THE HEALTH NEEDS OF THE CHILDREN OF OPERATION GRAPPLE AND VIETNAM VETERANS

**A Critical Appraisal Undertaken for Veterans' Affairs
New Zealand Defence Force**

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EXECUTIVE SUMMARY

The purpose of this report has been to:

- Conduct a comprehensive and critical review of all available international research on the health of Vietnam and nuclear test veterans' children;
- Consider that research within the New Zealand context;
- Identify the range of health conditions (if any) for which there is an elevated risk for the children of veterans;
- Identify the health care needs of those identified conditions; and
- Evaluate the various models of care for the identified conditions.

The literature has been reviewed systematically. The primary focus was on studies of veterans' children. However, the directly relevant literature was limited and the review was extended to include studies of paternal occupational and environmental exposures to provide some additional information.

OPERATION GRAPPLE

New Zealand Naval personnel were involved in a series of nine atmospheric nuclear weapons tests carried out by the United Kingdom between 1957 and 1958 in the Christmas and Malden Islands, known as 'Operation Grapple'.

There has been concern among nuclear test veterans and their families about potential health outcomes for their children as a result of their participation in the tests, in particular, anxiety about the effects of exposure to ionising radiation.

The sources of evidence available to the research community suggest that New Zealand nuclear test veterans were not exposed to significant levels of ionising radiation at the time of the tests. It should be noted, however, that most film badges were not processed (Crawford 1989), and the potential for residual radiation exposure may have existed.

There is no high-quality epidemiological literature available to support an association between the paternal exposure of New Zealand nuclear test veterans to ionising radiation before conception and an increased risk of adverse health outcomes for their children. Further, there are no high-quality epidemiological studies dealing directly with the health of children of nuclear test veterans internationally. Epidemiological studies investigating outcomes for this population have not generally been considered feasible.

The evidence from studies of occupational, environmental, and medical exposures of an association between paternal exposure to ionising radiation before conception and adverse health outcomes is inconsistent. The biological potential of paternal exposure to induce adverse health outcomes in children is recognised, but this has not been shown conclusively in human populations to date.

The studies undertaken by Roff have highlighted the presence of a number of undesirable health conditions in the children of New Zealand nuclear test veterans (Roff 1998; Roff et al. 2000). The dearth of literature on the psychological effects for the offspring of nuclear test veterans makes it difficult to draw conclusions about this outcome.

VIETNAM

New Zealand Vietnam veterans and veterans from other countries have for some time been concerned about the effects of their military service in Vietnam on the health of their children. Concerns relate primarily to exposure to herbicides widely used in Vietnam to defoliate areas of jungle. The different herbicides used have come to be grouped together under the term 'Agent Orange'.

The primary concern relates to the contamination of Agent Orange by trace amounts of the dioxin tetrachlorodibenzo-ρ-dioxin (TCDD). Over the decades since the Vietnam War there has been accumulating evidence that TCDD is a highly toxic substance and a potent carcinogenic.

The birth of children with a range of defects is unfortunately not uncommon and 2-3% of Vietnam veterans would be expected to have a child with a birth defect. It is understandable that veterans would question whether their exposure to Agent Orange contributed to their child's birth defect.

As a result of veterans' concerns a number of epidemiological studies have been undertaken comparing the health of veterans' children with a comparison group. There have been three high quality cohort studies and a number of good case control studies undertaken both in the United States and Australia. These studies have considered the potential effects of exposure to Agent Orange on all birth defects combined, on specific birth defects and on adverse reproductive outcomes such as still birth and spontaneous abortion.

The risk estimates calculated for the category 'all birth defects' are remarkably consistent and overall show no increased risk for Vietnam veterans for fathering children when all birth defects are considered. High quality epidemiological studies have shown no consistent positive association between exposure to Agent Orange or a range of chemicals or pesticides and any specific birth defect. However, there has been a tendency towards a slight but not significant association between paternal exposure to dioxins, pesticides and herbicides and an increased risk of the birth defect spina bifida. It is this association which has resulted in the United States Committee to Review the Health Effects of Agent Orange concluding that there is limited suggestive evidence of an association between spina bifida and Agent Orange exposure.

Similarly there has been a slight increased risk of childhood acute myelogenous leukaemia (AML) after paternal exposure to service in South East Asia and after exposure to pesticides. AML has also been accepted by the Committee as a condition for which there is limited suggestive evidence of an association between paternal exposure and adverse outcomes. There is no evidence available to permit

interpretation of international evidence for an increased risk of AML in a New Zealand context.

The extent to which decisions about associations between Agent Orange and adverse health outcomes for veterans' children can be made is affected by the limitations of epidemiological studies. Namely:

- Studies have not been large enough to detect rare outcomes;
- It is difficult to classify paternal exposure. The misclassification of unexposed men as exposed reduces the ability of the studies to detect a difference;
- Recall bias is inherent in self-reported data from veterans about their own and their children's health status;
- Background levels of TCDD in Western Society are relatively high; and
- A statistically significant result may not be biologically meaningful. A small proportion of results will be statistically significant due to chance.

Interpretation of these data in a New Zealand context must take into account the very limited potential New Zealand troops had for exposure to Agent Orange. The information available to the authors was that ANZAC Forces generally served in Phuoc Tuy province where there was no aerial spraying. In this context, and given the small increased risks found in studies of very exposed populations, the conclusion reached by this appraisal of the literature is that there is no evidence that exposure to chemicals in Vietnam has affected the health of the children of New Zealand Vietnam veterans.

The mental health of some Vietnam veterans has been linked to their service in Vietnam. Overseas and New Zealand studies suggest Vietnam veterans are more likely to suffer from post-traumatic stress disorder (PTSD) than civilians. Veterans with high exposure to combat are at higher risk of PTSD. Veterans with PTSD often have other psychological symptoms.

Living with a parent with mental illness can affect the family environment. Effects on the family environment represent a risk factor for the mental health of children of veterans. The health outcomes for children of veterans with PTSD are variable. International studies of psychosocial functioning show more similarities than differences between the children of veterans and civilians. Most children are unaffected. However, a small number of children may be affected. Health outcomes for affected children include a range of conditions such as lowered self-esteem, alcohol and substance abuse, and increased rates of suicide. Such effects may result from reduced quality of parenting or as a result of an increase in social disadvantage and adverse life events due to the disability associated with the parent's PTSD.

HEALTH CARE AND SUPPORT FOR VETERANS' CHILDREN

There are children of New Zealand veterans with disabilities resulting from birth defects and these people, and other New Zealanders with disability, need support. Appropriate models of support based on the New Zealand Health and Disability Support Strategy are discussed.

In New Zealand guidelines for health care professionals have been developed for caring for people with depression, anxiety, and alcohol or cannabis addiction. Guidelines describe recommended care based on the best evidence available. Summaries of the guidelines are appended (Appendix Two).

Children of veterans with PTSD may need assistance to access the health care recommended in New Zealand guidelines, as access to this care through the publicly funded health system may be limited.

The uncertainty and debate that has surrounded the potential risks for the children of veterans of Operation Grapple and Vietnam has undoubtedly caused high levels of concern amongst veterans and their families, and may have negatively impacted on their psychological wellbeing. It is hoped that the conclusions of this review will ease these concerns for some of those involved.

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SECTION ONE: OUTLINE OF REPORT

BACKGROUND

Objectives of this report

In 1998 the Prime Minister directed that an inquiry be undertaken into the health status of children of Vietnam and Operation Grapple veterans (Advisory Committee on the Health of Veterans' Children, 1999). The purpose of the Inquiry was to ascertain whether the parent's possible exposure to chemical agents or radiation during service had been responsible for health problems in their children and, if so, to recommend appropriate measures to assist those affected.

One of the recommendations arising from the Inquiry was that a research capability be established to provide information on the health of veterans' children. In this context the Office of Veterans' Affairs commissioned the following:

- A comprehensive and critical review of all available international research on the health of Vietnam and nuclear test veterans' children;

- Consideration of that research within the New Zealand context;

- Identification of the range of health conditions (if any) for which there is an elevated risk for the children of veterans;

- Identification of the health care needs of those identified conditions; and

- Evaluation of the various models of care for the identified conditions.

New Zealand servicemen and Operation Grapple

The United Kingdom carried out 21 atmospheric nuclear weapons tests in Australia and islands in the Pacific Ocean between 1952 and 1958. Personnel from the Royal New Zealand Navy were involved in tests at Malden and Christmas Islands between 1957 and 1958. This series of tests, known as 'Operation Grapple', involved nine tests in total and 563 New Zealand Naval personnel.

New Zealand servicemen and Vietnam

New Zealand was involved in the Vietnam war between 1964 and 1971 (Advisory Committee on the Health of Veterans' Children, 1999). Initially, in 1964, New Zealand's contribution was limited to engineers and medical personnel, but extended to include combat personnel in 1965 (Leepson, 1999). New Zealand began to withdraw combat troops in 1970, and completed withdrawal in 1971 (Leepson, 1999).

A total of 3368 Service men and women served in Vietnam (Advisory Committee on the Health of Veterans' Children, 1999).

Potential effects on the health status of children of veterans

The health of children of veterans could potentially be affected:

- By parental exposure to toxins or to chemicals such as herbicides or pesticides in Vietnam or by parental exposure to radiation in Operation Grapple.

Or

- As a result of impacts on the health of their veteran parent.

Parental exposure to harmful substances

Parental exposure has the potential to affect the conceiving spermatozoon or oocyte or their precursors or germ cells from which they originated, so exposure could cover a period from the parents' own foetal life until the conception of their offspring (Kristensen, 1999). Maternal exposure can also act during pregnancy or postnatally during lactation.

Manifestations of adverse outcome can occur at any point during the life-span of the offspring: during pregnancy, delivery, or the postnatal period including adolescence and adulthood. Adverse outcomes can be manifested by:

- Death (spontaneous abortion, stillbirth, postnatal death);

- Structural abnormalities – birth defects;

- Alterations in growth or functional competence of organ systems (birthweight, nervous system development, cancer); and by

- Chronic disease in adult life.

Impacts on the health of a veteran parent

The health of a child could potentially be affected by exposure to a parent whose health has been compromised as a result of service. Such conditions might include exposure to a parent with mental illness.

Health effects included in this report

The potential for both direct and indirect effects on the health of the children of New Zealand veterans of Vietnam and Operation Grapple has been considered in this report. As all of the New Zealand Navy personnel involved in Operation Grapple were male and most of the New Zealand personnel in Vietnam were male, the report has focused on male mediated health effects.

METHOD

Literature review

Literature for this report was reviewed systematically. A systematic literature review consists of the following stages (Cochrane Collaboration, 2000):

1. Question formulation
    Defining a specific question to guide the search for evidence.

2. Development of a search strategy
    Working with expert librarians to define the scope of the search for evidence, appropriate search terms, search limits, Boolean operators and databases.

3. Accessing papers and reports
    Obtaining papers from the published literature and from the unpublished or 'grey' literature such as theses and reports. Extracting relevant information using a standardised data extraction form.

4. Critical appraisal
    Conducting a detailed critique of the reliability and validity of the study objectives, design, methods and analysis. The purpose of appraising a paper is to discover if the methods and results of the research are sufficiently valid to produce useful information (Fowkes & Fulton, 1991).

5. Study categorisation and assignment of levels of evidence
    Categorising a study on the basis of the quality of the study design into an appropriate level of evidence. Level 1 studies are accorded the highest level of quality for determining association. Level 5 studies are the lowest level (Table 1).

Table 1: Levels of Evidence

Level 1 Evidence: Meta-analyses
Meta-analysis is the combination of data from several studies to generate one measurement. The advantages of meta-analysis are an increase in the power of the studies to detect small differences. Studies can only be reliably combined in this way if they have used the same methods of data collection and the same outcome measures.

Level 2 Evidence: Cohort Studies
A cohort study is an observational study of a group of people with a specified characteristic or disease who are followed up over a period of time to detect new events. Good quality cohort studies include a control group for comparison (Fowkes & Fulton, 1991). Data are usually presented as Odds Ratios.[i]

Level 3 Evidence: Case Control Studies
Case control studies are observational studies in which characteristics of people with a disease (cases) are compared with selected people without a disease (controls) (Fowkes & Fulton, 1991). Data are usually presented as Relative Risks[i].

Level 4 Evidence: Cohort Studies with Comparison with National Data sets
Data from the cohort are compared with national statistics. This type of study is less reliable than level 2 cohort studies because there is no consistency between the ways in which the national comparative data are collected and the study data.

Level 5 Evidence: Includes a range of low quality designs: cross-sectional comparative study, single cohort study with no comparison group and no comparison with national statistics, descriptive study with no comparison group. Cross sectional studies are surveys of the frequency of disease, risk factors or other characteristics of a defined population at one particular time (Fowkes & Fulton, 1991).

Question formulation

The primary question for which a search strategy was developed was:

> *'What is the strength and direction of the association between veterans' exposure to physical, chemical or psychological factors as a result of serving in Operation Grapple or Vietnam and health outcomes of their offspring?'*

Sub-questions were developed for specific outcomes:

> *'Did parental exposure to ionising radiation in Operation Grapple/ herbicides in Vietnam affect the health of their offspring?'*

> *'Did parental exposure to military service in Operation Grapple/ Vietnam affect the psycho-social functioning of offspring?'*

A secondary search was undertaken to answer the following question:

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[i] An Odds Ratio or Relative Risk estimates the magnitude of an association between an exposure and the risk of an outcome, such as a birth defect. When the event rate is low Odds Ratios (OR) are very similar to Relative Risks (RR). For both OR and RR a value of 1 indicates no difference. Less than 1 indicates the exposure reduces the likelihood of the event occurring. A value of greater than 1 indicates the exposure increases the chance of an event occurring (Cochrane Collaboration, 2000).

'What evidence is there of an association between occupational or environmental exposure to physical, chemical or psychological factors at similar levels to which veterans would have been exposed, on the impaired health of their offspring?'

It was not within the scope of this review to critically review the literature on any association between exposures and the veteran's own health.

Search strategy

All locally available references were accessed. References not locally available were accessed if they were written in the English language or if an English language abstract was available, if they were accessible within the time frame, and if the cost of accessing the material was within the scope of the budget.

The following sources of evidence were searched:

Electronic databases

- Medline 1966 to December Week 4 2000
- Psychlit
- PsychINFO 1967 to February Week 2 2001
- Cochrane Library
- Embase
- Digital Dissertations
- AMED (Allied and Complementary Medicine) 1985 to January 2001
- Cancerlit 1975 to November 2000
- Current Contents/All Editions 1993 Week 26 to 2001 Week 09
- Expanded Academic
- Health module (Proquest)
- Index New Zealand (INNZ)
- Social Science Citation Index
- Social Science Plus (Proquest)

Two experienced medical librarians were consulted in the construction of the following search strategy. The key search terms used included:

Vietnam; Veteran; Agent Orange; Dioxin; Defoliant; Pesticide (2,4,5-T or 2,4-D); Herbicide; Nuclear test; Operation Grapple; Christmas Island; Radiation; Atomic test; H-bomb; Health; Disease; Disability; Deformity; Congenital; Operation Ranch Hand; Cancer; Post-traumatic stress disorder; Mental health; Toxic chemical; Haematological cancer; SAPHO syndrome; paternal exposure; maternal exposure; AND children OR offspring.

Variations and combinations of these terms were used to search individual databases, dependent on the thesaurus available.

Internet search

The World Wide Web was searched using the Copernic 2001 Plus meta-search tool. Nineteen search engines were searched simultaneously (AltaVista; AOL.COM search;

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Direct Hit; Euroseek; Excite; FAST Search; FindWhat; Google; GoTo.com; HotBot; LookSmart; Lycos; MSN Web Search; My CompuServe; NBCi; Netscape Netcenter; Open Directory Project; Web Crawler; Yahoo). The following search terms were entered:

- Vietnam veteran health child
- Paternal radiation health
- Operation Grapple health

Search results were limited to the first 100 results for each search engine, sorted by relevance score. Web-sites were visited and searched for relevant content. No further studies were identified in this manner, with the exception of the report *"Morbidity of Vietnam Veterans. Suicide in Vietnam Veterans' Children: Supplementary Report No 1"*, (Australian Institute of Health and Welfare, 2000) which was available on-line. Key web-sites searched are listed in Appendix One.

Expert consultation

Several international researchers with expertise on the health effects of the Vietnam War or Operation Grapple were asked to identify sources of evidence and studies on the health effects on the children of veterans ('the topic area') (Table 2).

Table 2: Experts contacted in relation to the review

Name	Institution/organisation	Area of expertise
Rodney Jackson	Effective Practice Institute, Division of Community Health Auckland University	Epidemiologist
Sarah Darby	Imperial Cancer Research Fund Cancer Epidemiology Unit, University of Oxford, Radcliffe Infirmary	Nuclear test veterans
Neil Pearce	Massey University Wellington	Epidemiologist – the effects of exposure to nuclear radiation
Sue Rabbitt Roff	University of Dundee	Operation Grapple
John Probert	Auckland	Radiation
Terry Keane	Director Behavioral Science Division National Center VA Medical Center Boston MA	Vietnam veterans and PTSD
Lynda & Daniel King Paula Schnurr	Center for PTSD University of Adelaide	PTSD
Sandy McFarlane	University of Adelaide	PTSD
Wes O'Kane Ann Kilham	Vietnam Veterans Counselling Service, Australia	PTSD

Name	Institution/organisation	Area of expertise
David Butler	Senior Program Officer US National Academy of Sciences, Institute of Medicine	Agent Orange exposure
Keith Horsley	DVA, Canberra	Australian veterans' health

Bibliographies of published research

The bibliographies of published studies on the topic area were examined for any references missed in the literature searching.

Conference proceedings

Reports on the proceedings of conferences that included presentations on the topic area were examined.

Critical appraisal

Study categorisation

Levels of evidence for this report were graded using an adapted version of the US Preventive Services Task Force protocol, 1989.

An independently developed critical appraisal tool called the GATE (Generic Appraisal Tool for Epidemiology) was used to assess the quality of the studies and to categorise them within the hierarchy (Jackson, 2001).

Data extraction

The following standard form was used to extract data from studies (Table 3). The data extraction form included fields for: type of study, methods, types of participants, and outcome measures. Where necessary additional information was requested from authors or organisations on unpublished data or additional analysis of published data.

Meta analysis

The data from the papers directly relating to the children of Vietnam veterans were considered for meta-analysis. Dr David Butler of the US National Academy of Sciences, Institute of Medicine had sat on the Committee to Review the Health Effects in Vietnam Veterans of Exposure to Herbicides, which considered issues relating to meta-analysis.

The Committee concluded that while meta-analysis can be a useful tool for gaining an understanding of the direction of literature, it is a problematic choice for informing policy decisions on herbicide exposure health issues for veterans[ii]. There are two primary reasons for this.

[ii] Dr Butler, personal communication

Table 3: Guidelines and checklist for appraising a medical article (Fowkes & Fulton, 1991)

Guideline	Checklist		
1 Study design appropriate to objectives?	Objective:	Common design:	
	Prevalence	Cross sectional	
	Prognosis	Cohort	
	Treatment	Controlled trial	
	Cause	Cohort, case control, cross sectional	
2 Study sample representative?	Source of sample		
	Sampling method		
	Sample size		
	Entry criteria/exclusions		
	Non-respondents		
3 Control group acceptable?	Definition of controls		
	Source of controls		
	Matching/randomisation		
	Comparable characteristics		
4 Quality of measurements and outcomes?	Validity		
	Reproducibility		
	Blindness		
	Quality control		
5 Completeness?	Compliance		
	Drops outs		
	Death		
	Missing data		
6 Distortion influences?	Extraneous treatments		
	Contamination		
	Changes over time		
	Confounding factors		
	Distortion reduced by analysis		

++ = Major problem. + = Minor problem. 0 = Non problem. NA = Not applicable.

1. The first is that the literature is so disparate that a number of uncomfortable assumptions must be made in order to combine studies for analysis. While there is knowledge to be gained from occupational studies, studies of industrial accidents at sites such as Seveso, and Vietnam veterans' health studies, there is tremendous variation in the intensity, duration, and exact chemical composition of the exposures of such groups. The quality of the exposure assessments and the epidemiologic studies themselves (their control for confounding variables, for example) also vary widely. These facts leave the individual doing a meta-analysis with the difficult choice of either discounting the profound differences in the studies or excluding potentially informative studies from their analysis.

2. The second primary reason is that the uncertainty inherent in the summary values generated by a meta-analysis is not always well appreciated by policy makers, the media and others. Numbers tend to take on a life of their own and, rightly or otherwise, be compared to other numbers that may have been generated under quite different circumstances.

Exclusion of studies

Studies examining the health outcomes for the children of Gulf War veterans were excluded from the appraisal because the exposures of Gulf War veterans differed from the exposures of Vietnam veterans. Studies of Gulf War veterans have examined health effects after exposure to "multiple agents including petroleum solutions, insecticides, sandstorm dust, arthropod borne pathogens, sarin mustard gas, prophylactic drugs such as pyridostigmine bromide and other medications and vaccines administered to military personnel during the Gulf War" (Araneta et al., 1997; Araneta et al., 2000).

INTERPRETATION OF STUDIES

The Bradford-Hill criteria for causation (Bradford-Hill, 1965) have been used as a framework to consider the implications of the evidence in a New Zealand context. The criteria take into account:

- Strength of the association - Is there a strong association between the exposure and the outcome?

- Consistency - Has the association between the outcome and the exposure been observed in different studies of different cohorts at different times?

- Specificity - Is the association limited to specific workers and to particular sites or diseases?

- Temporality - Did the exposure precede the outcome? Does a particular occupation promote the disease or are men or women who work in that occupation more vulnerable to the disease?

- Biological gradient – Is there a dose response relationship between exposure and outcome?

- Plausibility – Is the causation biologically plausible?

- Coherence – Does the interpretation of the data conflict with the generally known facts of the natural history and biology of the disease?

- Experimental – Is there experimental evidence for the association?

It is essential the exposure precede the outcome. No other criterion is essential but the more criteria found in the study report the more likely the observed association is causal.

Important considerations in interpreting data from epidemiological studies of veterans

The power of the study to detect a difference

The 'power' of a study (or more formally statistical power) refers to the ability or sensitivity of the study to detect true or real differences in outcomes for groups exposed to different factors. There is a direct relationship between the power of a study and the total number of participants (sample size) in the study. Generally as sample size increases, power increases. Power ranges from 0% to 100%. It is generally agreed that a minimum of 80% power is required to be reasonably sure that an outcome of a given size has not been missed. Therefore studies that fall below 80% are deemed to lack adequate statistical power and their results must be viewed with greater caution. Studies with low power are more likely to not detect the true effects of exposures. The power of a study is an indication of the quality of the study.

Confounding

Confounding is the mixing of effects between the exposure, the disease and a third factor that is associated with the exposure and independently affects the risk of developing the disease (Hennekens & Buring, 1987).

Socio-demographic variables which are associated with both the adverse reproductive outcomes and the likelihood of an individual being a veteran will confound the outcome measures reported in studies. Selection for military service was not a random event (Goldberg, 1992). New Zealand servicemen who went to Vietnam were volunteers. Mäori are thought to have been over-represented in the New Zealand servicemen who served in Vietnam compared to the proportion of Mäori in the New Zealand population. One way of controlling for that confounding is to take these variables into account in the analysis, for example by using multi-variate analysis.

Birth outcomes are influenced by family planning (birth order, age of mother and so on) and past reproductive history. Any studies of the effects of parental exposure should take these factors into account (Kristensen, 1999). The term 'infertile worker effect' has been coined to describe women who have an adverse reproductive history. Women who have fertility problems may have a higher risk of adverse reproductive events and may also be more likely to stay in the workforce because of their childless status. These women are also therefore more likely to be in the exposed group in any study of occupational exposures.

Socio-economic status is also a determinant for pregnancy outcome. An association has been found between socio-economic status and preterm delivery (Hartikainen-Sorri & Sorri, 1989). In a case control study in Finland of 284 women, unmarried status (OR 2.0) and current smoking (OR 2.4) were associated with preterm birth. There are suggestive data from both New Zealand and overseas studies that Vietnam veterans may by socio-economically deprived compared to non-veterans (Chamberlain et al., 1994; Vincent et al., 1991).

Bias

Bias is a difference between the exposed and the unexposed groups resulting from some aspect of the study design or selection of participants rather than as a result of the exposure.

Recall bias

Recall bias is a difference in the way exposed and unexposed participants in a study report events. In the case of veterans' studies, concern about an association between exposure, either to radiation or to chemicals in Vietnam, and having a child with a birth defect may result in veterans' recall differing from the unexposed group. Medical record verification of all cases of birth defect is a method of controlling for recall bias.

Spontaneous abortions are difficult to record accurately. There is a high probability that women will not recognise them and will perceive spontaneous abortion as a delayed menstrual period if it occurs early in pregnancy. Recall of spontaneous abortion over time is unreliable. Wilcox et al compared data gathered in a prospective

study with participants' recall of spontaneous abortions at the end of the study (Wilcox & Horney, 1984). They found that women recalled only 75% of recorded abortions and the gestational age at which the abortion occurred was a major determinant of recall. Many malformations lead to early foetal death. A high proportion of anencephalic conceptions will be lost in this way that if recognised would be classified as a spontaneous abortion. An alternative measure of spontaneous abortion is the time to recognised pregnancy, as each spontaneous abortion will increase this time.

Selection bias

Some of the studies have high rates of non-response. If the veterans who choose to respond to a survey are different in some way from the non-respondents then bias will occur. For example, veterans who have children with a birth defect may be more interested in replying to surveys about birth defects than other veterans.

Misclassification bias

Misclassification bias can occur with regard to the misclassification of exposures, confounding variables or outcomes. Classification and grouping of outcome measures is undertaken in many studies to increase the power of the study to detect a difference if a difference exists. However, pre-term birth and neural tube defects are etiologically heterogeneous. Many conditions are rare and some are difficult to diagnose. Evaluating all congenital malformations together or using large heterogenous groups is likely to result in misclassification bias (Kogevinas & Sala, 1998).

Most studies use the number of births or the number of live births as a denominator for birth defect statistics. Ideally the number of conceptions should be used as the denominator but measurement of this is impossible to achieve (Kristensen, 1999). Selective loss of the outcome being studied before observation begins results in underestimation of the true incidence of the outcome. This is a particular problem in the study of spontaneous abortion. Ignoring induced abortion in a birth defects study may also result in bias, as induced abortion may be the result of prenatally diagnosed birth defects. If only recognised pregnancies are studied then an effect called the 'dose response' fallacy may occur. Congenital malformations, spontaneous abortions, subclinical abortions and infertility fall on a continuum according to biological severity. If the most severe effects are not recognised due to non-recording of spontaneous abortion then the outcome for a study based on births may be misleading (Sallmen et al., 2000).

Inaccurate reporting and registration of birth defects also has the potential to bias results. Validation using double registration systems has demonstrated that even major birth defects are not completely recorded (Erickson et al., 1984b; Lie et al., 1994). Restrepo et al (1990) in a Columbian study found that a birth defect was confirmed for only 38% of children reported by their parents as abnormal and that 8% of children reported as normal were malformed. No New Zealand data were found.

Misclassification of exposure

Measuring the levels of exposure of veterans and control groups has been difficult. Misclassification of unexposed individuals into the exposed group, or vice versa, has the effect of weakening the observed association in a study.

Measures of exposure effects: Odds Ratios and Confidence Intervals

The 'effect' of a given exposure can be described in terms of its size or magnitude. Exposures with large effects produce correspondingly large differences on outcome measures between groups.

The Odds Ratio (OR) is a statistical measure of the effect of an exposure that is commonly used in epidemiological studies. Exposures with large effects on outcomes produce large ORs. Exposures with small effects on outcomes produce small ORs. An exposure with an OR of 1.0 has essentially no effect on outcomes. ORs greater than 2 would be considered large, suggesting the risk of an adverse outcome was twice as great for the exposed compared to the unexposed.

Any measurement of the effect of an exposure will involve some degree of error. This error can be described statistically by way of a Confidence Interval (CI). A confidence interval is placed around a particular OR to indicate how precise the OR is. A CI of 95% is traditionally used in epidemiological studies. This means that there is a 95% probability that the CI includes the underlying or true OR. If the CI includes 1.0 then the study result is non-significant at the 5% level and is thus likely to have arisen by chance. Studies with low statistical power are more likely to produce results with very wide CIs that include 1.0. Studies with high statistical power are more likely to produce narrow CIs. High quality studies cite 95% CI in their reporting of results.

SECTION TWO: OPERATION GRAPPLE

BACKGROUND

New Zealand participation in Operation Grapple

The United Kingdom carried out 21 atmospheric nuclear weapons tests in Australia, and in islands in the Pacific Ocean between 1952 and 1958. Two Royal New Zealand Navy ships and 563 personnel participated in tests conducted by the United Kingdom in 1957 and 1958 at Malden and Christmas Islands (Advisory Committee on the Health of Veterans' Children, 1999). This series of tests, known as 'Operation Grapple', comprised nine tests in total divided into two series:

- Three thermonuclear detonations in the area of Malden Island in May and June of 1957; and
- Four thermonuclear detonations near Christmas Island between November 1957 and September 1958, as well as two atomic devices.

The role of the two Royal New Zealand Navy ships, the HMNZS Pukaki and HMNZS Rotoiti, was primarily to collect meteorological information. Secondary tasks included air-sea rescue, anti-submarine surveillance, monitoring thermal flashes, and water sampling. HMNZS Rotoiti participated in the first four tests, while HMNZS Pukaki was involved in all nine tests (Crawford, 1989; Advisory Committee on the Health of Veterans' Children, 1999).

EXPOSURE TO IONISING RADIATION

One of the primary concerns of personnel who participated in the testing of nuclear weapons is potential exposure to ionising radiation and the possible health effects associated with that exposure.

Ionising radiation[iii]

Exposure to ionising radiation comes from a variety of sources, both natural and human-made. Individuals are exposed to natural background radiation in their everyday life from cosmic rays and other radioactive substances occurring naturally in the earth and in humans (Clarke, 2000). Levels of exposure vary depending on factors such as place of residence and lifestyle (United Nations Environment Programme, 1991). According to UNSCEAR (2000), the average annual collective

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[iii] Ionising radiation refers to radiation that has the ability to ionise matter to produce positively and negatively charged particles (ARPNSA, 2001).

per caput dose is 2.4mSv[iv]. In New Zealand, the total effective annual dose from radiation of natural origin is, on average, 1.8mSv per person (Royal Society of New Zealand, 1998). Individuals are also potentially exposed to radiation in the environment (e.g. from atmospheric weapons testing or from nuclear power generation), in medical diagnosis and treatment (e.g. x-rays or radiotherapy) and in occupational settings (United Nations Environment Programme, 1991; UNSCEAR, 2000; Clarke, 2000).

Health effects of exposure to whole body ionising radiation

The health effects of exposure to ionising radiation have been well-documented in animal studies. Much of the information on health outcomes for humans has been derived from large-scale studies of the health outcomes for the A-bomb 'survivors' of Hiroshima and Nagasaki. There is also literature relating to nuclear accidents such as Chernobyl, as well as the health effects of occupational, environmental, and medical exposures to radiation.

Exposure to ionising radiation has the ability to affect organs and tissue and cause damage to human cells, and at high doses, cell death (UNSCEAR, 2000).

Figure 1: Effects of ionising radiation on tissue

HOW RADIATION LEADS TO DAMAGE IN TISSUE
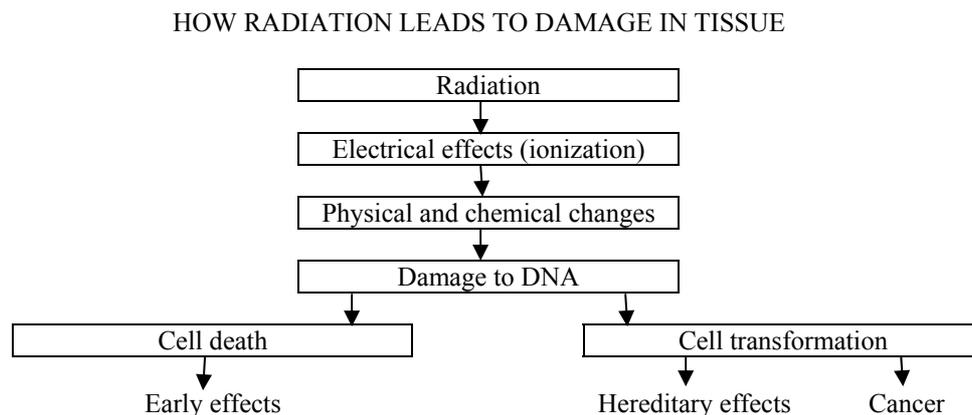
Source: United Nations Environment Programme (1991), p.66

The biological effects of radiation exposure are related to both the level of the dose and the dose rate (Institute of Medicine, 1995), as well as individual "sensitivity or resistance" to radiation (RadEFX, 2000).

Health effects resulting from irradiation can be broadly considered as fitting into two categories: acute or 'deterministic' health effects and long-term or 'stochastic' health effects.

[iv] Radioactivity is measured in decays per second. The term used to describe this is *becquerel* (Bq). In terms of radiation dose, the absorbed dose is measured in *grays* (Gy). A further measurement for dose, known as the effective dose, is also used. The effective dose is a weighted measurement that factors in the type and quality of radiation as well as the part of body exposed. The effective dose is measured in *sieverts* (Sv) (IOM, 1995; UNSCEAR,2000; ARPNSA, 2001).

Acute/deterministic health effects

There are a range of acute health effects that can occur in humans, often due to cell death from exposure to high doses and high dose rates of radiation. Acute effects will usually appear within hours, days (United Nations Environment Programme, 1991) or weeks of exposure (Nuclear Energy Agency (NEA), 2001), and are often thought to have a threshold (Institute of Medicine, 1995). This means that an effect can be expected to occur in all individuals exposed to a dose above the threshold (UNSCEAR, 2000).

The strength or severity of the effect is dependent on the dose to which an individual is exposed to (Institute of Medicine, 1995). According to Bulman and Kang (1994), a dose under 250mSv would be unlikely to result in an observable effect. The Institute of Medicine (1995)[v] suggests that harm is unlikely in the majority of healthy individuals if a dose is less than 100mSv.

Documented acute/deterministic effects include: erythema; radiation sickness (nausea, diarrhoea, vomiting, fatigue, and so on); blood changes; loss of hair; developmental problems (in exposed children); and death (at high levels of exposure) (United Nations Environment Programme, 1991).

Long-term/ stochastic health effects

Aside from causing cell death, exposure to ionising radiation can result in damage to living cells. Many cells are able to be repaired by the body; however, if cells are not repaired correctly there can be modification of the cell (Clarke, 2000).

The frequency of long-term effects, rather than the severity, is dependent on the dose (Institute of Medicine, 1995; NEA, 2001). As long-term outcomes are not specific to radiation exposure, they can not be connected directly to an individual's exposure (NEA, 2001). That is, a cancer manifests itself the same way in a radiation-exposed person as it would in a non-exposed person (Institute of Medicine, 1995; UNSCEAR, 2000).

Recognised long-term health effects for humans include, among other things, cataracts, specific cancers and hyperparathyroidism. Cancer is one of the most evident long-term effects of exposure to radiation and can appear many decades after the exposure (United Nations Environment Programme, 1991). In the Japanese atomic bomb survivors, the cancer incidence is increased for leukaemia (except for chronic lymphocytic leukaemia), thyroid, breast, ovary, lung, lower oesophagus, gastric, colon and rectum, bladder, skin (squamous and basal cell), and meningioma (Radiation Effects Research Foundation (RERF) 2001).

There is also evidence of adverse outcomes for individuals exposed *in utero* to radiation, including both teratogenic and carcinogenic effects (Sever, 1991).

Genetic effects are a potential long-term effect of exposure to ionising radiation. The risk of genetic effects has been documented in animal and plant studies, but has not been demonstrated conclusively in humans (Sever, 1991; Institute of Medicine, 1995; Meinert et al., 1999). In terms of preconceptional exposure, Brent (1999) suggests the

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[v] mSv: millisievert

following four risks from exposure to toxicants, such as ionising radiation, prior to conception:

Table 4: Risks of preconceptional exposure to reproductive toxicants

Risks of preconception exposure to reproductive toxicants
1. Sterility and infertility (threshold phenomenon)
2. Chromosomal abnormalities that can be transmitted or result in the death of the cell (stochastic phenomenon)
3. Abnormalities of the DNA at the molecular level due to deletions, substitutions, or shifting in the sequences of the nucleotides that provide the genetic messages to the cell (stochastic phenomenon)
4. Genetically determined congenital malformations and cancer (stochastic phenomenon)

Source: Based on Brent (1999), p.185

Aside from sterility, the other potential risks from preconceptional exposure are stochastic and the severity of the disease is therefore not dependent on the dose (Brent, 1999).

Exposure to low-dose ionising radiation

There is less evidence available surrounding the biological effects of exposure to low doses and low dose rates of ionising radiation. The effect of low levels of exposure on humans has been extrapolated from studies of high dose effects as well as from experimental studies on animals.

It is assumed that there is no dose that is without potential harm and, therefore, the frequency of effects at a low dose would be proportional to those at a high dose (Institute of Medicine, 1995; NEA, 2001). However, as a dose becomes lower, outcomes are increasingly more difficult to identify as being related to exposure. According to RadEFX (2000), in the long-term, exposure to low doses of ionising radiation primarily affects the thyroid gland, immune system, central nervous and cardiovascular systems, and the blood forming organs.

Doll (1998) discusses four types of effects from exposure to low-dose ionising radiation: cancer production, non-cancer effects, foetal and genetic effects. There has been evidence of cancer induction, production of other non-cancer and foetal effects at low doses (Doll, 1998). The evidence for genetic effects is more limited in terms of studies of low dose exposure. As mentioned previously, low dose studies have relied on assumptions from high dose studies and have not consistently found evidence for adverse health effects on the offspring of individuals exposed at low levels.

Exposure of New Zealand personnel to ionising radiation

The two main avenues of potential exposure for nuclear test personnel are:

- Initial exposure (exposure from the detonation of the device); and
- Exposure to residual radiation (environmental exposure from being in the locality after the detonation) (Bulman & Kang, 1994).

The main task of the New Zealand ships involved in Operation Grapple was to collect meteorological information in order for the tests to be conducted safely. Accordingly, New Zealand ships did not have a primary role in the tests and were stationed between 20 and 150 nautical miles upwind at the time of the detonations (MacDonald, 1997; Advisory Committee on the Health of Veterans' Children, 1999). However, it is reported that approximately 5 to 6 hours after the Grapple 1 test, HMNZS Pukaki passed within 6 nautical miles of ground zero,[vi] and through ground zero the day following Grapple Y (Crawford, 1989). All of the Operation Grapple tests were air bursts[vii].

Various protective measures and procedures were in place on the New Zealand ships, including protective clothing, and monitoring equipment (Crawford, 1989; Advisory Committee on the Health of Veterans' Children, 1999). According to Crawford (1989) the protective precautions taken by New Zealand personnel decreased as the test series progressed, apparently due to significant levels of radiation not being present (MacDonald, 1997).

The possibility that New Zealand troops were exposed to residual radiation has been raised (Pearce et al., 1990; Roff, 1996). Crawford (1989) reports on a log entry recorded after the Grapple II test that indicates rain at the time of the detonation, introducing the potential for exposure to residual radiation from radiation fallout for this particular test. Problems with the processing of film badges meant that gamma radiation that may have been received by the servicemen was not recorded.

As radiation doses are cumulative, the more tests a veteran witnessed, the greater the dose. In the case of New Zealand veterans who participated in Operation Grapple, there has been no evidence of significant exposure to ionising radiation (Advisory Committee on the Health of Veterans' Children, 1999; McEwan, 1999), although it can not be absolutely ruled out.

[vi] Crawford (1989) defines ground zero as: "The point on the ground surface at, or directly below, the initiating point of a nuclear explosion".
[vii] Air bursts are explosions conducted at altitudes sufficiently high to ensure that the fireball does not touch the surface (Crawford, 1989). This method of testing reduces the potential for local fallout.

HEALTH OUTCOMES FOR NUCLEAR TEST VETERANS

Possible health outcomes for nuclear test veterans as a result of participation in Operation Grapple have been identified from the literature. The health outcomes for nuclear test veterans are summarised in Table 5.

Table 5: Health outcomes for nuclear test veterans exposed to ionising radiation (increased risk of mortality)

Outcome	*Studies showing significantly increased mortality**
All cause mortality	For veterans receiving radiation dose $\geq$ 5 rem (Dalager et al, 2000)
	Unadjusted and adjusted for veterans receiving radiation dose >1000 mrem (Watanabe et al, 1995; Johnson et al,1997)
Injury/poisoning	Darby et al, 1993
Bronchitis/emphysema/chronic obstructive lung diseases	Darby et al, 1993
Digestive system disorders	Raman et al, 1987
Cirrhosis of the liver	Raman et al, 1987
External causes	Thaul et al, 2000
	Adjusted (Watanabe et al, 1995)
Cancers **	
Lymphopoietic	For veterans receiving radiation dose $\geq$ 5 rem (Dalager et al, 2000)
Miscellaneous lymphopoietic	For veterans receiving radiation dose $\geq$ 5 rem (Dalager et al, 2000)
All haematological	Pearce et al, 1990; Pearce et al, 1997
Leukaemia	Darby et al, 1988; Darby et al, 1993
	Caldwell et al, 1980; Caldwell et al, 1983; Pearce et al, 1990; Pearce et al, 1997 ***
Multiple myeloma	Darby et al, 1988; Darby et al, 1993
Digestive organs	Unadjusted and for veterans receiving dose 0-250 mrem (Watanabe et al, 1995)
Pancreas	For veterans receiving dose 250-1000mrem (Watanabe et al, 1995)
Liver	For veterans receiving dose >1000 mrem (Watanabe et al, 1995)
Prostate	Watanabe et al, 1995; Thaul et al, 2000
Bladder	Darby et al, 1993
Nasal	Thaul et al, 2000

* Results from studies by Garcia,(1994), Murphy (1990) and Roff (1997, 1998, 1999, Roff et al, 2000) were not included in this summary table as they were descriptive studies that did not attempt to demonstrate an increased risk and the results are therefore not comparable with the other studies. Results from an Australian study of atomic test veterans (Donovan et al., 1983) were not included in this summary table as the report was not able to be accessed.

** Cancer outcomes have been summarised under the categories used within individual studies. There will therefore be some overlap in categories because of differing methodological approaches.

*** These studies also found significantly increased incidence.

HEALTH OUTCOMES FOR THE CHILDREN OF NUCLEAR TEST VETERANS

Studies of veterans' children

Only two studies were found on the health outcomes for children of New Zealand nuclear test veterans.

Quality Level	Study Type	Number
1.	Meta-analysis of cohort or/ case control studies	0
2.	Cohort with comparison group	0
3.	Case control	0
4.	Cohort/ comparison with national dataset	0
5.	All other studies	Roff 1998b, Report on morbidity study of members of the British Nuclear Test Veterans Association and the New Zealand Nuclear Tests Veterans Associations and their families. Roff et al, 2000, Family history protocol study report.

In addition, a questionnaire had been sent to New Zealand veterans as part of the Inquiry into the Health Status of Children of Vietnam and Operation Grapple Veterans (Advisory Committee on the Health of Veterans' Children 1999). The results included only a proportion of veterans and no comparison group was available. Data from this survey were reviewed by Dr Patrick Tuohy[viii], who concluded that the results of the study were likely to be biased towards the children of veterans with health concerns. He was unable to draw any further conclusions based on the information.

The search was expanded to include studies of paternal preconceptional exposure to ionising radiation in occupational, medical, and environmental settings. Studies of maternal or population exposures or post-conception paternal exposure were generally excluded on the basis of relevance. The rationale behind this was:

- There were no female personnel from New Zealand involved in Operation Grapple;
- For an outcome for a child to be linked to exposure of the father, the exposure would have to have taken place prior to conception.

[viii] Chief Advisor Child and Youth Health, New Zealand Ministry of Health.

KEY STUDIES OF THE CHILDREN OF NUCLEAR TEST VETERANS

Level 5 evidence: Other studies

Morbidity study of members of the British Nuclear Test Veterans Association and the New Zealand Nuclear Tests Veterans Association and their families
Roff 1998b

1. Study description
- A descriptive study of a sample of New Zealand Nuclear Tests Veterans Association (NZNTVA) members. The primary outcome measure was self-reported morbidity of veterans, their children and grandchildren. Data were collected through questionnaires.

2a. Participant selection and source
- Questionnaires were distributed to 380 members of the NZNTVA to complete.
- The participants were selected from members of the NZNTVA and did not include all New Zealand veterans of Operation Grapple. The responses to this survey represent less than half the full cohort of Operation Grapple veterans.

2b. Outcome measurement
- The outcome measurement was self-reported mortality and morbidity.

Results
- 235 (62%) of the questionnaires distributed were completed and returned. 97 of those (41%) were from the families of veterans who were deceased.
- Descriptive results were presented on the health of the veteran and immediate blood relatives. Morbidity and/or mortality was not independently validated. It is unclear whether or not children born before the exposure are included in the results.
- There were no mortality or morbidity rates reported in the study.

Conclusions
- There is the potential for bias from confounding factors and the methods of sample selection and data collection.

Family History Protocol Study
Roff et al 2000

1. Study description
- A descriptive follow-up study of a sample of New Zealand Nuclear Tests Veterans Association (NZNTVA) members. The primary outcome measure was self-reported morbidity of veterans and their children and grandchildren. Data were collected in telephone interviews.

2a. Participant selection and source
- Members of the NZNTVA were sent an invitation in the mail to participate in a telephone interview.
- Participants were selected from members of the NZNTVA, and did not represent the full cohort of Operation Grapple veterans.

2b. Outcome measurement
- The outcome measurement was self-reported response to 74 questions on the health of the veteran and immediate blood relatives.

Results
- Descriptive results were presented on the health of the veteran and immediate blood relatives.
- Morbidity was not independently validated.

Conclusions
- There is the potential for bias from confounding factors. Those who responded to the request for an interview may have been more likely to have concerns about the health of their children and grandchildren. The 110 veterans in the study represent less than 20% of the total veterans involved in Operation Grapple.

SUMMARY OF THE OUTCOMES OF STUDIES

Literature searches failed to locate any high quality case control or cohort studies of the health outcomes for the offspring of nuclear test veterans from New Zealand or other countries. The researchers located only two studies that dealt directly with health outcomes for the children of New Zealand veterans who participated in Operation Grapple. These studies (Roff, 1998b; Roff et al., 2000) are descriptive studies that utilise self-reported data from the veterans and/or their families.

The 1998 study considers health outcomes for the New Zealand nuclear test veterans in the study as well as pregnancy outcomes and morbidity of their children and grandchildren. It was part of a wider study looking at the health of British nuclear test veterans and their families. The study provides information on numbers of conceptions and live-births, as well as on adverse reproductive outcomes including miscarriages, stillbirths, abortions, and peri-natal and infant deaths.

The study also reports on the morbidity of the children of the veterans. A range of conditions was identified, with the most common being: skin, skeletal, arthritic, and cardiovascular conditions.[ix] Many of these conditions were also identified in the grandchildren of veterans. The study did not include a comparison group and it is therefore difficult to determine whether rates of health outcomes differ from national rates. However, Roff reports that the rates of neural tube defects were higher in this study than those reported in a New Zealand study of birth defects among the children of parents exposed to 2,4,5-T (Smith et al., 1982).

The second study by Roff et al (2000) found that over half of the 109 families involved reported morbidity in their children. The aim of the study was to investigate familial issues surrounding morbidity. Morbidity overall was similar to that reported in the 1998 study of 235 veterans and their families, and included disorders of the blood, and skin, skeletal, arthritic, respiratory and cardiovascular conditions. The author comments on two families who reported Marfan syndrome and suggests that:

> Since approximately half the families in this follow up study report conditions for their children in the skeletal, ocular and cardiovascular systems, and many of these families report conditions in two or more of the systems in the one child, it is suggested that this population should be screened for Marfan syndrome and other connective disorders (p.4).

Roff also proposes that screening for spina bifida and other neural tube defects be made available for this population. Once again, it is difficult from these studies to determine whether or not the rates of morbidity are increased relative to the general population.

[ix] Other conditions reported in the children included: infertility, hearing, other vision conditions, emotional conditions, multiple sclerosis, respiratory, diabetes, stroke, migraines/headaches, thyroid, blood disorders, noncancer tumours, spina bifida, gastrointestinal, kidney, Down's syndrome, cerebral palsy, Marfan syndrome, and cancers.

There is also information on the children of nuclear test veterans available from the study of United Kingdom veterans (Roff, 1998b). The results were based on an analysis of the first 1000 questionnaires returned (out of 1041 returned from a total of 2087 sent out). This study reported numbers of miscarriages, stillbirths, live births, and neonatal and early childhood deaths. The most common conditions reported in the children were musculoskeletal, visual, dermatological, respiratory, fertility/reproductive, and gastrointestinal. Many of these conditions were also reported in the grandchildren. Roff states:

> Nearly half of this morbidity consists of dermatological, musculoskeletal and gastrointestinal conditions which are compatible with the SAPHO syndrome and its variants (p.22).

There are little data available from studies of children of veterans on the possible psychosocial outcomes for children in relation to their parent's participation in Operation Grapple. Two studies of United States veterans suggest a possible psychological impact on nuclear test veterans and their families (Garcia, 1994; Murphy et al., 1990). The studies by Roff (1998b; 2000) of New Zealand veterans indicate the presence of 'emotional' conditions in some children of veterans. However, there are no high quality studies specifically focusing on this outcome.

In 1995, the Institute of Medicine in the United States evaluated the feasibility of conducting epidemiological studies into adverse reproductive outcomes for atomic veterans. The Committee appointed concluded that epidemiological studies were not feasible because of a number of difficulties they regarded as "insurmountable", including the ability to:

- Have a sufficiently large sample;
- Ascertain accurate dose measures for individual veterans;
- Detect small risks at low doses of exposure;
- Identify and document reproductive outcomes over the 50-year period involved; and
- Accurately measure confounding factors (Institute of Medicine, 1995).

As there is limited evidence that relates directly to the children of New Zealand nuclear test veterans, combined with a general lack of high quality epidemiological studies on health outcomes for offspring of nuclear test veterans, estimates of health effects for this population are largely based on results of studies of parental occupational, medical, and environmental exposure.

As previously discussed, for the purposes of this review, only studies dealing with paternal preconceptional exposure were considered.

Studies of occupational exposure

There are a number of studies that have investigated health outcomes for the children of parents occupationally exposed to ionising radiation, such as nuclear industry workers and radiographers. The outcomes most frequently considered have been cancer, in particular leukaemias and lymphomas, and adverse reproductive outcomes. Studies of parental occupational exposure to ionising radiation vary in design and quality. In terms of exposure, there is variation in the types of exposures investigated (e.g. internal or external), and in the way in which exposure is assessed (e.g. using quantified dose estimates from records or self-report, doses estimated from occupation or job title, or occupation or job title as a surrogate for exposure). This makes direct comparisons of the results of different studies difficult. However, there are some general points for discussion that arise from the literature.

Cancer outcomes

There have been several studies of parental exposure to ionising radiation that have focused on nuclear workers and/or localities surrounding nuclear power plants. (Studies of cancer outcomes from occupational exposure are summarised in Table 6). In 1990, Gardner et al reported findings from a case control study of 52 cases of leukaemia, 22 of non-Hodgkin's lymphoma (NHL), and 23 of Hodgkin's disease in young people near the Sellafield nuclear plant in West Cumbria and 1001 controls. Area and local controls were matched for gender and date of birth. Relative to area controls, paternal employment at Sellafield at conception was associated with significantly raised risks for leukaemia (RR 2.79, 95% CI 1.04-7.52, n=8) and for leukaemia and NHL combined (RR 2.44, 95% CI 1.04-5.71, n=10). There was no significantly increased risk for employment before conception, employment at birth, or ever employed. Significantly raised relative risks were also found for leukaemia with paternal radiation dose record at conception when compared with area controls (RR 3.07, 95%1.09-8.65, n=8) and for leukaemia and NHL combined before conception when compared with area controls (RR 2.71, 95% CI 1.12-6.60, n=10). For the specific dose periods examined, significantly raised relative risks for leukaemia in offspring were found for paternal cumulative doses ≥100mSv compared with both area controls (RR 6.24, 95% CI 1.51-25.76, n=4) and local controls (RR 8.38, 95% CI 1.35-51.99, n=4), although the numbers were small and the confidence intervals wide. Relative risks remained significant when leukaemia and NHL were analysed together. A significant association between leukaemia and a paternal dose ≥10mSv in the 6 months preceding conception was found when compared with both area controls (RR 7.17, 95% CI 1.69-30.44, n=4) and local controls (RR 8.21, 95% CI 1.62-41.73, n=4), with similar results when leukaemia and NHL were analysed together. A dose-response gradient was also indicated. Gardner et al interpreted the results as suggesting a link between paternal preconceptional irradiation and leukaemia incidence in children. The findings were controversial and attracted wide debate. (Slightly adjusted figures were published in 1992 (Gardner, 1992), but did not alter the overall findings of the study).

A number of studies both in the United Kingdom and elsewhere have further investigated the 'Gardner' hypothesis that paternal preconceptional exposure to ionising radiation was associated with leukaemia in offspring (McKinney et al., 1991; Urquhart et al., 1991; McLaughlin et al., 1993; Kinlen et al., 1993; Roman et al.,

1993; Pobel & Viel, 1997; Draper et al., 1997; Roman et al., 1999). McKinney et al (1991) found a significantly increased risk for leukaemia and NHL by self-reported preconceptional paternal radiation exposure. When exposure was limited to ionising radiation or employment either in the nuclear industry or health related occupations, there was no significantly increased risk. However, exposure was self-reported and the study design meant it was not possible to investigate any dose-response relationship.

Urquhart et al (1991) found there was no significantly increased relative risk of leukaemia or NHL in the offspring of fathers employed in the nuclear industry at the time of conception. None of the fathers in their study had a lifetime dose greater than 100mSv and only one had a dose in the six months prior to conception greater than 10mSv. The study concluded that paternal preconceptional exposure could not explain the leukaemia excess in the study area, although the numbers in the study were small.

Kinlen et al (1993) looked specifically at paternal preconceptional exposure to radiation in the nuclear industry in Scotland and its relationship with the incidence of leukaemia and NHL in children. They found no significantly increased risks evident for any of the dose periods considered (total lifetime, six months preconceptional, and three months preconceptional) nor any significant dose response gradient.

A further study of parental employment in the nuclear industry and leukaemia and NHL incidence in children undertaken by Roman et al (1993) also found no increased relative risk for leukaemia or NHL incidence in offspring for fathers ever employed, employed before conception, or employed from conception to diagnosis, in the radiation industry. There was a statistically significant increased risk for leukaemia and NHL in children of fathers who had ever been monitored for ionising radiation (RR 8.0, 95% CL 1.4-54.6, n=4), although confidence intervals were wide.

A case control study in Ontario (McLaughlin et al., 1993) examined paternal radiation exposure and the risk of leukaemia in offspring. There was no significant association between fathers being monitored for radiation or job type and incidence of leukaemia. No significant associations were found for any of the time periods, dose categories, or types of exposure considered and no dose response gradient was apparent. Exposure was assessed through record linkage and many of the potential confounding factors were controlled for in the analysis.

Pobel and Viel (1997) examined the relationship between childhood leukaemia and a range of risk factors including x-ray exposure, parental occupational exposure, and lifestyle factors in the area of the La Hague nuclear reprocessing plant in France. Occupational information gathered in interviews and dosimetry data from nuclear facility records was used to calculate doses. None of the fathers in the study were found to have detectable doses of preconceptional exposure to radiation.

Draper et al (1997) investigated associations between parental preconceptional radiation exposure and childhood cancer by linking Cancer Registry data with data on the National Registry for Radiation Workers in the United Kingdom. Analysis was carried out both including and excluding data from West Cumbria that overlapped with the Gardner et al study (1990). When the Gardner cases were excluded,

significantly increased risks for leukaemia and NHL by total paternal preconceptional exposure <0.1mSv (RR 8.17, 95% CI 1.18-∞, n=6) and 3 month preconceptional exposure of between 0.1-2.4mSv (RR 2.82, 95% CI 1.10-7.82, n=16) were found. No significantly increased risks were found for other cancers excluding leukaemia and NHL, or for all cancers combined. When continuous dose categories were analysed, there was no evidence of any significant findings for any cancer group or dose periods studied. When the Gardner cases were included, significantly increased risks for leukaemia and NHL associated with a total preconceptional dose >100mSv (RR 2.13; 95% CI 1.02-5.13), a six month preconceptional dose of 0.1-4.9mSv (RR 2.35, 95% CI 1.06-5.47, n=21) and a three month preconceptional dose of 0.1-2.4mSv (RR 3.38, 95% CI 1.37-9.16, n=20), were found. The relative risk for leukaemia and NHL associated with the father being a radiation worker was significant for both sets of data. No significant dose-response gradient was found.

In a 1999 cohort study, Roman et al found cancer risk in offspring was not significantly associated with paternal employment in the nuclear industry or being monitored for radiation exposure. When children from Gardner's study (1990) were excluded, there were significantly increased risks for all malignancies by paternal preconceptional cumulative exposures ≥100mSv (RR 4.1, 95 % CI 1.4-11.8, n=4) and a 6 month preconceptional dose ≥10mSv (RR 5.1, 95% CI 1.4-16.9, n=3). When the Gardner data were included, significantly increased risks associated with cumulative preconceptional exposures ≥100mSv were found for leukaemia and NHL combined (RR 3.9, 95% CI 1.0-13.7, n=3), and for leukaemia (RR 5.8, 95% CI 1.3-24.8, n=3). Significantly increased risks associated with total preconceptional exposures ≥10mSv were also found for leukaemia (RR 7.7, 95% CI 1.9-31.0) and for all malignancies excluding leukaemia and NHL (RR4.4, 95% CI 1.1-18.5, n=2). Most of the significant findings were based on small numbers, and overall risk for cancer was not different from that of the general population. A dose-response trend was also not demonstrated.

Studies that have not focussed specifically on the nuclear industry include a study by Hicks et al (1984) of occupational exposure to ionising radiation. When all childhood cancers were considered as a group, there was no significantly increased risk for the children of fathers with potential occupational exposure. The study did find positive associations for bone cancer and Wilms' tumour for industries with some potential exposure. However, positive findings were based on small numbers of cases and confidence intervals were wide. Further, the method of assessing exposure by using self-reported occupation or industry as a surrogate measure introduced potential for misclassification bias. A dose-response relationship was not demonstrated.

Two studies using data from the Oxford Survey of Childhood Cancer examined associations between childhood cancer and paternal occupational exposure to ionising radiation. In the first study (Sorahan & Roberts, 1993), for all dose categories of paternal exposure to human-made ionising radiation in the six months prior to conception, there were no statistically significantly raised relative risks for any of the diagnostic groups. Relative risks calculated for potential paternal exposure to radionuclides in the six months prior to conception were statistically significant for all cancers excluding leukaemia and NHL (RR 3.20; 95% CI 1.17-8.74, n=16) and all childhood cancers (RR 2.70; 95% CI1.31-5.58, n=27). In the second study by Sorohan et al (1995), cancer in offspring was compared for six specific occupational

groups: radiologists (clinical), surgeons and anaesthetists, veterinary surgeons, dental surgeons, nuclear industry workers, and industrial radiographers. A significant association was found for both pre-conception (OR 1.86, 95% CI 1.08-3.29) and post-conception employment in the nuclear industry (OR 2.19, 95% CI 1.28-3.86) and all childhood cancers. This association did not remain significant when pre- and post-employment were analysed simultaneously. There was no significantly increased risk for leukaemia by paternal preconceptional employment as a nuclear worker. In both studies, exposures were inferred from self-reported employment information and no validated individual exposure information was available.

Roman et al (1996) considered a range of health outcomes for the children of radiographers, including cancer outcomes. Observed rates for all malignancies, leukaemia and NHL, and all malignancies except leukaemia and NHL in the offspring of male radiographers were higher than expected but non-significant.

A case control study by Smulevich et al (1999) in Moscow found paternal exposure to ionising radiation at any time prior to conception was significantly associated with an increased risk of leukaemia (OR 6.7, 95% CI 2.8-15.8, n=21), Hodgkin's disease (OR 10.6, 95% CI 1.05-106.9, n=5), NHL (OR 13.9, 95% CI 1.05-106.9, n=5), and soft-tissue tumours (OR 7.9, 95% CI 1.6-39.4, n=7). However, exposure was not measured, and there was potential for both recall and misclassification bias in the self-reporting of exposures.

Meinert et al (1999) investigated the relationships between parental exposures to various sources of ionising radiation and childhood leukaemia and NHL. Paternal occupational exposure to ionising radiation in the year before conception or involving domestic surveillance was not significantly associated with an increased risk of leukaemia, NHL, or solid tumours in offspring. If analysis was limited to children diagnosed with leukaemia before 1.5 years of age, there was a statistically significant association with paternal exposure in the year before conception (OR 2.74, 95 % CI 1.01-7.44, n=12). Again, exposure was self-reported and the authors suggest cautious interpretation of the findings.

Table 6: Studies of paternal occupational exposure to ionising radiation: Cancer outcomes

Study	*Title*	*Study group*	*Comparison/control group*
Cohort studies: Level 2 evidence			
Roman et al (1999)	Cancer in the children of nuclear industry employees: report on children aged under 25 years from nuclear industry family study	39 557 children of male employees 8883 children of female employees	Annual cancer incidence rates Offspring-years at risk
Case control studies: Level 3 evidence			
Meinert et al (1999)	Associations between childhood cancer and ionizing radiation: Results of a population-based case control study in Germany	2358 cancer cases (1184 leukaemia, 234 NHL, 940 solid tumours) Identified from German Childhood Cancer Registry Included children under 15 years, living in west Germany	2588 controls Matched for gender, date of birth, district of residence
Smulevich et al (1999)	Parental occupation and other factors and cancer risk in children: II. Occupational factors	593 cancer cases Identified from Moscow Central Cancer Dispensary Included children aged 0-14 years, diagnosed 1986-88	1181 controls (2 per case) Matched for age, gender, residence
Draper et al (1997)	Cancer in the offspring of radiation workers: a record linkage study	35 949 cancer cases Identified from cancer registers and other studies	38 323 controls Matched for residence at birth, sex, age
Pobel and Viel (1997)	Case-control study of leukaemia among young people near La Hague nuclear reprocessing plant: the environmental hypothesis revisited	27 leukaemia cases Included cases under 25 years and diagnosed between 1978-93	192 controls Matched for age, sex, place of birth, residence at time of diagnosis
Sorohan et al (1995)	Childhood cancer and paternal exposure to ionizing radiation: A second report from the Oxford Survey of Childhood Cancers	14 869 cancer cases Identified from Oxford Survey of Childhood Cancers	14 869 matched controls Identified from Oxford Survey of Childhood Cancers
Sorohan and Roberts (1993)	Childhood cancer and paternal exposure to ionizing radiation: Preliminary findings from the Oxford Survey of Childhood Cancers	15 279 cancer cases Identified from Oxford Survey of Childhood Cancers	15 279 controls Identified from Oxford Survey of Childhood Cancers
Kinlen et al (1993)	Paternal preconceptional exposure in the nuclear industry and leukaemia and non-Hodgkin's lymphoma in young people in Scotland	Fathers of 1104 children with leukaemia and 253 with NHL Identified from cancer registers and other studies Included cases under 25 years and born in or after 1958	Fathers of 3783 controls (3 controls per case) Matched for sex and county of birth
McLaughlin et al (1993)	Paternal radiation exposure and leukaemia in offspring: the Ontario case-control study	112 leukaemia cases Included children 0-14 years, diagnosed 1950-1988 and mothers living near a nuclear facility at birth	890 controls (8 controls per case) Matched for date of birth and residence at birth
Roman et al (1993)	Case-control study of leukaemia and non-Hodgkin's lymphoma among children aged 0-4 years living in West Berkshire and North Hampshire health districts	54 leukaemia or NHL cases Included children aged 0-4 living in study area, resident when diagnosed, and born and diagnosed 1972-89	324 controls (6 controls per case) Matched for gender, date of birth, residence at birth and diagnosis
Urquhart et al (1991)	Case-control study of leukaemia and non-Hodgkin's lymphoma in children in Caithness near the Dounreay nuclear installation	14 leukaemia and NHL cases Included children under 15 years, diagnosed 1970-86	55 controls Matched for sex, date of birth, residence at birth
McKinney et al (1991)	Parental occupations of children with leukaemia in west Cumbria, north Humberside and Gateshead	109 leukaemia or NHL cases Identified from cancer registries Included children under 15 years, diagnosed 1974-88	206 (2 controls per case) Matched for sex, date of birth, district of birth
Gardner et al (1990b)	Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria	52 leukaemia cases, 22 NHL cases, and 23 Hodgkin's disease Included children under 25 years, born in area, diagnosed 1950-85	1001 controls Matched for date of birth and sex

Hicks et al (1984)	Childhood cancer and occupational radiation exposure in parents	298 fathers and 298 mothers of children treated for cancer Included children treated for cancer in a Texas clinic between March 1976 and December 1977	3 sets of controls - Parents of clinic attenders (283 fathers, 283 mothers), siblings of case parents (413 uncles, 425 aunts), neighbourhood parents (228 fathers, 237 mothers)
Cohort studies with nested case control: Level 3 evidence			
Roman et al (1996)	Health of children born to medical radiographers	6730 members of College of Radiographers Cases were children whose parents reported an adverse outcome	Incidence rates Controls were children with no reported adverse outcome

Adverse reproductive outcomes

Several studies have investigated the relationship between occupational exposure to ionising radiation and adverse reproductive outcomes in offspring. The results of some of the key studies are discussed below. Study designs are summarised in Table 7.

In a study by Sever et al (1988), analyses were carried out looking at all congenital malformations, major malformations, and specific malformations by parental employment at Hanford nuclear plant and by continuous dose estimates calculated from annual dose totals. There was no significant increased risk for all malformations combined. However, there was a statistically significant increased risk for two specific defects: tracheoesophageal fistula ($0.025 < p < 0.05$, n=4) and congenital dislocation of the hip ($0.01 < p < 0.025$, n=2). There was a significantly increased risk found for neural tube defects (p=0.04, n=11) by paternal cumulative exposure. The authors suggest that the positive findings could be false positive because of the number of categories of specific defects that were analysed.

Green et al (1997b) also found no increased risk of congenital anomalies in the children of fathers employed at Ontario Hydro, or by monitoring status. Analyses of paternal exposure by radiation dose and congenital anomalies classified by aetiological subgroups did not find significant associations, with the exception of a significantly reduced risk for multifactorial aetiology for cumulative exposure (adjusted OR 0.61, 95% CI 0.42-0.90). There was also a reduced risk of anomalies of the circulatory system (adjusted OR 0.51, 95% CO 0.27-0.95).

Parker et al (1999) recently reported a study that focused specifically on stillbirth and a relationship with paternal occupational exposure to radiation in male radiation workers at the Sellafield nuclear plant. Overall a significant association was found for total paternal preconceptional dose in both the cohort and nested case control study and still-birth risk, and a higher risk for stillbirth with congenital anomalies, particularly neural tube defects. Exposure data were prospectively routinely collected data and the study involved large numbers.

Doyle et al (2000) investigated foetal death and congenital malformation among the offspring of employees of the Atomic Weapons Establishment, the Atomic Energy Authority, and British Nuclear Fuels in the years 1993 to 1996. There were no increased risks either overall or by specific malformation grouping associated with whether or not the father had been monitored for radiation exposure. Similar results were reported when analysis was limited to the six months prior to conception, by type of exposure and by dose estimates. Pregnancy outcomes in this study were self-reported, introducing the potential for recall bias. However, exposure data were estimated from employer records.

In the 1996 study by Roman et al discussed previously, adverse reproductive outcomes for the offspring of radiographers were also examined. There were no significantly increased risks for any of the congenital anomalies considered for the children of male radiographers.

Table 7: Studies of paternal occupational exposure to ionising radiation: Adverse reproductive outcomes

Study	Title	Study group	Comparison/control group
Cohort studies: Level 2 evidence			
Doyle et al (2000)	Fetal death and congenital malformation in babies born to nuclear industry employees: report from the nuclear industry family study	11 697 male workers and 1903 female workers Included those who had one or more singleton pregnancies	
Case control studies: Level 3 evidence			
Green et al (1997b)	Risk of congenital anomalies in children of parents occupationally exposed to low level ionising radiation	763 fathers and 165 mothers of child with congenital anomaly Included children born between April 1979 and December 1986 and diagnosed in first year of life	763 fathers and 165 mothers of matched live-born child without anomaly
Sever et al (1988)	A case-control study of congenital malformations and occupational exposure to low level ionising radiation	672 children with malformations Included births occurring 1957-80	672 controls (Further controls selected for major malformations making total of 977 controls) Matched for sex, maternal age, and race
Cohort studies with a nested case control: Level 3 evidence			
Parker et al (1999)	Still births among offspring of male radiation workers at Sellafield nuclear reprocessing plant	248 097 singleton births and 3715 stillbirths in Cumbria Included cases between 1950-89 9 208 cases in nested case control	For the nested case control, controls were livebirths to radiation workers matched for sex and date of birth
Roman et al (1996)	Health of children born to medical radiographers	6730 members of College of Radiographers Cases included children whose parents reported an adverse outcome	Incidence rates Controls were children with no reported adverse outcome

Medical exposure

As with studies of parental occupational exposure, studies of medical exposure varied in the types of exposures measured and the way in which exposure was assessed and characterised (Table 8).

Cancer outcomes

There have been some recent studies investigating the relationship between paternal diagnostic x-ray exposure and outcomes in offspring. In a case control study in Shanghai, Shu et al (1988) found paternal preconceptional exposure to 6-10 x-rays was associated with significantly increased risks for total leukaemia (OR 2.4, 95% CI 1.5-5.0, n=77), and acute lymphocytic leukaemia (ALL) (OR 1.9, 95% CI 1.2-2.8, n=46). Paternal exposure to ≥11 x-rays prior to conception was significantly associated with increased risk for total leukaemia (OR 3.9, 95% CI 1.7-8.6, n=53), ALL (OR 2.6, 95% CI 1.5-4.6, n=26) and acute non-lymphocytic leukaemia (ANLL) (OR 3.7, 95% CI 2.0-7.0, n=20). The findings were limited as x-rays of all sites were included and exposures were not independently validated. In a later study Shu et al (1994) found significantly increased risks for leukaemia in offspring after paternal x-ray exposure of some specific sites (including chest, limb, upper gastro, and lower gastro or abdomen) for some exposure periods and some leukaemia types. As with the earlier study by Shu et al, because exposure was self-reported there was potential for recall bias, and actual exposures were not validated.

Meinert et al (1999) also considered parental x-ray exposure in the case control study of children with leukaemia, NHL, or solid tumours. Pre-natal x-ray exposure in the two years prior to the relevant birth was considered; however, a distinction was not able to be made between preconceptional exposure and exposure after conception but before birth. Paternal exposure to x-rays at any site in the 2 years prior to the relevant birth was significantly associated with an increased risk of leukaemia (OR 1.33, 95% CI 1.10-1.61, n=466), although it was not significant when the x-ray site was limited to the abdomen or intestinal tract (OR 1.76, 95% CI 0.88-3.56, n=24) or when other malignancies or sub-groups were considered. As with the findings relating to occupational exposure, as exposure was self-reported there is the potential for misclassification of exposure and recall bias.

A 1994 study was conducted by Andersson et al to look at the relationship of preconceptional irradiation of patients treated with Thorostat and cancer in their children. Overall, mortality in the offspring was lower than expected, incidence of all site cancers was not higher than expected, and there were no cases of leukaemia or NHL. The male patients had mean estimated doses preconception of 941mSv, significantly higher than the usual occupational exposures.

Table 8: Studies of medical exposure to ionising radiation: Cancer outcomes

Study	Title	Study group	Comparison/control group
Case control studies: Level 3 evidence			
Meinert et al (1999)	Associations between childhood cancer and ionizing radiation: Results of a population-based case control study in Germany.	2358 cancer cases (1184 leukaemia, 234 NHL, 940 solid tumours) Identified from German Childhood Cancer Registry Included children under 15 years	2588 controls Matched for sex, date of birth, district or residence
Shu et al (1994)	Association of paternal diagnostic x-ray exposure with risk of infant leukemia.	Exact numbers are unclear	Exact numbers are unclear
Shu et al (1988)	A population-based case-control study of childhood leukemia in Shanghai.	309 cases of childhood leukaemia Included children under 15 years	618 control children from general population Matched for sex and birth calendar year
Cohort studies with a national comparison: Level 4 evidence			
Andersson et al (1994)	Effects of preconceptional irradiation on mortality and cancer incidence in the offspring of patients given injections of Thorotrast.	369 Children (offspring of 260 females and 320 males from a cohort of 999 patients)	Compared with national rates

Adverse reproductive outcomes

Shea (1997) compared parental x-ray exposure and birth outcomes among a sample from the Avon Longitudinal Study of Pregnancy and Childhood (ALSPAC). Birth weight (adjusted and unadjusted), foetal growth, and mean gestational age were not significantly different by paternal x-ray exposure, and there was no significant increase in rates of preterm delivery. Actual individual data were unavailable and self-reported exposure introduced the potential for recall bias. The preconceptional period was not able to be considered separately (Table 9).

Dodds et al (1993) looked at adverse outcomes in the children of cancer patients to establish if there was an association between cancer treatments, including radiotherapy, and the risk of congenital anomalies in offspring. No significant increase in risk was associated with therapy type, dose of radiotherapy, or any sub-group of analysis. Byrne et al (1998) reported on a study investigating genetic disease in the offspring of cancer survivors. Exposure to radiotherapy was not statistically significantly associated with an increased risk of genetic disease in offspring, with a difference in sex ratio or rates of cytogenic diseases, or with single-gene defects or malformations. The study had good statistical power to detect differences.

Environmental exposure

The majority of epidemiological studies that have considered the genetic effects of environmental exposure have looked at parental exposure, and have not considered paternal preconceptional exposure independently.

There has been a significant amount of literature on the exposure of atomic bomb survivors to radiation and the health effects for their children. Yoshimoto (1990) in reviewing evidence from Radiation Effects Research Foundation (RERF) studies of cancer risks in the offspring of atomic bomb survivors of Hiroshima and Nagasaki concluded that there had been no demonstration of a statistically significant increased cancer risk for the children of atomic-bomb survivors as a result of parental irradiation. Yoshimoto also found no evidence of a dose-response relationship for cancer risk in this cohort (Yoshimoto, 1990). Schull (1981) found no statistically significant association for four measures of adverse reproductive outcome for the offspring of A-bomb survivors, although the associations were in the positive direction.

A further body of literature has come from studies of the health effects of the Chernobyl accident. A review of studies of reproductive outcomes relating to Chernobyl concluded that there was not consistent evidence of an adverse effect in terms of congenital anomalies or other pregnancy outcomes (Little, 1993a). A recent study however has found a significant increase in mutation rates in offspring of 'liquidators' (Clean-up teams) (Weinberg et al., 2001).

Table 9: Studies of medical exposure to ionising radiation: Adverse reproductive outcomes

Study	*Title*	*Study group*	*Comparison/control group*
Cohort studies with a comparison group: Level 2 evidence			
Shea and Little (1997)	Is there an association between preconception paternal x-ray exposure and birth outcome?	From 7678 birth records, infants whose fathers received an x-ray within one year of pre-conception	Infants whose fathers did not receive a x-ray within one year of pre-conception Exact numbers unclear
Case control studies: Level 3 evidence			
Dodds et al (1993)	Case-contol study of congenital anomalies in children of cancer patients	45 200 mothers and 41 158 fathers Included parents of children with congenital anomalies diagnosed in first year of life	45 200 mothers and 41 158 fathers Included parents of children without congenital anomalies
Cohort with a nested case control studies: Level 3 evidence			
Byrne et al (1998)	Genetic disease in offspring of long-term survivors of childhood adolescent cancer	2198 offspring of eligible cancer survivors	4544 offspring of controls (siblings of cancer survivors)

HEALTH OUTCOMES AND CAUSATION

The health outcomes primarily considered in studies of paternal preconceptional occupational, environmental and/or medical exposure to ionising radiation can be divided into two groups of genetic outcomes: cancer and adverse reproductive outcomes. These two outcomes will be considered separately.

Radiation and hereditary cancer: causation

There is a strong association between exposure to ionising radiation and the induction of specific cancers. It is generally accepted that some cancers are radiogenic in humans. The association between paternal preconceptional exposure and the risk of cancer in offspring is less clear. Some studies of occupational and medical exposures have demonstrated associations with cancer, particularly haematological cancers such as leukaemia, NHL, and Hodgkin's disease (Shu et al., 1988a; Gardner et al., 1990b; Roman et al., 1993; Shu et al., 1994; Draper et al., 1997; Smulevich et al., 1999; Meinert et al., 1999). The studies overall, however, do not consistently support a causal role of paternal exposure and positive associations have not always been accompanied by significant dose-response gradients. For example, Draper (1997) found the strongest association was with fathers who had exposures below the recordable level. Dose response gradients have been unable to be considered in all studies because of the study designs, in particular the ways in which exposure has been measured. Some studies of occupational exposure to ionising radiation categorised subjects as exposed or not exposed on the basis of job title or employment in a particular industry, and were therefore unable to consider individual doses received, or dose-response gradients. Although Gardner (1990) suggested a causative association in his 1990 study, several studies since have failed to confirm this hypothesis.

Three studies that considered the potential association between paternal preconceptional x-ray exposure and leukaemia found statistically significant associations (Shu et al., 1988a; Shu et al., 1994; Meinert et al., 1999). The 1988 study by Shu also identified a significant dose-response gradient. However, data on x-ray exposure in both studies by Shu were collected through interviews and was not independently validated. The study by Andersson of patients treated with Thorostat (1994) is significant in that fathers in this study were exposed to high levels of radiation directly to the testes. No significant cancer outcomes were demonstrated for offspring.

When taking into consideration the available literature as a whole, as well as current scientific understandings, the association between paternal exposure to low-level doses of radiation and the risk of cancer in offspring, including leukaemia and lymphomas, is not strong, and the positive associations have also not been consistently demonstrated. It has been suggested that the significant associations with leukaemia do not fit with current knowledge of leukaemia and radiation genetics (Doll et al., 1994; Wakeford, 1995). Brinkworth (2000) suggests that in recent studies there is generally "little evidence that radiation can induce germ-line mutations leading to cancer in offspring". Doll in discussing findings relating to leukaemia states:

The idea that ionizing radiation could cause a gonadal mutation that caused a child to have leukaemia is, nevertheless, plausible, but has to be judged against the background of what is known about the hereditability of childhood leukaemias and about the radiation exposures required to produce mutations in mammalian genomes (1994, p.678).

In terms of biological plausibility, radiation-induced tumours and susceptibility have been demonstrated in mice. In recent animal studies, it has been shown that susceptibility of offspring to the induction of lympho-haemopoietic malignancy when exposed to a secondary carcinogen may increase with paternal irradiation before conception (Lord et al., 1998).

In conclusion, while radiation-induced cancer in the offspring of those exposed before conception is theoretically plausible, it has not been demonstrated consistently or conclusively in human studies.

Radiation and adverse reproductive outcomes: Causation

In studies of paternal preconceptional exposure to ionising radiation, a number of reproductive outcomes have been considered, including spontaneous abortion, stillbirth, neonatal death, and congenital anomalies. In general, there is no consistent association between this type of exposure and a range of adverse reproductive outcomes. Studies conducted with the Japanese atomic bomb survivors did not find significant associations between exposure and adverse reproductive health outcomes, although small non-significant increases have been found.

Although there have been a few studies that have demonstrated a statistically significant association, this has not been demonstrated consistently in any setting (environmental, medical, occupational, or natural exposures). In the studies reviewed, Parker (1999) and Sever (1998) found significant associations. Sever however suggested the associations were likely to be due to chance due to the number of outcomes measured. Little (1999) has suggested that Parker's findings are incompatible with other studies of paternal exposure. Roman (1996), Green (1997b), and Doyle (2000) found no significant positive associations, and Green also documented significantly reduced risks for some types of congenital abnormalities. Adverse reproductive effects associated with paternal preconceptional exposure to ionising radiation would be expected to have a dose-response gradient.

Adverse reproductive outcomes can be both maternally or paternally mediated. In reviews of occupational exposure, increasing attention is being paid to the 'potential role' of paternal occupational exposure. There is evidence from animal studies to support a relationship between paternal preconceptional exposure to ionising radiation and adverse reproductive outcomes. An association is biologically plausible; however, there are little data available to support this for humans (Institute of Medicine, 1995). However, Savitz (1994) suggests that while there is currently little literature to support an association with spontaneous abortion, the theory behind the assumption is sufficiently plausible to warrant further study.

An association between paternal preconceptional exposure and adverse pregnancy outcomes or congenital anomalies has not been demonstrated, although it is thought to be biologically plausible.

CONCLUSIONS

The sources of evidence available to the research community suggest that New Zealand nuclear test veterans were not exposed to significant levels of ionising radiation at the time of the tests. It should be noted, however, that most film badges were not processed (Crawford 1989), and the potential for residual radiation exposure may have existed.

There is no high-quality epidemiological literature available to support an association between the paternal exposure of New Zealand nuclear test veterans to ionising radiation before conception and an increased risk of adverse health outcomes for their children. Further, there are no high-quality epidemiological studies dealing directly with the health of children of nuclear test veterans internationally. Epidemiological studies investigating outcomes for this population have not generally been considered feasible.

The evidence from studies of occupational, environmental, and medical exposures of an association between paternal exposure to ionising radiation before conception and adverse health outcomes is inconsistent. The biological potential of paternal exposure to induce adverse health outcomes in children is recognised, but this has not been shown conclusively in human populations to date.

The studies undertaken by Roff have highlighted a number of undesirable health conditions in the children of New Zealand nuclear test veterans (1998b; Roff et al, 2000).

The uncertainty and debate that has surrounded this issue, and, in particular, the potential risks for the children of nuclear test veterans, has undoubtedly caused high levels of concern among nuclear test veterans and their families, and may have had a negative effect on their psychological wellbeing. However, the dearth of literature on the psychological effects for the children of nuclear test veterans makes it difficult to draw conclusions about psycho-social outcomes.

SECTION THREE: VIETNAM WAR

BACKGROUND

New Zealand troop participation in Vietnam

New Zealand troops served with Australian Forces in the Vietnam war between 1964 and 1972 (Advisory Committee on the Health of Veterans' Children, 1999). Initially, in 1964, New Zealand's contribution was limited to engineers and medical personnel, but extended to include combat personnel in 1965 (Leepson, 1999). New Zealand began to withdraw combat troops in 1970 and completed withdrawal in 1971 (Leepson, 1999).

A total of 3368 service men and women served in Vietnam (Advisory Committee on the Health of Veterans' Children, 1999). It is likely that Mäori were over represented in the New Zealand Servicemen serving in Vietnam compared with the proportion of Mäori in the New Zealand population (MacDonald et al., 1997; Vincent et al., 1994). The New Zealand Department of Defence (Office of Veterans Affairs, 2001) records New Zealand personnel who served in Vietnam as including:

- 3338 service men and 30 women (nurses)
- 186 civilians (teachers and aid workers)

Vietnam veterans were exposed to factors with the potential to affect their health or the health of their children. The exposures considered in this review are exposures which have been linked with adverse health outcomes for veterans and which have the potential to result in adverse health outcomes for the veterans' children. The two main exposures in this category are:

- Exposure to toxins such as those present in herbicides or pesticides or in the Vietnam environment; and

- General exposure to the environment in Vietnam, 'the Vietnam experience'.

EXPOSURE TO TOXINS SUCH AS THOSE PRESENT IN HERBICIDES OR PESTICIDES

Herbicides were widely used as defoliants by the United States Military Forces in Vietnam between 1962 and 1971. The main herbicides used were Agents White, Blue and Orange, named after the colour of the containers they were stored in. Early spraying also included Agents Pink, Purple and Green.

Agents Orange and White were systemic defoliants, effective against woody and broadleaf plants. Agent Orange was composed of two herbicides: 2,4-D (2,4 dichlorophenoxyacetic acid) and 2,4,5-T (2,4,5-trichlorophenoxyacetic acid). 2,4,5-T was frequently contaminated by small amounts of dioxin, in particular 2,3,7,8-tetrachlorodibenzo-ρ-dioxin (TCDD). Agent White consisted of 2,4-D and Picloram (4-amine-3,5,6-trichloropicolinic acid). Agent Blue was a formulation of cacodylic acid and was a non-systemic desiccant used primarily against grasses, bamboo, rice and other crops intended for the enemy.

Agent Orange was the most widely used of these herbicides. According to US military records, at least 70 kilograms of Agent Orange was sprayed on Vietnam. Most of the spraying was done between 1967 and 1969 from fixed wing aircraft as part of Operation Ranch Hand. All herbicide spraying had ended by 1971. There was potential for military and civilian personnel serving in Vietnam and the Vietnamese civilian and military populations to be exposed to varying doses of Agent Orange and other herbicides. Agent Orange has come to be used as a generic term to describe veterans' exposure to chemicals in Vietnam.

Information about the exposure of New Zealand and Australian troops to herbicide spraying has been compiled by comparing the Herbs tapes (magnetic computer tape print-outs detailing spraying missions) with troop movements (O'Keefe & Smith, 1994). There is only one recorded case where ANZAC troops were in an area where they could have been exposed to aerial spraying (Advisory Committee on the Health of Veterans' Children, 1999).

Service personnel also had the potential to be exposed to weed killers used around the bases to control grasses and shrubs, and to insecticides used to control mosquito vectors (or carriers) of diseases such as malaria and dengue fever. Paraquat and Reglone were commonly used weed killers. Malthion and DDT were the most frequently used insecticides (O'Keefe & Smith, 1994).

It is exposure to the TCDD contaminating Agent Orange that is of most concern when considering health outcomes. TCDD and dioxin-like compounds are generated as by-products in trace quantities in various combustion, industrial and biological processes. Dioxin-like compounds are biologically stable and, as a result, human exposure is chronic and widespread (Grassman et al., 1998).

There is no doubt that TCDD is toxic. TCDD is an extremely potent animal carcinogen and has been shown to cause increases in lung cancer and all cancers combined in a variety of industrial settings (Smith & Lopipero, 2001). The

International Agency for Research on Cancer has concluded that TCDD is carcinogenic to humans (IARC, 1997).

HEALTH OUTCOMES FOR THE VETERANS EXPOSED TO TOXINS

The Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange (Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange, 2001) determined an association between exposure and the health outcomes listed in Table 10.

Table 10: Health outcomes for veterans of the Vietnam War exposed to herbicides and pesticides

Condition	*Strength of association**
Cancers	
Soft-tissue sarcoma	Sufficient evidence
Non-Hodgkin's lymphoma	Sufficient evidence
Hodgkin's disease	Sufficient evidence
Respiratory cancers	Limited/suggestive evidence
Prostate cancer	Limited/suggestive evidence
Multiple myeloma	Limited/suggestive evidence
Non-cancers	
Chloracne	Sufficient evidence
Acute and sub-acute transient peripheral neuropathy	Limited/suggestive evidence
Porphyria cutanea tarda	Limited/suggestive evidence
Adult-onset Type II diabetes	Limited/suggestive evidence

*Source: Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange (2001). *Update 2000*. Washington, D.C.: National Academy Press. (Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange, 2001)

HEALTH OUTCOMES FOR THE CHILDREN OF VIETNAM VETERANS EXPOSED TO TOXINS

Studies of veterans' children

A total of 11 studies were found directly relating to the children of Vietnam veterans. Many of the key studies were published as reports initially (Erickson et al., 1984a; Walsh et al., 1983; Wolfe et al., 1992) and papers were subsequently published based on the reports. Reports are not listed as separate studies. Further studies were found relating to paternal occupational or agricultural exposure to chemicals. Studies of maternal or population exposures were excluded on the basis of relevance, with the exception of New Zealand specific studies.

Quality Level	Study Type	Count	Key Studies
1.	Meta-analysis of cohort or case control studies	0	
2.	Cohort with comparison group	3	Centers for Disease Control, 1988c, Vietnam Experience Study, 1988 Health Status of Vietnam Veterans III. Reproductive Outcomes and Child Health Wolfe et al, 1995, Paternal Serum Dioxin and Reproductive Outcomes among veterans of Operation Ranch Hand Michalek et al, 1998b, Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death
3.	Case control	5	Donovan et al, 1984, Vietnam service and the risk of congenital anomalies. Erickson et al, 1984b, Vietnam veterans' risks for fathering babies with birth defects. Aschengrau & Monson, 1989, Paternal military service in Vietnam and risk of spontaneous abortion Aschengrau & Monson, 1990, Paternal military service in Vietnam and the risk of late adverse pregnancy outcomes Wen et al, 2000, Paternal military service and risk for childhood leukaemia in offspring
4.	Cohort/ comparison with national dataset	1	AIHW, 1999, Morbidity of Vietnam Veterans: A study of the health of Australia's Vietnam veteran community. Volume 3 Validation Study
5.	All other studies	2	Stellman et al, 1988, Health and Reproductive Outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam Field and Kerr, 1988, Reproductive behaviour and consistent patterns of abnormality in offspring of Vietnam veterans

Studies of the children of New Zealand veterans

The only information specifically available about New Zealand veterans comes from a survey carried out to inform the Inquiry into the Health Status of Children of Vietnam and Operation Grapple veterans (Advisory Committee on the Health of Veterans' Children, 1999). This survey included only a proportion of veterans and no comparison group was available. Data from this survey were reviewed by Dr Patrick Tuohy[x]. Dr Tuohy concluded that the results of the study were likely to be biased towards the children of veterans with health concerns and that he was unable to draw any conclusions based on the information.

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[x] Chief Advisor Child and Youth Health, NZ Ministry of Health

KEY STUDIES OF THE OFFSPRING OF VIETNAM VETERANS

Level 2 evidence: Cohort studies with a comparison group

Health status of Vietnam veterans III. Reproductive outcomes and child health
The Centers for Disease Control Vietnam Experience Study 1988c

1. Study description
- This study is part of the Vietnam Experience (VES) study, an historical cohort study of a random sample of men who enlisted in the US Army from 1965 to 1971. Vietnam veterans were compared with veterans who did not serve in Vietnam. Reproductive outcomes were examined using data collected from veterans during telephone interviews and data from hospital birth records of selected veterans' children.

2a. Participant selection and source
- The VES study consisted of telephone interviews with 15 288 veterans. As a result of an interim analysis of self-reported data showing differences in total birth defects and cerebro-spinal malformations (CSMs), two substudies were added to the main study.
   - A comparison of the rates of total birth defects recorded on hospital records for Vietnam veterans and non-Vietnam veterans. The study included 2282 veterans and 4122 offspring participating in the interview and medical examination components of the VES after Jan 1 1986.
   - In the second substudy hospital records were examined for all offspring reported to have CSMs, reported to have conditions suggestive of CSMs and all stillborn children. Hospital records were used for validation.
- Veteran status was determined from army records.
- Birth defects were coded using ICD-9 systems.

2b. Exposure and comparison subgroup similarities
- The exposure assessed was exposure to the Vietnam experience.
- All Birth defects group: no significant differences in demography/history between groups.
- CSM group: significant differences in demography/history and reporting between groups.

2c. Exposure and comparison measurement
- The exposure comparison groups were well defined.

2d. Outcome measurement
- Hospital birth records of birth defects/CSM were defined using an objective internationally accepted coding system ICD-9. Paternal interview data for birth defects/CSM were defined using ICD-9.

Results
- Birth records: the sample size for the All Birth defects group was based on a statistical power calculation for the primary outcome measure of Total Birth defects. The study had 80% power to detect a relative risk of 1.4.
- The study did not have adequate power to detect small effect sizes for specific defects, including CSM.
- Effect size estimates for the All Birth defects group are presented as Odds Ratios with 95% confidence intervals. Point estimates for self-reported data were generally slightly greater than 1.0. Confidence intervals generally included 1.0 indicating the effect was not significant.
- There was appropriate adjustment for a variety of socio-demographic characteristics for the veterans in the analyses for the All Birth defects group.
- The substudy based on reproductive outcomes validated from hospital records produced Odds Ratios that approximated 1.0.
- Observed and expected numbers of outcomes are presented for the CSM substudy. The observed number is similar to that expected on the basis of rates from two US surveillance systems. A much lower than expected number was found in the children of non-Vietnam veterans.

Conclusions
- A good quality cohort study. The objectives were well formulated and the study conclusions do not go beyond the results. The limitations of the study are comprehensively identified.
- The differences between self-reported and validated data suggest differential recall or reporting between Vietnam veterans and non-Vietnam veterans.
- One limitation of the studies is the lack of information about the mothers of the babies studied, in particular maternal exposure to alcohol and tobacco.

Paternal serum dioxin and reproductive outcomes among veterans of Operation Ranch Hand
Wolfe et al 1995

1. Study description
▪ A prospective cohort study of Vietnam veterans of Operation Ranch Hand (exposure) and Airforce veterans (no exposure). Outcome measures were specific birth defects in the children of veterans. Data sources comprised hospital records and parental interviews.

2a. Participant selection and source
▪ Hospital records of the children of exposed and unexposed veterans were identified through parents. Exposed and unexposed parents were matched on date of birth, race and military rank.

2b. Exposure and comparison subgroup similarities
▪ The report provides minimal details on the demographic variables of the two study groups. However, the analyses involved adjustment for the potential confounding influence of these variables.

2c. Exposure and comparison measurement
▪ The exposure/comparison groups were well defined.

2d. Outcome measurement
▪ Hospital records of birth defects were defined using an independently developed coding system ICD-9.

Results
▪ Effect size estimates are presented as relative risks with 95% confidence intervals.
▪ No analysis of statistical power was performed. Sample numbers for some comparisons were very low. Confidence intervals were generally wide suggesting the study lacked adequate power. Confidence intervals generally included 1.0 indicating there was insufficient evidence to suggest an excess risk.

Conclusions
▪ A good quality cohort study. The objectives were well formulated and the study conclusions did not go beyond the results. A strength of the study is the attempt to specify the exposure status of Vietnam veterans in terms of dioxin levels. However, the issue of adequate statistical power was not addressed.

Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death
Michalek et al 1998b

1. Study description
▪ A prospective cohort study of newborn children of Vietnam veterans of Operation Ranch Hand (exposure) and Airforce veterans (no exposure). Outcome measures were risk of preterm birth, intrauterine growth retardation, and infant death. Data comprised hospital records and parental interviews.

2a. Participant selection and source
▪ Hospital records of infants were identified through parents.

2b. Exposure and comparison subgroup similarities
▪ The report provides comprehensive details on the demographic variables of the two study groups. Results indicated significant differences on some variables, and analyses involved adjustment for the potential confounding influence of these variables.

2c. Exposure and comparison measurement
▪ The exposure/comparison groups were well defined.
▪ Exposure status was defined in terms of three different levels of dioxin exposure: Background, Low, High.

2d. Outcome measurement
▪ Hospital records of study outcomes were defined using an independently developed coding system ICD-9.

Results
▪ Effect size estimates are presented as relative risks with 95% confidence intervals.
▪ No analysis of statistical power was performed. Sample numbers for some comparisons were very low. Confidence intervals were generally very wide suggesting the study lacked adequate power. Confidence intervals generally included 1.0 indicating there was insufficient evidence to suggest an excess risk.
▪ Effect size did not increase in a consistent manner as exposure level increased. The latter finding is consistent with the general finding of no effect for all outcomes.

Conclusions
▪ A good quality cohort study. The objectives were well formulated and the study conclusions did not go beyond the results. A strength of the study is the attempt to specify the exposure status of Vietnam veterans in terms of dioxin levels.

Level 3 evidence: Case control studies

Vietnam service and the risk of congenital anomalies
Donovan et al 1984

1. Study description
▪ A retrospective case control study. Cases were infants with anomalies diagnosed at or shortly after birth. Control infants were infants born without an anomaly. The veteran status of the father was obtained from army records.

2a. Classification of case status
▪ Cases were selected from children born in any of the 34 hospitals in New South Wales and defined using ICD-9 codes.

2b. Selection of controls
▪ Potential controls were selected from the same hospital matched on maternal age, time of birth and socio-economic status where possible.
▪ Controls were discounted if no paternal information was available. Controls were individually matched to cases on appropriate measures. Analyses indicated matching was successful.

2c. Exposure and comparison measurement
▪ The exposure/comparison groups were well defined.
▪ Case/control status was identified independently of exposure status.

2d. Outcome measurement
▪ The presence or absence of anomalies was defined using an independent coding system: BPA using information obtained from hospital records.

Results
▪ This study had 87% power to detect an Odds Ratio of 1.5 for all anomalies combined.
▪ Effects size estimates were presented as Odds Ratios with 95% confidence intervals only for the all anomalies combined measure (risk of fathering a malformed infant).
▪ Odds ratios for the 7 specific anomalies all showed no effect. However, confidence intervals were not reported.

Conclusions
▪ A good quality case control study. The objectives were well formulated and the study conclusions did not go beyond the results. However, reporting of the results of the statistical analyses is insufficient.

Vietnam veterans' risks for fathering babies with birth defects
Erickson et al 1984b

1. Study description
-   A retrospective case control study of newborn children in the Metropolitan Atlanta Congenital Birth Defects Programme. Case babies were babies born with birth defects. The veteran status of the father was compared between cases and controls.
-   Data were extracted from hospital and military records, and parental interviews. The study aimed to test the following hypotheses:
    1. Whether veterans, excluding Vietnam veterans, were at different risk than non-veterans for fathering babies with birth defects.
    2. Whether Vietnam veterans were at different risk for fathering babies with birth defects (the main focus for the study).
    3. Whether Vietnam veterans who were judged by the army Agent Orange Task Force to have had greater opportunity for exposure to Agent Orange, had different risks for fathering babies with defects.
    4. Whether Vietnam veterans who said during interview that they had been exposed to herbicides such as Agent Orange were at different risk.

2a. Classification of case status
-   Case records were obtained from a single large city register of birth defects for the period 1968-1980. Only records with ICD-8 diagnoses were selected.

2b. Selection of controls
-   Control records were obtained from a general population registry.
-   Controls were approximately matched to cases. However it is unclear from the analyses whether matching was successful for case/control infants.

2c. Exposure and comparison measurement
-   Exposure was defined in two ways:
    a. Paternal veteran status – whether the father was a veteran or non-veteran and whether he had served in Vietnam.
    b. An exposure opportunity index (EOI) was created to measure exposure to the herbicide Agent Orange and was based on times and places of service in Vietnam.
-   Case/control status was identified independently of exposure status.

2d. Outcome measurement
-   Hospital records of anomalies were defined using an independent coding system: ICD-8.

Results
-   This study had 70% power to detect an Odds Ratio of 1.2 for the all types of birth defects measure and greater than 99% power to detect an Odds Ratio of 1.5 or greater. Power was generally very low for detecting specific defects.
-   Effects size estimates for the various defects were presented as Odds Ratios and regression coefficients. However, with the exception of the all birth defects measure, 95% confidence intervals were not provided, nor were standard errors provided for regression coefficients.

- The Odds Ratio for the all birth defects measure (Vietnam veterans) was close to no effect (0.97 with CI 0.83-1.14).
- Spina bifida: a significant association (regression coefficient) between spina bifida and exposure to Agent Orange was found on the two self-reported EOI measures (see previous comments on EOI). However, the magnitudes of the regression coefficients are small. Odds ratios for spina bifida were not significant.

Conclusions
- The objectives were well formulated and the study conclusions did not go beyond the results. The limitations of the study are comprehensively identified. Reporting of results of statistical analyses is insufficient. The authors concluded "Vietnam veterans do not have an increased risk for fathering children with major birth defects, nor do veterans with greater estimated exposures to Agent Orange seem to have an increased risk."

Paternal military service in Vietnam and the risk of late adverse pregnancy outcomes
Aschengrau and Monson 1989
Paternal military service in Vietnam and the risk of spontaneous abortion
Aschengrau et al 1990

1. Study description
▪   The two papers are separate analyses of data derived from a nested case control study of women who delivered infants from August 1977 until March 1980 at Boston Hospital for Women, US. Paternal military history was compared between babies with adverse reproductive outcomes (cases) and normal controls. Data were sourced from military and hospital records.

2a. Classification of case status
▪   Cases were identified through hospital records and included congenital anomalies (1314), stillbirths (121) and neonatal deaths (76).
▪   Birth defects were defined using an independently developed coding system ICD-9-CM.
▪   Cases were not randomly selected, increasing the risk of confounding by demographic variables.

2b. Selection of controls
▪   Controls were randomly selected. There was minimal reporting on characteristics of sample populations.

2c. Exposure and comparison measurement
▪   Paternal veteran status was obtained from military records.
▪   Case/control status was identified independently of exposure status.
▪   Analyses involved adjustment for group differences in demographic variables.

2d. Outcome measurement
▪   Effect size estimates were presented as crude and adjusted Odds Ratios with 95% confidence intervals.
▪   No statistical power analysis was performed. Confidence intervals were generally wide suggesting the study may have lacked power.

Conclusions
▪   The objectives were well formulated and the study conclusions did not go beyond the results. However, the limitations of the study are not adequately identified, in particular the issue of adequate statistical power.

Paternal military service and risk for childhood leukaemia in offspring
Wen et al 2000

1. Study description
- A retrospective case control study of children with leukaemia (cases) matched with randomly selected controls. The analysis was part of a series of studies undertaken by the Children's Cancer Group (CCG). Data were collected from interviews with fathers.

2a. Classification of case status
- 2300 cases were identified through registrations with the CCG.

2b. Selection of controls
- Controls were selected using a random digit telephone dialling procedure and individually matched on year of birth, location of residence, sex and race.

2c. Exposure and comparison measurement
- Case/control status was identified independently of exposure status.
- There were slight differences between the case and control populations and these are defined in detail. There were higher non-response rates in the control group.
- Analyses involved adjustment for group differences in demographic variables.

2d. Outcome measurement
- Paternal occupation was self defined as service in Vietnam or Cambodia.

Results
- Effect size estimates were derived from a conditional logistic regression model adjusted for paternal education, race, income, smoking status, exposure to X-rays and marijuana. 95% confidence intervals are presented.
- No statistical power analysis was performed. Confidence intervals were generally narrow.

Conclusions
- A good quality case control study. The objectives were well formulated and the study conclusions did not go beyond the results. A limitation of the study is self-reported exposure status.

Level 4 evidence: Cohort studies with a national comparison group

Australian Morbidity of Vietnam Veterans Study
Australian Institute of Health and Welfare 1999

1. Study description
▪ The Morbidity of Vietnam Veterans study (Commonwealth Department of Veterans' Affairs, 1998a) was undertaken by the Commonwealth Department of Veteran Affairs and was a study of a cohort of Australian veterans (exposure). The study aimed to survey the health of Vietnam veterans, their spouses and their children, and to compare their health with the number expected to have different conditions based on Australian community standards. Data were collected by postal questionnaire.

2a. Participant selection and source
▪ The cohort consisted of all male Vietnam veterans able to be traced from military records. The list is believed to be reliable. A total of 59 036 males and 484 females were identified as Vietnam veterans. Of these 501 died in service or were listed as missing and 3840 were known to be deceased at the time of the survey. Questionnaires were mailed to 49 944 male Vietnam veterans, 278 female and 1531 widower, divorced or separated partners of veterans. Questionnaires were returned by 40 030 male veterans (80%).
▪ Comparable data were extracted from unmatched data from national databases.

2b. Exposure and comparison subgroup similarities
▪ Community data were accessed for people of a similar age. The definitions of the outcomes compared differed between data from the cohort and from the national database so no direct comparison was available for a number of outcomes.

2c. Exposure and comparison measurement
▪ The exposure/comparison groups were not directly comparable.
▪ Exposure was defined as any service in Vietnam.

2d. Outcome measurement
▪ Outcomes were self-reported based on responses to generalised questions in a postal survey.

Results
▪ Differences between the cohort and comparison group are presented as rates in the cohort group compared with expected rates based on national statistics. Confidence intervals were not available.
▪ No statistical power analysis was performed.

Conclusions
▪ The study results are indicative only. Comparison groups were inadequate. However, the report recommended that immediate action be taken to validate the findings of the survey by validating the self-reported health conditions against medical records.

A validation study was undertaken on a sub-sample of 6842 veterans and their children. Outcomes accepted for validation included cancers, congenital abnormalities and death. Response rates for children ranged from 54% to 86%. In analysis of the data the validity of reported conditions by non-respondents was assumed to be at the same rate as respondents. The results of the validation study and comparison with the rates in the main survey are shown in Table 11.

Table 11: Comparison of self-reported rates of health conditions in Australian veterans' children with validated and expected rates.

Condition	Rates in Survey	Conditions validated (n)	Conditions not validated (n)	Conditions not able to be validated (n)	Conditions with no response (n)	Estimated validated conditions (n)	Expected number of conditions (95% CI)
Leukaemia	78	30	13	13	29	39	64 (48-80)
Wilms' tumour	47	7	15	8	22	10	7 (2-12)
Cancer of the nervous system	126	26	44	13	52	31	48 (34-62)
Other cancer	716	101	309	84	266	122	333 (297-369)
Spina bifida-maxima	379	34	185	102	149	50	33 (22-44)
Down Syndrome	143	49	27	28	43	67	92 (73-111)
Tracheooesophageal fistula	128	7	60	26	38	10	23 (14-32)
Anencephaly	51	10	27	10	11	13	16 (8-24)
Cleft lip/palate	304	57	63	77	107	94	64 (48-80)
Absent external body part	394	14	166	105	110	22	34 (23-45)
Extra body part	355	38	97	129	119	74	-

Level 5 evidence: Other studies

Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam
Stellman et al 1988

1. Study description
- A cross-sectional survey of health and reproductive outcomes in US Vietnam War veterans (exposure) and non-Vietnam military veterans (no exposure).
- Data collection was by self-administered questionnaire.

2a. Participant selection and source
- Participants in the two groups (exposure/no exposure) were all adult male veterans randomly selected from military records.
- The exposed group were Vietnam veterans who belonged to The American Legion.

2b. Exposure and comparison subgroup similarities
- It is unclear from the report whether the two groups were similar in terms of standard demographic variables. It is also unclear whether the analyses involved adjustment for these potentially confounding variables.

2c. Exposure and comparison measurement
- The exposure/comparison groups were well defined.

2d. Outcome measurement
- Outcomes relevant to this review included reported difficulties with conception, specific birth outcomes and birth weight.
- Data comprised self-reported unvalidated responses to questionnaire items.

Results
- It is unclear what the response rate of the survey was.
- Effect size estimates are presented as Odds Ratios with *P* values.
- There is no analysis of the statistical power of the study.

Conclusions
- A low quality descriptive study. Data were wholly self-report based and therefore potentially biased. There was essentially no attempt by the authors to identify the limitations of the study.

Reproductive behaviour and consistent patterns of abnormality in offspring of Vietnam veterans
Field and Kerr 1988

1. Study description
▪ A cross-sectional survey of reproductive outcomes in 1395 Tasmanian, Australian serviceman (705 conscripts plus 690 regular army) Vietnam War veterans (exposure) and a non-veteran community sample (no exposure). Data collection was by interview.

2a. Participant selection and source
▪ Veterans were selected using military records. It is unclear whether sampling was random.
▪ The non-veteran sample was not randomly selected thereby raising the potential for sampling bias.

2b. Exposure and comparison subgroup similarities
▪ Results indicate minimal differences between the groups on standard demographic variables.

2c. Exposure and comparison measurement
▪ The exposure/comparison groups were well defined.

2d. Outcome measurement
▪ Outcomes relevant to this review included a range of measures of child health including birth weight, birth defects, child mortality, behavioural/learning problems, and specific physical illnesses.
▪ Data comprised self-report responses to questionnaire items. Additional information was sought from participants' doctors. However, the quality of this information is unclear.

Results
▪ It is unclear what specific statistical analyses were performed.
▪ *P* values are presented without effect size estimates.
▪ There is no analysis of the statistical power of the study.

Conclusions
▪ A low quality descriptive study. There is insufficient identification of the limitations of the study design and methodology. Claims by the authors that previous studies have over-emphasised 'statistical aspects' are unsubstantiated and poorly conceived. Criticism of Field and Kerr's study was reported by O'Keefe. (1994). Data from the study were presented to the Evatt Commission. Examination of data by the Commission revealed the following concerns:
  - The sample of veterans included in the study was selected by the Vietnam Veterans Association of Australian (VVAA);
  - The interviewing was carried out by the wives of veterans;
  - Controls were selected by the veterans; and
  - Data were misclassified.
After review of the data, Dr Field offered to withdraw the submission from the Commission.

SUMMARY OF THE OUTCOMES OF STUDIES

All birth defects

Most of the key studies of Vietnam veterans considered the combined outcome 'all birth defects' (Aschengrau & Monson, 1989; Aschengrau & Monson, 1990; Centers for Disease Control, 1988c; Donovan et al., 1984) for exposure to the Vietnam experience or for exposure to Agent Orange. Summarised results of these studies are shown in Table 12.

Two studies of paternal exposure of Vietnamese men have been reviewed by Sterling and Arundel (1986). Studies evaluating paternal occupational exposure to dioxins, pesticides or herbicides have also been reviewed (Table 13).

The only study of Vietnam veterans where an excess risk for all birth defects combined was found was the CDC study comparing Vietnam veterans and non-veterans. This study relied upon self-reported information about birth defects. Recalculation of risks based on data from a sub-sample of veterans for whom medical records were checked showed no increased risk.

An increased risk for all birth defects was found in the Vietnamese studies. The studies have been critically reviewed by Constable and Hatch (1985). Two types of studies have been carried out in Vietnam:

- Studies comparing reproductive outcomes in the South where there was herbicide spraying with reproductive outcomes in the North where there was no spraying.
- Studies comparing the reproductive outcomes for women who stayed in the North, but whose husbands served in the South, with women whose husbands did not serve in the South.

Problems with accepting the results of the Vietnamese studies include (Constable and Hatch, 1985):

- Insufficient detail about the methods used in subject selection, case finding and data collection;
- Variation in the exposures of individuals would not be reflected in the definition of exposure based on area of residence. Comparison between villages sprayed and not sprayed was problematic because it depended on self-reported data and no account was taken of movement between villages (O'Keefe & Smith, 1994);
- A lack of information about the timing of exposures in relation to pregnancies;
- The potential for maternal as well as paternal exposure;
- Low rates of birth abnormalities in the control groups and near normal rates in the exposed groups. There is only limited comparative data available for birth defects in Vietnam prior to any spraying. Validation of a sub-sample of women by Lang et al found disparities;
- Limited efforts to consider potentially confounding variables in the analysis;
- The absence of a dose response relationship.

The majority of studies of occupational and environmental exposure to pesticides have found no increased risks for all birth defects. Slight excess risks were found by Garry (1996a) and Restrepo et al (1990). These studies are not directly comparable with the studies of Vietnam veterans as they include the potential for maternal exposure as well as paternal.

Summary
The Odds Ratios and Relative Risks calculated from these data are remarkably consistent and overall show no increased risk for Vietnam veterans for fathering children when all birth defects are considered (Figure 2).

Table 12: Health outcome for offspring of Vietnam veterans: All birth defects

Study	Number	Groups	Objective/ Subjective	Outcome measure	Exposure		All defects Odds Ratio (95% CI)
Cohort studies: Level 2 evidence							
Wolfe et al (1995)	872 Ranch Hand veterans 1036 comparison subjects	Ranch Hand veterans with dioxin results and Air Force veterans serving in SE Asia at same time with dioxin results	Reported by study participants All conceptions verified	ICD-9 (740 –759)	Exposure to dioxin Background Low High		1.0 (0.7 – 1.3) 1.3 (1.0 – 1.6) 1.0 (0.8 – 1.3)
CDC (1988)	7924 Vietnam and 7364 non-Vietnam veterans	Vietnam veterans and non-Vietnam veterans	Subjective Data validated for a random sample	ICD-9 (740-759)	Vietnam experience	Self-report: Validated:	1.3 (1.2 – 1.4) 1.0 (0.8 – 1.4)
Case control studies: Level 3 evidence							
Aschengrau & Monson (1990)	1314 anomalies, 201 spontaneous abortions 1490 controls	Vietnam veterans vs. non-Vietnam veterans and no known service	Objective	ICD-9 (modified)	Vietnam experience	Vietnam vs. non-Vietnam: Vietnam vs. no known service:	1.2 (0.8 – 1.9) 1.3 (0.9 – 1.9)
Aschengrau & Monson (1989)	201 women with spontaneous abortions, 1119 controls	Vietnam veterans and non-Vietnam veterans vs. no known service	Objective	Any spontaneous abortion to 27 weeks	Vietnam experience	Vietnam veterans vs. no known service:	No all defects data
Donovan et al (1984)	8517 babies with anomalies and 8517 control babies	Vietnam veterans vs. all other men Vietnam veterans vs non-Vietnam veterans	Objective	ICD-9	Vietnam experience	Adjusted: Unadjusted: Adjusted: Unadjusted:	1.02 (0.78 – 1.32) 1.03 (0.80 – 1.33) 0.80 (0.55-1.16) 0.79 (0.56-1.13)
Erickson et al (1984b)	7133 case babies and 4246 control babies	Vietnam veterans vs. all other fathers	Objective	ICD – 9	Agent Orange Exposure	Vietnam veterans vs. all other fathers	0.97 (0.83 – 1.14)
Other studies: Level 5 evidence							
Field and Kerr (1988)	Children of 1395 Tasmanian veterans 281 comparison families	Veterans vs. unmatched general population group	Subjective	Self-reported	Vietnam experience	Veterans vs. no known service in Vietnam	A significant increase

Table 13: Health outcome for offspring after paternal exposures to toxins: All birth defects

Study	Number	Groups	Objective/ Subjective	Outcome Measure	Exposure	All Defects Odds Ratio (95% CI))
Cohort studies: Level 2 evidence						
Kristensen et al (1997)	200 000 births between 1967-1991	Farmers vs. non-farmers	Objective	ICD-8	Pesticides in a farming environment	1.02 (0.96-1.09) - adjusted
Townsend et al (1982)	737 conceptions	Wives of exposed and unexposed workers at the Dow chemical plant	Subjective	ICD-8	All dioxins TCDD	0.97 (0.76-1.22) All unfavourable outcomes - adjusted 0.85 (0.53-1.35) All congenital malformations - adjusted 0.98 (0.72-1.32) All unfavourable outcomes - adjusted 1.08 (0.56-1.83) All congenital malformations - adjusted
Suskind and Hertzberg (1984)	204 exposed workers 163 non-exposed workers	Exposure partners vs. unexposed partners from the same workplace	Subjective	Not specified	Manufacture of 2,4,5-T	RR 1.074 (no CI)*
Case: control studies: Level 3 evidence						
Garcia (1998)	261 matched pairs	Cases matched with a referent	Objective	ICD-9	Direct handling of pesticides by fathers	1.49 p=0.087
Blatter et al (1997)	Multi-centre case: referent study	Live born children with spina bifida vs. a general population referent group	Objective	ICD-9	Exposure to pesticides Low exposure High exposure	0.9 (0.4-1.9) n=11 0.2 (0.0-1.4) 1.7 (0.7-4.0)
Garry et al (1996)	4935 births to pesticide appliers linked to 210 723 live births	Pesticide appliers compared with general population	Objective	1989 National Centres for Health Statistics Revised Guidelines	Exposure to pesticides	1.41 (1.18-1.69) n=125
Can et al (1984)	Cases: 32 069 pregnancies Controls: 121 993 pregnancies	Wives of men exposed during military service in Vietnam vs. wives of unexposed men	Objective	Not specified	Paternal exposure to South Vietnam	1.38 (1.18-1.65) - unadjusted
Other studies Level 5 evidence						
Restrepo et al (1990)	8867 people	Before vs. after working in the floriculture industry	Objective	Study defined categories	Occupational exposure to pesticides	1.53 (1.04-2.25)
Lang et al (1983) Reviewed bySterling	Birth defects in 18 communities	Compared exposed and unexposed fathers	Subjective	Not specified	Paternal exposure to South Vietnam	4.9 (2.5-9.5) - unadjusted
Smith et al (1982)	989 sprayers	Professional New Zealand 2,4,5-T sprayers vs. agricultural contractors	Subjective	Not specified	Exposure to pesticides	RR 1.19 (0.58 – 2.45) – unadjusted*
Hanify et al (1981)	37 751 babies born in Northland hospitals, New Zealand: 510 diagnosed malformations	Exposed vs. unexposed	Objective	UK Ministry of Health classification	Aerial 2,4,5-T spray	1.73 (1.44-2.08)

* RR = relative risk

**Figure 2: Summarised Odds Ratios for the outcomes all Birth Defects**
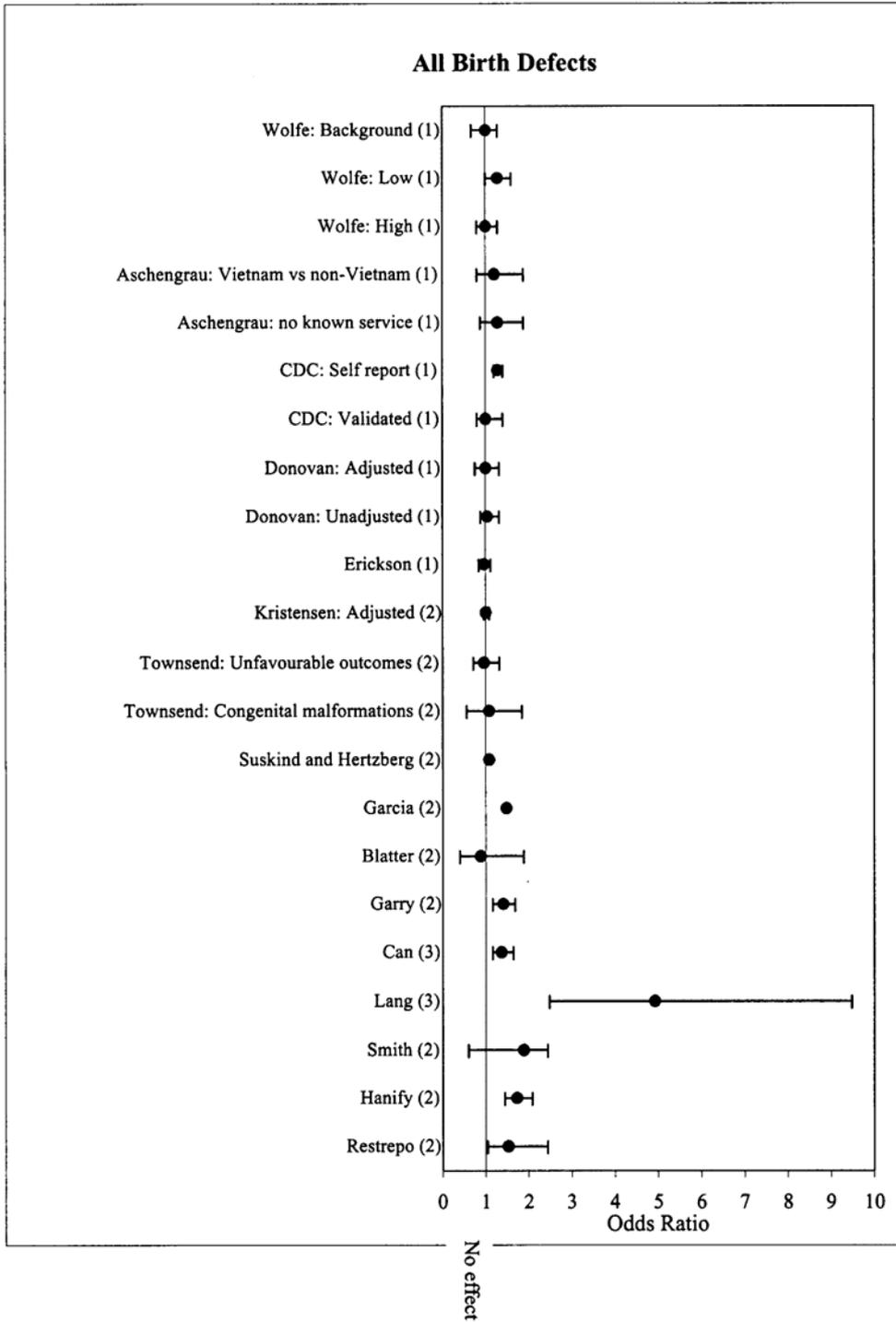
Figure 2: Summarised Odds Ratios for the outcome "all defects"

1. Vietnam veterans' studies
2. Occupational/Environmental exposure
3. Vietnam studies

Key:

● Odds Ratio or Relative Risk

⊢—⊣ 95% Confidence Interval

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Specific birth defects

As discussed previously, grouping all birth defects together into one category may be inappropriate due to the heterogeneity of birth defects. Studies of specific birth defects have also been undertaken and are summarised in Tables 14 and 15.

The CDC studies of the offspring of Vietnam veterans found slightly increased risks of nervous system defects and hydrocephalus but no significant increased risk of spina bifida (Centers for Disease Control, 1988c). Erickson et al (1984b) analysed 95 defect groups and found no increased risk for most defects. The exceptions were spina bifida for veterans thought to have had increased exposure to Agent Orange and cleft lip for veterans with intermediate exposure. Veterans also had significantly lower risks of fathering babies with complex cardiovascular defects. Erickson notes that while these results were statistically significant they may not be biologically significant. A statistically significant result does not necessarily mean that there are true differences in risk. When a large number of hypotheses are tested, as in this study, some significant results are expected as a result of chance. Erickson concludes that the lack of an association for both anencephalus and spina bifida suggests that the statistically significant result for spina bifida is due to chance. Similarly the other positive associations found were all small and may have been the result of chance or an unaccounted for confounding variable.

The AIHW study (1999) found elevated rates of spina bifida in the offspring of veterans, but this was based on comparison with national statistics rather than with a matched control group. Spina bifida has been considered in occupational and environmental studies. Significantly elevated risks were found by Kristensen et al (1997) with spina bifida only for men who sprayed pesticides inside glasshouses and on orchards. However, although not significant, there was a small positive association between spina bifida and exposure to a range of chemicals in most of the studies reviewed. Summarised OR and RR for the outcome spina bifida are shown in Figure 3.

Wolfe et al (1995) found some elevations of risk in specific organ categories but the numbers were too small to permit analyses. The authors concluded that the results were not biologically meaningful.

The Vietnamese study by Can (1984) also estimated Odds Ratios for wives of exposed veterans with molar pregnancies (OR 1.52, 95 % CI 0.98-2.35) and for children with limb deformities (OR 0.90, 95% CI 0.58-1.39) but found no increased risk.

A range of other specific birth defects have also been considered in studies of occupational and environmental paternal exposure. Central nervous system, neural tube and cleft palate defects are summarised in Table 16. In addition a study by Garry et al (Garry et al., 1996a) found no increased rates of gastrointestinal (OR 3.63, 95% CI 1.51-8.70), circulatory/respiratory (OR 1.69, 95% CI 1.04-2.76) or chromosomal (OR 1.06, 95% CI 0.53-2.10) defects between Minnesota pesticide appliers and a general population control group. Rates of urogenital defects were slightly elevated (OR 1.69, 95% CI 1.06-2.64).

Hanify et al (1981) found a correlation between aerial top-dressing spraying and slightly increased rates of talipes in Northland, New Zealand (OR 1.66, 95% CI 1.20-2.29). However, Hanify's study reflects both paternal and maternal exposure. In a study of paternal exposure to 2,4,5-T, Smith et al (1982) found no increased rates of talipes.

Summary

There was no consistent positive association between exposure to Agent Orange or a range of chemicals or pesticides and any specific birth defect. However, the Odds Ratios tended to be higher than 1.0 indicating a slightly increased risk even though these increases for individual studies were not significant. None of the studies had sufficient power to determine if rare birth defects were significantly associated with paternal exposure to chemicals such as Agent Orange.

Table 14: Health outcome for offspring of Vietnam veterans: Central nervous system, neural tube and cleft palate defects

Study	Exposure	Groups	Nervous system OR (95% CI)	Spina bifida OR (95% CI)	Hydrocephalus OR (95% CI)	Anencephaly OR (95% CI)	Cleft lip or palate OR (95% CI)	Neural tube defects OR (95% CI)
Cohort studies with a comparison group: Level 2 evidence								
CDC (1988)	Vietnam experience	Vietnam veterans vs. non-veterans	2.3 (1.2-4.5)	1.7 (0.6-5.0) unadjusted	5.1 (1.1-23.1) unadjusted			
Case control Studies with a comparison group: Level 3 Evidence								
Aschengrau & Monson (1990)	Vietnam experience	Vietnam veterans vs. non-veterans	3.2 (not significant)					
		Veterans vs. no known service	2.5 (not significant)					
Donovan et al (1984)	Vietnam experience	Vietnam veterans vs. non-veterans	1.25 (no CI)				0.91 (no CI)	
Erickson et al (1984)	Agent Orange exposure	Vietnam veterans vs. all other fathers	0.91 (no CI)	1.05 (no CI)	0.85 (no CI)	0.89 (no CI)		
		Based on self-reported exposure scores	0.78 (no CI)	1.19 (no CI)	0.25 (no CI)	0.80 (no CI)		
Cohort Studies with a comparison group Level 4 Evidence								
AIHW – validation study (1999)	Vietnam experience	Vietnam veterans vs. national statistics		1.5 (no CI)		0.82 (no CI)	1.47 (no CI)	

Table 15: Health outcome for offspring of Vietnam veterans: Other specific birth defects

Study	Exposure	Groups	Eye OR (95% CI)	Ear/face/neck OR (95% CI)	Circulatory system/ heart OR (95% CI)	Respiratory system OR (95% CI)	Digestive system OR (95% CI)	Genital system OR (95% CI)	Urinary system OR (95% CI)	Musculo-skeletal OR (95% CI)	Skin OR (95% CI)
Cohort studies with a comparison group: Level 2 evidence											
Wolfe et al (1995)	Bkgd Low High	Exposed veterans vs. unexposed veterans	2.0 (0.6 – 6.7) 1.2 (0.2 – 5.6) 1.6 (0.4 – 6.0)	1.6 (0.6 – 4.5) 0.7 (0.2 – 3.3) 1.7 (0.6 – 4.7)	0.9 (0.3 – 2.6) 2.3 (1.0 – 5.1) 0.9 (0.3 – 2.7)	Insufficient numbers	0.9 (0.4 – 2.1) 1.2 (0.5 – 2.7) 0.8 (0.3 – 2.0)	0.2 (0.0 – 1.4) 1.8 (0.8 – 4.1) 1.2 (0.5-3.0)	1.2 (0.4 – 3.6) 2.0 (0.8 – 5.4) 2.1 (0.8 - 5.4)	0.9 (0.6 – 1.3) 1.0 (0.7 – 1.5) 0.9 (0.6 – 1.2)	0.8 (0.3 – 2.2) 1.4 (0.6 – 3.2) 0.5 (0.2 – 1.7)
CDC (1988)	Vietnam experience	Vietnam veterans vs. non-veterans	1.3 (0.7 – 2.8)	1.6 (0.9 – 2.8)	1.1 (0.8 – 1.6)	1.5 (0.6 – 3.5)	1.2 (0.9 – 1.6)	1.3 (0.8 – 2.2)	1.4 (0.9 – 2.3)	1.2 (1.1 – 1.5)	
Case: control studies Level 3 evidence											
Aschengrau & Monson (1990)	Vietnam experience	Vietnam veterans vs. non-veterans	0.0*	0.0*	1.8*	0.0*	0.8*	1.6*	0.8*	1.1*	
		Veterans vs. no known service	0.0*	0.0*	3.7*	0.0*	0.9*	3.0*	1.9*	1.5*	
Donovan et al (1984)	Vietnam experience	Vietnam veterans vs. non-veterans			1.03					0.94	
Erickson (1984)	Agent Orange exposure	Vietnam veterans vs. all other fathers	0.91		0.69	0.87	0.98	0.92	0.93	0.98	
		Based on self reported exposure scores	0.42		0.55	1.08	1.09	1.16	0.21	1.06	

*all non-significant

Table 16: Health outcome for offspring for other Paternal Exposures: Central nervous system, neural tube and cleft palate defects

Study	Exposure	Groups	Nervous system OR (95% CI)	Spina bifida OR (95% CI)	Hydrocephalus OR (95% CI)	Anencephaly OR (95% CI)	Cleft lip or palate OR (95% CI)	Neural tube defects OR (95% CI)
Case control studies Level 3 evidence								
Can (1984)	Paternal exposure to South Vietnam	Wives of potentially exposed men vs. wives of unexposed men		0.97 (0.12-8.00)	1.45 (0.78-2.67)	1.92 (0.93-3.80)	2.31 (1.55-3.44) - lip	
Dimich-Ward et al (1996)	Paternal exposure to dioxin contaminated chlorphenols in the sawmill industry	Record linkage of sawmill cohort records and stillbirth records with general population Paternal exposure 3 months prior to conception		1.8 (0.8-4.1)		1.11 (no CI) - Anencephaly or spina bifida 2.4 (1.1-5.3) – (comparing 75th and 25th percentiles)		
Kristensen et al (1997)	Paternal exposure of Norwegian farming families to pesticides	Farmers vs. general population	0.94 (0.73-1.20) unadjusted	0.76 (0.51-1.13) – all farmers unadjusted 1.6 (0.9-2.7) - Tractor sprayers unadjusted 2.8 (1.1-7.1) - Greenhouse/orchard sprayers unadjusted		(0.68-1.79) - unadjusted	0.93 (0.6-1.43) - unadjusted	1.6 (0.9-2.7) - " in orchards and green houses" 2.8 (1.1-7.1) - unadjusted
Blatter et al (1997)	Paternal exposure to pesticides	Live born children with spina bifida vs. live born, children who experienced a trauma capitis or meningitis		1.7 (0.7-4.0) - pesticides use 1.6 (0.6-4.0) - herbicide use				
Garry et al(1996)	Case referent study	Linked data from Minnesota national registries 3472 children of pesticide appliers: 4935 births, linked to 210 723 live births	1.10 (0.50-2.40) n=6					
Brender and Suarez (1990)	Paternal occupational exposure to pesticides	Linked Texas live-birth-death defect records				1.28 - pesticides (no CI)		
Other studies Level 5 evidence								
Smith (1982)	Paternal exposure to 2,4,5-T	Pesticide sprayers vs. agricultural contractors		No significant difference				
Hanify (1981)	Population exposure to pesticide spray	Pre and post aerial spraying Northland, New Zealand		1.13 (0.62-2.05)		1.42 (0.69-2.90)		

**Figure 3: Summarised Odds Ratios for the outcome Spina Bifida**
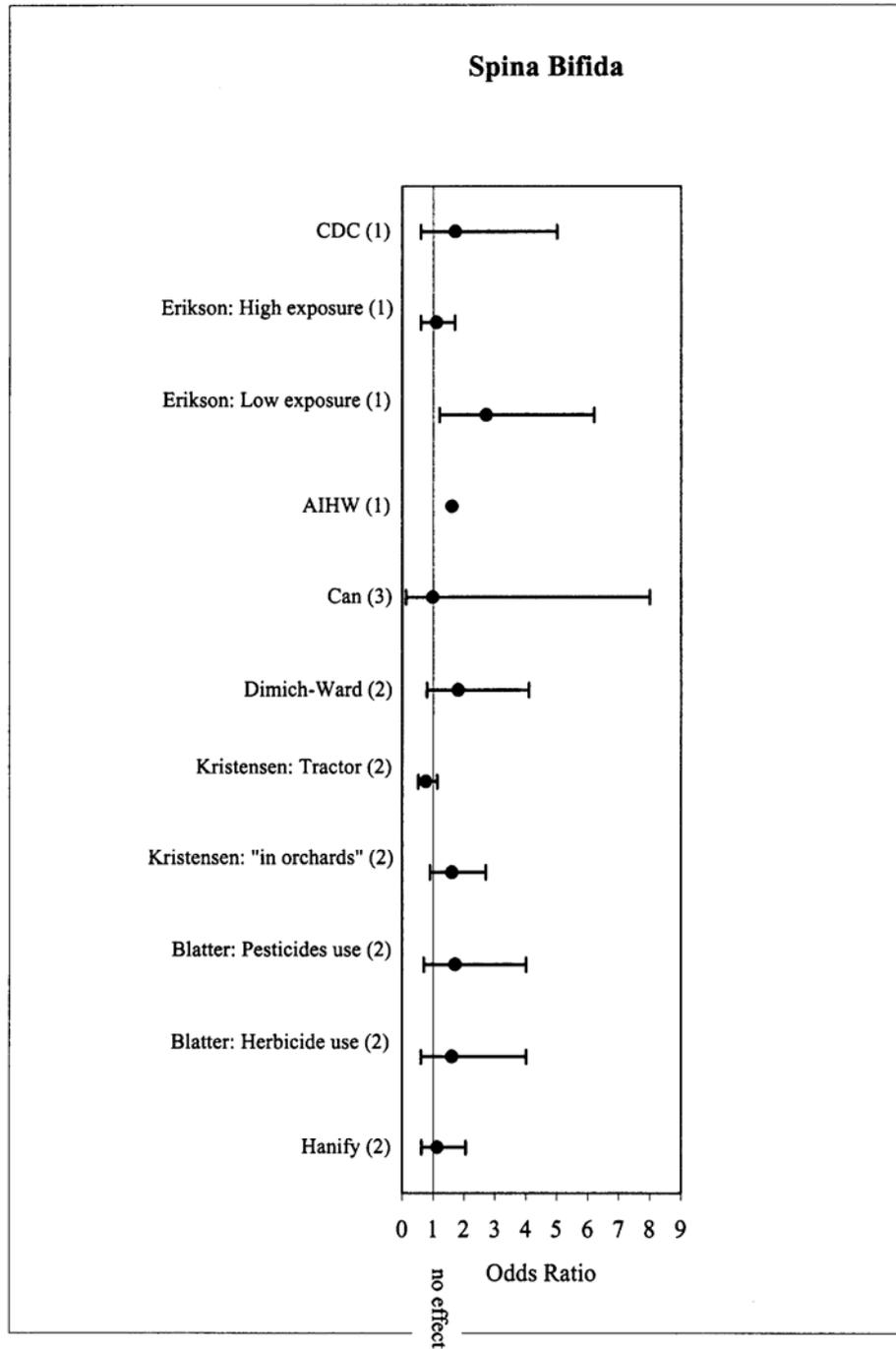
Figure 3: Summarised Odds Ratios for the outcome "spina bifida"

1. Vietnam veterans' studies
2. Occupational/Environmental exposure
3. Vietnam studies

Key:

●   Odds Ratio or Relative Risk

├──┤   95% Confidence Interval

Adverse reproductive outcomes

Studies of live births may miss adverse effects expressed during foetal development, possibly leading to spontaneous abortion. However, no significantly elevated risks of spontaneous abortion, stillbirth or intrauterine growth retardation were found in studies of Vietnam veterans, with the exception of the CDC study where elevated rates of spontaneous abortion were reported by veterans (Tables 17 and 18). The Committee to Review the Health Effects of Agent Orange (2001) has concluded that there is inadequate or insufficient evidence to determine whether an association existed between exposure to herbicides used in Vietnam and spontaneous abortion, stillbirth, neonatal death, low birth weight and infant death.

Effects of TCDD exposure on the male reproductive system

There have been several studies investigating the effects of TCDD exposure on the male reproductive system. A reduction in testosterone has been found to correlate with increasing serum TCDD levels (Sweeney et al., 1997/1998). There have been reports of an increase in the number of female newborns in the most exposed areas of Seveso, a population exposed to TCDD as a result of an industrial accident in 1976. The male to female ratio returned to normal at a later stage. It has been suggested that the reason for the observed excess of female births is lowered testosterone as well as high gonadotropin levels as this hormone profile is associated with female offspring (Egeland et al., 1994). Sex ratios may be useful as a potential marker of genetic damage, although there is debate about whether altered sex ratios are the result of differential effects of damage to the paternal X chromosome or to changes in paternal hormone levels at conception.

Mocarelli et al (2000) found an increasing probability of female births with increasing TCDD levels in paternal serum. Fathers exposed when they were younger than 19 years of age had significantly more girls than boys (OR 0.38, 95% CI 0.30-0.47). The median concentration of dioxin in Seveso fathers was similar to doses that induced epidiymal impairments in rats and is about 20 times the concentration of TCDD currently found in humans in industrialised countries.

There is debate about whether TCDD does affect the male to female birth ratio. The only veterans' study to examine the ratio of male to female births was the Ranch Hand study where Michalek et al (1998) found no reduction in male births. The proportion of male births in the comparison group was 49.6%, in the background exposure group 49.5%, in the low exposure group 51.3% and in the high exposure group 46.5%. The slight differences they did find were not related to exposure.

Table 17: Health outcome for offspring of Vietnam veterans: In utero and neo-natal outcomes

Study	Exposure	Groups	Spontaneous abortion OR (95% CI)	Still birth OR (95% CI)	Pre-term birth OR (95% CI)	Infant death OR (95% CI)	Interuterine growth retardation OR (95% CI)
Cohort studies Level 2 evidence							
Wolfe et al (1995)	Bkgd exposure to dioxin: Low: High:	Exposed veterans vs. unexposed veterans	1.1(0.8 – 1.5) 1.3 (1.0 – 1.7) 1.0 (0.7 – 1.3)	1.8 (0.7 – 4.5) 1.8 (0.7 – 4.7) 0.3 (0.0 – 2.3)			
Michalek et al (1998)	Bkgd exposure to dioxin Low: High:	Exposed veterans vs. unexposed veterans			1.4 (0.9 – 2.3) 0.5 (0.2 – 1.2) 1.3 (0.8 – 2.3)	3.2 (1.0 – 10.3) 1.5 (0.3 – 7.5) 4.5 (1.5 – 14.0)	0.9 (0.6 – 1.4) 0.9 (0.6 – 1.3) 0.9 (0.6 – 1.3)
CDC (1988c)	Vietnam experience	Self-report: Validated:	1.3 (1.2 – 1.4)	Not significant			1.1 (0.8 – 1.4)
Case control studies Level 3 evidence							
Aschengrau & Monson(1990)	Vietnam experience	Vietnam vs. non-Vietnam: Vietnam vs. no known service:		3.2 (0.7 – 14.5) 1.5 (0.6 – 3.9)		1.1 (0.2 – 4.5) 1.2 (0.4 – 4.2)	
Aschengrau & Monson (1989)	Vietnam experience	Vietnam vs. no known service: To 27 weeks To 13 weeks	0.88 (0.42-1.86) 1.24 (0.56-2.77)				
Other studies Level 5 evidence							
Stellman et al (1988)	Vietnam experience	Vietnam veterans vs. Non-Vietnam veterans High exposure	1.35 (no CI) 1.74 (no CI)				
Field and Kerr (1988)	Vietnam experience	Vietnam veterans vs. non-Vietnam veterans	Significant increase	Significant increase		Significant increase	

Table 18: Health outcome after paternal exposures to chemicals: In utero and neo-natal outcomes

Study	*Exposure*	*Groups*	*Spontaneous abortion* *OR (95% CI)*	*Still birth* *OR (95% CI)*	*Pre-term birth* *OR (95% CI)*	*Infant death* *OR (95% CI)*	*Interuterine growth retardation* *OR (95% CI)*
Cohort studies with a comparison group Level 4 evidence							
Suskind and Hertzberg (1984)	Paternal workplace exposure to manufacture of 2,4,5-T	Exposed workers vs. non-exposed workers.	0.87 - unadjusted	1.45- unadjusted		1.45 - unadjusted	
Townsend et al (1982)	Paternal workplace exposure to polychlorinated dioxins	Wives of exposed workers vs. wives of unexposed					
		Any dioxin (adjusted)	1.03 (0.77-1.39)	1.06 (0.54-2.09)		0.63 (0.27-1.39)	
		TCDD (adjusted)	0.96 (0.65-1.42)	0.97 (0.38-2.36)		0.82 (0.30-2.09)	
Case control studies with a comparison group Level 3 evidence							
Sterling and Arundel (1986) Can (1984)	Paternal exposure to South Vietnam	Wives of potentially exposed men vs. wives of unexposed men	(1.16-1.28) - unadjusted	0.87 (0.78-0.94) - unadjusted			
Dimich-Ward et al(1996)	Paternal exposure to dioxin contaminated chlorphenols in the sawmill industry	Record linkage of sawmill cohort records and stillbirth records with general population		1.01 (0.98-1.08)	0.99 (0.98-1.00)	1.00 (0.96-1.02)	1.00 (0.92-1.01)
Petrelli et al (2000)	Paternal exposure to a range of pesticides	Pesticide applicators vs. food retailers	3.8 (1.2-12.0) - adjusted maternal age				
Restrepo et al (1990)	Paternal occupational exposure to 127 types of pesticides	Before vs. after working in the floriculture industry	1.79 (1.16-2.77)	0.87 (0.42-1.83)	2.75 (2.01-3.76)		
Smith et al (1982)	Paternal exposure to 2,4,5-T	Pesticide sprayers vs. agricultural contractors	0.89 (0.61-1.30)				

Childhood Cancer

Leukaemia is the most common cancer in children, accounting for about one third of childhood cases. There are two forms of childhood leukaemia, acute lymphocytic leukaemia (ALL) and acute myelogenous leukaemia (AML). AML is by far the most common form of the disease. The second most common group of cancers are those of the central nervous system – brain and spinal cord.

The risk of childhood leukaemia has been examined in studies of the children of veterans by Wen et al (2000), CDC (1988c), Erickson (1984b), and the AIHW (1999) (Table 19). Erickson found no increased risk when all cancers were considered and the CDC study found no increased risk of leukaemia. In a large case control study of the children of veterans of Cambodia and Vietnam, Wen et al found a small elevated risk of AML for children of veterans, especially those diagnosed under two years of age. Childhood cancers diagnosed at very young ages are more likely to be etiologically related to preconceptional or in utero exposures (Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange, 2001). There was no association with self-reported exposure to Agent Orange.

The AIHW study (1998) asked veterans if any of their children had ever been diagnosed by a doctor as having leukaemia, Wilms' tumour, tumour of the nervous system and other cancers. Self-reported rates were higher than rates expected based on national comparison data. However, in the validation study (Commonwealth Department of Veterans' Affairs, 1998a) the number of estimated conditions was substantially lower and did not exceed expected rates.

Childhood cancers have also been studied after paternal exposure to occupational and environmental chemicals (Table 20). Elevated risks were found by Heacock et al (2000) for brain cancer. Cancer of the kidney was examined by Pearce and Parker (2000) and Fear et al (1998) for much the same group of children, with elevated risks found by Fear et al but not by Pearce and Parker. The difference was suggested to result from misclassification of paternal occupation by Fear et al.

Rates of all cancers combined were found to be increased in men with occupations involving exposure to pesticides in gardens (Meinert et al., 2000), and in farmwork (Sharpe et al., 1995). Use of pesticides on farms was associated with risks of leukaemia by Meinert et al and any paternal occupations with exposure to pesticides by Buckley et al (1989).

The United States Committee to Review the Health Effects in Vietnam veterans of exposure to herbicides (2001) has accepted that there is limited suggestive evidence of an association between herbicides and AML in the children of veterans, based primarily on the results of studies by Wen et al (2000) and the AIHW study (1998).

Table 19: Health outcome for offspring of Vietnam veterans: Cancers

Study	Number	Groups	Objective/ Subjective	Exposure OR (95% CI)	All cancers OR (95% CI)	Leukaemia OR (95% CI)
Cohort studies Level 2 evidence						
Wen et al (2000)		Data Source: Children's Cancer Group data		Paternal military service: Service in SE Asia:		1.2 (0.9-1.6) AML & ALL all cases 1.7 (1.0-2.9) AML only 4.6 (1.3-16.1) AML only children under 2
CDC (1988)	7924 Vietnam and 7364 non-Vietnam veterans.	Vietnam veterans and non-Vietnam veterans		Vietnam experience	1.5 (0.8-2.8)	1.6 (0.6-4.1)
Erickson et al (1984)	13,000 babies with birth defects	Vietnam veterans vs. all other fathers		Agent Orange Exposure	1.8 (1.0-3.3)	
Cohort studies comparison with national data set Level 4 evidence						
AIHW (2000) Validation study					No increased risk	AML no increased risk

Table 20: Health outcome for offspring after paternal exposures to chemicals: Cancers

| *Study*	*Number*	*Groups*	*Exposure*	*All cancer* *OR (95% CI)*	*Leukaemia* *OR (95% CI)*	*Kidney* *OR (95% CI)*	*Lymphoma* *OR (95% CI)*	*Brain cancer* *OR (95% CI)*
Cohort study Level 2 evidence								
Heacock (2000)			Sawmill workers		SIR 1.0 (0.5-1.8)* 0.8 (0.2-3.6) High exposure			1.3 (0.6-2.5)*SIR 1.5 (0.4-6.9) High exposure
Pearce and Parker (2000)	298,188 live births 1950-1993 in Cumbria, UK 8851 deaths		Paternal employment in occupations with exposure to herbicides and/or pesticides			0.88 (0.20-3.84)		
Fear et al (1998)	449 deaths from cancer	Childhood death records in England and Wales for 167 703 childhood deaths.	Men with potential exposure to pesticides.	PMR 0.89 (0.81-0.80)		PMR 1.59 (1.18-2.15)		
Case control study Level 3 evidence								
Meinert et al (2000)	Cases: 1184 children with leukaemia, 234 with non-Hodgkins lymphoma, 940 with a solid tumour Controls: 2588 matched controls	Children with cancer vs. general population	Paternal exposure to a range of pesticides in Germany pre-pregnancy		1.5 (1.0-2.2) - Use of pesticides on farms 1.0 (0.8-1.2) - Use in gardens		1.5 (0.7-3.1) - Residential use of pesticides	
Meinert et al (1996)	Cases: 219 newly diagnosed cases of childhood leukaemia. 82% response Controls: sex and age matched from the same community.	Childhood cancer cases vs. general population	Exposure to a range of pesticides in Germany	2.52 (1.0-1.6) - Pesticide use in gardens				
Sharpe et al (1995)	Cases: 109 children with Wilm's tumour (nephroblastoma) Controls: 218 children hospitalised from other causes.			3.24 (1.2-9.0) - Farmwork and use of pesticides by fathers				
Buckley et al 1989)	Cases: Registrations with CCSG, 154 fathers Controls: matched by DOB and race, 138 fathers		Paternal pesticide exposure		2.3 - AML any paternal exposure 2.7 (1.0-7.0) - AML paternal exposure>1000 days			

*SIR – standardised incidence ratio

INTERPRETING THE EVIDENCE

Reproductive outcomes in men exposed to toxins in a variety of settings have been reviewed in this report. The most direct evidence comes from studies of the reproductive outcomes of Vietnam veterans. Epidemiological studies quantify associations between exposure and an outcome(s). A key concern in the studies of Vietnam veterans is misclassification of veterans with regard to exposure.

Measuring exposure

Measuring levels of exposure of Vietnam veterans to herbicides and dioxin contaminants has been problematic. Exposure has been assessed in the published literature in the following ways (Goldberg, 1992).

Basic dichotomous exposure classification → Served in Vietnam → Exposed to combat / Not exposed to combat

Basic dichotomous exposure classification → Did not serve in Vietnam

Measuring exposure to herbicides → Plasma dioxin / Clinical outcomes
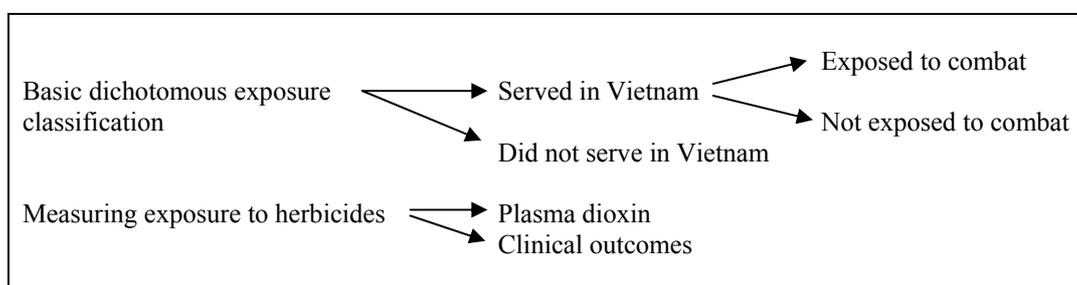
Studies of the Vietnam experience as a whole are not accurate studies of exposure to herbicides. Accurate classification of exposure is required to ascertain the effects of herbicides (Resnik et al., 1984). If the exposure considered is the Vietnam experience then there are problems in extrapolating from these data to infer the effects of exposure to herbicides. For example if only a subgroup of veterans were exposed then studying the whole group of veterans would weaken the ability of the study to detect a difference in that subgroup.

Exposure to Agent Orange could be defined by the length of time spent in Vietnam, by self-report or military record information. Self-reported exposure can be unreliable, as found when serum dioxin levels were compared with self-reported exposure (Booth, 1987). A CDC study (Patterson et al., 1987) found no association between a veteran's self assessed exposure to herbicides and elevated levels of dioxin in serum. This lack of association confirmed concerns about the reliability of exposure classification in earlier studies relying on self-reported data (Needham et al., 1991). Defining exposure from military records can be incomplete, requires assumptions to be made about spray drift and does not include ad hoc spraying missions known to have occurred but not to have been well recorded.

Clinical examination can provide evidence of exposure to dioxins. Chloracne has been linked with exposure but only occurs in a subset of exposed individuals. Dioxin assays provide accurate information about the current levels of serum dioxin but these assays are costly and levels need to be extrapolated to estimate levels of exposure for veterans at the time they served in Vietnam. Extrapolation may be inaccurate because the decay of dioxin depends on the proportion of body fat and cannot differentiate

between exposure in Vietnam and any exposure which may have occurred in the intervening years. Therefore there is more potential for serum dioxin levels to overestimate exposure than to underestimate exposure.

Serum dioxin concentrations in veterans

Serum dioxin concentrations of US Vietnam veterans have been compared with serum dioxin levels of populations exposed to dioxin after industrial accidents (Figure 4). Veterans' exposure levels were extrapolated based on a half life of dioxin of 7 years to obtain estimated levels at the time they were in Vietnam (Wolfe et al., 1990). Results of serum testing indicated that comparison subjects had background levels of dioxin, Vietnam Ranch Hand veterans (the most exposed veterans) had higher dioxin levels than other veterans, non-flying enlisted Ranch Hand personnel had the highest levels and officers the lowest. However, dioxin levels in veterans were lower than those seen in workers exposed industrially and in exposed residents of Seveso (Needham et al., 1991).
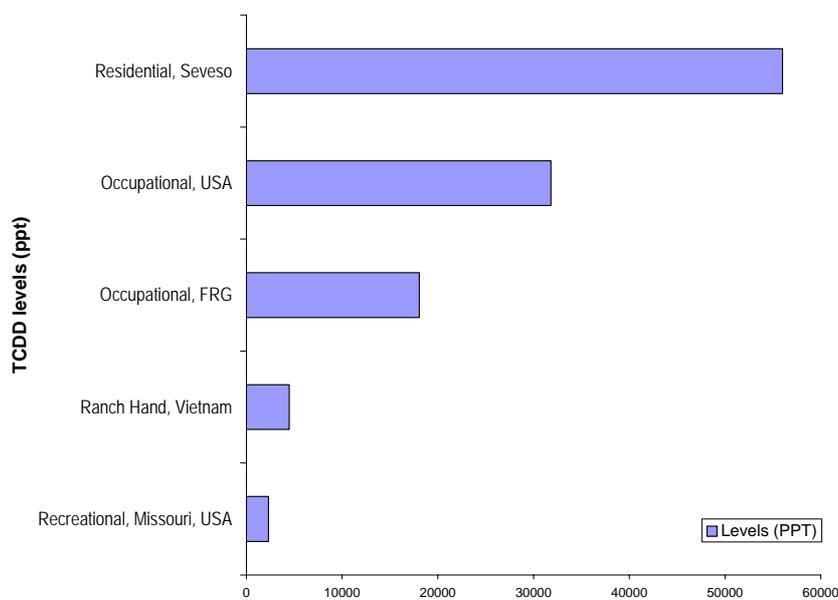
Figure 4: Highest extrapolated TCDD levels in humans

Source: Needham, 1991

Other issues in interpreting the results of studies

Recall bias is inherent in any study design where the outcome measures for the study are based on self-reported data. Recall bias has been demonstrated in self-reported data about medical outcomes. In the CDC study (1998c) self-reported data differed from data validated against medical records. Recall bias resulted in reports of an increased risk. A similar difference between self-reported and validated rates was found in the AIHW studies. For example, self-reported rates of cancer in the children

of veterans exceeded expected values and many of the reported cancers were unable to be validated (Australian Institute of Health and Welfare, 1999).

Studies of other sources of paternal exposure

Studies of paternal exposure in occupational and agricultural settings have also been included. Levels of exposure in occupational settings exceeded levels to which veterans were exposed (Needham et al., 1991). Interpretation of these studies is complicated by the possibility of maternal exposure either directly to pesticides in the environment or by 'para-occupational' exposure, to toxic substances such as on contaminated work clothing or in the home environment (Garcia et al., 1998).

IS THERE AN ASSOCIATION BETWEEN PATERNAL EXPOSURE FOR NEW ZEALAND VETERANS TO TOXINS OR CHEMICALS AND ADVERSE HEALTH OUTCOMES FOR THEIR CHILDREN?

Strength of the association

The strongest evidence of no effect comes from the large cohort and case control studies of the reproductive outcomes for veterans. These studies have been consistent in their reports of no increased risk for all birth defects when considered together. The fact that the studies have been undertaken on different populations and using different methods but producing consistent results showing no effect, is an indication of the likelihood that no effect exists. The Odds Ratios produced from these studies are very similar and the confidence intervals narrow.

A weak association was identified between exposure to chemicals and the birth defect spina bifida based on the data from Vietnam veterans. Slightly stronger associations were found based on paternal occupational exposure to a range of pesticides. Interpreting data from studies of paternal exposure in occupational and agricultural settings is complicated by the possibility of maternal exposure, either directly to pesticides in the environment or by 'para-occupational' exposure to toxic substances such as on contaminated work clothing or in the home environment (Garcia et al., 1998). In addition, exposure in these occupational and agricultural settings was to a mixture of pesticides.

A weak association has been found between both paternal exposure to the Vietnam experience and paternal exposures to pesticides, and an increased risk of some childhood cancers. Wen et al (2000) found confusing results when comparing childhood leukaemia rates with the length of time veteran fathers had served in South East Asia.

In interpreting any data from studies where the association is weak, accounting for bias and confounding is particularly important. As discussed previously, socio-economic status is likely to be a confounding variable in studies of birth defects. There are suggestive data from both New Zealand and overseas studies that Vietnam veterans may be socio-economically deprived compared to non-veterans. Unfortunately the numbers are too small to allow the analysis to be adjusted for these variables.

Participation in the Vietnam War was not a random event. New Zealand servicemen who went to Vietnam were volunteers. Mäori are thought to be over represented in the New Zealand servicemen who served in Vietnam compared to the proportion of Mäori in the New Zealand population. There are reported differences between Mäori and non-Mäori for some reproductive outcomes. Higher rates of the birth deformities cleft palate and talipes have been reported for Mäori (Hanify et al., 1980). High rates of club foot in Mäori have been linked to a single dominant gene and rates are estimated as 6 to 7 per 1000 (Chapman et al., 2000). There are also differences in socio-economic deprivation between Mäori and non-Mäori in New Zealand (Statistics New Zealand, 2000).

Consistency

There is a body of evidence to suggest that direct exposure and maternal exposure to the dioxin contaminants of pesticides is associated with adverse health outcomes. TCDD is accepted by the International Agency for Research on Cancer (IARC) as a potent carcinogen (IARC, 1997).

An association between paternal exposure to toxins and adverse reproductive effects has been observed in some animal studies, some studies of Vietnam veterans and in some studies of paternal exposure to toxins after industrial accidents and occupational exposure to pesticides. However, the results of different studies are not consistent.

Plausibility

Carcinogenic effects of dioxins

TCDD is the most widely studied of all the dioxin-like compounds. Dioxin-like compounds are absorbed through the gastrointestinal tract, skin and lungs (Smith & Lopipero, 2001). Animal studies indicated that after exposure TCDD is distributed via the blood, principally to the liver and adipose tissue but also to the skin and muscles.

The health effects of TCDD have been reviewed in a recent report by the New Zealand Ministry for the Environment (Smith & Lopipero, 2001). Direct exposure to TCDD has been shown to affect a wide range of organ systems in many animal species. A review of published studies with animals by Friedman (1984) concluded that there is evidence that the constituents of Agent Orange are capable of producing gene mutations and chromosomal aberrations, at least in some experimental circumstances. Maternal exposure to TCDD and 2,4,5-T is teratogenic in mice and perhaps in other mammals. Smith et al (2001) conclude in their review that TCDD has been shown to cause both benign and malignant tumours at multiple sites in several animal species.

Increases in lung cancers and all-cancers combined have now been identified in highly exposed cohorts of workers in industrial settings. Based on evidence to date the IARC has concluded that TCDD is carcinogenic to humans (IARC, 1997). The mechanism of TCDD toxicity seems to be via binding to the aryl hydrocarbon receptor (Ah receptor) (Smith & Lopipero, 2001).

Paternal exposure and birth defects

Birth defects can occur as a result of either mutagenesis (genetic damage before conception) or more commonly teratogenesis (abnormalities of embryonic or foetal development initiated after conception). The most plausible effects of male mutation of germ cells are reduced fertility, spontaneous abortion, some birth defects and child cancer (Garcia et al., 1998).

Teratogenesis requires an in utero exposure. The most vulnerable period for the human embryo is the first three months after conception. There are three mechanisms

by which exposure of the male to toxic substances may lead to poor reproductive performance or congenital malformations in the offspring.

- A direct effect on pituitary hypothalmic function in the male or on male sex hormones leading to a reduction in libido and impairment of related physiological functions;
- A direct effect on the sperm itself leading to chromosome damage or alterations in sperm motility;
- The presence of toxins in seminal fluid (Friedman, 1984; Sterling & Arundel, 1986). Intercourse during pregnancy must then lead to maternal systemic absorption of the toxin and eventually an effect on the fetus. There is some evidence from animal models that a variety of chemicals can be absorbed through the vaginal mucosa (Garcia et al., 1998).

However, the potential of TCDD to produce teratogenic birth defects in children born several years after paternal exposure to chemicals is less clear (Pearn, 1983).

Evidence from animal studies

Animal studies pre-1983 have been reviewed by Friedman (1984). More recently Smith et al (2001) reported on the key animal studies. There is evidence from animal studies of maternal exposure that 2,4,5-T can produce teratogenic effects. In 1971 Courtney and Moore found exposure to 2,4,5-T in utero resulted in cleft palate and cystic kidney disease.

In laboratory animals paternal exposure of adult animals to dioxins has been found to:
- Produce testicular abnormalities and reduced plasma levels of testosterone (Moore et al., 1985);
- Decrease sperm count but not affect fertility (Lindstrom et al., 1995);
- Produce pups of low birthweight but with no abnormalities (Friedman, 1984).

A few animal studies have considered the effects of paternal exposure on subsequent offspring. Exposure of male animals in utero has been found to impair reproductive capabilities in the male rat offspring (Gray & Ostby, 1995). Courtney and Moore (1971) explored the effects of paternal exposure on subsequent offspring and found that exposure of male rats to 2,4,5-T in utero did not result in birth defects in their subsequent offspring. A later three generation study by Hansen (cited in Smith et al, 1976) also found no effect on offspring after administration of 2,4-D in the diet. Litters were of normal size and sex ratios. Khera et al (cited in Smith et al, 1976) exposed male rats to a dose of 4ug/kg of TCDD, a dose found to be fatal to pregnant females if administered to the pregnant mother. Although the dose was toxic to the male rat, no defects were found in their offspring. Lamb et al (cited in Smith et al, 1976) fed TCDD to male monkeys for long periods and found no increase in teratospermia, no reduction in reproductive capacity and no defects in offspring.

Evidence from human males

The effects of environmental chemicals on the male reproductive system are difficult to evaluate from animal data due to interspecies variation, high doses in experimental

protocols and the route of administration, and the low sensitivity and specificity of reproductive markers used in some studies (Traina et al., 1994).

Evidence of alterations in male reproductive hormone levels has been observed (Egeland et al., 1994). Serum dioxin was significantly associated with decreased testicular size in data from studies of Operation Ranch Hand veterans (Wolfe et al., 1992). Chromosomal changes have been found in a 1978 New Zealand study, Crossen et al (1978), where pesticide sprayers had a higher rate of sister chromatid exchange than a control group.

In summary, animal studies have provided information about the potential for male mediated teratogenesis. However, the evidence for biological mechanisms remains unclear. In particular, the mechanism by which male exposure can affect the development of offspring conceived some years later is unclear.

Exposure levels of New Zealand servicemen

Much of the data on direct exposure comes from studies of health outcomes after accidental exposure to dioxin resulting from an industrial accident. Residents of Seveso, Italy were exposed to TCDD after a cloud of TCDD was released over the township in 1976. The health of this population has since been studied extensively. The most obvious health effect of direct exposure was the development of chloracne by the most exposed. There was no substantial change in observed rates of spontaneous abortions or birth defects in this very exposed population. Rates of development of cancers are being monitored.

The key issue in interpreting the implications of the evidence about associations between exposure to chemicals in Vietnam, birth defects and adverse reproductive outcomes, is the extent to which New Zealand servicemen were exposed.

New Zealand servicemen in Vietnam served with Australian forces. An individual could have been exposed to herbicide either directly by being in an area when aerial spraying occurred, or indirectly by ingesting food or water which had been contaminated by spray. Exposure of Australian troops was considered in detail by the Evatt Commission (Hall, 1986) who concluded that Australian Vietnam veterans had not been exposed directly to Agent Orange or to any other herbicides or insecticide and that the potential for indirect exposure was minimal. In the worst possible case it was estimated that the level of exposure of an Australian veteran would have been at 4% of the safe or no-effects level for 2,4,5-T, 4% of the no-effects level for 2,4-D and 7% of that for TCDD. Low levels of exposure were supported by the lack of any reports of acute toxic effects such as chloracne (O'Keefe & Smith, 1994). Chromosomal analysis of a small sample of Australian veterans showed no significant difference in the incidence of chromosomal damage between 15 veterans and eight controls (O'Keefe & Smith, 1994). Levels of exposure of US veterans from Operation Ranch Hand were likely to be in the order of 1000 times the exposure of Australian and New Zealand veterans.

The New Zealand population is exposed to background levels of dioxin. 2,4,5-T has also been used extensively in New Zealand as an agricultural herbicide. Dioxin residues can be detected in areas that have been used for sawmilling. Average levels

of dioxin in the New Zealand general population aged 15 and older are 19.7 ng TEQ kg^{-1} on a lipid adjusted basis (Smith & Lopipero, 2001). There is no evidence available to the authors of this report to suggest that the serum dioxin levels of New Zealand Vietnam veterans would be different to those of the New Zealand general population.

Coherence

The weak associations between spina bifida and exposure to Agent Orange are difficult to interpret, as spina bifida is etiologically linked with anencephaly and hydrocephalus. Increased rates of spina bifida should be linked with increased rates of anencephaly and hydrocephalus. In the study by Erickson et al (1984b) a weak association with spina bifida was found between veterans with low exposure to dioxin, but not with veterans with higher exposure. No increased risk was found for hydrocephalus or anencephaly (Erickson et al., 1984b). In the CDC study (1988c), slightly increased risks were found for nervous system defects and hydrocephalus, but not for spina bifida.

Conclusion

The birth of children with a range of defects is unfortunately not uncommon and 2-3% of Vietnam veterans would be expected to have a child with a birth defect. It is understandable that veterans would question whether their exposure to Agent Orange contributed to their child's birth defect.

As a result of veterans' concerns, a number of epidemiological studies have been undertaken comparing the health of veterans' children with a comparison group. There have been three high quality cohort studies and a number of good case control studies undertaken both in the United States and Australia. These studies have considered the potential effects of exposure to Agent Orange on all birth defects combined, on specific birth defects and on adverse reproductive outcomes such as stillbirths and spontaneous abortion.

The risk estimates calculated for the category 'all birth defects' are remarkably consistent and overall show no increased risk for Vietnam veterans for fathering children when all birth defects are considered.

High quality epidemiological studies have shown no consistent positive association between exposure to Agent Orange or a range of chemicals or pesticides and any specific birth defect. However, there has been a trend towards a slight but not significant association between paternal exposure to dioxins, pesticides and herbicides and an increased risk of the birth defect spina bifida. It is this association which has resulted in the United States Committee to Review the Health Effects of Agent Orange concluding that there is limited suggestive evidence of an association between spina bifida and Agent Orange exposure.

Similarly, there has been a slight increased risk of childhood acute myelogenous leukaemia (AML) after paternal exposure to service in South East Asia and after

exposure to pesticides. AML has also been accepted by the committee as a condition for which there is limited suggestive evidence of an association between paternal exposure and adverse outcomes. There is no evidence available to permit interpretation of international evidence for an increased risk of AML in a New Zealand context.

The extent to which decisions about associations between Agent Orange and adverse health outcomes for veterans' children can be made is affected by the limitations of the cited epidemiological studies. Namely:

- Studies do not have sufficient power to detect an increased risk of rare outcomes;
- It is difficult to classify paternal exposure, and misclassification of unexposed men as exposed reduces the ability to detect a difference;
- Recall bias is inherent in self-reported data from veterans about their own and their children's health status;
- Background levels of TCDD in Western Society are relatively high; and
- A statistically significant result may not be biologically meaningful. A small proportion of results will be statistically significant due to chance.

Interpretation of these data in a New Zealand context must take into account the very limited potential New Zealand troops had for exposure to Agent Orange. The information available to the authors was that ANZAC Forces generally served in Phuoc Tuy province where there was no aerial spraying. In this context and given the small increased risks found in studies of very exposed populations, the conclusion reached by this appraisal of the literature is that there is no evidence that exposure to chemicals in Vietnam has affected the health of the children of New Zealand Vietnam veterans.

Overseas studies of veterans have conclusively demonstrated no overall increased risk when the category 'all birth defects' is considered. There would be no value in repeating such studies in New Zealand. The evidence on specific birth defects is slightly less conclusive. Unfortunately there are insufficient numbers of Vietnam veterans in New Zealand to enable an epidemiological study of specific birth defects to be carried out.

RECOMMENDATIONS

1. If individual servicemen are concerned about the extent to which they were exposed, measuring the levels of dioxin in their serum would confirm their exposure. Low levels would provide veterans with some reassurance about the health risks to their children.

2. Children of veterans have been born with birth defects, as are a proportion of children of non-veterans. The support of children and adults with disability is a responsibility which is shared by a society. Suggested models of disability support are appended in Section Four of this report.

3. Consideration could also be given to involvement of the Office of Veterans' Affairs in assessing the health needs of veterans' children with disabilities and

reviewing the extent to which the New Zealand public health care system is able to meet these needs.

VETERANS' EXPOSURE: THE VIETNAM EXPERIENCE

HEALTH OUTCOMES FOR VETERANS

Vietnam veterans were exposed to a range of potential hazards as a result of their participation in the Vietnam War. In this section of the report the range of psychosocial outcomes identified from the literature as a result of exposure to the Vietnam experience will be reported and the potential health outcomes for the children of veterans reviewed.

Outcomes related to involvement in the Vietnam War

Potential health outcomes for veterans as a result of their experience in Vietnam and in particular as a result of exposure to combat were identified from the literature. Health outcomes for veterans are summarised in Table 21. It was not within the scope of this study to critically appraise the literature on health outcomes for veterans.

Table 21: Health outcomes for veterans associated with service in the Vietnam War (excluding those specifically relating to exposure to herbicides and pesticides)

Outcome:	Studies showing a significant association
Psychosocial	
Alcohol abuse/dependence	Higher rates (VES, Centers for Disease Control, 1988a), (Jordan et al., 1991; Kulka et al., 1988).
Anxiety	Higher rates (VES, Centers for Disease Control, 1988a).
Depression	Higher rates (VES, Centers for Disease Control, 1988a; Jordan et al, 1991).
PTSD (combat-related)	Higher rates (VHS**, Centers for Disease Control, 1988a; Long et al., 1996; O'Toole et al., 1996; Kulka et al., 1988).
Insomnia / Sleep disturbances	Higher rates (Neylan, 1998).
Generalised anxiety disorder (GAD)	Higher rates (Jordan et al., 1991; Centers for Disease Control, 1988a; Kulka et al., 1988).
Anti-social personality disorder (ASPD)	Higher rates (Jordan et al., 1991).
Lower socio-economic attainment	More likely to be unemployed (Davidson & Mellor, 2001). Veterans with PTSD more likely to be in lower socio-economic groups (Long et al., 1992).
Physical	
Hearing loss, Melanoma of the skin*, Prostate cancer*, Multiple sclerosis**, Ischaemic heart disease**, High blood pressure**, Asthma**, Diabetes**, Disability from injury**, skin disease**	(VES, Centers for Disease Control, 1988b)

   * Based on validated data
   ** Based on self-reported data

Psycho-social outcomes

A number of studies have produced estimates of the prevalence of psychological illness in veterans compared with the general community (Table 22).

Table 22: Current prevalence rates of mental illness in Vietnam veterans

PTSD Prevalence*	Mental Illness in Vietnam Veterans	Community Rates of Mental Illness
New Zealand		
Long et al., (1996) 10% of veterans MacDonald et al., (1997) 27% Māori veterans, 15% non-Māori Vincent et al., (1991) 12% of veterans	Veterans with PTSD (Long et al., (1996) Anxiety 15%; Depression 6% Both anxiety and depression 73% More than 1 additional disorder 94% Veterans without PTSD Long et al., (1996) Anxiety 27%, Depression 1% Both anxiety and depression 12%	Christchurch Community Study (Oakley-Browne et al., 1989) Anxiety 7.7% Depression 3.4% Alcohol abuse/ dependence 14.1% Drug abuse/ dependence 2.3%
Australia		
O'Toole et al., (1996) Lifetime prevalence 18.7%	All Vietnam veterans O'Toole et al., (1996) Any DIS diagnosis 59.6% Depression 0.7%, Anxiety 3.2% Alcohol abuse/ dependence 17.7% Drug abuse/ dependence 0.9% ASPD 0.9%, OCD 1.3%	Australian Bureau of Statistics (1998) Depression 54.9% Anxiety disorder 20.6% Alcohol related disorders 11.7% Any mental health disorder 29.4%
Commonwealth Department of Veterans' Affairs, (1998a) PTSD 31% Morbidity of Vietnam Veterans Survey		Commonwealth Department of Veterans' Affairs, (1998a) PTSD in men 2.3% PTSD in women 4.2%
United States		
Kulka et al., (1988) NVVRS PTSD Current prevalence in male Vietnam theatre veterans 15.2% Vietnam era Veterans (did not serve in Vietnam) 2.5%	All veterans Jordan et al., (1991) Depressive episode 2.8% GAD 4.5% Alcohol abuse/ dependence 11.2% Drug abuse and dependence 1.8% ASPD 2.0%, OCD 1.5%, Any NSVG/DIS disorder 17.1%	Kulka et al., (1988) PTSD 1.2% Jordan et al., (1991) Depressive episode 0.4% OCD 0.0%, GAD 2.9% Alcohol abuse/ dependence 7.0% Drug abuse and dependence 0.8% ASPD 0.0% Any NSVG/DIS disorder 11.6%
Centers for Disease Control, (1988a) 16.5% for Vietnam veterans 3% of other Vietnam era veterans	All veterans Centers for Disease Control, (1988a) Major depression 4.5% Generalised anxiety 4.9% Alcohol abuse/ dependence 13.7% Norquist et al., (1990) Alcohol abuse Lifetime 30.6%, Current 11.6% Lifetime drug abuse and dependence 11.5%, Lifetime ASPD 8.0%	Robins et al., (1988) Anxiety 2.0% Depression 7.7% OCD 2.0% Alcohol abuse/ dependence 14.1% Drug abuse/ dependence 5.1%

PTSD Prevalence*	Mental Illness in Vietnam Veterans	Community Rates of Mental Illness
Hankin et al., (1999) PTSD 20%	All veterans Hankin et al., (1999) Depression 31% Alcohol related disorders 12% Any mental health disorder 40%	

* Prevalence rates are not directly comparable as studies used slightly different cut off points on assessment scales and different criteria for assessing PTSD
NSVG National Survey of the Vietnam Generation
DIS-Diagnostic Interview Schedule
Long, et al, 1996 : Postal survey returned by 756 New Zealand Vietnam War veterans (55% response). PTSD defined by responses to Mississippi scale
O'Toole et al, 1996 (O'Toole et al., 1996) : Interviews with a random sample of 641 Australian Army Vietnam veterans. PTSD defined by DSM-III criteria
Morbidity of Vietnam Veterans Survey: A sample of more than 40,000 male and female Vietnam veterans compared with rates in adult Australians using ICD-10 criteria.
National Vietnam Veterans Readjustment Study (NVVRS): PTSD assessed by the Diagnostic Interview Schedule (DIS) based on DSM-III. Case control study, 1990.
CDC Vietnam experience study(Centers for Disease Control, 1988a): 2490 male Vietnam veterans and 1972 non-Vietnam veterans. PTSD defined by DSM-III criteria. 1988.
Hankin (Hankin et al., 1999) Mental health disorders and mental health treatment among US Department of Veterans Affairs Outpatients 1999.

Increased rates of post-traumatic stress disorder (PTSD) have been identified in all studies comparing veterans and civilian populations. In New Zealand Long et al (1996) investigated the prevalence of depression and anxiety in a community sample of 756 New Zealand Vietnam War veterans. Results revealed that 10% of the veterans could be classified as having PTSD. In New Zealand PTSD cases also differed significantly from non-cases in terms of their age, marital status, income, educational qualifications, and employment status (Vincent, 1994). Mäori veterans reported higher levels of PTSD than their non-Mäori counterparts. However, it is likely that higher levels of psychological symptoms reported by Mäori veterans can be accounted for by their experience of higher levels of combat stressors (MacDonald et al., 1997). That is, the different rates of PTSD are likely to be due to different experiences in Vietnam rather than different vulnerability to PTSD.

Elevated rates of PTSD in Vietnam veterans have also been reported in studies from Australia of 18.7% (O'Toole et al., 1996) and 31% (Commonwealth Department of Veterans' Affairs, 1998a), and the United States of 16.5% (Centers for Disease Control, 1988a) and 15.2% (Kulka et al., 1988). Anecdotal comment suggests that higher US rates of PTSD may be due to higher vulnerability of conscripts to PTSD than regular soldiers. New Zealand troops were deployed as units on a six or twelve month rotational basis. US troops were deployed individually on a twelve or thirteen month rotational basis (Vincent, 1994).

The DSM-IV (American Psychiatric Association, 1994) description of PTSD is "the development of characteristic symptoms following exposure to an extreme traumatic stressor involving direct personal experience of an event that involves actual or threatened death or serious injury, or other threat to one's physical integrity or witnessing an event that involves death, injury, or a threat to the physical integrity of another person or learning about unexpected or violent death, serious harm or threat of death or injury experienced by a family member or other close associates."

PTSD has three major components (American Psychiatric Association, 1994):

- Recurrent and intrusive recollections or dreams of the stressful event;
- Emotional numbing or withdrawal from the external world;
- Associated symptoms such as flatness of effect, sleep disturbance, memory impairment and hyperalertness.

The prevalence of PTSD in veterans has been associated with exposure to combat (Chamberlain et al., 1994; Jordan et al., 1991). Bullman et al (1991) found that US veterans were more likely to have PTSD if they were wounded or had faced combat in Vietnam. A New Zealand study found significant differences reported between veterans with PTSD and other veterans in terms of combat exposure, combat duties, length of service in Vietnam, length of service after Vietnam, total military service, and rank (Vincent, 1994).

The most common symptoms experienced by veterans suffering from PTSD are flashbacks, nightmares, startle responses, irritability, depression and violent behaviour. Interpersonal problems and fulfilling the roles of husband and father may be difficult for veterans with PTSD. A descriptive study of New Zealand veterans found that higher levels of PTSD affect the ability of veterans to initiate and maintain interpersonal relationships and that these interpersonal problems are evident in poorer levels of family functioning, and poorer marital dyadic adjustment (MacDonald et al., 1999).

The effect on partners has been reported as increased stress, feelings of worthlessness, social isolation, confusion, self blame, loss of control over their lives and increased violence in homes, lower levels of life satisfaction and happiness, higher scores on demoralisation and greater fears of having a nervous breakdown (Jordan et al., 1992). The effects of emotional numbing (Soloman, 1988) and other symptoms of PTSD are particularly significant for veterans' families (Scaturo & Hayman, 1992).

Other mental health disorders

PTSD may also affect the general health of veterans, and veterans with PTSD frequently have other mental problems in conjunction with the disorder (Vincent, 1994). Mental disorders which accompany PTSD include anxiety, depression, panic disorders, antisocial personalities, phobic disorders, atypical psychosis and intermittent explosive disorder. Veterans with PTSD frequently have problems with violent behaviour, poor interfamilial relationships, problems with employment, paranoia, introversion and/or aggression. Communication problems prevent them from expressing themselves, dealing with personal relationships or adjusting properly to society. The prevalence of these other mental health problems is summarised in Table 22.

In New Zealand Long et al (1992) reported that Vietnam veterans with PTSD reported more illness symptoms, chronic illness and disability days then veterans who did not have PTSD. Correspondingly, Vietnam veterans with PTSD had higher rates of contact with health care providers (Table 23).

Table 23: Contact with health care providers by Vietnam veterans (Long et al., 1992)

Health care contact	PTSD cases (%)	Non-PTSD cases (%)
General practitioner	76	56
Medical specialist	41	24
Pharmacist	49	34
Dentist	30	27
Psychiatrist or psychologist	17	1
Counsellor	11	2
Accident and Emergency services	20	4
Hospital admission	20	4

Published studies are not able to resolve the issue of whether the differences between veteran and civilian groups are due to selection factors associated with entering the military. However, researchers working with veterans with PTSD make the point that regardless of the etiology the disorders are associated with genuine suffering for veterans and their families (Jordan et al., 1991).

HEALTH OUTCOMES FOR OFFSPRING OF A VIETNAM VETERAN WITH MENTAL ILLNESS

A search of the relevant literature found no high quality cohort or case control studies had been published. No meta-analyses were found. Most of the available data were from cross-sectional studies. The cross sectional studies utilised a range of data collection instruments and multiple outcome measures.

Quality Level	Study Type	Count*
1.	Meta-analysis of cohort or/case control studies	0
2.	Cohort with comparison group	0
3.	Case control	1
4.	Cohort/comparison with national dataset	1
5.	All other studies	15

*There were a small number of level 5 studies of the children of veterans with PTSD which were unable to be accessed in New Zealand.

Summary of Studies

Details of the studies of the psychological health of veterans' children are summarised in Tables 24 and 25. Studies of the psychological health of veterans' children began appearing in the literature in the 1980s as case studies (Glassman et al., 1987; Rosenheck & Nathan, 1985).

Later studies have mainly been cross-sectional surveys of the children of Vietnam veterans comparing either veterans' children with civilian children (Dansby & Marinelli, 1999; Unkovich, 2001) or the children of veterans with PTSD with the children of veterans without PTSD (Davidson et al., 1989; Parsons et al., 1990; Jordan et al., 1992; Long et al., 1992; Caselli & Motta, 1995; Beckham et al., 1997; Rosenheck & Fontana, 1998; Westerink & Giarratano, 1999; Davidson & Mellor, 2001).

The only cohort study found in the literature (Australian Institute of Health and Welfare, 1999) reported higher rates of suicide in a cohort of the children of Vietnam veterans than in the general Australian population. The analysis of rates did not include adjustment for the other risk factors for suicide.

Table 24: The psychosocial impact of PTSD on the children of veterans: Comparison of veterans' children with children of civilians

Author	Data Source	Results
Cohort study with comparison with a national sample Level 4 evidence		
AIHW (2000)	Survey of 40 030 male Australian Vietnam veterans. Child health data reported by the veteran Comparison with national general population rates.	Increased rates of suicides for the children of Australian veterans
AIHW Validation Study (1999)	Data from the morbidity study validated against National Death Index for a sub-sample	Veterans reported 247 suicides, 111 were validated, 4 not validated, 123 not able to be validated Expected rates in the community were 75 (58-92)
Cross sectional studies Level 5 evidence		
Unkovich (2001)**	64 children of 38 male Western Australian veterans Data: personality inventory (MMPI-2) completed by the child	Most of the veterans' children were the same as their peers A small group of children reported high levels of overall emotional distress
Dansby and Marinelli (1999)	Parents of 28 children of US Vietnam combat veterans Comparison peer sample randomly selected Data: PTSD measured on Mississippi score; Self-reported adolescent data, BRP, School records, Personality questionnaire	The majority of outcomes were not significantly different Significant differences: The children of combat veterans showed poorer attitudes toward school, more negative attitudes toward their fathers, elevated scores of depression, tension, apprehension and anxiety, lowered scores on creativity and their behaviour was more problematic
Motta et al (1997)	45 children of veterans and 47 children of non-veterans Data: Impact of event scale, the MMPI - II PTSD scale	A suggestion of secondary trauma in children of veterans compared with children of civilians
Matsakis (1989)**	Survey of US veterans attending Veterans' Centres Data: Child's behaviour was reported by Veterans Centre Counsellors	Children of veterans had low self esteem, developmental difficulties, impaired interpersonal relationships and duplication of the aggressive symptoms of the father
Case studies Level 5 evidence		
Glassman et al (1987)	Expressions of the veteran's paranoid schizophrenia involved delusions and hallucinations relating to Vietnam	The veteran's wife and children shared his paranoia
Rosenheck and Nathan (1985)	Describes a veteran's child	Child has symptoms of secondary traumatisation

*PTSD=Post-traumatic Stress Disorder, CBCL scores = Child Behaviour Check list, BRP= Behaviour rating profile
**Abstract only accessed

Table 25: The psychosocial impact of PTSD on the children of veterans: Comparison of the children of veterans with and without PTSD

Author	Data Source	Results
Case control study Level 3 evidence		
Davidson et al (1989)	Cases: 108 veterans meeting DSM-III criteria for PTSD who attended VA Medical Centre Controls: 60 medical outpatients at the same centre, age matched	Increased rates of psychiatric treatment and disorder among the children of Vietnam veterans compared to the children of civilians
Cross sectional studies Level 5 evidence		
Davidson and Mellor (2001)	50 children of 50 male Vietnam veterans subgrouped according to PTSD status (60% response) Comparison group: age matched, selected by snowball sampling (n=33)	Veterans and their children were more likely to be unemployed. No significant differences were found between the self-esteem and PTSD symptomatology scores for any offspring groups. Scores of children of veterans with PTSD ranged widely reflecting the heterogeneity of the PTSD group offspring. Unhealthy family functioning was the area in which the effect of the veteran's PTSD appeared to manifest itself.
Westerink and Giarratano (1999)	Families of veterans with PTSD, NSW, Australia. Comparison group: Unmatched, families of volunteers from university or hospital staff.	Veteran's children lived in families with significantly higher levels of conflict. There was a small number of veteran's children who had very low self esteem and high levels of distress as measured by the GHQ.
Rosenheck and Fontana (1998)	Representative national sample of 1198 veterans who served during the Vietnam era Data – CBCL	Participation in abusive violence affects child behaviour independently of PTSD. Children of veterans more likely to have CBCL scores in the clinical range.
Beckham et al (1997)	40 children of 28 fathers who are Vietnam veterans with PTSD Data- MMPI	78% of children had at least one clinically elevated scale. Children of veterans with PTSD were more likely than children of a healthy parent to report illicit drug use, behaviour problems or violent behaviour.
Caselli and Motta (1995)	40 male Vietnam war veterans and their spouses. The veterans were self selected from veteran centres by advertising and word of mouth	Children of veterans with PTSD were more likely to have behaviour problems. Their parents were more likely to have marital adjustment problems than children of veterans without PTSD
Jordan et al (1992)	Veterans who served during the Vietnam era; 122 with PTSD, 252 without PTSD Child behaviour data reported by father	Men with PTSD reported higher levels of parenting problems. Spouses of partners with PTSD reported more marital problems. Children of veterans with PTSD were more likely to have behaviour problems than children of veterans without PTSD.
Long et al (1992)	1023 male NZ Vietnam veterans	Children of veterans with PTSD were more likely to grow up in a socio-economically deprived family, or have parents who were divorced or separated.
Parsons et al (1990)	Vietnam combat veteran's perceptions of their children's social and emotional functioning	Fathers with PTSD perceived their children as exhibiting a greater degree of dysfunctional social and emotional behaviour. Children were more likely to exhibit inadequate self control resulting in aggression, hyperactivity and delinquency and to have difficulty in establishing and maintaining friendships.
Harkness (1989)	Descriptive study of the profile of veterans' children. Data CBCL	Differences in CBCL significantly correlated to level of family functioning but not to severity of PTSD symptoms. Family functioning was affected by violence, exposure to combat and employment.

Two recent cross-sectional studies of Australian children of Vietnam veterans found few differences between the veterans' children and other children (Davidson & Mellor, 2001; Unkovich, 2001; Westerink & Giarratano, 1999). The partners of veterans with PTSD often act as a buffer between the veteran and the rest of the world. Westerink and Giarratano (1999) suggest that effective buffering may be a reason why so few Australian children show signs of serious problems. Davidson and Mellor (2001) suggest that the difference between the Australian and U.S. studies may reflect differences between the U.S. and Australian Vietnam veterans, including fundamental character differences, the differing nature of their traumatic war experiences and post-war readjustment, including level of substance abuse or violence, and marital status. Any of these may have influenced their children's self-esteem.

There are no studies of the psychological health of the children of New Zealand Vietnam veterans. However, 17% of the clients of Nga Whanau a Tu, a pilot counselling project targeting Vietnam veterans and their families, were veterans' children (Deane et al., 1998).

Children living with a parent with PTSD may also be affected by secondary traumatisation or the intergenerational effects of PTSD. Evidence for long-term transgenerational effects from a parent's combat experience comes from studies of the adult children of World War II veterans (Rosenheck, 1986).

The effects of living with a parent with PTSD, reported by the above studies, are variable. Not all children are affected and many studies have found more similarities in the results of psychological assessment tools than differences between the children of Vietnam veterans with PTSD, children of veterans without PTSD and children of civilians. Common responses include depression, guilt, irritability (Rosenheck, 1986) and low self esteem (Westerink & Giarratano, 1999). Individual characteristics such as gender, child's temperament and mitigating positive relationships may be associated with resilience.

INTERPRETATION OF STUDIES

The studies of the psychological health of veterans' children have been mainly descriptive based on small sample sizes. There have been no case control or cohort with comparison group studies.

The method used to select study groups has direct consequences on the statements that can be made about the relationship between exposures and outcomes (Goldberg, 1992). While some of the reported studies have used comparison groups as a control population, the comparison groups have frequently had different characteristics. Other limitations of the studies include only selecting children of veterans from a veteran population seeking help.

Different studies have used different instruments to measure the mental health of veterans and their children. In some studies measurement of children's health has been taken directly from interviews with children and in others measurement of the

behaviour of the adolescent has been as perceived by the veteran parent with PTSD. The measurement of PTSD and alcohol use or abuse is also complex.

Assessing causality is a major issue in the interpretation of these studies. There may be some aspect of the veteran which determines their susceptibility to PTSD and it is this factor, rather than the PTSD, which increases the likelihood of problems in the child.

Despite the limitations of individual studies, there are now a number of studies of veterans from different countries showing elevated risks of PTSD and some other mental illness compared with the general population. However, given the limitations of the studies it is not possible to draw any conclusions about the association between the veterans' PTSD from their Vietnam experience and the mental health of their children. However, there is a body of literature which suggests that the interplay between risk and protective factors which occur for the child will contribute to a mental health disorder. These have been outlined for a New Zealand population by Fergusson et al (1997) as:

- Risk factors which increase the likelihood of mental illness - Social disadvantage, family history of the disorder (genetic), poor family functioning and exposure to adversity; and

- Protective factors which decrease the likelihood of mental illness – Intelligence and problem solving, external interests and affiliations, parental bonding and attachment and development of resilience contributed to by early temperament.

Kendler et al (1993) has suggested that these all contribute in a multifactorial fashion towards increasing or decreasing the risk of an episode of a mental health disorder. This is summarised in Figure 5.

Figure 5: Risk and Resilience factors in determining the onset of mental illness

Childhood parental loss — Social support — Stressful life events in last 3 months — Neuroticism — History of Major Depression — Recent difficulties — Perceived parental warmth — Genetic factors — Lifetime traumas — Episode of Major Depression in last year

-.06 .35 -.13 -.21 .08 .18 -.22 -.15 .33 .15 .39 .09 -.08 .14 .20 .12 .19 -.20 .17 .09 .21 .09 .14 -.24 -.21 .17 .08

Risk Factor
Protective Factor
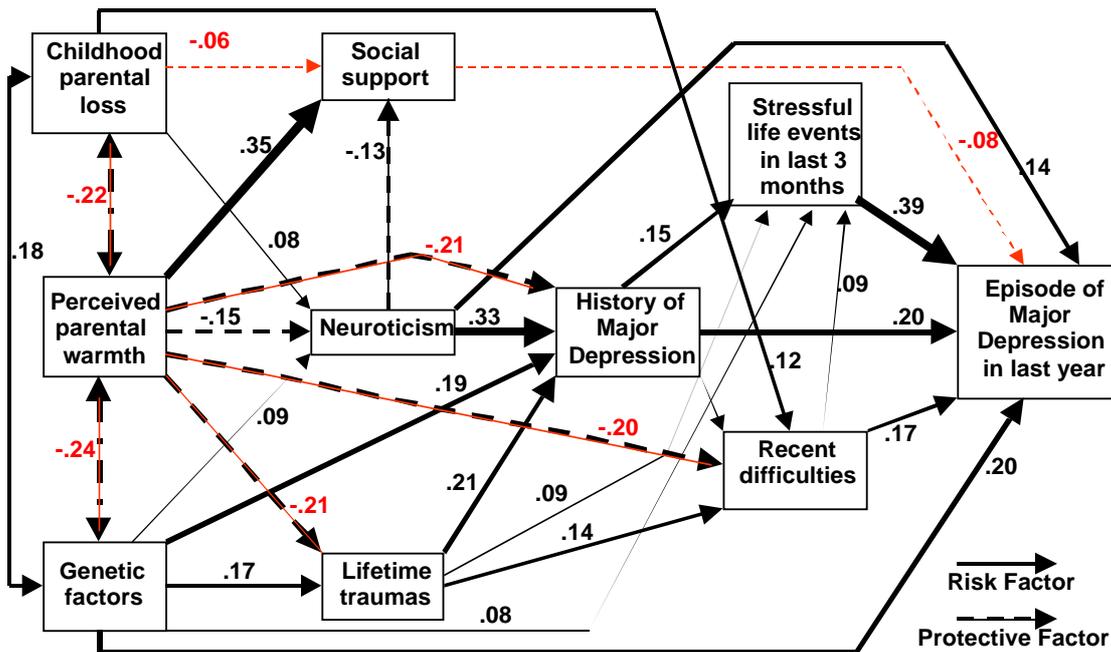
Source: Kendler et al (1993)

It is important to realise that the risk (and protective) factors which predict the likelihood of a disorder are not necessarily the same as those which will predict the onset of the disorder (Zubrick et al., 2000). Thus, a group of people may be subject to the same level of pre-morbid risk (and/or lack of protective) factors but not all will be exposed to the factors which determine the onset of the disorder. Similarly, some will have developed a resilience, by virtue of their temperament, which is itself protective on the onset of a disorder.

As the most frequently reported influence on the health of children of Vietnam veterans is the disrupted family functioning (Jordan et al., 1992; Westerink & Giarratano, 1999), it is plausible that the potential for intergenerational effects of PTSD are via the strain on the family and relationships of the veteran with their spouse and children (Figley & Kleber, 1995), rather than though a predisposing genetic inheritance for a disorder.

SUMMARY

- There are no level one or level two studies comparing the mental health of the children of veterans with the mental health of the children of civilians.

- New Zealand Vietnam veterans are more likely to suffer from post-traumatic stress disorder than civilians.

- Veterans with high exposure to combat are at higher risk of PTSD. Veterans with PTSD often have other psychological symptoms.

Living with a parent with mental illness can affect the family environment. Effects on the family environment represent a risk factor for the mental health of children of veterans.

The health outcomes for children of veterans with PTSD are variable. International studies of psychosocial functioning show more similarities than differences between the children of veterans and civilians. However, a small number of children are affected. Health outcomes for children include a range of conditions such as lowered self esteem, alcohol and substance abuse and increased rates of suicide. Such effects may result from reduced quality of parenting (resulting in lower levels of the protective factor of 'parental warmth' and increase in the risk factor of 'childhood parental loss') or as a result of an increase in social disadvantage and adverse life events due to the disability associated with the parent's PTSD.

There are no data available for New Zealand children. As rates of PTSD seem to be lower for New Zealand veterans, there may be less risk for the children of New Zealand and Australian veterans than for the children of Vietnam veterans in the United States.

SECTION FOUR: HEALTH CARE AND SUPPORT FOR THE CHILDREN OF OPERATION GRAPPLE AND VIETNAM VETERANS

INTRODUCTION

Physical disability

The United States Committee to review the Health Effects in Vietnam Veterans of Exposure to Herbicides has concluded that there is limited suggestive evidence of an increased risk of AML and spina bifida in the children of Vietnam veterans.

The review of the literature undertaken in this report and interpretation of this evidence in a New Zealand context suggests that there is no increased risk of spina bifida for the children of New Zealand Vietnam veterans. The review of the literature regarding the health risk for the children of Operation Grapple veterans has also found there is insufficient evidence to support an association between the levels of exposure of New Zealand veterans to radiation and adverse health outcomes for their children. However, there are children of veterans who have physical disability and these children need support. Models of disability support are included in this section.

Models of care for AML have not been included in this review for the following reasons:

- At this time very few children of veterans are aged under two years; and
- Care for children with AML is available through the publicly funded health care system.

Mental illness

Living with a parent with mental illness can affect the family environment. Effects on the family environment represent a risk factor for the mental health of children of veterans. Models of mental health care are discussed.

Age distribution of children

The only data available about the age distribution of the children of New Zealand veterans of Vietnam and Operation Grapple is based on a questionnaire survey of a sample of veterans undertaken for the Inquiry into the Health Status of Children of Vietnam and Operation Grapple veterans. Analysis of data from this sample found that the average number of children of Vietnam veterans was 2.44. Based on this the estimated total number of children is 8218. The age distribution of those children is shown in Table 26. No data are available for the children of Operation Grapple veterans.

Table 26: The age distribution of children of Vietnam veterans

Age group of children	Proportion	Estimated numbers
1-15 years	10.5%	864
16-25 years	43.2%	35 510
26-36 years	34.1%	2 803
36-45 years	11.6%	954
46-55 years	0.5%	42

A FRAMEWORK OF SUPPORT SERVICES FOR PEOPLE WHO ARE DISABLED

Introduction

One in five New Zealanders have a disability (Minister for Disability Issues, 2001). There is huge variation in the degree of disability that people experience. Disability can exist from birth, be acquired through accident or illness at any stage of life, or arise as a result of the ageing process. However, the predominant need for people with disabilities, as with all people, is self determination to achieve quality of life, living within the community of their choice (Munford & Sullivan, 1998). This report focuses on disabilities evident at birth and considers children born with physical disabilities.

The disability sphere is wider than just the professionals involved in it and the organisations that define its scope. There are varying constituencies and interests that hold differing levels of power and influence. Included are people with disabilities, their families, friends and social communities, workers involved within the formal services which impact on the disability sphere, government influences and others that regulate the field, educators, researchers and academics as well as the general public influence (Kendrick, 1999b).

Background

Historically the notion of disability has arisen from a process causing the isolation and marginalisation of people with physical and mental impairments. There are many reasons why this has occurred. These include the disabled person's reduced ability to participate in productive enterprise as society has moved from producing goods by hand through the industrial revolution to sophisticated production techniques (Finkelstein, 1998).

The philosophy of support for people with disabilities has changed markedly over the last forty years. A number of differing models have been proposed which conceptualise disability. These include scientific, interpretative and critical models (Munford & Sullivan, 1998).

Conceptualisation of disability

The scientific or medical model equates disability with illness (Begum, 1996), or with having a need (McKnight, 1998). Thus clinical practice "…strives to produce normally functioning individuals, with the definition of 'normal' being 'as they were before they became disabled'" (Silburn, 1993, p.224). Although the medical model has made huge contributions to the lives of people with disability through technological advances assisting mobility and sensory awareness, the experience of what it is like to live with a disability has largely been ignored. Large scale institutionalisation of disabled people whose lives are controlled by medical professionals has been seen as an appropriate model of care (Bennie, 1998).

Until recently health professionals have predominantly held the role of gate keepers (Harrison, 1993) to medical, social and welfare services, thus reinforcing the view that disability is a medical problem (Finkelstein, 1998). This has legitimised a notion of 'dependency', of needing to be 'cared for'. The construction of 'care' (McKnight, 1998) has been applied to a service which should predominantly be seen as support through partnership (Swartz, 1992; McKnight, 1998; Kendrick, 2000c). In New Zealand some people believe that gate keeping to support services is still largely retained by organisations such as the Needs Assessment Service Co-ordination agencies (NASC) which represent the medical model of service provision (Scown & Sullivan, 2000).

The interpretative perspective of disability focuses on the experience of disability. Policies such as normalisation and integration have contributed to understanding what constitutes quality of life, thus combating the stigma associated with disability (Kendrick, 1997). Such a perspective can assist individuals in conceptualising their personal view of disability and the types of services required to assist them. It addresses the assumption that people with disabilities may not want to be other than what they already are (Morris, 1993; Scown & Sullivan, 2000). This perspective is criticised because it does not challenge the dominant political power structures and values which create the notion that a person with a disability is different (Munford & Sullivan, 1998).

A critical perspective advances the potential for empowerment and advocacy by focusing on legal and human rights. As a result, there has been a rapid expansion of self help groups for people with disabilities. Similarly, groups have developed which teach individuals with disability and support workers advocacy skills (Kendrick, 2000a). These groups attempt to direct attention to the impact which society has on disabled people's lives rather than looking at the effects of disability at an individual level (Munford & Sullivan, 1998).

If the dominant view of disability is of people being ill or suffering disease, then they will be treated within service systems in the model of hospitals (residential settings). Conversely, if people with disabilities are viewed as people with potential for growth who are part of family and community groups, then services will be tailored to support these outcomes (Cocks & Stehlik, 1996; Finkelstein, 1998). Thus this model focuses on social (Barnes & Mercer, 1996) or critical political (Munford & Sullivan, 1998) rather than biological factors in understanding disability.

Cultural conceptualisation of disability

Maori and Pacific people are believed to conceptualise disability in differing ways. In addition to traditionally accepted forms of disability, Maori identify the loss of land, government policies, loss of knowledge of whakapapa and identity and the ongoing effects of colonisation and assimilation as disabling (Kingi & Bray, 2000). Similarly, Pacific people identify issues of disability linked to identity, gender, power, culture and religious practice, and socio-economic factors (Huakau & Bray, 2000).

Enabling communities

International (Swartz, 1992; Barnes & Mercer, 1996; Finkelstein, 1998) and New Zealand authors (Munford & Sullivan, 1998) write about a philosophical approach of enabling or inclusive communities. Citizens of enabling inclusive communities recognise people can be disabled by their environment, the attitudes of society, health systems and health professionals even more than their own impairment (Scullion, 2000).

Moving to models of community support can result in differing problems by giving the gatekeeping role to a differing group of support professionals. Community support workers can see their roles as providing solutions to the problems in disabled people's lives (Kendrick, 2000d), rather than mentoring them to construct their own solutions (Finkelstein, 1998; Kendrick, 2000d). Professional services can reconstruct the needs of disabled people as deficiencies, such as: 'you are deficient'; 'you are a problem'; 'you have a collection of problems'. Professional services then define themselves as the answer to these needs: 'we are the solution to your problem'; 'we know the problem you have'; 'you cannot understand the problem or the solution'; 'only we can decide whether the solution has dealt with the problem' (McKnight, 1998).

However, there are successful international models which resolve the above tensions (Bartnik, 2000; Kendrick, 2000b). One model is the Local Area Co-ordination (LAC) model in Western Australia. This model is based on a set of principles, values and beliefs that each person with a disability and their family are best placed to identify their own needs and that given time and support can make choices that positively impact on their quality of life. The LAC has few defined support services, believing that they should not expect individuals and families to fit in with formulated services. Instead they assist individuals and their families to purchase supports and services that cannot be met through existing structures. This may include approaching local or government funding bodies for financial support (Maher, 1999; Bartnik, 2000).

The New Zealand disability perspective

Within New Zealand, recent disability philosophy is expressed in the Disability Strategy released in April 2001 (Minister for Disability Issues, 2001). This strategy addresses the overarching need for people with disabilities to be able to live in a world that generally does not choose to take account of the impairments that they have. Although a number of agencies such as New Zealand CCS (formally the Crippled Children's Society) and Enable (formally the New Zealand Disabilities Resource Centre) have espoused this philosophical view of disability for many years, the delivery of health and other related services have been based around the medical model of care delivery. The medical model of care focuses predominantly on the presenting symptom, attempting to 'fix' the problem, rather than addressing holistic contextual issues. The disability model focuses on strengthening the child/adult's capacity to live with disability (Kendrick, 1999b) using a personalised form of care which appropriately individualises support using existing or new services (Kendrick, 1999a).

Since the early 1990s there has been a move to articulate a specific disability philosophy. In 1994 the Ministry of Health released the Standards for Needs

Assessment for People with Disabilities. In 1995 the final transfer took place from the Department of Social Welfare of the Disabled Persons Community Welfare Act programmes including services to support people with a physical disability to the Regional Health Authorities.

Purchasing strategies developed since 1996 have focused on a far wider range of services which might be required to meet the day-to-day needs of disabled people (Central Regional Health Authority, 1996). An integral part of these changes was the development of agencies to undertake assessment and co-ordination of services from the very young to the elderly who require support. In 1997 the NASC Agencies began to undertake assessments of people requiring support and to co-ordinate provision of support services. These agencies are contracted to provide this service, are largely owned by public hospitals, and are said to function from a medical rather than a disability framework. Services offered are said to focus on the provision of care, protection, nursing and medication rather than those which might support the life-defining needs of sustainable relationships, supported living, community participation and supported employment (Scown & Sullivan, 2000). An exception to this is 'Access Ability' a NASC which operates within a disability framework. Access Ability is part owned by New Zealand CCS and the Community Living Trust. It now holds contracts in Southland, Otago, Taranaki, South Auckland (and wider Auckland for some services) (Sullivan, 2001).

In 1996 a survey (including both NZ household and specific disability residential facilities settings) was undertaken to plan the delivery of services to people with disability and to monitor the effectiveness of existing programmes, laws and services. The survey focused on functional abilities, use of medication and aids, and use of support services including specialist health and education support. The survey, although asking why people believed they had a disability, did not focus on the medical diagnosis. A similar survey undertaken in 2001 aims to establish the prevalence of activity limitations and the barriers that people face in everyday life.

In September 2000 the New Zealand Disability Strategy Discussion Document (Minister for Disability Issues, 2000) was released. The discussion document was written by a number of people representing the agencies currently involved with people with disabilities. The resulting document 'The New Zealand Disability Strategy, Making the world of difference, Whakanui Oranga' was released in April 2001. The Summary of this document is incorporated here.

The New Zealand Disability Strategy: Summary

The New Zealand Disability Strategy presents a long-term plan for changing New Zealand from a disabling to an inclusive society. It has been developed in consultation with disabled people and the wider disability sector, and reflects many individuals' experiences of disability.

Disability is not something individuals have. What individuals have are impairments. They may be physical, sensory, neurological, psychiatric, intellectual or other impairments. Disability is the process which happens when one group of people create barriers by designing a world only for their way of living, taking no account of the impairments other people have.

Along with other New Zealanders, disabled people aspire to a good life. However, they also face huge barriers to achieving the life that so many take for granted. These barriers are created when we build a society that takes no account of the impairments other people have. Our society is built in a way that assumes we can all see signs, read directions, hear announcements, reach buttons, have the strength to open heavy doors and have stable moods and perceptions.

Underpinning the New Zealand Disability Strategy is a vision of a fully inclusive society. New Zealand will be inclusive when people with impairments can say they live in:

'A society that highly values our lives and continually enhances our full participation.'

Achieving this vision will involve ensuring that disabled people have a meaningful partnership with Government, communities and support agencies, based on respect and equality. Disabled people will be integrated into community life on their own terms, their abilities will be valued, their diversity and interdependence will be recognised, and their human rights will be protected. Achieving this vision will also involve recognising the principles of the Treaty of Waitangi.

To advance New Zealand towards a fully inclusive society, the Strategy includes fifteen Objectives, underpinned by detailed Actions. The Objectives are to:

1. Encourage and educate for a non-disabling society
2. Ensure rights for disabled people
3. Provide the best education for disabled people
4. Provide opportunities in employment and economic development for disabled people
5. Foster leadership by disabled people
6. Foster an aware and responsive public service
7. Create long-term support systems centred on the individual
8. Support quality living in the community for disabled people
9. Support lifestyle choices, recreation and culture for disabled people
10. Collect and use relevant information about disabled people and disability issues
11. Promote participation of disabled Mäori
12. Promote participation of disabled Pacific peoples
13. Enable disabled children and youth to lead full and active lives
14. Promote participation of disabled women in order to improve their quality of life
15. Value families, whänau and people providing ongoing support

Key government departments will produce an implementation work plan for the 2001/02 year showing what they are doing towards implementation of the Strategy. This annual planning process will then be rolled out to other departments in 2001/03. The Minister for Disability Issues will report to Parliament annually on progress in implementing the Strategy and full reviews of progress will be conducted after five and ten years.

Source: 'The New Zealand Disability Strategy, Making the world of difference, Whakanui Oranga'

New Zealand models of health care support for people with disability

There is no standardised New Zealand model of health care for children/adolescents with a disability. New Zealand provides differing services according to the geographic region and the funding that is available in each area. As with all aspects of health care, models of care and services to support children/adolescents have changed substantially over the last twenty years.

In the Wellington region up until 1997, a Physical Disability Service existed that focused solely on the needs of people (all ages) with disabilities. In 1996 a new purchasing framework was devised by the Centre Health Funding Authority (CRHA) based on the Ministry of Health's Framework for Disability Support Service. An emphasis was placed on people with disabilities being able to use a process to access disability support services, the key components of this service being needs assessment, service co-ordination and service provision, with NASC agencies undertaking the 'needs assessment' and 'service co-ordination' components and 'service provision' being supplied by a number of government funded, private and voluntary agencies. As well, Assessment, Treatment and Rehabilitation (AT&R) units were established to provide short-term care addressing specific disability related issues.

The support needs of children/adolescents who have a disability

The needs of the child/adolescent appear to be related to their presenting clinical problems and developmental stage. These needs are often different to those of adults. From birth there are a number of clinical issues that require assessment and treatment, either surgically or medically. Similarly, it can be anticipated that developmental steps may not be achieved and children will need ongoing assessment and support. A framework of disability support from birth focuses on the child and family as a unit of care where the needs of the parents must equally be addressed. Parent(s) may require education and assistance to care for, to retain hope for (Kiripalai et al., 2000; Marcias et al., 2000), and re-nurture the dreams for the future of their child (Sullivan, 2001).

Specialist health care service co-ordination does not appear to fit into the disability model and currently continues to be provided by tertiary public hospitals. For children and adolescents this is provided by paediatric services ranging from specialist paediatric community nurses, paediatric specialists, and multidisciplinary clinics including Spina Bifida Clinics.

Although the paediatric stream of health care is funded up until fourteen years, most specialist paediatric services (those services that see children with disability or a chronic illness) continue until the adolescent reaches the end of secondary schooling (Austin, 2001). From that time onward, ongoing care is continued by individual medical specialists with perhaps an increasing co-ordination role undertaken by the individual's general practitioner.

Long term health support for children/adolescents with spina bifida ideally requires assessment and input by paediatric, neurological, urological and neurosurgical services, as well as allied health support from community paediatric nurses, occupational therapists, physiotherapists and social work. Ideally this type of support

is best delivered using a multidisciplinary model, perhaps using a case management approach where all team members attempt to take account of physical issues as well as accounting for the child/family's own values and life situation (Austin, 2001; Zwarenstein et al., 2001). Integral to this model is appointing a smaller group or individual to mentor the child/family through the many associated complex choices (Zwarenstein et al., 2001). However, most New Zealand Spina Bifida Clinics are clinics where specialists are available in the same location on the same day, but do not undertake joint assessment or care-support planning.

Informing health professionals about appropriate disability support is pivotal in attempting to change the dominant medical model paradigm of health care delivery (Kendrick, 2000d) and assuring quality services by using performance indicators defined by people with disabilities (Kendrick, 1997). International initiatives have been reported which involve medical paediatric registrars in home based health support (Anon., 1995). Interactive educational approaches which inform general practitioners about disability issues have been utilised within Australia (Newell & Meumann, 1997). Similarly, new education initiatives for nurse practitioners focus on enabling the person with a disability (Scullion, 2000).

Ongoing home support centres on assessment, education and support for activities of daily living, particularly appropriate continence support, provision of equipment to support continence, assessment for mobility aids, and general family support (Ransfield, 2001). Several new surgical procedures such as the 'ACE' procedure for bowel continence and the Mitronaff procedure for urinary continence are undertaken on an individual basis (Gill, 2001; Ransfield, 2001). These procedures are funded by the Paediatric Service with provision of ongoing continence supplies being funded by Community Health Services.

There is also a range of equally important support, which perhaps focuses on the more contextual needs of the children/adolescents. This includes paediatric neuro-developmental therapists, the Ministry of Education Special Education Service (SES) or CCS funded 'early intervention service', SES funding for specialist mobility aids and the work of non-governmental agencies such as CCS, IHC and Enable (Hill, 2001). A number of support groups initiated by parents and, similarly, children and adolescents, exist.

A number of parents believe that current funded therapies are not evidence based, and purchase therapies (neuro-developmental/physical/educational) from outside of New Zealand (Sullivan, 2001).

The support needs of adults who have a disability

Adults with disabilities have seen many changes in care and support provision as they have aged. Such changes in service delivery are disruptive and stressful, as people constantly have to adjust to increasing or decreasing services, different funding arrangements, and changes in the role they are expected to undertake.

A major issue for adults with a disability is where they live, whether independently or within a residential setting. The de-institutionalisation of residential settings such as Kimberley Hospital in Levin meant new models of living arrangements developed.

There are a number of small residential services such as Spring Lodge (Upper Hutt), Emmerson House (Porirua) and Laura Fergusson Trust residential settings (Hutt Valley and Auckland). These small residential living centres have been labelled by some as trans-institutionalisation or re-institutionalisation because the original conceptualisations of disability residential care have not been addressed (Scown & Sullivan, 2000). There are also small communal groupings or supported, independent living arrangements. New Zealand CCS and Access Ability work to support the latter living arrangements (Hill, 2001; Sullivan, 2001).

It appears that once growth and maturation have occurred, the health needs for many people with disability are static and can be similar to the general population (Harrison, 1993). There will be exceptions where there are complications arising from deteriorating function relating to the original disability or childhood management, such as those relating to renal or neurological damage.

The provision of health care for adults is undertaken by adult medical specialists, some of whom may have been involved with the person from childhood. It is also possible that that adult may not require or have avoided specialist care. Their health care support needs may most appropriately be addressed by general practitioner care or they may not require formal health care. The fee for service primary health care system in New Zealand is a barrier to the co-ordination of disability care by general practitioners.

Agencies such as Workbridge, which is contracted by Work and Income, provide a specialist employment placement service for people with all types of disabilities (Workbridge, 2001). This includes identifying career goals, identifying training requirements, employment preparation, employment search, accessing support funding, and ongoing support after employment. Other organisations such as 'Enable' (formally the New Zealand Disabilities Resource Centre) manage health funding to improve the quality of life of people with disabilities through provision of access to information, research and funding of equipment, housing alterations and vehicle purchase and modification (www.enable.co.nz, 2001).

Genetic counselling

Genetic counselling is a service which assists in assessing the risk of transmission of congenital disability. People who have had a child with spina bifida have an increased risk of having another child with the condition. A similar increased risk exists that a person with spina bifida will have a child who is also affected. Genetic counselling and prenatal diagnosis with selective abortion is an integral part of the management of families with central nervous system malformation. Genetic counselling is fully funded by the Ministry of Health. In the Central/Southern region the service is based in Wellington Hospital and is available to people living in the South Island up to New Plymouth and across to Napier. There is a toll-free phone number available and regular outreach clinics.

It is now widely accepted that folic acid supplementation has a role in the prevention of neural tube defects and the prevention of recurrence of neural tube defect (MRC Vitamin Study Research Group, 1991; Czeizel & Dudas, 1992).

Support services

Organisations such as New Zealand CCS continue to provide a range of services from childhood through adult life (New Zealand CCS, 2000). These services include:

1. Early childhood: New Zealand CCS provide a number of early intervention early childhood centres.
2. Community support: this includes identification of the needs of people with disabilities and the implementation of holistic planned services that support their ability to live in the community of their choice.
3. Vocational support: this includes the support of people with disabilities within their communities of choice to achieve their vocational goals.
4. Recreational support: this includes the support of people with disabilities in their communities of choice to achieve their chosen recreational goals.
5. Supported living: this includes supporting people with disabilities.

Recommendations

1. Implement the New Zealand Disability Strategy within the Office of Veterans Affairs service policies for veterans with disabilities. Consultation with veterans and their children is an important part of this process.

2. Consider whether separate support services are required for veterans with disabilities, perhaps using a person(s) to mentor the person with a disability in identifying quality of life choices (case worker model, or the LAC model (Maher, 1999; Bartnik, 2000) or the Nova Scotia model (Kendrick, 2000b). Alternatively, consider whether resources should be appropriately used to support people to use existing disability service focused delivery systems (Kendrick, 1999c), or directly support the services themselves. This may include funding arrangement for general practitioner consultations to support health service needs.

3. Develop a resource booklet for New Zealand people with disabilities identifying all organisations that directly and indirectly offer support including therapies not currently funded or available in New Zealand, how they can be accessed, costs of access, and government and non-governmental funding available.

MENTAL HEALTH CARE NEEDS OF CHILDREN OF VIETNAM VETERANS

The first step in providing mental health care to the children of Vietnam veterans is to ascertain what their difficulties actually are. This will mean that each child of a veteran who has difficulties will need to be assessed to determine the nature, severity and associated disabilities (e.g. anxiety disorder, depression) and then have access to the appropriate effective treatments.[xi]

The models of health care for the different mental health conditions for which veterans' children are at increased risk have been defined by a range of clinical practice guidelines developed for New Zealand health professionals.

Clinical practice guidelines are tools to provide guidance in decision-making at each level of interaction: between health professional and patient; between purchaser and provider; and between 'funder' and 'purchaser'.[xii] Guidelines are developed based on the best available evidence and can provide a useful estimate to service planners and funders as to what might be expected for a usual population with a particular disorder.

The following clinical guidelines have been developed for New Zealand health care providers (by order developed and also approximate frequency of the disorder):

- The guidelines for the 'Treatment and Management of Depression in Primary Care' have been developed by the National Health Committee for primary health care providers and the National Advisory Committee for Health and Disability, September, 1996.
- The guidelines for 'Assessing and Treating Anxiety Disorders' have been developed by the National Health Committee and the National Advisory Committee for Health and Disability for primary health care providers, November 1998.
- The guidelines for 'Recognising, Assessing and Treating Alcohol and Cannabis Abuse in Primary Care' have been developed by the National Health Committee for primary health care providers and the National Advisory Committee for Health and Disability, July 1999.
- The guidelines for the 'Detection and Management of Young People at Risk of Suicide' have been developed by the Ministry of Youth Affairs and the RNZCGP for primary health care providers, September 1999.

Summaries of the models of care recommended by these guidelines are appended (Appendix Two).

[xi] Personal communication Debbie Lovell, Senior Clinical Psychiatrist, Clinical Trials Unit, Oxford University

[xii] The NZ Guideline Group http://www.nzgg.org.nz.

Accessing Mental Health Care in New Zealand

The best practice care recommended in the guidelines is not necessarily readily available in New Zealand through the publicly funded health care system.

Cognitive behaviour therapy is recommended but very difficult to access via the public health system. Secondary mental health services for children and youth in Auckland are at 20-25% of benchmark and for the rest of the country about 50%. Thus any implementation of the guidelines may need to consider services being purchased from private providers when they are not available from District Health Boards. In order to maximise the use of available services, it is suggested that there is case management by an experienced clinician who assesses the person, develops a treatment plan for their needs and supervises the provision (both access to DHB and purchase of private) services that they need.

It is possible that there may be advantages in developing specific programmes for veterans and their families in larger population areas (e.g. Auckland).

Specific veterans programmes

New Zealand Pilot Study

It is only in recent years that the needs of veterans' families have been recognised. In New Zealand the Nga Whanau a Tu was established, as a pilot project, to provide counselling for veterans' families. The project was co-ordinated through the Department of Psychology, Massey University (Deane et al., 1998). 112 individuals registered for counselling through the programme, and were referred to 57 counsellors throughout New Zealand: 37% were wives; 17% ex-wives; 4% widows; 21% were veterans; and 17% veterans' children. Most frequently, help was sought with emotional problems (71%), relationship difficulties (56%) and physical complaints (13%). The largest single categories of emotional distress were anger (10%) and diffuse distress (10%). The programme was evaluated with a postal survey to clients. Response rates of 54% for the post-test questionnaire and 36% for the follow up questionnaires were achieved. On average clients reported that counselling had been beneficial and indicated satisfaction with services received. At the end of the trial therapists reported that 50% of clients were in need of further treatment.

Australian Vietnam Veterans Counselling Service (VVCS) Youth Services Project Plan

The Australian Veterans Counselling Service Youth Services Project Plan has been developed to increase the capacity of the VVCS and key partners and stakeholders to promote and enhance the mental health of their children to reduce the current level of suicide risk.[xiii].

The service aims to:
- Be accessible and appropriate. Guidance and participation by young people in the project is critical to ensure needs are appropriately identified and met;

[xiii] Ann O'Kane, personal communication

- Establish partnerships with a range of specialist and community resources available across Australia;
- Establish service responses which are sustainable and evaluated.

VVCS will follow the broad national directions for suicide prevention recommended in the Australian National Suicide Prevention Strategy (2000–2004). The target group is the 80,000 children identified through the Health Study (1998) who were born to Vietnam veterans since the beginning of the Vietnam War.

Estimated costs of the provision of care in New Zealand

A model to estimate the costs of providing mental health care to the children of veterans has been developed by Don Smith,[xiv] specifically for this paper. The model draws on a model initially developed by The Treasury for prediction of primary and secondary mental health services, and which is currently being reviewed by the Department of Psychological Medicine, Wellington School of Medicine, University of Otago. This model is based on the current assumptions used in work previously completed for the Mental Health Commission's Blueprint for mental health services and for the Ministry of Health's Mental Health Strategy. A significant development from these two methods is that the model assumes an integrated primary and secondary health service delivery of treatments based on the National Health Committee's primary mental health practice guidelines.

The likely rates of mental health disorder amongst children of veterans

As indicated in earlier sections of this report, it has not been possible to locate any research specifically reporting rates of mental health disorders amongst children of veterans. Thus the estimate offered is conceptual and is based on the research on rates of mental health in the total New Zealand community with an increased loading for children of veterans due to the likely increase in risk factors and decrease in parental support factors during their childhood years.

First, the level of mental health disorders in the general New Zealand community is outlined. The prevalence (number of people likely to have a disorder in any month) and associated level of disability of the main mental health disorders is listed in Table 27. Overall, the Ministry of Health, National Mental Health Strategy, estimates that 3% of the population will require access to a mental health service at any time. Current services cater for about 2% accessing these services.

If all the disorders with associated disability are considered, then 7.85% of the adult population (18-64 years) and 4.68% of youth (0-17 years) will require access to treatment services. However, not all will require all services at the same time and not everyone requiring services will choose to present.

[xiv] Research Associate, Wellington School of Medicine, University of Otago

Table 27: Estimates of prevalence of mental health disorders, by level of severity, for model (one month prevalence if possible) – as percentage of the age group population.

Mental health disorder clusters	1 month prevalence of only or main problem	Severity and disability (% of the age group population[xv])		
		Mild	*Moderate*	*High*
Anxiety Disorders (18 – 64 years)	2.7%	0.52	0.88	0.83
Dysthymia (18 – 64 years)	0.6%[xvi]	0.12	0.18	0.26
Major Depressive Disorder[xvii] (18 – 64 years)	1.7%[xviii]	0.34	0.50	0.73
Schizophrenia and related disorders (18 – 64 years)	0.4%	0.08[xix]	0.16	0.16
Disabling personality disorders (18 – 64 years)	3.4%	1.04	0.59	0.31
Substance abuse and dependence (18 – 64 years)	2.8%	0.60	0.38	0.17
Conduct and oppositional disorders (10 – 17 years)	4.5%[xx]	1.37[xxi]	0.78	0.40
Serious mental health disorders of childhood (0 – 17 years)	2.43%[xxii]	0.48[xxiii]	0.75	0.90

Estimation of the number of children of veterans likely to present for treatment services

In any six month period it might be expected that (given 1.5 times the usual level of morbidity amongst the children of veterans) there will be 225 people with a mild mental health disorder, 351 with a moderately severe disorder and 442 with a high severity disorder. However, not all these people will present for a treatment service should it be offered, seeking help from other sources or not considering that they need assistance. Using the presentation rates found by the United States Epidemiological Catchment Area studies we would expect that in any six months that 571 people (65 mild, 174 moderate and 332 severe) would present for treatment (adults and youth).

[xv] Note that the combined percentages for the three levels of disability do not equal the 1 month prevalence as some people have the disorder with no associated disability. The assumption is made that if there is no associated disability then there is no significant need for treatment.

[xvi] The data supplied was for all Affective Disorders being 2.3%. The proportion of this being for Dysthymia was estimated to be 25.7% based on that being the proportion for total 1 month prevalence in the study.

[xvii] Includes Bipolar Disorder.

[xviii] The data supplied was for all Affective Disorders being 2.3%. The proportion of this being for Affective Disorders other than Dysthymia was estimated to be 74.3% based on that being the proportion for total 1 month prevalence in the study.

[xix] The distribution of severity was assigned to include all cases. Based on Australian information 33% of cases had no disability and the rest moderate disability

[xx] Estimated from the prevalence of the Dunedin and Christchurch birth cohort studies and discounted for 50% co-morbidity – see argument later in this section.

[xxi] The distribution to the three levels of severity was done using the severity distribution for adult personality disorder as there is no comparable information from the two NZ studies

[xxii] Estimated from Goodman 1997 – see argument later in this section.

[xxiii] The distribution to the three levels of severity was done using the mean severity distribution for adult anxiety disorders and affective disorders as there is no comparable information from the two NZ studies

Access to the treatments generally indicated in the best practice guidelines for this group of people would cost in the order of $431,000 for a 6 month period (assuming that any specialist secondary services required are available and not a cost to this system and that all primary care treatments would be at full cost (i.e. no community service card entitlements, etc). This provides for one third to be in an initial assessment and treatment phase, one third to be continuing an established treatment and one third to be provided with ongoing relapse prevention services. In the initial implementation of any programme these loadings may be towards more initial treatment, and, once established, should increase to greater relapse prevention (possibly with higher numbers–so no difference in cost).

Recommendations

1. The Office of Veterans' Affairs should assess the numbers of Vietnam and Operation Grapple veterans who have been diagnosed with PTSD, the mental health care needs of the children of veterans and the extent to which these needs are being met in the publicly funded health care system.
2. Mental health care should be consistent with the models of care recommended in the appropriate New Zealand guidelines and made accessible to the children of veterans.

REFERENCES

Abrahamson, S., Bender, M. A., Conger, A. D., & Wolff, S. (1973). Uniformity of radiation-induced mutation rates among different species. *Nature, 245*(5426), 460-462. (Not accessed)

Adelstein, S. J. (1987). Uncertainty and relative risks of radiation exposure. *JAMA, 258*(5), 655-657.

*Advisory Committee on the Health of Veterans' Children. (1999). *Inquiry into the health status of the children of Vietnam and Operation Grapple veterans*. Wellington, New Zealand.

Aisner, J., Wiernik, P. H., & Pearl, P. (1993). Pregnancy outcome in patients treated for Hodgkin's disease. *J Clin Oncol, 11*(3), 507-512.

Alexander, F. (1998). Cancer in the offspring of radiation workers. Connection between leukaemia and radiation needs to be considered. *BMJ, 316*(7145), 1672; discussion 1673.

Alexander, F. E., Cartwright, R. A., & McKinney, P. A. (1992). Paternal occupations of children with leukaemia. *BMJ, 305*, 715-716.

Alexander, G. R., Baruffi, G., Mor, K. M., Kieffer, E. C., & Hulsey, T. C. (1993). Multiethnic variations in the pregnancy outcomes of military dependents. *Am J Public Health, 83*, 1721-1725.

*American Psychiatric Association. (1994). *Diagnostic and statistical manual for mental disorders (DSM-IV)* (4th ed.). Washington DC.

Anderson, L. M., Diwan, B. A., Fear, N. T., & Roman, E. (2000). Critical windows of exposure for children's health: Cancer in human epidemiological studies and neoplasms in experimental animal models. *Environ Health Perspect, 108*(Suppl 3), 573-594. (Not accessed)

Andersson, M., Juel, K., Ishikawa, Y., & Storm, H. H. (1994). Effects of preconceptional irradiation on mortality and cancer incidence in the offspring of patients given injections of Thorotrast. *J Natl Cancer Inst, 86*(24), 1866-1867.

Anon. (1987). RE: "Do atomic veterans have excess cancer? New results correcting for the healthy soldier bias" [Letter]. *Am J of Epidemiol, 126*(6), 1214.

Anon. (1989). *Film badge dosimetry in atmospheric nuclear tests*. Washington D.C.: National Academy Press.

*Anon. (1995). Paediatricians made house calls. *Exceptional Parent, Oct 1995*, 51-54.

Anonymous. (1983). Agent Orange and birth defects [letter]. *N Engl J Med, 309*(8), 491-492.

Anonymous. (1984). Vietnam veterans' risks for fathering babies with birth defects. *MMWR Morb Mortal Wkly Rep, 33*(32), 457-459.

*Araneta, M. R., Moore, C. A., Olney, R. S., Edmonds, L. D., Karcher, J. A., McDonough, C., Hiliopoulos, K. M., Schlangen, K. M., & Gray, G. C. (1997). Goldenhar syndrome among infants born in military hospitals to Gulf War veterans. *Teratology, 56*(4), 244-251.

*Araneta, M. R. G., Destiche, D. A., Schlangen, K. M., Merz, R. D., Forrester, M. B., & Gray, G. C. (2000). Birth defects prevalence among infants of Persian Gulf War veterans born in Hawaii, 1989-1993. *Teratology, 62*(4), 195-204.

Armstrong, B. K., & Stanley, F. J. (1984). Birth defects and Vietnam service [editorial]. *Med J Aust, 140*(7), 388-389.

*Aschengrau, A., & Monson, R. R. (1989). Paternal military service in Vietnam and risk of spontaneous abortion. *J Occup Med, 31*, 618-623.

*Aschengrau, A., & Monson, R. R. (1990). Paternal military service in Vietnam and the risk of late adverse pregnancy outcomes. *Am J Public Health, 80*(10), 1218-1224.

*Austin, N. (2001). Care of children with Spina bifida.: personal communication.

*Australian Bureau of Statistics. (1998). *Mental health and well being profile of adults*. Canberra.

Australian Department of Veterans Affairs. (1983). *Case-control study of congenital abnormalities and Vietnam service.* Canberra.

*Australian Institute of Health and Welfare. (1999). *Morbidity of Vietnam Veterans: A study of the health of Australia's Vietnam veteran community. Volume 3 Validation Study*. Canberra.

*Australian Institute of Health and Welfare. (2000). *Morbidity of Vietnam Veterans. Suicide in Vietnam Veterans' Children: Supplementary Report No 1*. Canberra: AIHW.

*Australian Radiation Protection and Nuclear Safety Agency. (2001). *Ionizing radiation and health*. Australian Radiation Protection and Nuclear Safety Agency, Commonwealth Department of Health and Aged Care. Available: www.arpansa.gov.au.

Awa, A., Honda, T., Neriishi, S., Sofuni, T., Shimba, H., Ohtaki, K., Nakano, M., Kodama, Y., Itoh, M., & Hamilton, H. (1989). *Cytogenetic study of the offspring of atomic bomb survivors, Hiroshima and Nagasaki.*: Radiation Effects Research Foundation.

Axmon, A., Rylander, L., Stromberg, U., & Hagmar, L. (2000). Miscarriages and stillbirths in women with a high intake of fish contaminated with persistent organchlorine compounds. *Int Arch Occup Environ Health, 73*, 204-208.

Baird, J., Anderson, T., Newcombe, H., & Lowry, B. (1988). Genetic disorders in children and young adults: A population study. *Am J Hum Genet, 42*, 677-693.

Barcinski, M., Abreu, M., De Almeida, J., Naya, J., Fonesca, L., & Castro, L. (1975). Cytogenetic investigation in a Brazilian population living in an area of high natural radioactivity. *Am J Hum Genet, 27*, 802-806.

*Barnes, C., & Mercer, G. (1996). Introduction: exploring the divide. In C. Barnes & G. Mercer (Eds.), *Exploding the divide: Illness and disability* (Vol. One, pp. 1-16). Leeds: The Disability Press.

*Bartnik, E. (2000). *Advocacy for change.* Paper presented at the Access to a quality of life, Auckland.

Baverstock, K. F. (1991). DNA instability, paternal irradiation and leukaemia in children around Sellafield. *Int J Radiat Biol, 60*, 581-595. (Not accessed)

*Beckham, J. C., Braxton, L. E., Kudler, H. S., Feldman, M. E., Lytle, B. L., & Palmer, S. (1997). Minnesota Multiphasic Personality Inventory profiles of Vietnam combat veterans with posttraumatic stress disorder and their children. *J Clin Psychol, 53*(8), 847.

Beckham, J. C., Lytle, B. L., & Feldman, M. E. (1996). Caregiver burden in partners of Vietnam War veterans with Posttraumatic Stress Disorder. *J Consult Clin Psychol, 64*, 1068-1072.

*Begum, N. (1996). General practitioners' role in shaping disabled women's lives. In C. Barnes & G. Mercer (Eds.), *Exploring the divide*. Leeds: The Disability Press.

Bell, E. M., Hertz-Picciotto, I., & Beaumont, J. J. (2001). A case-control study of pesticides and fetal death due to congenital anomalies. *Epidemiology, 12*, 148-156.

Bender, R. A., & Young, R. C. (1978). Effects of cancer treatment on individual and generational genetics. *Semin Oncol, 5*(1), 47-56. (Not accessed)

*Bennie, G. (1998). Employment services and disabled people: models, methods and mayhem. In R. Munford & M. Sullivan (Eds.), *Thinking critically about disability* (Vol. Two, pp. 1-14). Palmerston North: Department of Social Policy and Social Work, Massey University.

Berry, R. J. (1995). Preconception paternal occupational radiation exposure and the risk of childhood leukaemia: a paradox within an enigma. *Occup Med (Oxford), 45*(1), 5-10.

Bertazzi, P., Bernucci, I., Brambilla, G., Consonni, D., & Pesatori, A. C. (1998). The Seveso studies on early and long-term effects of dioxin exposure: a review. *Environ Health Perspect, 106*, 625-633.

Bertazzi, P. A., Zocchettic, C., C, P. A., Guercilena, S., Consonni, D., Tironi, A., & Landi, M. T. (1992). Mortality of a young population after accidental exposure to 2,3,7,8-tetrachlorodibenzodioxin. *Int J Epidemiol, 21*(1), 118-123.

Bhatia, S., & Neglia, J. P. (1995). Epidemiology of childhood acute myelogenous leukemia. *J Pediatr Hematol Oncol, 17*(2), 94-100.

Bisanti, L., Bonetti, F., Caramaschi, F., Del Corno, G., Favaretti, C., Giambelluca, S. E., Marni, E., Montesarchio, E., Puccinelli, V., Remotti, G., Volpato, C., Zambrelli, E., & Fara, G. E. (1980). Experiences from the accident of Seveso. *Acta Morphol Acad Sci Hung, 28*, 139-157. (Not accessed)

Bithell, J. F., Dutton, S. J., Draper, G. J., & Neary, N. M. (1994). Distribution of childhood leukaemias and non-Hodgkin's lymphomas near nuclear installations in England and Wales. *BMJ, 309*, 501-505.

Bithell, J. F., & Stewart, A. M. (1975). Pre-natal irradiation and childhood malignancy: a review of British data from the Oxford survey. *Br J Cancer, 35*, 271-287. (Not accessed)

Black, R., Sharp, L., Harkness, E., & McKinney, P. A. (1994). Leukaemia and non-Hodgkin's lymphoma: incidence in children and young adults resident in the Dounreay area of Caithness, Scotland in 1968-91. *Epidemiology Community Health, 48*, 232-236. (Not accessed)

Bland, J. M. (1994). Cancer in nuclear test veterans. Statistical analysis inappropriate [letter; comment]. *BMJ, 308*(6924), 339; discussion 339-340.

*Blatter, B., Hermens, R., Bakker, M., Roeleveld, N., Verbeek, A. L., & GA, Z. a. (1997). Paternal occupational exposure around conception and spina bifida in offspring. *Am J Ind Med, 32*, 283-291.

Bonde, J. P., & Giwercman, A. (1995). Occupational hazards to male fecundity. *Reproductive Medicine Review, 4*, 59-73. (Not accessed)

*Booth, W. (1987). Agent orange study hits a brick wall. *Science, 237*, 1285-1286.

Bound, J. P., Francis, B. J., & Harvey, P. (1995). Down's syndrome:prevalence and ionising radiation in an area of north west England 1957-91. *J Epidemiol Community Health, 49*, 164-170.

Boyle, C. A., Decoufle, P., & O'Brien, T. R. (1989). Long-term health consequences of military service in Vietnam. *Epidemiol Rev, 11*, 1-27.

*Bradford-Hill, A. (1965). The environment and disease: Association or Causation? *P Roy Soc Med, 58*, 295-300.

Brandt, E. N., Jr. (1984). The CDC study of Vietnam veterans' risks of fathering infants with birth defects [editorial]. *Public Health Rep, 99*(6), 529-530.

*Brender, J. D., & Suarez, L. (1990). Paternal occupation and anencephaly. *Am J Epidemiol, 131*, 517-521.

*Brent, R. L. (1999). Utilization of developmental basic science principles in the evaluation of reproductive risks from pre- and postconception environmental radiation exposures. *Teratology, 59*, 182-204.

*Brinkworth, M. H. (2000). Paternal transmission of genetic damage: findings in animals and humans. *Int J Androl, 23*(3), 123-135.

British Medical Association (Board of Science and Education). (1983). *The medical effects of nuclear war. The report of the British Medical Association's Board of Science and Education.*: John Wiley & Sons.

Bross, I. D., & Bross, N. S. (1987). Do Atomic Veterans have excess cancer? New results correcting for the healthy soldier bias. *Am J Epidemiol, 126*(6), 1042-1050.

Bryne, J., Nicholson, H. S., & Mulvihill, J. J. (1992). Absence of birth defects in offspring of women treated with dactinomycin. *N Engl J Med, 326*(2), 137.

Buckley, J. D., Pendergrass, T. W., Buckley, C. M., Pritchard, D. J., Nesbit, M. E., Provisor, A. J., & Robison, L. L. (1998). Epidemiology of osteosarcoma and Ewings-sarcoma in childhood - a study of 305 cases by the childrens cancer group. *Cancer, 83*(7), 1440-1448.

*Buckley, J. D., Robison, L. L., Swotinsky, R., Garabrant, D. H., LeBeau, M., Manchester, P., Nesbit, M. E., Odom, L., Peters, J. M., Woods, W. G., & Hammond, G. D. (1989). Occupation exposures of parents of children with acute nonlymphocytic leukemia: a report from the Children's Cancer Study Group. *Cancer Res, 49*, 4030-4037.

*Bullman, T., Kang, H., & Thomas, T. (1991). Posttraumatic stress disorder among Vietnam veterans on the Agent Orange registry: a case-control analysis. *Ann Epidemiol, 1*, 505-512.

Bullman, T., Kang, H., & Watanabe, H. (1990). Proportionate mortality among US Army Vietnam veterans who served in military region 1. *Am J Epidemiol, 131*, 517-521.

Bullman, T. A., & Kang, H. K. (1994). The effects of mustard gas, ionizing radiation, herbicides, trauma, and oil smoke on US military personnel: The results of veteran studies. *Annu Rev Public Health, 15*, 69-90.

Busby, C., & Cato, M. S. (1998). Cancer in the offspring of radiation workers. Exposure to internal radioisotopes may be responsible. *BMJ, 316*(7145), 1672-1673; discussion 1673.

Byrne, J. (1999). Long-term genetic and reproductive effects of ionizing radiation and chemotherapeutic agents on cancer patients and their offspring. *Teratology, 59*, 210-215.

Byrne, J., Mulvihill, J. J., Myers, M. H., Connelly, R. R., Naughton, M. D., Krauss, M. R., Steinhorn, S. C., Hassinger, D. D., Austin, D. F., Bragg, K., Holmes, G. F., Holmes, F. F., Latourette, H. B., Weyer, P. J., Meigs, J. W., Teta, M. J., Cook, J. W., & Strong, L. C. (1997). Effects of treatment on fertility in long-term survivors of childhood or adolescent cancer. *N Engl J Med, 317*(21), 1315-1321.

*Byrne, J., Rasmussen, S., Steinhorn, S., Connelly, R., Myers, M., Lynch, C., Flannery, J., Austin, D., Holmes, F., Holmes, G., Strong, L., & Mulvihill, J. (1998). Genetic disease in offspring of long-term survivors of childhood and adolescent cancer. *Am J Hum Genet, 62*, 45-52.

*Caldwell, G. G., Kelley, D. B., & Heath, C. W. (1980). Leukemia among participants in military maneuvers at nuclear bomb test. A preliminary report. *JAMA, 224*, 1575-1578.

*Caldwell, G. G., Kelley, D. B., Zack, M., Falk, H., & Heath, C. (1983). Mortality and cancer frequency among military nuclear test (SMOKY) participants, 1957 through 1979. *JAMA, 250*, 620-624.

Caldwell, G. (1990). Twenty-two years of cancer cluster investigations at the Centers for Disease Control. *Am J Epidemiol, 132*(Suppl. No. 1), S43-S47.

Caldwell, G., Kelley, D., Heath, C., & Zack, M. (1984). Polycythemia vera among participants of a nuclear weapons test. *JAMA, 252*(5), 662-664.

*Can, N. (1984). Effects on offspring of paternal exposure to herbicides. In A. H. Westing (Ed.), *Stockholm International Peace Institute. Herbicides in war: the long-term ecological and human consequences* (pp. 137-140). London: Taylor and Francis.

Carmelli, D., Hofherr, L., Tosmic, J., & Morgan, R. (1981). *A case-control study of the relationship between exposure to 2,4 - D and spontaneous abortions in humans.*: SRI International. Prepared for the National Forest Products Association and the US Department of Agriculture, Forest Services. (Not accessed)

*Caselli, L. T., & Motta, R. W. (1995). The effect of PTSD and combat level on Vietnam veterans' perceptions of child behavior and marital adjustment. *J Clin Psychol, 51*(1), 4-12.

Catherall, D. (1997). Family treatment when a member has PTSD. *NCP Clinical Quarterly, 7(2) Spring*.

*Centers for Disease Control. (1988a). Health status of Vietnam Veterans: I. Psychosocial characteristics. *JAMA, 259*, 2701-2702.

*Centers for Disease Control. (1988b). Health status of Vietnam Veterans: II. Physical health. *JAMA, 259*, 2708-2714.

*Centers for Disease Control. (1988c). Health status of Vietnam veterans. III. Reproductive outcomes and child health. The Centers for Disease Control Vietnam Experience Study. *JAMA, 259*(18), 2715-2719.

*Central Regional Health Authority. (1996). *Physical, neurological and sensory disability services* (Strategy document). Wellington: Central Regional Health Authority.

*Chamberlain, K., Vincent, C., & Long, N. (1994). *New Zealand Vietnam War Veterans twenty years on: II: Post-traumatic stress disorder and its effects*. Palmerston North: Department of Psychology, Massey University.

*Chapman, C., Stott, S., Port, R. V., & Nicol, R. (2000). Genetics of club foot in Maori. *J Med Genet, 37*, 680-683.

Chinh, R. R., Phi, P. T., & Thuy, N. T. (1996). Sperm auto-antibodies and anti-nuclear antigen antibodies in chronic dioxin-exposed veterans. *Chemosphere, 32*(3), 525-530.

Clarke, R. (1998). Report on a recent publication: a records linkage study of the gardner hypothesis, *Low doses of ionizing radiation: biological effects and regulatory control. Invited papers and discussions* (pp. 209-213): IAEA, Austria.

*Clarke, R. (2000). UNSCEAR 2000 Report. *Radiological Protection Bulletin, 224*, 5-9.

*Cochrane Collaboration. (2000). *Cochrane Collaboration Reviewers Handbook* (Vol. Version 4).

*Cocks, E., & Stehlik, D. (1996). History of services. In J. Annison & J. Jenkinson & W. Sparrow & E. Bethune (Eds.), *Disability*. South Australia: Nelson ITP.

Cohen, B. H., Lilienfeld, A. M., Kramer, S., & Hyman, L. C. (1977). Parental factors in Down's syndrome-results of the second Baltimore case-control stugy. pp. 301-52. *In: Hook EB, Porter IH, ed. Population cytogenetics. New York, Academic Press, 455*.

Colt, J. S., & Blair, A. (1998). Parental occupational exposures and risk of childhood cancer. *Environl Health Perspect, 106*(Suppl 3), 909-925.(Abstract only)

Committee on the Biological Effects of Ionizing Radiation (BEIR V). (1990). *Health effects of exposure to low levels of ionizing radiation: BEIR V*. Washington D.C.: National Academy Press.

Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange. (1999). *Veterans and Agent Orange. Update 1998*. Washington D.C.: National Academy Press.

*Committee to Review the Health Effects in Vietnam Veterans of Exposure to Agent Orange. (2001). *Veterans and Agent Orange. Update 2000 [Prepublication copy]*. Washington D.C.: National Academy Press.

*Commonwealth Department of Veterans' Affairs. (1998a). *Morbidity of Vietnam Veterans: A study of the health of Australia's Vietnam veteran community. Volume 1 Male Vietnam Veterans Survey and Community Comparison Outcomes*. Canberra: Commonwealth Department of Veterans' Affairs.

Commonwealth Department of Veterans' Affairs. (1998b). *Morbidity of Vietnam Veterans: A study of the health of Australias Vietnam veteran community. Volume 2 Female Vietnam Veterans Survey and Community Comparison Outcomes*. Canberra: Commonwealth Department of Veterans' Affairs.

*Constable, J. D., & Hatch, M. C. (1985). Reproductive effects of herbicide exposure in Vietnam: recent studies by the Vietnamese and others. *Teratog Carcinog Mutagen, 5*, 231-250.

Cook, R. R. (1980). Agent Orange and spontaneous abortions. *JAMA, 243*, 1423.

Cookson, C. (1979). Emergence ban on 2,4,5,-T herbicide in US. *Nature, 278*, 108-109.

Cordier, S., Lefeuvre, B., Filippini, G., Perisbonet, R., Farinotti, M., Lovicu, G., & Mandereau, L. (1997). Parental occupation, occupational exposure to solvents and polycyclic aromatic hydrocarbons and risk of childhood brain tumors (italy, france, spain). *Cancer Causes Control, 8*(5), 688-697.

Correa-Villasenor, A., Ferencz, C., Boughman, J., Neill, C., & The Baltimore Washington Infant Study Group. (1991). Total anomalous pulmonary venous return: Familial and environmental factors. *Teratology, 44*, 415-428.

*Courtney, K. D., & Moore, J. A. (1971). Teratology studies with 2,4,5-T and 2,3,7,8-TCDD. *Toxicol Appl Pharmacol, 20*, 396-403.

Cowan, D. N., DeFraites, R. F., Gray, G. C., Goldenbaum, M. B., & Wishik, S. M. (1997). The risk of birth defects among children of Persian Gulf War veterans [see comments]. *N Engl J Med, 336*(23), 1650-1656.

Cowan, D. N., Gray, G. C., & DeFraites, R. F. (1998). Counterpoint: Responding to inadequate critique of birth defects paper [comment]. *Am J Epidemiol, 148*(4), 326-327; discussion 334-328.

*Crawford, J. (1989). *The involvement of the Royal New Zealand Navy in the British nuclear testing programmes of 1957 and 1958.* Wellington: Ministry of Defence.

Croen, L. A., Shaw, G. M., Sanbonmatsu, L., Selvin, S., & Buffler, P. A. (1997). Maternal residential proximity to hazardous waste sites and risk for selected congenital malformations [see comments]. *Epidemiology, 8*(4), 347-354.

*Crossen, P. E., Morgan, W. F., Horan, J. J., & Stewart, J. (1978). Cytogenetic studies of pesticide and herbicide sprayers. *NZ J Med, 88*, 192-195.

Crow, J. F. (1955). Comparison of fetal and infant death rates in progeny of radiaologists and pathologists. *Am J Roentgenol, 73*, 467. (Not accessed)

Crow, J. F. (1981). *How well can we assess genetic risk? Not very.* Washington DC: National Council on Radiation Protection and Measurements.

*Czeizel, A. E., & Dudas, I. (1992). Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med, 327*, 1832-1835.

Dai, L. C., Phuong, N. T. N., Thom, L. H., Thuy, T. T., Van, N. T. T., Cam, L. H., Chi, H. T. K., & Thuy, L. B. (1990). A comparison of infant mortality rates between two Vietnamese villages sprayed by defoliants in wartime and one unsprayed village. *Chemosphere, 20*, 1005-1912.

*Dalager, N. A., Kang, H. K., & Mahan, C. M. (2000). Cancer mortality among the highest exposed US atmospheric test participants. *J Occup Environ Med, 42*, 798-805.

Dalton, L. (1991). *Radiation exposures: The hidden story of the health hazards behind official 'safety' standards*. Australia: Scribe.(Not accessed)

Dan, B. B. (1984). Vietnam and birth defects [editorial]. *JAMA, 252*(7), 936-937.

Dan, E. (1995). *Secondary traumatization in the adolescent offspring of Vietnam veterans with Post Traumatic Stress Disorder.* Unpublished PhD, The Fielding Institute. (Not accessed)

Daniels, J., Olshan, A. F., & Savitz, D. A. (1997). Pesticides and childhood cancers. *Environ Health Perspect, 105*, 1068-1077.

Dansak, D. A. (1998). Childhood abuse and parental disorders reported by Navy outpatient mental health patients. *Military Medicine, 163*(8), 510-514.(Not accessed)

*Dansby, V. S., & Marinelli, R. P. (1999). Adolescent children of Vietnam combat veteran fathers: a population at risk. *J Adolescence, 22*(3), 329.

*Darby, S., Kendall, G., Fell, T., O'Hagen, J., Muirhead, C., Ennis, J., Ball, A., DEnnis, J., & Doll, R. (1988). A summary of the mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes. *BMJ, 296*, 332-338.

Darby, S. C. (1994). Cancer in nuclear test veterans: Author's reply: [letter]. *BMJ, 308*, 339-340.

Darby, S. C., & Doll, R. (1987). Fallout, radiation doses near Dounreay, and childhood leukaemia. *BMJ, 294*, 637-638.

Darby, S. C., Kendall, G. M., Fell, T. P., Doll, R., Goodill, A. A., Conquest, A. J., Jackson, D. A., & Haylock, R. G. (1993a). Further follow up of mortality and incidence of cancer in men from the United Kingdom who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes [see comments]. *BMJ, 307*(6918), 1530-1535.

Darby, S. C., Kendall, G. M., Fell, T. P., Doll, R., Goodill, A. A., Conquest, A. J., Jackson, D. A., & Haylock, R. G. (1993b). *Mortality and cancer incidence 1952-1990 in UK participants in the UK atmospheric nuclear weapon tests and experimental programmes*.: National Radiological Protection Board.

*Davidson, A., & Mellor, D. (2001). The adjustment of children of Australian Vietnam veterans: Is there evidence for the transgenerational transmission of the effects of war-related trauma. *Accepted for publication Australian & New Zealand Journal of Psychiatry*.

*Davidson, J. R., Smith, R. D., & Kudler, H. S. (1989). Familial psychiatric illness in chronic posttraumatic stress disorder. *Compr Psychiatry, 30*(4), 339-345.

*De Wals, P., Bertrand, F., De la Mata, I., & Lechat, M. (1988). Chromosomal anomalies and Chernobyl. *Int J Epidemiol, 17*, 230-231.

Deane, F., MacDonald, C., Chamberlain, K., Long, N., & Davin, L. (1998). New Zealand Vietnam veteran's family programme, nga whanau a tu (families of war): Development and outcome. *Australian & New Zealand Journal of Family Therapy, 19*(1), 1-10.

Deprez, R. D., Carvette, M. E., & Agger, M. S. (1991). *The health and medical status of Maine veterans: a report to the Bureau of Veterans Services, Commission of Vietnam and Atomic Veterans.*: Public Health Resource Group.(Not accessed)

*Dimich-Ward, H., Hertzman, C., Teschke, K., Hershler, R., Marion, S. A., Ostry, A., & Kelly, S. (1996). Reproductive effects of paternal exposure to chlorophenate wood preservatives in the sawmill industry. *Scand J Work Environ Health, 22*, 267-273.

*Dodds, L., Marrett, L., Tomkins, D. J., Green, B., & Sherman, G. (1993). Case-control study of congenital anomalies in children of cancer patients. *BMJ, 307*, 164-168.

*Doll, R. (1998). Effects of small doses of ionising radiation. *Journal of Radiological Protection, 18*(3), 163-174.

*Doll, R., Evans, H. J., & Darby, S. C. (1994). Paternal exposure not to blame. *Nature, 367*, 678-680.

Doll, R., Sharp, C., Muirhead, C., & Darby, S. (1998). Study of UK men who had participated in the UK nuclear weapons test programme [letter]. *Journal of Radiological Protection, 18*(3), 209-210.

*Donovan, J. W., MacLennan, R., & Adena, M. (1984). Vietnam service and the risk of congenital anomalies. A case-control study. *Med J Aust, 140*(7), 394-397.

Donovan, J. W., Stevenson, & Ariotti. (1983). *Survey of health of former atomic test personnel.* Canberra: Commonwealth Department of Health. (Not accessed)

*Doyle, P., Maconochie, N., Roman, E., Davies, G., Smith, P. G., & Beral, V. (2000). Fetal death and congenital malformation in babies born to nuclear industry employees: report from the nuclear industry family study. *Lancet, 356*(9238), 1293-1299.

Doyle, R., E, Maconochie, N. (1997). Birth defects among children of persian gulf war veterans. *N Engl J Med, 337*(16), 1175-1176.

*Draper, G. J., Little, M. P., Sorahan, T., Kinlen, L. J., Bunch, K. J., Conquest, A. J., Kendall, G. M., Kneale, G. W., Lancashire, R. J., Muirhead, C. R., O'Connor, C. M., & Vincent, T. J. (1997). Cancer in the offspring of radiation workers: a record linkage study. *BMJ, 315*, 1181-1188.

Driscoll, R. (1998). *Epidemiologic study of adverse reproductive outcomes among women in the U. S forest service. Section 2, health hazard evaluation report no. 93-1035-2686.* Washington DC: US Department of Agriculture, U.S. Forest service. (Not accessed)

Dummer, T. J. B., Dickinson, H. O., Pearce, M. S., Charlton, M. E., Smith, J., Salotti, J., & Parker, L. (1998). Stillbirth rates around the nuclear installation at Sellafield, North West England: 1950-1989. *Int J Epidemiol, 27*, 74-82.

*Egeland, G., Sweeney, M., Fingerhut, M., Wille, K., Schnorr, T., & Halperin, W. (1994). Total serum testosterone and gonadotropins in workers exposed to dioxin. *Am J Epidemiol, 139*, 272-281.

Elwood, J. M., & Elwood, J. H. (1980). *Epidemiology of anencephalus and spina bifida*. Oxford: Oxford University Press.(Not accessed)

Elwood, J. M., Little, J., & Elwood, J. H. (1992). *Epidemiology and control of neural tube defects* (2nd Ed ed.): Oxford University Press.(Not accessed)

*Erickson, J. D., Mulinare, J., & McClain, P. W. (1984a). *Vietnam Veterans' risks for fathering babies born with birth defects*. Atlanta: Centers for Disease Control.

*Erickson, J. D., Mulinare, J., McClain, P. W., Fitch, T. G., James, L. M., McClearn, A. B., & Adams, M. J., Jr. (1984b). Vietnam veterans' risks for fathering babies with birth defects. *JAMA, 252*(7), 903-912.

Ericson, A., Kallen, B., & Winberg, J. (1977). Surveillance of malformations at birth: a comparison of two record systems run parallel. *Int J Epidemiol, 6*, 35-41.

Evans, R., Webb, K., Knutsen, A., Roodman, S., Robers, D., Bagby, J., Garrett, W., & Andrews, J. (1988). A medical follow-up of the health effects of long-term exposure to 2,3,4,8-tetrachlorodibenzo-p-dioxin. *Arch Environ Health, 43*, 273-278.

*Fear, B., Roman, E., Reeves, G., & Pannett, B. (1998). Childhood cancer and paternal employment in agriculture: the role of pesticides. *Br J Cancer, 77*(5), 825-829.

Fein, G. G., Jacobson, J. L., Jacobson, S. W., Schwartz, P. M., & Dowler, J. K. (1984). Prenatal exposure to polychlorinated biphenyls: effects on birth size and gestational age. *J Pediatr, 105*, 315-320.

*Fergusson, D., Horwood, J., & Lynskey, M. (1997). Children and adolescents. In E. P. a. C. SCD (Ed.), *Mental health in New Zealand from a public health perspective*. Wellington: Ministry of Health.

Fett, M. J., Dun, M., & Adena, M. (1984). The mortality study, part 1: a retrospective cohort study of mortality among Australian national servicemen of vietnam conflict. *Australian Government Printing Service*. (Not accessed)

Field, B., & Kerr, C. (1979). Herbicide use and incidence of neural-tube defects. *Lancet, 1*(1341-1342).

*Field, B., & Kerr, C. (1988). Reproductive behaviour and consistent patterns of abnormality in offspring of Vietnam veterans. *J Med Genet, 25*, 819-826.

Figatalamanca, I., & Hatch, M. C. (1994). Reproduction and the workplace - what we know and where we go from here. *Int J Occup Med J, 3*(3), 279-303.

Figley, C. R. (1988). A five-phase treatment of Post-Traumatic Disorder in families. *J Trauma Stress, 1*, 127-141.

*Figley, C. R., & Kleber, R. J. (1995). Beyond the "victim": Secondary traumatic stress. In R. J. Kleber & C. R. Figley (Eds.), *Beyond trauma: Cultural and societal dynamics. Plenum series on stress and coping.* (pp. 75-98). New York, NY, USA: Plenum Press.

*Finkelstein, V. (1998). The commonality of disability. In J. Swain & V. Finklestein & S. French & M. Oliver (Eds.), *Disabling barriers - enabling environments* (pp. 9-17). London: Sage Publications.

Fitzgerald, J. (1993). *Needs assessment for Alaskan families of combat veterans.* Unpublished MS, University of Alaska, Anchorage. (Not accessed)

*Fowkes, F., & Fulton, P. (1991). Critical appraisal of published research: introductory guidelines. *BMJ, 302*, 1136-1140.

Frederikson, L., Chamberlain, K., & Long, N. (1996). Unacknowledged casualties of the Vietnam war: Experiences of partners of New Zealand veterans. *Qualitative Health Research, 6*(1), 49-70.

*Friedman, J. M. (1984). Does Agent Orange cause birth defects? *Teratology, 29*, 193-221.

Friedman, M. (1998). Current and future drug treatments for PTSD. *Psychiatric Annals, 28*, 461-468.

Friedman, M. J. (1991). Biological approaches to the diagnosis and treatment of post-traumatic stress disorder. *J Trauma Stress, 4*, 67-91.

Garcia, A. M. (1998). Occupational exposure to pesticides and congenital malformations: a review of mechanisms, methods, and results. *Am J Ind Med, 33*, 232-240.

*Garcia, A. M., Benavides, F. G., Fletcher, T., & Orts, E. (1998). Paternal exposure to pesticides and congenital malformations. *Scand J Work Environ Health, 24*(6), 473-480.

*Garcia, B. (1994). Social-psychological dilemmas and coping of atomic veterans. *Am J Orthopsychiatry, 64*(4), 651-655.

Gardner, M. (1988). Cancer among participants in tests of British nuclear weapons. *BMJ, 296*, 309-310.

Gardner, M., Hal, A., Downes, S., & Terrell, J. (1987a). Follow up study of children born elsewhere but attending schools in Seascale, West Cumbria (schools cohort). *BMJ, 295*, 819-822.

Gardner, M., Hall, A. J., Downes, S., & Terrell, J. D. (1987b). Follow up study of children born to mothers resident in Seascale, West Cumbria (birth cohort). *BMJ, 295*, 822-827.

Gardner, M., Hall, A. J., Snee, M. P., Downes, S., Powell, C. A., & Terrell, J. D. (1990a). Methods and basic data of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria. *BMJ, 300*, 429-434.

*Gardner, M. J. (1992). Paternal occupations of children with leukaemia. *BMJ, 305*, 715.

*Gardner, M. J., Snee, M. P., Hall, A. J., Powell, C. A., Downes, S., & Terrell, J. D. (1990b). Results of case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in west Cumbria. *BMJ, 300*, 423-429.

*Garry, V. F., Schreinemachers, D., Harkins, M. E., & Griffith, J. (1996a). Pesticide appliers, biocides, and birth defects in rural Minnesota. *Environmental Health Perspective, 104*, 394-399.

Garry, V. F., Tarone, R. E., Long, L., Griffith, J., Kelly, J., & Burroughs, B. (1996b). Pesticide appliers with miced pesticide exposure: G-banded analysis and possible relationship to non-Hodgkin's lymphoma. *Cancer Epidemiol Biomarkers Prev, 5*(1), 11-16.

Gill, K. (2001). Ace procedure.: personal communication.

*Glassman, J. N., Magulac, M., & Darko, D. F. (1987). Folie a famille: shared paranoid disorder in a Vietnam veteran and his family. *Am J Psychiatry, 144*(5), 658-660.

*Goldberg, J. (1992). Health effects of military service. Lessons learned from the Vietnam experience. *Ann Epidemiol, 2*(6), 841-853.

Gordon, J., & Shy, C. (1981). Agricultural chemical use and congenital cleft lip and/or palate. *Arch Environ Health, 36*, 213-221.

Graham, S., Levin, M. L., & Lilienfeld, A. M. (1966). Preconception, intrauterine and postnatal irradiation as related to leukaemia. *J Natl Cancer Inst, 19*, 347-371.

*Grassman, J. A., Masten, S. A., Walker, N. J., & Lucier, G. W. (1998). Animal models of human response to dioxins. *Environmental Health Perspective, 106*, 761-775.

Gratton, R. T. (1998). *A descriptive study of children born to Vietnam veterans diagnosed with PTSD.* Unpublished PhD, Smith College for Social Work.(Not accessed)

Gray, G., Knoke, J., Berg, S. W., Wignall, F. S., & Barrett-Connor, E. (1998). Counterpoint: Responding to suppositions and misunderstandings. *Am J Epidemiol, 148*(4), 328-333.

*Gray, L. E. J., & Ostby, J. S. (1995). In utero 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) alters reproductive morphology and function in female rat offspring. *Toxicol Appl Pharmacol, 133*, 285-294.

Green, D. M., Fiorello, A., Zevon, M., Hall, B., & Seigelstein, N. (1997a). Birth defects and childhood cancer in offspring of survivors of childhood cancer. *Arch Pediatr Adolesc Med, 151*, 379-383.

Green, D. M., Hall, B., & Zevon, M. A. (1989). Pregnancy outcome after treatment for acute lymphoblastic leukemia during childhood or adolescence. *Cancer, 64*, 2335-2339.

Green, D. M., Zevon, M. A., Lowrie, G., Seigelstein, N., & Hall, B. (1991). Congenital anomalies in children of patients who received chemotherapy for cancer in childhood and adolescence. *N Engl J Med, 325*(3), 141-146.

*Green, L. M., Dodds, L., Miller, A. B., Tomkins, D. J., Li, J. H., & Escobar, M. (1997b). Risk of congenital anomalies in children of parents occupationally exposed to low level ionising radiation. *Occup Environ Med, 54*(9), 629-635.

Grillon, C., Dierker, L., & Merikangas, K. R. (1998). Fear-potentiated startle in adolescent offspring of parents with anxiety disorders. *Biol Psychiatry, 44*(10), 990-997. (Not accessed)

Gulbransen, G. (1989). New Zealand radiation veterans: Christmas Island 1957-58. *N Z General Practice, 2*, 11-15.

Haeusler, M., Berghold, A., Schoell, W., Hofer, P., & Schaffer, M. (1992). The influence of the post-Chernobyl fallout on birth defects and abortion rates in Austria. *Am J Obstet Gynecol, 167*, 1025-1031.

*Hall, W. (1986). The Agent Orange controversy after the Evatt Royal Commission. *Med J Aust, 145*, 219-225.

Hall, W. (1989). The logic of a controversy: The case of Agent Orange in Australia. *Soc Sci Med, 29*(4), 537-?

*Hanify, J. A., Metcalf, P., & Nobbs, C. L. (1981). Aerial spraying of 2,4,5-T and human birth malformations: An epidemiologic investigation. *Science, 212*, 349-351.

*Hanify, J. A., Metcalf, P., Nobbs, C. L., & Worsley, K. J. (1980). Congenital malformations in the newborn in Northland 1966-1977. *NZ J Med, 92*, 245-248.

*Hankin, C., Spiro, A., Miller, D., & LKazis. (1999). Mental health disorders and mental health treatment among US Department of Veterans Affairs Outpatients: The Veterans Health Study. *Am J Psychiatry, 156*, 1924-1930.

*Harkness, L. L. (1989). *Children of war: A study of the offspring of Vietnam veterans with Post Traumatic Stress Disorder.* Unpublished PhD, New York University.

*Harrison, J. (1993). Medical responsibilities. In J. Swain & V. Finklestein & S. French & M. Oliver (Eds.), *Disabling barriers-enabling societies*. London: Sage Publications.

*Hartikainen-Sorri, A.-L., & Sorri, M. (1989). Occupational and socio-medical factors in preterm birth. *Obstet Gynecol, 74*(1), 13-16.

Hatch, M. C., & Stein, Z. A. (1986). Agent Orange and risks to reproduction. *Teratog Carcinog Mutagen, 6*, 185-202.

Hawkins, M. M. (1991). Is there evidence of a therapy-related increase in germ cell mutation among childhood cancer survivors? *J Natl Cancer Inst, 83*(22), 1643-1650.

Hawkins, M. M., Draper, G. J., & Winter, D. L. (1995). Cancer in the offspring of survivors of childhood leukaemia and non-Hodgkin lymphomas. *Br J Cancer, 71*, 1335-1339.

Hawkins, M. M., & Smith, R. A. (1989). Pregnancy outcomes in childhood cancer survivors: provbable effects of abdominal irradiation. *Int J Cancer, 43*, 399-402.

*Heacock, H., Hertzman, C., Demers, P. A., Gallagher, R., Hogg, R. S., Teschke, K., Hershler, R., Bajdik, C. D., Dimich-Ward, H., Marion, S. A., Ostry, A., & Kelly, S. (2000). Childhood cancer in the offspring of male sawmill workers occupationally exposed to chlorophenate fungicides. *Environmental Health Perspective, 108*, 499-503.

Heacock, H., Hogg, R., Marion, S. A., Hershler, R., Teschke, K., Dimich-Ward, H., & Demers, P. (1998). Fertility among a cohort of male sawmill workers exposed ot chlorophenate fungicides. *Epidemiology, 7*, 352-357.

*Hennekens, C., & Buring, J. (1987). *Epidemiology in Medicine*. Boston/Toronto: Little, Brown and Co.

Henriksen, G. L., & Michalek, J. E. (1996). Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology, 7*(4), 454-455.

Henriksen, G. L., Michalek, J. E., Swaby, J. A., & Rahe, A. J. (1996). Serum dioxin, testosterone, and gonadotropins in veterans of Operation Ranch Hand. *Epidemiology, 7*(4), 352-357.

*Hicks, N., Zack, M., Caldwell, G. G., Fernback, D. J., & Falletta, J. M. (1984). Childhood cancer and occupational radiation exposure in parents. *Cancer, 53*, 1637-1643.

*Hill, M. (2001). Support services for people with disability.: personal communication.

Hjalmars, E. A. (1994). Risk of acute childhood leukaemia in Sweden after the Chernobyl reactor accident. *BMJ, 309*(16), 154.(Not accessed)

Hoar, S. K., Morrison, A. S., Cole, P., & Silverman, D. T. (1980). An occupation and exposure linkage system for the study of occupational carcinogenesis. *J Occup Med, 22*, 722-726.

Hoffman, R. E. (1986). Health effects of long term exposure to 2,3,7,8 - Tetrachlorodibenzo - p Dioxin. *JAMA, 255*(15), 2031-2038.

Hogg, R. D. (1987). Royal commission on the use and effects of chemical agents on Australian personnel in Vietnam: an assessment and recommendatons as a basis for a final cabinet submission. *The Senate*.(Not accessed)

*Huakau, G., & Bray, A. (2000). *Talking disabilities from a pacific perspective*. Dunedin: Donald Beasley Institute Inc.

Humphrey, G. F. (1986). Scientists and Royal Commissions. *Search, 17*, 63-64.

IARC Study Group on Cancer Risk among Nuclear Industry Workers. (1994). Direct estimates of cancer mortality due to low doses of ionising radiation: an international study. *Lancet, 344*, 1039-1043.

IARC. (1997). Polychlorinated dibenzo-para-dioxins and polychlorinated dibenzofurans. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans.* Col, 69. Lyon.

*Institute of Medicine. (1995). *Adverse reproductive outcomes in families of atomic veterans: The feasibility of epidemiologic studies*. Washington, D.C.: National Academy Press.

International Atomic Energy Agency. (1978, 13-17 March). *Late biological effects of ionizing radiation. Proceedings of a symposium, Vienna*, Vienna.

International Atomic Energy Agency. (1998). *Low doses of ionizing radiation: biological effects and regulatory control. Invited papers and discussions*.: IAEA, Austria.

Jablon, S. (1987). Re: "Do Atomic Veterans have excess cancer? New results correcting for the healthy soldier bias" [letter]. *Am J Epidemiol, 126*(6), 1214.

Jablon, S., Hrubec, Z., & Boice, J. (1991). Cancer in populations living near nuclear facilities - A survey of mortality nationwide and incidence in two states. *JAMA, 265*(11), 1403-1408.

Jablon, S., & Kato, H. (1970). Childhood cancer in relation to prenatal exposure to A-bomb radiation. *Lancet*, 1000-1003.(Not accessed)

*Jackson, R. (2001). *Unpublished paper*. Auckland: Effective Practice Institute Division of Community Health, University of Auckland.

James, W. (1997). Reproductive effects of male dioxin exposure. The use of offspring sex ratios to detect reporductive effects of male exposure to dioxins. *Environmental Health Perspective, 105*(2), 162-163.

Jansson, B., & Vogg, L. (1989). Dioxin from Swedish municipal incinerators and the occurance of cleft lip and palate malformations. *Int J Environ Stud, 34*, 99-104.

Jensen, P. S., Martin, D., & Watanabe, H. (1996). Children's response to parental separation during operation desert storm. *J Am Acad Child Adolesc Psychiatry, 35*(4), 433-441.(Not accessed)

Johnson, J. (1996). Veterans study suggests dioxin, spina bifida link. *Environmental Science & Technology, 30*(5), A 193.

Johnson, J. C., & Thaul, S. (1996). *Mortality of veteran participants in the CROSSROADS nuclear test*. Washington D.C.: National Academy Press.

*Johnson, J. C., Thaul, S., Page, W. F., & Crawford, H. (1997). Mortality of veteran participants in the CROSSROADS nuclear test. *Health Phys, 73*(1), 187-189.

*Jordan, B. K., Marmar, C. R., Fairbank, J. A., Schlenger, W. E., & et al. (1992). Problems in families of male Vietnam veterans with posttraumatic stress disorder. *J Consult Clin Psychol, 60*(6), 916-926.

*Jordan, B. K., William, E. S., Hough, R., Kulka, R. A., Weiss, D., Fairbank, J. A., & Marmar, C. R. (1991). Lifetime and current prevalence of specific psychiatric disorders among Vietnam veterans and controls. *Arch Gen Psychiatry, 48*, 207-215.

Josefson, D. (1997). US admits radiation experiments on 20000 veterans [news]. *BMJ, 315*(7108), 566.

Kang, H. K., Mahan, C. M., Lee, K. Y., Magee, C. A., Mather, S. H., & Matanoski, G. (2000). Pregnancy outcomes among U.S. women Vietnam veterans. *Am J Ind Med, 38*(4), 447-454.

*Kendler, K., Kessler, R., & al., e. (1993). The prediction of major depression in women: Towards an integrated aetiological model. *Am J Psychiatry, 150*, 863-870.

*Kendrick, M. (1997). The leadership challenge of service quality. *Interaction, 11*(1).

*Kendrick, M. (1999a). Formal individualisation systems: their potential & limitations. *Crucial Times, July 1999*, 9-11.

*Kendrick, M. (1999b). Some observations on key leadership challenges in the field of disability. www.srv.21century.com.au/resource/MK1.htm.

*Kendrick, M. (1999c). *Some observations on what one person can do in human services.* Paper presented at the Sharing the road in 1999: proceedings of the 1999 Conference for direct support workers, Brisbane.

*Kendrick, M. (2000a). Advocacy and the challenging of authority.

*Kendrick, M. (2000b). *An evaluation of the Nova Scotia Community Based Options community residential service delivery system.* Nova Scotia: Nova Scotia Department of Community Services.

*Kendrick, M. (2000c). Person-centredness: a characteristic of people, not systems. *Crucial Times, 18*, 9-11.

*Kendrick, M. (2000d, March 2000). *When people matter more than systems.* Paper presented at the The Promise of Opportunity, Albany, New York.

Kenney, L. B., Nicholson, H. S., Brasseux, C., Mills, J. L., Robison, L. L., Zeltzer, L. K., Meadows, A. T., Reaman, G. H., & Byrne, J. (1996). Brith defects in offspring of adult survivors of childhood acute lymphoblastic leukemia. *Amercian Cancer Society, 78*(1), 169-176.

Khoury, M. J., Botto, L., Mastroiacovo, P., Skjaerven, R., Castilla, E., & Erickson, J. D. (1994). Monitoring for multiple congenital anomalies: an international perspective. *Epidemiol Rev, 16*, 335-350.

*Kingi, J., & Bray, A. (2000). *Maori concepts of disability.* Dunedin: Donald Beasley Institute Inc.

Kinlen, L. J. (1993). Can paternal preconceptional radiation account for the increase of leukaemia and non-Hodgkins lymphoma in Seascale? *BMJ, 306*, 1718-1721.

*Kinlen, L. J., Clarke, K., & Balkwill, A. (1993). Paternal preconceptional radiation exposure in the nuclear industry and leukaemia and non-Hodgkin's lymphoma in young people in Scotland. *BMJ, 306*, 1153-1158.

Kinlen, L. J., Dickson, M., & Stiller, C. A. (1995). Childhood leukaemia and non-Hodgkin's lymphoma near large rural construction sites, with a comparison with Sellafield nuclear site. *BMJ, 310*, 763-768.

*Kiripalai, H., Parkin, P., Willan, A., Fehlings, D., Rosenbaum, P., King, D., & Nie, A. V. (2000). Quality of life in spina bifida: importance of parental hope. *Arch Dis Child, 83*, 293-297.

Kizer, K. W. (1996). From the Veterans Health Administration. *JAMA, 275*, 351.

*Kogevinas, M., & Sala, M. (1998). Pesticides and congenital malformations - how many studies will it take to reach a conclusion? [Editorial]. *Scand J Work Environ Health, 24*, 445-447.

*Kristensen, P. (1999). Parental exposure, adverse pregnancy and offspring effects -perspectives in developmental epidemiology. *Scand J Work Environ Health, 25*(6), 541-549.

*Kristensen, P., Irgens, L. M., Andersen, A., Bye, A. D., & Sundheim, L. (1997). Birth defects among offspring of Norwegian farmers. *Epidemiology, 8*, 537-544.

*Kulka, R. A. S., William, E., Fairbank, J. A., Hough, R. L., Jordan, B. K., Marmar, C. R., & Weiss, D. S. (1988). *PTSD among Vietnam veterans: a family perspective (National Vietnam Veterans Readjustment Study).* Research Triangle Park, North Carolina: Research Triangle Institute.

Kunstadter, P. (1982). *A study of herbicides and birth defects in the Republic of Vietnam: An analysis of hospital records.* Washington, D.C.: National Academy Press.(Not accessed)

Lang, J. M., Lieberman, E., & Cohen, A. (1996). A comparison of risk factors for preterm labor and term small-for-gestational-age birth. *Epidemiology, 7*, 369-376.

Larson, S. B., Joffe, M., & Bonde, J. P. (1998). Time to pregnancy and exposure to pesticides in Danish farmers. *Occup Environ Med, 55*(4), 278-283.

LaVecchio, F. A., Pashayan, H. M., & Singer, W. (1983). Agent Orange and birth defects [letter]. *N Engl J Med, 308*(12), 719-720.

Lawson, R. (1994). Cancer in nuclear test veterans. Important questions unanswered [letter; comment]. *Br J Cancer, 308*(6924), 339; discussion 339-340.

Lawson, R. H. (1987). Radiation experiments on British soldiers [letter]. *Lancet, 2*(8572), 1404.

Leck, I. (1974). Causation of neural tube defects: Clues from epidemiology. *BMJ, 30*, 158-163.

*Leepson, M. (Ed.). (1999). *Websters New World Dictionary of the Vietnam War*. New York: Simon & Schuster, Inc.

Lerda, D., & Rizzi, R. (1991). Study of reproductive function in persons occupationally exposed to 2,4-dichlorophenoxyacetic acid (2,4-D). *Mutat Res, 262*, 47-50.

Levine, R. S., Hersch, C. B., & Hodder, R. A. (1990). Historical patterns of pesticide epidemiology research from 1945 to 1988. *Epidemiology, 1*, 181-184.

Lie, R., Irgens, L., Skjaerven, R., Reitan, J., Strand, P., & Strand, T. (1992). Birth defects in Norway by levels of external and food-based exposure to radiation from Chernobyl. *Amercian Journal of Epidemiology, 136*, 377-388.

*Lie, R. T., Heuch, I., & Irgens, l. (1994). Maximum likelihood estimation of the proportion of congenital malformations using double registration systems. *Biometrics, 50*, 433-444.

Limoli, C. L., Corcoran, J. J., Jordan, R., Morgan, W. F., & Schwartz, J. L. (2001). A role for chromosomal instability in the development of and selection for radioresistant cell variants. *Journal of Cancer, 84*(4), 489-492.

Limoli, C. L., Ponnaiya, J. J., Corcoran, J. J., Giedzinski, E., & Morgan, W. F. (2000). Chromosomal instability induced by heavy ion irradiation. *Int J Radiat Biol, 76*(12), 1599-1606.

*Lindstrom, G., Hooper, K., Petreas, M., Stephens, R., & Gilman, A. (1995). Workshop on perinatal exposure to dioxin-like compounds. *Environmental Health Perspective, 103*, 135-142.

*Little, J. (1993a). The Chernobyl accident, congenital abnormalities and other reproductive outcomes. *Paediatr Perinat Epidemiol, 7*(2), 121-151.

Little, J., & Elwood, J. H. (1992). Socio-economic status and occupation. In J. M. Elwood & J. Little & J. H. Elwood (Eds.), *Epidemiology and control of nueral tube defects. Monographs in epidemiology and biostatistics* (Vol. 20, pp. 456-520). Oxford: Oxford University Press.

Little, M. P. (1990a). A comparison between the risks of childhood leukaemia from parental exposure to radiation in the Sellafield workforce and those displayed among Japanese bomb survivors. *Journal of Radiological Protection, 10*, 185-198.

Little, M. P. (1990b). A comparison of the apparent risks of childhood leukaemia from parental exposure to radiation in the six months prior to conception in the Sellafield workforce and the Japanese bomb survivors. *Journal of Radiological Protection, 11*, 77-90.

Little, M. P. (1992). The risks of leukaemia and non-cancer mortality in the offspring of the Japanese bomb survivors and a comparison of leukaemia risks with those in the offspring of the Sellafield workforce. *Journal of Radiological Protection, 12*, 203-218.

Little, M. P. (1993b). A comparison of the risks of leukaemia in the offspring of the Japanese bomb survivors and those of the Sellafield workforce with those in the offspring of the Ontario and Scottish workforces. *Journal of Radiological Protection, 13*, 161-175.

*Little, M. P. (1999). A comparison of the risk of stillbirth associated with paternal pre-conception irradiation in the Sellafield workforce with that of stillbirth and untoward pregnancy outcome among Japanese atomic bomb survivors. *Journal of Radiological Protection, 19*(4), 361-373.

Little, M. P., Wakeford, R., & Charles, M. W. (1994). An analysis of leukaemia, lymphoma and other malignancies together with certain categories of non-cancer mortality in the first generation offspring (F1) of the Japanese bomb survivors. *Journal of Radiological Protection, 14*, 203-218.

Little, M. P., Wakeford, R., Charles, M. W., & Andersson, M. (1996). A comparison of the risks of leukaemia and non-Hodgkin's lymphoma in the first generation offspring (F1) of the Danish Thorotrast patients with those observed in other studies of parental preconception irradiation. *Journal of Radiological Protection, 16*(1), 25-36.

*Long, N., Chamberlain, K., & Vincent, C. (1992). The health and mental health of NZ Vietnam war veterans with post traumatic stress disorder. *NZ J Med, 105*, 417-419.

*Long, N., MacDonald, C., & Chamberlain, K. (1996). Prevalence of posttraumatic stress disorder, depression and anxiety in a community sample of New Zealand Vietnam war veterans. *Aust N Z J Psychiatry, 30*(2), 253-256.

Lord, B. I. (1999). Transgenerational susceptibility to leukaemia induction resulting from preconception, paternal irradiation. *Int J Radiat Biol, 75*(7).

*Lord, B. I., Woolford, L. B., Wang, L., McDonald, D., Lorimore, S. A., Stones, V. A., Wright, E. G., & Scott, D. (1998). Induction of lympho-haemopoietic malignancy: impact of preconception paternal irradiation. *Int J Radiat Biol, 74*(6), 721-728.

Lowengart, R. A., Peters, J. M., Cicioni, C., Buckley, J. D., Bernstein, L., Preston-Martin, S., & Rappaport, E. (1987). Childhood leukaemia and parents' occupational and home exposures. *J Natl Cancer Inst, 79*, 39-46.

*MacDonald, C. (1997). *Mortality and health effects in participants of atmospheric nuclear weapons tests: a critical review*.

MacDonald, C., Chamberlain, K., & Long, N. (1995). Posttraumatic stress disorder (PTSD) and its effects in Vietnam veterans: The New Zealand experience. *NZ J Psychol, 24*(2), 63-68.

*MacDonald, C., Chamberlain, K., & Long, N. (1997). Race, combat and PTSD in a community sample of New Zealand Vietnam war veterans. *J Trauma Stress, 10*(1), 117-124.

*MacDonald, C., Chamberlain, K., Long, N., & Flett, R. (1999). Posttraumatic stress disorder and interpersonal functioning in Vietnam War veterans: A mediational model. *J Trauma Stress, 12*(4), 701-707.

Macleod, A. D. (1991). Posttraumatic stress disorder in World War Two veterans. *NZ J Med, 104*, 285-288.

Maconochie, N., Doyle, P., Roman, E., Davies, G., Smith, P., & Beral, V. (1999). Nuclear industry family sutdy: methods and description of a United Kingdom study linking occupational information held by employers to reproduction and child health. *Occupational and Environmental Medicine, 56*, 793-801.

Magnani, C., Pastore, G., Luzzato, L., & Terracini, B. (1990). Parental occupation and other environmental factors in the etiology of leukemias and non-Hodgkin's lymphomas in childhood: A case-control study. *Tumori, 76*, 413-419.(Not accessed)

*Maher, C. (1999). Strengthening families through local area co ordination. *Crucial Times, July 1999*, 7.

Mannino, J. A. (1978). *Effects of chronic exposure to low doses of ionizing radiation on the reproductive performance and outcome of an exposed population.*, Wayne State University, Detroit, MI.(Not accessed)

Mantel, N. (1987). Do atomic veterans have excess cancer? New results correcting for healthy soldier bias. *Am J Epidemiol, 126*, 1214-1216.

*Marcias, M., Saylor, C., Kreh, S., Clifford, S., & Romanczuk, A. (2000). Predictors of support service interest and participation by families of children with spina bifida. *Rehabilitation Nursing, 25*(2), 54-58.

Marshall, E. (1985). GAO find errors in A-bomb test data [news]. *Science, 230*(4732), 1361.

Mastroiacovo, P., Spagnolo, A., Marni, E., Meazza, L., Bertrollini, R., Segni, G., & Borgna-Pignattti, C. (1988). Birth defects in the Seveso area after TCDD contamination. *JAMA, 259*, 1668-1672.

Matheson, D. P., Smith, A. H., & Fisher, D. O. (1981). Methods used for a study of reproductive outcomes among New Zealand agricultural chemical sprayers. *Occupational Health, 3*, 17-20. (Not accessed)

*Matsakis, A. (1989). Surveying the damage: the effects of PTSD on family life. *VA Practitioner, 6*(8), 75-81.

May, G. (1982). Tetrachlorodibenzodioxin: A survey of subjects ten years after exposure. *Br J Ind Med, 39*, 128-135.

*McEwan, A. C. (1999). Report to the Advisory Committee on the Health of Veteran's Children: Report on the potential for radiation induced genetic effects in children of Christmas Island veterans, *Inquiry into the health status of children of Vietnam and Operation Grapple veterans*. Wellington: Department of the Prime Minister and Cabinet.

*McKinney, P. A., Alexander, F. E., Cartwright, R. A., & Parker, L. (1991). Paternal occupations of children with leukaemia in west Cumbria, north Humberside, and Gateshead. *BMJ, 302*, 681-687.

*McKnight, J. (1998). Professionalized service and disabling help. *SRV_VRS, 3*(1), 26-33.

*McLaughlin, J., King, W. D., Anderson, T. W., Clarke, E. A., & Ashmore, J. P. (1993). Paternal radiation exposure and leukaemia in offspring: the Ontario case-control study. *BMJ, 307*, 959-966.

McMahon, B. (1962). Prenatal x-ray exposure and childhood cancer. *J Natl Cancer Inst, 28*, 1173-1191.(Not accessed)

*Medical Research Council Vitamin Sutdy Research Group. (1991). Prevention of neural tube defects: results of the Medical Research Council vitamin study. *Lancet, 338*, 131-137.

*Meinert, R., Kaatsch, P., Kaletsch, U., Krummenauer, F., Miesner, A., & Michaelis, J. (1996). Childhood leukaemia and exposure to pesticides: Results of a case-control study in Northern Germany. *Eur J Cancer, 32A*, 1943-1948.

*Meinert, R., Kaletsch, U., Kaatsch, P., Schuz, J., & Michaelis, J. (1999). Associations between childhood cancer and ionizing radiation: Results of a population-based case-control study in Germany. *Cancer Epidemiol Biomarkers Prev, 8*(9), 793-799.

Meinert, R., Schuz, J., Kaletsch, U., Kaatsch, P., & Michaelis, J. (2000). Leukemia and non-Hodgkin's lymphoma in childhood and exposure to pesticides: results of a register-based case-control study in Germany. *Am J Epidemiol, 151*(7), 6390-6646.

*Michalek, J. E., Rahe, A. J., & Boyle, C. A. (1998a). Paternal dioxin and the sex of children fathered by veterans of Operation Ranch Hand [letter]. *Epidemiology, 9*(4), 474-475.

*Michalek, J. E., Rahe, A. J., & Boyle, C. A. (1998b). Paternal dioxin, preterm birth, intrauterine growth retardation, and infant death. *Epidemiology, 9*(2), 161-167.

Miller, R. W. (1995). Looking for adverse reproductive outcomes in 'atomic veterans': Are such studies feasible? [Letter]. *JAMA, 274*(11), 865.

*Minister for Disability Issues. (2000). *The New Zealand Disability Strategy Discussion Document* (Discussion document). Wellington: Ministry of health.

*Minister for Disability Issues. (2001). *The New Zealand Disability Strategy* (Strategy). Wellington: Ministry of Health.

Mocarelli, P., Brambilla, P., Gerthoux, P. M., Patterson, D. G., & Needham, L. L. (1996). Change in sex ratio with exposure to dioxin [Letter]. *Lancet, 348*, 409.

*Mocarelli, P., Gerthoux, P. M., Ferrari, E., Patterson, D. G. J., Kiwszak, S. M., Brambilla, P., Vincoli, N., Signorini, S., Tramacere, P., Carreri, V., Sampson, E. J., Turner, W. E., & Needham, L. L. (2000). Paternal concentrations of dioxin and sex ratio of offspring. *Lancet, 355*(9218), 1858-1863.

*Moore, R. W., Potter, C. L., Theobald, H. M., Robinson, J. A., & Peterson, R. E. (1985). Androgenic deficiency in male rats treated with 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Toxicol Appl Pharmacol, 79*, 99-111.

Morgan, W. F., Day, J. P., Kaplan, M. I., McGhee, E. M., & Limoli, C. L. (1996). Genomic Instability Induced by Ionizing Radiation. *Radiat Res, 146*, 247-258.

*Morris, J. (1993). Prejudice. In J. Swain & V. Finklestein & S. French & M. Oliver (Eds.), *Disabling barriers - enabling communities* (pp. 101-107). London: Sage Publications.

*Motta, R. W., Josepf, J. M., Rose, R. D., Suozzi, J. M., & Leiderman, L. J. (1997). Secondary trauma: Assessing inter-generational transmission of war experiences with a modified Stroop procedure. *J Clin Psychol, 53*(8), 895-903.

Motta, R. W., Suozzi, J., & Joseph, J. (1994). Assessment of secondary traumatization with an emotional Stroop task. *Percept Mot Skills, 78*(3), 1274.

*MRC Vitamin Study Research Group. (1991). Prevention of neural tube defects: Results of the Medical Research Council Vitamin Study. *Lancet, 338*(8760), 131-137.

Mulvihill, J. J., Connelly, R. R., Austin, D. D., Cook, J. W., Holmes, F. F., Krauss, M. R., Steinhorn, S. C., Teta, M. J., Myers, H., Byrne, J., Bragg, K., Hassinger, D. D., Holmes, G. F., Latourette, H. B., Naughton, M. D., Strong, L. C., & Weyer, P. J. (1987a). Cancer in offspring of long-term survivors of childhood and adolescent cancer. *Lancet, 2*.

Mulvihill, J. J., McKeen, E. A., Rosner, F., & Hosein Zarrabi, M. (1987b). Pregnancy outcome in cancer patients. Experience in a large cooperative group. *Cancer, 60*, 1143-1150.

*Munford, R., & Sullivan, M. (1998). Introduction. In R. Munford & M. Sullivan (Eds.), *Thinking critically about disability* (pp. i-ii). Palmerston North: Department of Social Policy and Social Work, Massey University.

*Murphy, B. C., Ellis, P., & Greenberg, S. (1990). Atomic veterans and their families: responses to radiation exposure. *Am J Orthopsychiatry, 60*(3), 418-427.

Narod, S. A., Douglas, G. R., Nestmann, E. R., & Blakey, D. H. (1988). Human mutagens: evidence from paternal exposure [Review]. *Environ Mol Mutagen, 11*(3), 401-415.

National Council on Radiation Protection and Measurements. (1980). *Influence of dose and its distribution in time on dose-response relationships for low-let radiations* (64). Washingotn DC: National Council on Radiation Protection and Measurements.

National Council on Radiation Protection and Measurements. (1987). *Genetic effects from internally deposited radionuclides* (89): National Council on Radiation and Measurements.

National Radiological Protection Board. (1993). Estimates of late radiation risks to the UK population. *Documents of the NRPB, 4*, 15-157.

National Research Council Committee on the Biological Effects of Ionizing Radiation. (1990). *Health Effects of Exposure to Low Levels of Ionizing Radiation BEIRV*. Washington: National Academy Press.

*Needham, L. L., Gerthoux, P. M., Patterson, D. G., Brambilla, G., Turner, W. E., Beretta, C., Pirkle, J. L., Colombo, L., Sampson, E. J., Tramacere, P., Signorini, S., Meazza, L., Carreri, V., Jackson, R. J., & Mocarelli, P. (1997/98). Serum dioxin levels in Seveso, Italy, Population in 1976. *Teratog Carcinog Mutagen, 17*(225-240).

Needham, L. L., Patterson, D. G., & Houk, V. N. (1991). Levels of TCDD in selected human populations and their relevance to human risk assessment. In M. A. Gallo & R. Scheuplein & K. A. Can der Heijden (Eds.), *Biological basis for risk assessment of dioxins and related compounds, Banbury Report 35* (pp. 229-257). Cold Spring Harbour, NY: Cold Spring Harbor Laboratory Press.

Neel, J. V., Kato, H., & Schull, W. J. (1991). Mortality in the children of atomic bomb survivors and controls. In J. V. Neel & W. J. Schull (Eds.), *The children of atomic bomb survivors: A genetic study*. Washington: National Academy Press.

Neel, J. V., Satoh, C., Goriki, K., Asakawa, J., Fujita, M., Takahashi, N., & Kageoka, T. (1988). Search for mutations altering protein charge and/or function in children of atomic bomb survivors: Final report. *Am J Hum Genet, 42*, 663-676.

Nelson, C., Holson, J., HG, & Gaylor, D. (1979). Retrospective study of the relationship between agricultural use of 2,4,5-T and cleft palate occurence in Arkansas. *Teratology, 19*, 377-383.

Nevin, N. C., Johnston, W. P., & Merrit, J. D. (1981). Influence of socal class on the risk of recurrence of anencephalus and spina bifida. *Dev Med Child Neurol, 23*, 155-159.

*New Zealand CCS. (2000). *A better future for people with disabilities*. Wellington: New Zealand CCS.

*Newell, C., & Meumann, F. (1997). Training on the social nature of disability in general practice: a case study and model for further development. *Aust Dis J, 1*, 53-58.

Newell, G. R. (1984). *Development and preliminary results of pilot clinical studies. Report of the Agent Orange Advisory Committee to the Texas Department of Health.*: University of Texas System Cancer Center.

*Norquist, G., Hough, R., Golding, J., & Escobar, J. (1990). Psychiatric disorders in male veterans and non-veterans. *J Nerv Ment Dis, 178*(5), 328-335.

*Nuclear Energy Agency (NEA). (2001). *Chernobyl - Health Impact*. OECD Nuclear Energy Agency. Available: www.nea.fr/html/chernobyl/c05.html.

Nuriminen, T., Rantala, K., Kurrpa, K., & Holmberg, P. (1994). Agricultural work during pregnancy and selected structural malformations in Finland. *Epidemiology, 1*, 23-30.

Nygaard, R., Clausen, N., Siimes, M. A., Marky, I., Skjeldestad, F. E., Kristinsson, J. R., Vuoristo, A., Wegelius, R., & Moe, P. J. (1991). Reproduction following reatment for childhood leukemia: a population-based prospective cohort study of fertility and offspring [Abstract]. *Med Pediatr Oncol, 19*(6), 459-466.(Abstract only)

*Oakley-Browne, M., Joyce, P., Wells, J., Bushnell, J., & Hornblow, A. (1989). Christchurch Psychiatric Epidemiology Study: six month and other period prevalences. *Aust N Z J Psychiatry, 23*, 327-340.

*Office of Veterans Affairs. (2001). personal communication.

Oftedal, P., & Searle, A. G. (1980). An overall genetic risk assessment for radiobiological protection purposes. *J Med Genet, 17*, 15-20.

*O'Keefe, B., & Smith, F. B. (1994). *Medicine at war: medical aspects of Australia's involvement in Southeast Asia 1950-1972*. NSW, Australia: Allen & Unwin Pty Ltd.

O'Leary, L. M., Hicks, A. M., Peters, J. M., & London, S. (1991). Parental occupational exposures and risk of childhood cancer: a review. *Am J Ind Med, 20*, 17-35.

Olshan, A. F. (1995). Lessons learned from epidemiologic studies of environmental exposure and genetic disease [Review]. *Environ Mol Mutagen, 25 (Suppl)*, 74-80.

Olshan, A. F., Teschke, K., & Baird, P. A. (1991). Paternal occupation and congenital anomalies in offspring. *Am J Ind Med, 20*, 447-475.

Otake, M., Schull, W. J., & Neel, J. V. (1991). Congenital malformations, stillbirths, and early mortality among the children of atomic bomb survivors: A reanalysis. In J. V. Neel & W. J. Schull (Eds.), *The children of atomic bomb survivors: A genetic study*. Washington, D.C.: National Academy Press.

*O'Toole, B., Marshall, R., Grayson, S., Schureck, R., Dobson, M., French, M., Pulvertaft, B., Meldrum, L., Bolton, J., & Vennard, J. (1996). The Australian Vietnam veterans' Health Study: III. Psychological health of Australian Vietnam veterans and the relationship to combat. *Int J Epidemiol, 25*, 331-340.

Parker, L., Craft, A. W., Smith, J., Dickinson, H., Wakeford, R., & Binks, K. e. a. (1993). Geographical distribution of preconceptional radiation doses to fathers employed at the Sellafield nuclear installation, west Cumbria. *BMJ, 307*, 966-971.

*Parker, L., Pearce, M. S., Dickinson, H. O., Aitkin, M., & Craft, A. W. (1999). Stillbirths among offspring of male radiation workers at Sellafield nuclear reprocessing plant. *Lancet, 354*(9188), 1407-1414.

*Parsons, J. P. K., Thomas, J., & Owen, S. V. (1990). Incidence of behaviour problems among children of Vietnam war veterans. *School Psychology International, 11*(4), 253-259.

Pastore, L. M., Hertz-Picciotto, I., & Beaumont, J. J. (1997). Risk of stillbirth from occupational and residential exposures. *Occup Environ Med, 54*, 511-518.

Patandin, S., Koopman-Esseboom, C., de Ridder, M. A., Weisglas-Kuperus, N., & Sauer, P. J. (1998). Effects of environmental exposure to polychlorinated biphenyls and diosins on birth size and growth in Dutch children. *Pediatr Res, 44*(4), 538-545.

*Patterson, D., Hampton, L., Lapeza, C., Belser, W., Green, V., Alexander, L., & Needham, L. (1987). High resolution gas chromatographic/ high resolution mass spectrometric analysis of human serum on a whole weight and lipid basis for 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Anal Chem, 59*, 2000-2005.

*Pearce, M., & Parker, L. (2000). Paternal employment in agriculture and childhood kidney cancer. *Pediatr Hematol Oncol, 17*, 223-230.

Pearce, N. (1996). *Mortality and cancer incidence in New Zealand participants in United Kingdom nuclear weapons tests in the pacific: supplementary report.* Wellington: Department of Medicine.

*Pearce, N., Prior, I., Methven, D., Culling, C., Marshall, S., Auld, J., & Boer, G. d. (1990). Follow up of New Zealand participants in British atmospheric nuclear weapons tests in the Pacific. *BMJ, 300*, 1161-1166.

*Pearce, N., Winkelmann, R., Kennedy, J., Lewis, S., Purdie, G., Slater, T., Prior, I., & Fraser, J. (1997). Further follow-up of New Zealand participants in United Kingdom atmospheric nuclear weapons tests in the pacific. *Cancer Causes and Control, 8*, 139-145.

Pearn, J. (1985). Herbicides and congenital malformations: a review for the paediatrician. *Aust Paediatr J, 21*, 237-242.

*Pearn, J. H. (1983). Teratogens and the male: an analysis with special reference to herbicide exposure. *Med J Aust, 2*, 16-20.

Penrose, L. S. (1957). Paternal age in achondroplasia and mongolism. *Am J Hum Genet, 9*, 167-169.

Pesatori, A. C., Consonni, D., Tironi, A., Zocchetti, C., Fini, A., & Bertazzi, P. (1993). Cancer in a young population in a dioxin-contaminated area. *Int J Epidemiol, 22*, 1010-1013.

Peters, J. M., Preston-Martin, S., & Yu, M. C. (1981). Brain tumours in children and occupational exposure of parents. *Science, 213*, 235-237.

Peterson, L. E., & Abrahamson, S. (Eds.). (1998). *Effects of ionizing radiation: Atomic bomb survivors and their children (1945-1995).*: Joseph Henry Press.

*Petrelli, G., Figa-Talamanca, I., Tropeano, R., Tangucci, M., Cini, C., Aquilini, S., Gasperini, L., & Meli, P. (2000). Reproductive male-mediated risk: spontaneous abortion among wives of pesticide applicators. *Eur J Epidemiol, 16*(4), 391-393.

Phuong, N., Thut, T., & Phuong, P. (1989a). An estimate of reproductive abnormalities in women inhabiting herbicide sprayed and non-herbicide sprayed areas in the south of Vietnam, 1952-1981. *Chemosphere, 18*, 843-846.

Phuong, N., Thuy, N. T., & Phuong, P. (1989b). An estimate of differences among women giving birth to deformed babies and among those with hydatidiform mole seen at the Ob-Gyn hospital of Ho Chi Minh city in the south of Vietnam. *Chemosphere, 18*, 801-803.

*Pobel, D., & Viel, J. F. (1997). Case-control study of leukaemia among young people near La Hague nuclear reprocessing plant: the environmental hypothesis revisited. *BMJ, 314*, 101-106.

Pocchiari, F., Silano, V., & Zampieri, A. (1979). Human health effects from accidental release of tetrachlorodibenzo-p-dioxin (TCDD) at Seveso, Italy. *Ann N y Acad Sci, 320*, 311-320.(Not accessed)

Pollak, J. (1987). The agent orange controversy. *Med J Aust, 146*, 115.

Pour-Jafari, H. (1994). Congenital malformations in the progenies of Iranian chemical victims. *Vet Hum Toxicol, 36*(6), 562-563.

Preston, D., Kato, H., Kopecky, K. J., & Fujita, S. (1987). *Life span study report 10: Part 1. Cancer Mortality among A-Bomb survivors in Hiroshima and Nagasaki, 1950-1985*. Hiroshima, Japan: Radiation Effects Research Foundation. Technical Report RERFTR 1-86.(Not accessed)

Putnam, F. W. (1996). Child development and dissociation. *Child & Adolescent Psychiatric Clinics of North America, 5*(2), 285 ff.

*RadEFX. (2000). *Chernobyl Nuclear Power Plant Accident Health Effects*. RadEFX. Available: http://radefx.med.bcm.tmc.edu/chernobyl/default.htm.

*Radiation Effects Research Foundation (RERF) (2001). www.rerf.or.jp

Raman, J., Dulberg, C., Spasoff, R., & Scott, J. (1987). Mortality among Canadian military personnel exposed to low-dose radiation. *Can Med Assoc J, 136*, 1051-1056.

*Ransfield, S. (2001). Community paediatric care in Wellington.: personal communication.

Reggiani, G. (1978). Medical problems raised by TCDD contamination in Seveso, Italy. *Arch Toxicol, 40*, 161-188.(Not accessed)

Reggiani, G. (1979). Estimation of the TCDD toxic potential in light of the Seveso accident. *Arch Toxicol, 40 (suppl. 2)*, 291-302.(Not accessed)

*Resnik, R., Gold, J., & Mandrick, J. (1984). Vietnam service and congenital anomalies. *Med J Aust, 140*, 194-195.

Restrepo, M., Munoz, N., Day, N. E., Parra, J. E., de Romero, L., & Nguyen-Ding, X. (1990a). Prevalence of adverse reproductive outcomes in a population occupationally exposed to pesticides in Colombia. *Scand J Work Environ Health, 16*(232-8).

*Restrepo, M., Munoz, N., Day, N. E., Parra, J. E., Hernandez, C., & Blettner, M. (1990b). Birth defects among children born to a population occupationally exposed to pesticides in Colombia. *Scand J Work Environ Health, 16*, 239-246.

Rhoades, D., Leaveck, M., & Hudson, J. (Eds.). (1995). *The legacy of Vietnam veterans and their families: survivors of war: catalysts for change*. Washington: Agent Orange Class Assistance Programme.(Not accessed)

Roan, C. C., Matanoski, G. E., McIlnay, C. Q., Olds, K. L., Pylant, F., & Trout, J. R. (1984). Spontaneous abortions, stillbirths and birth defects in families of agricultural pilots. *Arch Environ Health, 39*, 56-60.

Roberts, J. (1994). Debate over US Gulf war syndrome continues [news]. *BMJ, 309*(6966), 1392-1393.

Robinette, C. D., Jablon, S., & Preston, D. L. (1985). *Studies of participants in nuclear tests. Final report*. Washington: National research council medical follow-up agency.(Not accessed)

*Robins, L., Wing, J., Wittchen, H., & Helzer, J. (1988). The Composite International Diagnostic Interview: an epidemiologic instrument suitable for use in conjunction with different diagnostic systems and different cultures. *Arch Gen Psychiatry, 45*, 1069-1077.

*Roff, S. R. (1996). *Problems in the estimation of risk of ill health arising from presence at the Christmas Island tests*. Dundee: University of Dundee Medical School.

*Roff, S. R. (1997). "Knocked over by a pile of nuclear bombs; hasn't felt well since". Profile of a pre-defined sample of veterans of UK nuclear weapons tests.: Unpublished.

Roff, S. R. (1998a). Puff the magic dragon: how our understanding of fallout, residual and induced radiation evolved over fifty years of nuclear weapons testing. *Medicine, Conflict & Survival, 14*(2), 106-119.

*Roff, S. R. (1998b). *Report on morbidity study of members of the British Nuclear Tests Veterans Association and the New Zealand Nuclear Tests Veterans Association and their families*. Dundee: Centre for Medical Education, Dundee University Medical School.

Roff, S. R. (1999a). The dark side of the nuclear family. *New Statesman, 12*(538), 28-29.

*Roff, S. R. (1999b). Mortality and morbidity of members of the British Nuclear Tests Veterans Association and the New Zealand Nuclear Tests Veterans Association and their families. *Medicine, Conflict & Survival, 15*(Suppl 1), i-ix, 1-51.

*Roff, S. R., Preece, P., McKenzie, R., & Sefton, R. (2000). *Family history protocol study report.* Dundee: Centre for Medical Education, Dundee University Medical School.

Rokicka-Milewska, R., Derulska, D., Armata, J., W, B., Boguslawska-Jaworska, J., Cyklis, R., Duczmal, B., Michalewska, D., Newecka, T., & Ochocka, M. (1986). Children cured of acute lymphoid leukemia. Long-term follow-up studies, including progeny. [Abstract]. *Am J Pediat Hematol, 8*(3), 208-212.(Abstract only)

Roman, E., Beral, V., Carpenter, L., Watson, A., Barton, C., & Ryder, H. (1987). Childhood leukaemia in the West Berkshire and Bsingstoke and North Hampshire District Health Authorities in relation to nuclear establishments in the vicinity. *BMJ, 294*, 597-602.

*Roman, E., Doyle, P., Ansell, P., Bull, D., & Beral, V. (1996). Health of children born to medical radiographers. *Occup Environ Med, 53*, 73-79.

*Roman, E., Doyle, P., Maconochie, N., Davies, G., Smith, P. G., & Beral, V. (1999). Cancer in children of nuclear industry employees: report on children aged under 25 years from nuclear industry family study. *BMJ, 318*, 1443-1450.

*Roman, E., Watson, A., Beral, V., Buckle, S., Bull, D., & Baker, K., et al. (1993). Case-control study of leukaemia and non-Hodgkin's lymphoma among children aged 0-4 years living in West Berkshire and North Hampshire health districts. *BMJ, 306*, 615-621.

Rose, K. S. B. (1990). Pre-1989 epidemiological surveys of low-level dose pre-conception irradiation. *Journal of Radiological Protection, 10*, 177-184.

Rose, K. S. B. (1994). A review of epidemiological studies concerning leukaemia and lymphoma among young people and the genetic effects of ionizing radiation. *Nuclear Energy-Journal of the British Nuclear Energy Society, 33*(6), 331-336.(Not accessed)

*Rosenheck, R. (1986). Impact of posttraumatic stress disorder of World War II on the next generation. *J Nerv Ment Dis, 174*(6), 319-327.

*Rosenheck, R., & Fontana, A. (1998). Transgenerational effects of abusive violence on the children of Vietnam combat veterans. *J Trauma Stress, 11*(4), 731-742.

*Rosenheck, R., & Nathan, P. (1985). Secondary traumatization in children of Vietnam veterans. *Hospital & Community Psychiatry, 36*(5), 538-539.

*Royal Society of New Zealand. (1998). *Radiation and the New Zealand community.* Wellington: Royal Society of New Zealand.

Rupa, D. S., Reddy, P. P., & Redd, O. S. (1991). Reproductive performance in population exposed to pesticides in cotton fields in India. *Environ Res, 55*, 123-128.

Rylander, L., Stromberg, U., Dyremark, E., Ostman, C., Nilsson-Ehle, P., & Hagmar, L. (1998). Polychlorinated biphenyls in blood plasma among Swedish female fish consumers in relation to low birthweight. *Am J Epidemiol, 147*, 493-502.

*Sallmen, M., Linbohm, M., & Nurminen, M. (2000). Paternal exposure to lead and infertility. *Epidemiology, 11*, 148-152.

Samet, J. M. (1996). Dioxin and cancer: the never-ending story. *Cancer Causes and Control, 7*, 302-304.

Sankaaranarayanan, K. (1998). Ionizing radiation and hereditary effects: emerging perspectives, *Low doses of ionizing radiation: biological effects and regulatory control. Invited papers and discussions* (pp. 145-162): IAEA, Austria.

Satoh, C., & Neel, J. V. (1988). Biochemical mutations in the children of atomic bomb survivors. *Gann Monogr Cancer Res, 35*, 191-208.(Not accessed)

*Savitz, D. A., Sonnenfeld, N. L., & Oshlan, A. F. (1994). Review of epidemiologic studies of paternal occupational exposure and spontaneous abortion. *Am J Ind Med, 5*, 361-383.

*Scaturo, D., & Hayman, P. (1992). The impact of combat trauma across the family-life cycle - clinical considerations. *J Trauma Stress, 5*(2), 273-288.

*Schull, W. J., Otake, M., & Neel, J. V. (1981). Genetic effects of the atomic bomb: A reappraisal. *Science, 213*(11), 1220-1227.

*Scown, J., & Sullivan, L. (2000). *Presentation to the National Health committee*. Wellington.

*Scullion, P. (2000). Enabling disabled people: responsibilities of nurse education. *British Journal of Nursing, 9*(15), 1010-1015.

Scurfield, R. (1993). Treatment of PTSD in Vietnam veternas. In J. P. Wilson & B. Raphael (Eds.), *The international handbook of traumatic stress syndromes*. New York: Plenum Press.

Sever, L. E. (1991). Parental radiation exposure and children's health: are there effects on the second generation [Review]. *Occup Med, 6*(4), 613-627.

Sever, L. E. (1995). Male-mediated developmental toxicity [editorial]. *Epidemiology, 6*, 573-574.

Sever, L. E., Arbuckle, T. E., & Sweeny, A. (1997). Reproductive and developmental effects of occupational pesticide exposure: the epidemiologic evidence. *Occup Med, 12*, 305-325.

*Sever, L. E., Gilbert, E. S., Hessol, N. A., & McIntyre, J. M. (1988). A case-control study of congenital malformations and occupational exposure to low-level ionizing radiation. *Am J Epidemiol, 127*(2), 226-242.

*Sharpe, C. R., Franco, E. L., de Camargo, B., Lopes, L. F., Barreto, J. H., Johnsson, R. R., & Mauad, M. A. (1995). Parental exposures to pesticides and risk of Wilms' tumor in Brazil. *Am J Epidemiol, 141*, 210-217.

*Shea, K. M., & Little, R. E. (1997). Is there an association between preconception paternal x-ray exposure and birth outcome. *Am J Epidemiol, 145*(6), 546-551.

Sheperd, M. (1997). Combat-induced post traumatic stress disorder. *New Zealand Journal of Disability Studies, 4*, 141-150.

*Shu, X., Reamna, G. H., & Lampkin, B., et al. (1994). Association of diagnostic x-ray exposure with risk of infant leukemia. *Cancer Epidemiol Biomarkers Prev, 3*, 645-653.

*Shu, X. O., Gao, Y. T., & Brinton, L. A., et al. (1988b). A population-based case-control sutdy of childhoood leukemia in Shanghai. *Cancer, 62*, 635-644.

*Silburn, L. (1993). A social model in a medical world: the development of an integrated living team as part of the strategy for younger physically disabled people in North Derbyshire. In J. Swain & V. Finkelstein & S. French & M. Oliver (Eds.), *Disabling barriers - enabling environments* (pp. 218-227). London: Sage Publications.

Skolnick, A. A. (1996). Discovery of 50-year-old naval logbook may aid follow-up study of radium-exposed veterans [news]. *JAMA, 276*(20), 1628, 1630.

Slanina, J., Musshoff, K., Ner, T., & Stiasny, R. (1977). Long-term side effects in irradiated patients with Hodgkin's disease. *Int J Radiat Oncol Biol Phys, 2*(1-2), 1-19.

Smejkal, V. P. (1989). *Second generation effects of the Vietnam conflict: Adjustment and development of adolescent children of combat veterans.* Unpublished EDD, West Virginia University.

*Smith, A., & Lopipero, P. (2001). *Evaluation of the toxicity of dioxins and dioxin like PCBs: A health risk appraisal for the New Zealand population* (ISBN 0-478-09091-9). Wellington: Ministry for the Environment.

*Smith, A. H., Fisher, D. O., & Pearce, N. (1982). Congenital defects and miscarriages among New Zealand 2,4,5-T Sprayers. *Arch Environ Health, 37*, 197-200.

Smith, A. H., Matheson, D. P., Fisher, D. O., & Chapman, C. J. (1981). Preliminary report of reproductive outcomes among pesticide applicators using. *NZ J Med, 93*, 177-179.

*Smith, F. A., Schwetz, B. A., & Nitshke, K. D. (1976). Teratogenicity of 2,3,7,8-tetrachlorodibenzo-p-dioxin in CF-1 mice. *Toxicol Appl Pharmacol, 38*, 517-523.

Smith, R. (1999). The ill children of nuclear test veterans: victims or just unlucky? *New Zealand International Review, 24*(3), 20-23.

Smith, R. J. (1983). Study of Atomic Veterans fuels controversy [news]. *Science, 221*(4612), 733-734.

*Smulevich, V. B., Solionova, L. G., & Belyakova, S. V. (1999). Parental occupation and other factors and cancer risk in children: II. Occupational factors. *Int J Cancer, 83*(6), 718-722.

Soloman, Z. (1988). The effect of combat-related Post-Traumatic Stress Disorder on the family. *Psychiatry, 51*, 323-329.

Sorahan, T. (1988). Cancer after nuclear weapons tests [letter]. *British Medical Journal Clinical Research Ed., 296*(6623), 716-717.

Sorahan, T. (1996). Parental exposure to radiation and childhood cancer. *Occup Environ Med, 53*(7), 503.

*Sorahan, T., Lancashire, R. J., Temperton, D. H., & Heighway, W. P. (1995). Childhood cancer and paternal exposure to ionizing radiation: a second report from the Oxford Survey of Childhood Cancers. *Am J Ind Med, 28*(1), 71-78.

*Sorahan, T., & Roberts, P. J. (1993). Childhood cancer and paternal exposure to ionizing radiation: preliminary findings from the Oxford Survey of Childhood Cancers. *Am J Ind Med, 23*, 343-354.

*Statistics New Zealand. (2000). *New Zealand official yearbook 2000*. Auckland: David Bateman Ltd.

*Stellman, S. D., Stellman, J. M., & Sommer, J. F. J. (1988). Health and reproductive outcomes among American Legionnaires in relation to combat and herbicide exposure in Vietnam. *Environ Res, 47*, 150-174.

Stephenson, J. (1996). New IOM report links agent orange exposure to risk of birth defect in Vietnam vets' children [news]. *JAMA, 275*(14), 1066-1067.

*Sterling, T. D., & Arundel, A. (1986). Review of recent Vietnamese studies on the carcinogenic and teratogenic effects of phenoxy herbicide exposure. *Int J Health Serv, 16*, 265-278.

Stewart, A. M., & Kneale, G. W. (1984). Non-cancer effects of exposure to A-bomb radiation. *J Epidemiol Community Health, 38*, 108-112.

Stockbauer, J. W., Hoffman, R. E., Schramm, W. F., & Edmonds, L. D. (1988). Reproductive outcomes of mothers with potential exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin. *Am J Epidemiol, 128*, 410-419.

Study, C. V. E. (1988). Health status of vietnam veterans. *JAMA, 259*(18), 2701-2707.

*Sullivan, L. (2001). Disability support in New Zealand.

*Suskind, R. R., & Hertzberg, V. S. (1984). Human health effects of 2,4,5-T and its toxic contaminants. *JAMA, 251*, 2372-2380.

*Swartz, D. (1992). *Crossing the river: creating a conceptual revolution in community & disability*. Cambridge, Massachusetts: Brookline Books.

*Sweeney, M. H., Clavert, G. M., Egeland, G. A., Fingerhut, M. A., Halperin, W. E., & Piacitelli, L. A. (1997/1998). Review and update of the results of the NIOSH medical study of workers exposed to chemicals contaminated with 2,3,7,8-tetrachlorodibenzodioxin. *Teratog Carcinog Mutagen, 17*(4-5), 241-247.

Tas, S., Luauwerys, R., & Lison, D. (1996). Occupational hazards for the male reproductive system. *Crit Rev Toxicol, 26*(3), 261-307.

*Thaul, S., Page, W. F., Crawford, H., & O'Maonaigh, H. (2000). *The Five Series Study: Mortality of military participants in U.S. nuclear weapons tests*. Washington D.C.: National Academy Press.

Thomas, H. F. (1980). 2,4,5-T use and congenital malformation rates in Hungary. *Lancet, 2*, 214-215.

Thomas, T. L., Kang, H. K., & Dalager, N. A. (1991). Mortality among women vietnam veterans, 1973-1987. *Am J Epidemiol, 134*, 973-980.

Togoni, G., & Bonaccorsi, A. (1982). Epidemiological problems with TCDD (a critical view). *Drug Metab Rev, 13*(3), 447-469.

*Townsend, J. C., Bodner, K. M., & VanPeenen, P. F. (1982). Survey of reproductive events of wives of employees exposed to chlorinated dioxins. *Am J Epidemiol, 115*, 695-713.

*Traina, M. E., Ade, P., Siepi, G., Urbani, E., & Petrelli, M. G. (1994). A review of the effect of pesticide formilations on male fertility. *Int J Environ Health R, 4*, 38-47.

U.S. Environmental Protection Agency. (1979). *Report of assessment of a field investigation of six year spontaneous abortion rates in three Oregon areas in relation to forest 2,4,5-T spray practices.* Washington: Epidemiologic Studies Program, Human Effects Monitoring Branch.(Not accessed)

*United Nations Environment Programme. (1991). *Radiation: doses, effects, risks.* UK: Blackwell Publishers.

*United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). (2000). *Report to the General Assembly - 2000.*: United Nations.

*Unkovich, D. (2001). *Emotional health of Vietnam veterans' children.* Unpublished PhD, Murdoch, Western Australia.

*Urquhart, J. D., Black, R. J., Muirhead, M. J., Sharp, L., Maxwell, M., & Eden, O. B. (1991). Case control study of leukaemia and non-Hodgkin's lymphoma in children in Caithness near the Dourneay nuclear installation. *BMJ, 302*, 687-692.

Van der Kolk, B. A., Dryfus, D., & Michaels, M. e. a. (1994). Fluxetine in post-traumatic stress disorder. *J Clin Psychiatry, 55*, 517-522.

Vartiainen, T., Jaakkola, J. J., Saarikoski, S., & Tuomisto, J. (1998). Birthweight and sex of children and the correlation to the body burden of PCDDs/PCDFs and PCBs of the mother. *Environmental Health Perspectives, 106*(2), 61-66.

Viel, J. F., & Richardson, S. T. (1990). Childhood leukaemia around the La Hague nuclear waste reprocessing plant. *BMJ, 300*, 580-581.

*Vincent, C. (1994). *Combat related posttraumatic stress disorder and interpersonal functioning in veterans of the Vietnam War.*, Massey University, Palmerston North.

*Vincent, C., Chamberlain, K., & Long, N. (1994). *The New Zealand Vietnam War veteran twenty years on: Part One: Mental Health, Physical Health and Stress.* Palmerston North: Massey University.

*Vincent, C., Long, N., & Chamberlain, K. (1991). *Health, Mental health and well-being of New Zealand Vietnam Veterans.* Palmerston North: Department of Psychology, Massey University.

*Vyner, H. M. (1988). The psychological dimensions of health care for patients exposed to radiation and the other invisible environmental contaminants. *Soc Sci Med, 27*(10), 1097-1103.

*Wakeford, R. (1995). The risk of childhood cancer from intrauterine and preconceptional exposure to ionizing radiation. *Environ Health Perspect, 103*, 1018-1025.

Wakeford, R., & Parker, L. (1996). Leukaemia and non-Hodgkin's lymphoma in young persons resident in small areas of West Cumbria in relation to paternal preconceptional irradiation. *Br J Cancer, 73*(5), 672-679.

Wakeford, R., & Tawn, E. J. (2000). Paternal irradiation and leukemia in offspring[Letter]. *Radiat Res, 154*(2), 222-223.

*Walsh, R., Donovan, J., Adena, M., Rose, G., & Battistutta, D. (1983). *Case control studies of congenital anomalies and Vietnam Service (Birth Defects Report).* Canberra: Commonwealth Institute of Health.

*Watanabe, K. K., Kang, H. K., & Dalager, N. A. (1995). Cancer mortality risk among military participants of a 1958 atmospheric nuclear weapons test. *Am J Public Health, 85*(4), 523-527.

*Weinberg, H., Korol, A., Kirzhner, V., Avivi, A., Fahima, T., Nevo, E., Shapiro, S., Rennert, G., Piatak, O., Stepanova, E., & Skvarskaja, E. (2001). Very high mutation rate in offspring of Chernobyl accident liquidators. *P Roy Soc Biol, 268*, 1001 -"".

Weisglas-Kuperus, N., Sas, T. C., Koopman-Esseboom, C., van der Zwan, C. W., De Ridder, M. A., Beishuizen, A., Hooijkaas, H., & Sauer, P. J. (1995). Immunologic effects of background

prenatal and postnatal exposure to dioxins and polychlorinated biphenyls in Dutch infants. *Pediatr Res, 38*(3), 404-410.

*Wen, W. Q., Shu, X. O., Steinbuch, M., Severson, R. K., Reaman, G. H., Buckley, J. D., & Robison, L. L. (2000). Paternal military service and risk for childhood leukemia in offspring. *Am J Epidemiol, 151*(3), 231-240.

*Westerink, J., & Giarratano, L. (1999). The impact of posttraumatic stress disorder on partners and children of Australian Vietnam veterans. *Aust N Z J Psychiatry, 33*(6), 841-847.

White, F., Cohen, F., Sherman, G., & McCurdy, R. (1988). Chemicals, birth defects and stillbirths in New Brunswick: associations with agricultural activity. *Can Med Assoc J, 138*, 117-124.

*Wilcox, A., & Horney, L. (1984). Accuracy of spontaneous abortion recall. *Am J Epidemiol, 120*(5), 727-733.

Wilcox, A. J., Skjaerven, R., & Irgens, L. M. (1994). Harsh social conditions and perinatal survival: an age-period-cohort analysis of the World war II occupation of Norway. *Am J Public Health, 84*, 1463-1467.

Williams, M. B., & Sommer, J. F. (1994). *Handbook of Post-Traumatic therapy*. Westport, CT.: Greenwood Press.

Withers, R., Madison-Smith, G., Flett, R., Long, N., Chamberlain, K., & MacDonald, C. (1997). Health care utilisation: A comparison between New Zealand war veteran's partners and civilian women. In G. Habermann (Ed.), *Looking back and moving forward: 50 years of New Zealand psychology* (pp. 289-302). Wellington: New Zealand Psychological Society Inc.

*Wolfe, W. H., Michalek, J. E., Miner, J. C., & Rahe, A. J. (1992). *The Air Force Health Study: An epidemiologic investigation of health effects in Air Force personnel following exposure to herbicides. Reporductive Outcomes.* San Antonio: Armstrong Laboratory, Brooks Air Force Base.

*Wolfe, W. H., Michalek, J. E., Miner, J. C., Rahe, A. J., Moore, C. A., Needham, L. L., & Patterson, D. G., Jr. (1995). Paternal serum dioxin and reproductive outcomes among veterans of Operation Ranch Hand [see comments]. *Epidemiology, 6*(1), 17-22.

*Wolfe, W. H., Michalek, J. E., Miner, J. C., Rahe, A. J., Silva, J., Thomas, W. F., Grubbs, W., Lustik, M. B., Karrison, T. G., Roegner, R. H., & Williams, D. E. (1990). Health status of Air Force veterans occupationally exposed to herbicides in Vietnam. 1. Physical health. *JAMA, 14*, 1824-1831.

*Workbridge. (2001). Workbridge at Work. *Workbridge at Work, 3*(2), 2-24.

World Health Organizaiton Regional Office for Europe Copenhagen. (1975). *Health implications of nuclear power production.* (European Series No. 3): World Health Organization.

World Health Organization. (1987). *Effects of nuclear war on health and health services. Second editition*. Geneva: World Health Organization.

*www.enable.co.nz. (May 2001).

Yamazaki, J. N., & Schull, W. J. (1990). Perinatal loss and neurological abnormalities among children of the atomic bomb: Nagasaki and Hiroshima revisited, 1949-1989. *JAMA, 264*, 605-609.

*Yoshimoto, Y. (1990). Cancer risk among children of atomic bomb survivors: A review of RERF epidemiologic studies. *JAMA, 264*, 596-600.

Yoshimoto, Y., Nell, J. V., Schull, W. J., Kato, H., Soda, M., Eto, R., & Mabuchi, K. (1990). Malignant tumours during the first 2 decades of life in the offspring of atomic bomb survivors. *Am J Hum Genet, 1990*(46).

Yoshimoto, Y., Schull, W. J., Kato, H., & Neel, J. V. (1991). Mortality among the offspring (F1) of atomic bomb survivors, 1946-85. In J. V. Neel & W. J. Schull (Eds.), *The children of atomic bomb survivors: A genetic study*. Washington, D.C.: National Academy Press.

Zahm et al. (1998). Pesticides and chilhood cancer. *Environmental Health Perspective, 106*(suppl 3), 893-908.

Zober, A., Messerer, P., & Ott, M. G. (1997/98). BASF Studies: epidemiological and clinical investigations on dioxin-exposed chemical workers. *Teratog Carcinog Mutagen, 17*, 249-256.

*Zubrick, S., Silburn, S., Burton, P., & Blair, E. (2000). Mental health disorders in children and young people: Scope, cause and prevention. *Aust N Z J Psychiatry, 34*, 570-578.

*Zwarenstein, M., Stephenson, B., & Johnson, L. (2001). Case mangement: effects on professional practice and health care options. *The Cochrane Data base of Sytematic Reviews, www.gareway2.ovid.com/ovidweb.cgi*.

Key:

* - reference cited in text

Not accessed – reference unable to be accessed (overseas, too old, not able to be found)

Abstract only – Only the abstract was able to be obtained

APPENDIX ONE: KEY WEBSITES SEARCHED

Some of the key web-sites searched included:

Australian Nuclear Veterans Association	www.tac.com.au/~anva/main.html
Australian Vietnam War Veterans Trust	www.accsoft.com.au/~vvt/index.html
Centers for Disease Control and Prevention	www.cdc.gov
Department of Veterans Affairs, Australia	www.dva.gov.au
Department of Veterans Affairs, U.S.	www.va.gov
International Atomic Energy Agency	www.iaea.org
National Association of Atomic Veterans	www.naav.com/
National Academy Press	www.nap.edu
National Academies	www4.nationalacademies.org
National Council on Radiation Protection and Measures	www.ncrp.com/
New Zealand Vietnam Veterans Association	grunt.space.swri.edu/nzorgs.htm
Nuclear Energy Agency	www.nea.fr/web.html
Radiation Effects Research Foundation	www.rerf.or.jp/eigo/experhp/rerfhome.htm
Radiation Research Society	www.radres.org
RadEFX	radefx.bcm.tmc.edu
Vietnam Veterans of America	www.vvz.org
World Health Organisation	www.who.org

APPENDIX TWO: SUMMARY OF GUIDELINES

Copies of guidelines can be accessed on line from the New Zealand Guidelines Group website; http://www.nzgg.org.nz/