data [28]. However, this study did find a suggestive increase in risk for suicide associated with insecticide and herbicide spraying among the subgroup of operators classified as most likely to be directly exposed to pesticides [1].

Our recent retrospective cohort study of cancer and mortality of pesticide-exposed workers in a range of industries found a significant excess of suicide mortality [standardized mortality ratio (SMR) = 1.35, 95% confidence interval (CI): 1.10–1.66] [29]. The aim of the present nested case–control study was to investigate in more detail the work types and pesticide exposures of these suicide cases. We hypothesized that suicide cases would have been more likely to have been occupationally exposed to anticholinesterase pesticides (OPs and carbamates) or to have had a history of acute cholinesterase inhibition.

Methods
The case–control study was nested within a cohort study of pesticide-exposed workers assembled from archive records, belonging to the New South Wales and Victorian state governments. Extensive state government programmes in the 1960s to 1980s offered free regular biomonitoring to pesticide-exposed workers. The programmes provided ongoing occupational health surveillance and identification of possible overexposure cases requiring follow-up. Personal identifiers including name, address, date of birth, job information and interview dates were collected from archive records.

The cohort consisted of 14 601 eligible workers, of whom 92% were male. The cohort included pesticide-exposed workers with jobs in agriculture and primary production, pesticide manufacturing/distribution and maintenance of municipal and sporting facilities, ornamental gardens and public utilities [29].

Relevant identifier variables for each cohort member were supplied to the Australian Institute of Health and Welfare (AIHW) for linkage to the National Death Index (NDI) for the years 1983–2004. For subjects matched to the NDI, the AIHW supplied dates and causes of death and 1338 cohort members were found to have died from any cause [29].

A case was defined as any cohort member who was matched to an NDI record during the period of follow-up and for whom the primary cause of death was intentional self-harm (ICD-9 E950–E959 or ICD-10 X60–X64). Ninety cases met these criteria. Three controls per case were selected from the rest of the cohort \( (n = 270) \) based on a sample size calculation, which assumed relative risks to be detectable with 80% power and exposure prevalence to vary between 5 and 50%. The power calculation showed that three controls per case offered some advantage over two controls; however, little advantage was to be gained by using more than three controls.

Cases and controls were matched by year of birth (5 year bands) and state of residence at the time of interview (New South Wales or Victoria) and controls needed to be alive at the time of the matched case’s death. State was matched because the cohort was composed of records from two distinct programmes that run independently by the state governments of New South Wales and Victoria. Live controls were chosen to ensure that, like the case, each control had the potential for exposure until the case’s death. All the cases and controls were males.

Exposure assessment for all cases and controls \( (N = 360) \) involved review of all interview records for each subject in the original archived records to determine any exposure to four pesticide classes, any overexposure to the same four pesticide classes and detailed job description information. The pesticide classes used were defined by the categories used on the original survey forms: OP/carbamate anticholinesterase insecticides, organochlorine insecticides, herbicides/fungicides and organometal pesticides. At each interview, subjects had been asked about their current pesticide exposure and reported pesticides were recorded. For the purpose of the case–control
analyses, exposure was defined as ever exposed, taking into account all interview records for each subject. Overexposure was defined as ever having a biomonitoring test result recorded for that pesticide class which was outside the reference range.

At interview, subjects had provided job title and employment details. For the purpose of the case–control analysis, jobs were coded using the 1988 International Standard Classification of Occupations (ISCO-88, International Labour Organisation Bureau of Statistics), an international coding system approximately contemporaneous with the period during which the cohort members were in the workforce. For the purpose of the case–control study, ISCO-88 jobs were grouped as follows: Agricultural jobs were defined as ISCO-88 6100–6112, 6114 (crop growers, excluding gardeners and nursery workers), 6114–6139 (animal producers and mixed crop/animal producers) and 9211 (agricultural labourers). Gardeners, horticultural and nursery workers were defined as ISCO-88 6113 (gardeners, horticultural and nursery growers). Grain storage workers were coded as ISCO-88 8100 (stationary-plant and related operators), all of whom were described as grain silo or related workers in their original records. Chemical manufacturing workers were defined as ISCO-88 8150 (chemical-processing plant operators). A further ‘other’ category was defined as all jobs, not included in the above groups.

Univariate and multivariate logistic regression models were used to determine odds ratios (ORs) and 95% CIs. All analyses were performed using STATA statistical software package, Version 9 (STATA Corporation, 2005).

This study was conducted under the approval of the Monash University Standing Committee on Ethics in Research Involving Humans. Linkage to the NDI was approved by the AIHW Ethics Committee.

**Results**

Table 1 shows demographic and exposure information for the cases and controls. The majority of the study group was born between 1950 and 1970 (66%) and these individuals were therefore aged from early 30s to early 50s by the end of cohort follow-up. Approximately one-third of the study group was classified as agricultural workers and a further third as horticulture, gardening and nursery workers. Job classifications were similar between cases and controls. Horticulture, gardening and nursery workers were a little more common among controls than among cases.

Three quarters of the study group reported exposure to OP and/or carbamate anticholinesterase insecticides. Organometal and organochlorine pesticides were reported by <5% of subjects in each group.

Overexposure events detected through the biomonitoring component of the surveillance programmes were detected in only a minority of subjects, with 87% of subjects having no recorded overexposures. OP/carbamate insecticides were the most common causes of recorded overexposures.

Eleven cases had a history of overexposure to anticholinesterase pesticides. However, three of these cases were classified as overexposed based on a blood test result that was dated within 10 days of their date of death. According to the original eligibility criteria, these subjects remain eligible for inclusion in the study and analyses based on job title. However, since their death was likely to be a direct toxic effect of their documented overexposure, these cases and their matched controls were removed from the analyses involving this metric: the univariate analysis of overexposure to OP/carbamates and the multivariate model.

The suicide vectors of the 90 cases have been reported elsewhere [29]. Hanging and firearms were the most common vectors, accounting for 57% of the suicide deaths. Poisonings accounted for 14% of the suicide deaths.

Table 2 shows univariate regression results for odds of suicide by various exposure metrics. The following

<table>
<thead>
<tr>
<th>Year of birth</th>
<th>Cases (N = 90)</th>
<th>Controls (N = 270)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1920</td>
<td>1 (1)</td>
<td>3 (1)</td>
</tr>
<tr>
<td>1920–1929</td>
<td>6 (7)</td>
<td>18 (7)</td>
</tr>
<tr>
<td>1930–1939</td>
<td>11 (12)</td>
<td>33 (12)</td>
</tr>
<tr>
<td>1940–1949</td>
<td>12 (13)</td>
<td>36 (13)</td>
</tr>
<tr>
<td>1950–1959</td>
<td>26 (29)</td>
<td>78 (29)</td>
</tr>
<tr>
<td>1960–1969</td>
<td>33 (37)</td>
<td>99 (37)</td>
</tr>
<tr>
<td>&gt;1969</td>
<td>1 (1)</td>
<td>3 (1)</td>
</tr>
</tbody>
</table>

Specific job groups (ISCO-88)

- Agricultural jobs: 30 (33%)
- Horticulture, gardening and nursery jobs: 24 (27%)
- Grain storage jobs: 5 (6%)
- Chemical manufacturing jobs: 28 (31%)
- Other jobs: 79 (29%)

Reported pesticide exposures

- OP/carbamates: 69 (77%)
- Organochlorines: 30 (33%)
- Herbicides/fungicides: 42 (47%)
- Organometal pesticides: 12 (13%)
- Exposures not recorded: 2 (2%)

Ever overexposed

- OP/carbamates: 11 (12%)
- Organochlorines: 1 (1%)
- Herbicides/fungicides: 6 (7%)
- Organometal pesticides: 1 (1%)
- No record of overexposure: 72 (80%)

Since individuals may have exposure/overexposure to more than one pesticide class, column totals for these variables may be >100%.
exposure categories were not included in the regression analyses due to small numbers: grain storage jobs, chemical manufacturing jobs and overexposure to organometals, herbicides/fungicides and organochlorines. In univariate analyses, none of these variables was significantly associated with risk of suicide (results not shown).

Odds of suicide were not significantly different from unity of reported exposure to OPs/carbamates, organochlorines or organometals. Reported exposure to herbicides/fungicides was negatively associated with suicide mortality. There was an approximately 2-fold increased odds of suicide among those classified as overexposed to cholinesterase inhibitors, although this finding was not statistically significant. Occupation was not associated with suicide risk and this was also the case when analyses were repeated using the ISCO-88 Major Group headings (results not shown).

Table 2. Univariate regression results—odds of suicide by reported pesticide exposure classes, OP/carbamate overexposure and major occupational groups

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Cases (N = 90), n (%)</th>
<th>Controls (N = 270), n (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported pesticide exposures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exposed OP/carbamates</td>
<td>21 (23)</td>
<td>70 (26)</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>69 (77)</td>
<td>200 (75)</td>
<td>1.15 (0.66–2.00)</td>
</tr>
<tr>
<td>Exposed OC</td>
<td>60 (67)</td>
<td>169 (63)</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>30 (33)</td>
<td>101 (37)</td>
<td>0.84 (0.51–1.38)</td>
</tr>
<tr>
<td>Exposed herbicides/fungicides</td>
<td>48 (53)</td>
<td>103 (38)</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>42 (47)</td>
<td>167 (62)</td>
<td>0.54 (0.33–0.87)</td>
</tr>
<tr>
<td>Exposed organometal pesticides</td>
<td>78 (87)</td>
<td>224 (83)</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>12 (13)</td>
<td>46 (17.0)</td>
<td>0.75 (0.38–1.49)</td>
</tr>
<tr>
<td>Over exposure OP/carbamates overexposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>79 (91)</td>
<td>249 (95)</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>8 (9)</td>
<td>12 (5)</td>
<td>2.10 (0.83–5.32)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Agricultural job</td>
<td>60 (67)</td>
<td>187 (69)</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>30 (33)</td>
<td>82 (31)</td>
<td>1.15 (0.69–1.91)</td>
</tr>
<tr>
<td>Horticulture/gardening/nursery job</td>
<td>66 (73)</td>
<td>179 (66)</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>24 (27)</td>
<td>91 (34)</td>
<td>0.72 (0.42–1.22)</td>
</tr>
</tbody>
</table>

Bold values are statistically significant.

OC, organochlorines.

*The following exposure categories were not included in the regression analyses due to small numbers: grain storage jobs, chemical manufacturing jobs and overexposure to organometals, herbicides/fungicides and organochlorines.

+Three cases and their respective matched controls were not included in the univariate analysis of OP/carbamate overexposure because the blood test result by which they were classified as overexposed was within 10 days of their date of death. The total number of individuals in this analysis is therefore 348.

Results of the multivariate regression model (Table 3) showed a similar pattern to the univariate results. Odds of suicide among those with a history of overexposure to OPs and carbamates were ~2-fold, although this was not statistically significant. Herbicide/fungicide exposure continued to have low odds of suicide, although the OR was not significant in the multivariate model. No significant associations were observed for occupational groups and this was also the case when the model was repeated using the ISCO-88 Major Group headings (results not shown).

**Discussion**

Elevated suicide risk was not significantly associated with self-reported exposure to any class of pesticides or with blood test-confirmed overexposure. A non-significant increased suicide risk was observed among those with a history of cholinesterase inhibition. This may be consistent with the body of evidence linking a history of the past cholinesterase inhibition with depressive symptoms, mood problems, anxiety and other neuropsychological and neurobehavioral deficits, which are likely to affect risk of suicide [16] since mental disorders, particularly depression, are implicated in the vast majority of suicidal behaviour [1,17].

In the present study, the ~2-fold OR for suicide mortality associated with past cholinesterase overexposure was not statistically significant in both the univariate and multivariate analyses. However, it is likely that there was bias from possible exposure misclassification. It is improbable that the surveillance programme detected every overexposure event in the lives of the workers in the cohort. The surveillance programme visited local areas intermittently and the programme records included notes of self-reported overexposure events that had occurred.

Table 3. Multivariate regression results—odds of suicide by reported pesticide exposure classes, OP/carbamate overexposure and major occupational groups, adjusted for reported pesticide exposure, overexposure to OP/carbamate pesticides and occupational groups

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported pesticide exposure</td>
<td></td>
</tr>
<tr>
<td>Exposed OP/carbamates</td>
<td>1.07 (0.59–1.95)</td>
</tr>
<tr>
<td>Exposed OC</td>
<td>0.95 (0.55–1.63)</td>
</tr>
<tr>
<td>Exposed herbicides/fungicides</td>
<td>0.65 (0.40–1.10)</td>
</tr>
<tr>
<td>Exposed organometal pesticides</td>
<td>0.84 (0.40–1.76)</td>
</tr>
<tr>
<td>Over exposure OP/carbamates overexposure</td>
<td></td>
</tr>
<tr>
<td>Overexposure: OP/carbamates</td>
<td>1.90 (0.73–4.93)</td>
</tr>
<tr>
<td>Occupation</td>
<td></td>
</tr>
<tr>
<td>Agricultural job</td>
<td>1.16 (0.64–2.12)</td>
</tr>
<tr>
<td>Horticulture, gardening or nursery job</td>
<td>0.93 (0.49–1.78)</td>
</tr>
</tbody>
</table>

OC, organochlorines.
since the programme’s last visit to the area or earlier in the participant’s career prior to involvement in the surveillance programme. These self-reports of overexposure were not used in the classification of subjects for the purpose of these analyses. Therefore, while we are confident of the overexposure status of individuals classified as (ever) overexposed, as this was based on biomonitoring results, it is likely that a proportion of the controls also experienced overexposure at some time. Although the extent of this cannot be estimated, differential exposure misclassification of this kind would be expected to bias the risk estimate towards the null, under-representing the true risk [29].

It is also reasonable to suspect that the 90 suicide deaths eligible for inclusion in this case–control analysis under-represents the true number of suicide deaths in the cohort and this would reduce the potential statistical power of the case–control analysis. There was a significant excess of unintentional poisoning mortality observed in the main cohort analysis (SMR = 1.83, 95% CI: 1.02–2.31), based on 10 deaths [28]. Given the tendency of coroners to under-represent suicide in favour of accident, it is plausible that some of these deaths may, in fact, have been suicides. However coroner’s data, which would be needed to investigate this possibility, are not available from the NDI. A negative association was found for herbicide/fungicide use. This finding is unexpected and may be a chance finding since it is improbable that herbicide/fungicide use itself is protective against suicide. It is possible that workers who use herbicides/fungicides may differ from the rest of the sample in other factors related to mental health and suicide, such as socio-economic status, geographic/social isolation, marital status, religious beliefs, stress or chronic physical illness [17]. Such factors may also have affected the possible association seen between suicide and cholinesterase inhibition. Unfortunately, the data available for the cohort under study did not permit exploration of such differences.

A major strength of this study was access to quantitative laboratory test data to confirm overexposure status, whereas in the past, studies have relied on self-reported poisoning or similar subjective data. However, as discussed above, although this provides a high degree of certainty that cases classified as overexposed truly were, this metric is likely to have underestimated the number truly overexposed.

A main limitation of this study is that information about cohort members is limited by the data items that were collected in the original surveillance programmes. This limits the possibilities for exploring other factors relevant to suicide and mental health. In particular, we were limited by the pesticide categories in which the exposure data were originally collected. Another important limitation of this study is the small numbers of cases in many of the subanalyses. Repeat linkage of the main cohort to the NDI in the future will enable these analyses to be repeated with larger numbers of cases and increased statistical power.

In conclusion, in this case–control study of suicide deaths in a cohort of pesticide-exposed workers, self-reported pesticide usage and occupational group were not associated with increased risk of suicide. We suggest that the non-significant increased risk of suicide associated with a history of blood test-confirmed cholinesterase inhibition warrants further research to investigate this association as such an association would have implications for the clinical care of individuals with a history of acute cholinesterase inhibition.

Key points

- An unusually high risk of suicide among agricultural workers is widely acknowledged but the aetiology remains largely unclear, especially the possible role of pesticide exposure.
- Using subject-specific exposure data collected at the time of exposure, this study found no significant increases in suicide risk associated with self-reported pesticide exposure or with blood test-confirmed overexposure.
- A non-significant association between previous overexposure to anticholinesterase pesticides and suicide mortality was observed.

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Conflicts of interest

None declared.

References