

**Investigation of a possible cluster of cancer cases at the Morven Brown Building,
University of New South Wales**

Project plan

Organisation

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Project team

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SUMMARY

The project is a detailed investigation of a possible cancer cluster involving staff at the Morven Brown Building, University of New South Wales, with associated review of relevant past and current exposures and work practices.

The project will involve:

- review of past exposures to hazardous substances, as well as relevant physical and biological hazards, and work practices relevant to these exposures;
- review of current exposures to hazardous substances, as well as relevant physical and biological hazards, and work practices relevant to these exposures;
- reviewing the literature to identify cancers associated with the identified main exposures;
- attempting to identify all incident cases of cancer amongst current and former UNSW staff of the Faculty of Arts and Social Sciences (or the equivalent in the past) who have worked in the Morven Brown Building at some time from the beginning of 1996 to the present by matching their names with information at State and Territory cancer registries;
- interviewing cases who contact the investigator and agree to be interviewed;
- reviewing the literature to identify work-related exposures associated with the identified cancers;
- comparison of the rate of cancer (overall and for specific cancers, if relevant) in the relevant staff with an age and sex-matched Australian population;
- an overall assessment of the likelihood that occupational exposures have contributed to the past and/or current employees having a higher than expected rate of one or more cancers;
- provision of recommendations based on the above information.

BACKGROUND

Following the occurrence of cancer in a number of members of staff who currently work, or previously worked, in the Morven Brown Building on the main campus at the University of New South Wales, concern was raised that the rate of cancer in such staff members was higher than would be expected. As a result, the University has commissioned a project to examine this possible cluster of cancers.

METHOD

OBJECTIVES

This project will aim to:

- provide an opinion on the likelihood of exposures in or around the Morven Brown Building having contributed to the occurrence of cancer in staff who have worked in the building;
- to recommend what, if any, further action might be warranted.

This work will include an assessment of past and current exposures of staff who have worked in the building to relevant physical, chemical and biological hazards, and an assessment of the type, number and rate of cancer in current and former staff.

INTRODUCTION

The project requires an epidemiological assessment of the suspected cluster, including a consideration of the current and past occupational exposures. It will also be very important to involve all interested parties in the project, so that all concerns are heard and addressed as much as is reasonably possible.

There are a number of approaches that can reasonably be taken when investigating an apparent cancer cluster, and many references that provide good guidance in this regard. Recurring themes in these publications are that:

- such investigations commonly do not provide a definitive answer;
- most apparent clusters are almost certainly chance occurrences of cancers due to non-work exposures;
- a small number of cluster investigations have identified important relationships between work-related exposures and cancer;
- investigation requires a careful and considered approach; and
- dismissing apparent clusters without appropriate investigation, consideration and consultation is likely to result in the acrimony of concerned staff and the escalation of tension and worries in the affected workforce¹.

Key questions that need to be answered are presented here. These are used as the basis for the methodology. The questions are:

- Are there known workplace exposures that could have contributed to the occurrence of the cancers?
- Have all the cases been identified?
- Are all the cases of the same (or similar) type?
- Do the cancer types have a known common cause, whether occupational or non-occupational?
- Did the persons diagnosed with cancer have a common occupational (or non-occupational) exposure?
- Did the cancers occur at an appropriate time in relation to the possible workplace exposures?
- Is there statistical evidence to suggest that the number of cases is in excess of what would be expected in this population?
- On the balance of probabilities, is it likely that the identified cancers occurred as a result of occupational exposures?
- Are there any plausible non-occupational causes for the apparent cluster?

The methodology takes the above questions into account.

APPROACH

1) Preliminary and later discussion with all interested parties

It is important for the success of the project that the project team gain a detailed understanding of the concerns of all persons with an interest in the issue being investigated by the project. This includes affected workers, other concerned workers and union representatives. Several such meetings have already been held (two with interested staff and two with the newly constituted Steering Committee). The project methodology presented here has been discussed with staff and refined in response to their comments.

A Steering Committee has been established. This is designed to provide a formal avenue for involvement and interaction of staff and management, a mechanism for efficient communication between the University and the study team, and a means of discussing progress with the project and resolving issues that might arise.

¹ AFOM Working Party on Occupational Cancer. *Occupational Cancer. A guide to prevention, assessment and investigation*. Sydney: 2003, The Australasian Faculty of Occupational Medicine.

Caldwell GG. Twenty-two years of cancer cluster investigations at the Centers for Disease Control. *Am J Epidemiol*, 1990; 132(Suppl 1):S43-47.

Fleming LE, Ducatman AM, Shalat SL. Disease clusters in occupational medicine: a protocol for their investigation in the workplace. *Am J Ind Med*, 1992; 22:33-47.

Frumkin H, Kantrowitz W. Cancer clusters in the workplace: an approach to investigation. *J Occup Med*, 1987; 29:949-952.

Rothman K. A sobering start to the cluster busters' conference. *Am J Epidemiol*, 1990; 132(Suppl 1):S6-13.

2) Hygiene assessment and literature review

Are there known workplace exposures that could have contributed to the occurrence of the cancers?

It is very important to gain a thorough understanding of the type, nature and extent of exposures to which staff working in the Morven Brown Building may have been exposed. This requires a detailed assessment by an occupational hygienist and occupational physician. It appears that considerable investigations have already been undertaken on behalf of the University to investigate the nature and level of possible relevant exposures. Documentation of all relevant hygiene investigations will be read by the project team. A thorough workplace inspection will be undertaken, looking at the relevant worksites and work tasks, and interviewing current (and, if relevant, former) building staff to ascertain how work practices and exposures might have changed over time. Until this work has started, it will not be known whether any further form of workplace monitoring or measurement should be undertaken. The focus of this assessment will be hazardous substances, but relevant physical and biological hazards will be included.

In addition, a brief review of the published literature will be undertaken to identify the known or suspected cancers associated with the identified exposures.

3) Identification and characterisation of cases

Have all the cases been identified?

Are all the cases of the same (or similar) type?

The extent to which all cancer cases can be identified, and the type of cancer confirmed, depends on the available data sources. Cancer is a notifiable disease in Australia, and State and Territory cancer registries record information on all cases of cancer, including details on the type of cancer and the person affected. These registries have been in operation for several decades. It is possible to obtain information from cancer registries concerning whether a particular person or group of persons have been diagnosed with cancer and, if so, to find out information about the case. However, this requires the name, sex and date of birth of the person, their permission (if this is reasonable to obtain, although this may not be necessary for all persons in this instance) and ethics approval by the relevant cancer registry. If information is required from all cancer registries in Australia (as would be needed in a comprehensive study), separate ethics applications would be required for all of them. It might be reasonable in some circumstances to limit enquiries to the registries of the States and Territories in close proximity to the site of the cluster (in this case, to the New South Wales (NSW) and the Australian Capital Territory (ACT)).

The Steering Committee expressed a strong view that, because academic staff members commonly move interstate with their occupation, all Australian cancer registries should be approached. Therefore, it is planned that all cancer cases be identified through a request of cancer registries from all States and Territories. In addition, it is usual in such studies to also use the National Deaths Index to allow calculation of cancer mortality rates in addition to cancer incidence rates. This will require ethics approval from 10 ethics committees:

- the University of New South Wales Human Research Ethics Committee;
- the relevant ethics committee for each of the eight States and Territories;
- the ethics committee of the Australian Institute of Health and Welfare (this covers cancer registry data and National Deaths Index data).

There will also need to be an independent review of study methodology, as this is required by several of the ethics committees. This will be requested from the Research Review Scheme conducted by the School of Public Health at the University of Sydney.

Gaining ethics approval can be very frustrating and can be expected to take a minimum of six months and possibly up to 12 months². Approach will be made to the University Human Research Ethics Committee as soon as possible, as this is required before application can be made to several of the other ethics committees.

² As a guide, obtaining approvals for the current investigation into a cancer cluster at the National Gallery of Australia took from October 2006 to July 2007.

Matching to cancer registry data will require a list of the name, sex and date of birth (and, if available, last known address) of all staff who have worked in the Morven Brown Building back to a particular point in time. Information from the Human Resources section suggests that this information is available for:

- all current staff, regardless of when they were first hired;
- all previous staff who worked at some time from the beginning of 1996, regardless of when they were first hired.

The previous database that was used for staff is a read-only database that cannot provide information on all people who have worked in the Faculty during a particular time period – it can only provide information on individuals if their name or staff number is known. Therefore, it will not be possible to identify staff members who no longer work at the University and who did not work for the University for at least some time from the beginning of 1996.

It is expected that the information from the database, plus information from Steering Committee members or others within the Faculty, will allow reasonably accurate determination of when individuals worked in the Morven Brown building.

Non-Faculty members (e.g. people working in the shops housed in the building, or working in the bank adjacent to the building) will not be included because there is insufficient information about such staff who have ever worked in the building, there are not many such people, it would require liaison with other employers, and the results of the study found for Faculty members should apply to these people. This is because Faculty members are likely to have spent more time in the building, and so to have greater potential for “exposure” than these other workers.

Similarly, casual tutors, graduate students, and other students will not be included because records on these tutors and students appear to be incomplete, their numbers are relatively small and their exposures are likely to be less than those of Faculty members.

Therefore, the study population is planned to be all current and former staff members of the Faculty of Arts and Social Sciences (or the equivalent in the past) who have worked in the Morven Brown building at any time from 1 January 1996 onwards (with 30 June 2006 the likely cut-off date that will be used – the precise date used will depend on the date to which cancer registry data are available). No minimum period of work will be required at this stage, but a minimum time may be used as a cut-off during the analysis.

The alternative approach of attempting to contact all current and previous staff who have worked in the building to ascertain whether or not they have been diagnosed with cancer and, if so, the type of cancer, was considered by the project team and the Steering Committee. However, it was decided not to pursue this approach because it can be expected to be difficult to track down past employees, and it is likely that the self-report of cancer, especially the type of cancer, will be subject to error. This approach therefore has a lot of potential for under-recognition of cancer cases and information bias and so would not provide as good a level of evidence. However, a letter will be sent by the Faculty to the last known address of all eligible previous staff members to inform them about the study and provide them with an opportunity to obtain more information about the study. Information about the study will also be publicised through the University web site and the press.

Extent of information on individual cases

A related issue is whether individuals who have developed cancer should be contacted and interviewed in depth in order to identify evidence that might suggest the cancer was more likely or less likely to be related to occupational exposures or to non-occupational factors. This approach raises difficulties because some of the people with cancer can be expected to have died and so accurate detailed information is unlikely to be able to be obtained about them. In addition, although some people might identify themselves as cases, other people with cancer will only be identified via a cancer registry, and there are significant ethical concerns about contacting someone who has not initially consented to be contacted. Therefore, even if it is

thought desirable in theory to obtain detailed information about individual cases, there are practical limits on what might be possible. However, if detailed information could be obtained on most cases, this would probably add to the strength of the overall assessment, and might also emphasise for the cases the seriousness with which the possibility of a work-related contribution to their illness is being taken.

Following discussions with the Steering Committee, on balance it was decided that the study be advertised widely and that people who have worked in the Morven Brown Building and developed cancer be encouraged to contact the project leader to discuss the possibility of being interviewed. The project leader will then arrange to interview each person individually, if they agree, using a standardised protocol (which might differ somewhat depending on the type of cancer involved). However, people who are identified via the cancer registry search, but who do not contact the investigator, will not be approached.

4) Literature review of causes of identified cancers

Do the cancer types have a known common cause, whether occupational or non-occupational?

Once the cancer types have been identified, a review of the published literature is required to identify the known or suspected occupational (and non-occupational) causes or associations for each cancer type.

This will entail a search of the literature, critical appraisal of relevant articles and synthesis of the relevant information. A focussed critical review of relevant published, peer-reviewed literature will therefore be conducted, relying on review articles as much as possible. The review will seek to provide a concise summary of the current state of knowledge of the known and suspected occupational causes of each of the identified cancer types.

5) Assessment of exposure of cases

Did the persons diagnosed with cancer have a common occupational (or non-occupational) exposure?

Information on exposures of cases will be based on their occupation and, if the person is interviewed, on the information provided at interview.

6) Assessment of temporal plausibility

Did the cancers occur at an appropriate time in relation to the possible workplace exposures?

The latency between exposure and onset of cancer is believed to be typically of the order of at least ten to 15 years. This means that, in most cases, cancers that occur during the first five to ten years of employment are unlikely to be related to that employment. It is therefore important to try to obtain information on when and for how long each person worked in the Morven Brown Building prior to their diagnosis. Calculation of cancer incidence rates can then be made assuming no latency, and repeated taking into account the time between first employment and diagnosis. In addition, analyses taking into account period of exposure (time worked in the building) will also be conducted where possible.

7) Epidemiological assessment

Is there statistical evidence to suggest that the number of cases is in excess of what would be expected in this population?

Assessing whether there are more cases of cancer, either overall or of a particular type, requires comparing the rate of cancer in the employees with the rate expected, based on the rates in the general population for persons of the same age and sex.

To calculate rates for the relevant employees (the population at risk), it is necessary to know the number of cases of cancer, and to take into account the length of time the person was working in the Morven Brown Building, their age at diagnosis, their age when employed (in practice this requires information on date of birth and dates of employment) and their sex.

To calculate the expected rates, information will need to be obtained from the Australian Institute of Health and Welfare. This information is publicly accessible already.

Standardised rates based on this information will be calculated. However, it needs to be recognised that the interpretation of the statistics is fraught with difficulty. This is because the statistical tests are being conducted on a population that is already considered to have a higher rate than normal (that is why the investigation is being conducted), so it would not be surprising if a higher rate is found. The statistical tests that might be conducted are essentially post-hoc and therefore probably carry little weight. There are approaches that can be used to attempt to take this post-hoc nature into account, but none are very satisfactory. This difficulty has been explained to the Steering Committee, but the committee members have advised they do still want the rate calculations to be undertaken.

8) Overall assessment

On the balance of probabilities, is it likely that the identified cancers occurred as a result of occupational exposures?

Are there any plausible non-occupational causes for the apparent cluster?

The final advice as to the presence of a cluster and the likelihood of a connection to occupational exposures in or around the Morven Brown Building, or to non-occupational exposures, will be based on all the above information. Similarly, any recommendations will be made once all information has been considered.

9) Summary of methodology

The project will involve:

- review of past exposures to hazardous substances, as well as relevant physical and biological hazards, and work practices relevant to these exposures;
- review of current exposures to hazardous substances, as well as relevant physical and biological hazards, and work practices relevant to these exposures;
- reviewing the literature to identify cancers associated with the identified main exposures;
- attempting to identify all incident cases of cancer amongst current and former UNSW staff of the Faculty of Arts and Social Sciences (or the equivalent in the past) who have worked in the Morven Brown Building at some time from the beginning of 1996 to the present by matching their names with information at State and Territory cancer registries;
- interviewing cases who contact the investigator and agree to be interviewed;
- reviewing the literature to identify work-related exposures associated with the identified cancers;
- comparison of the rate of cancer (overall and for specific cancers, if relevant) in the relevant staff with an age and sex-matched Australian population;
- an overall assessment of the likelihood that occupational exposures have contributed to the past and/or current employees having a higher than expected rate of one or more cancers;
- provision of recommendations based on the above information.

ETHICAL ISSUES

The main ethical issue involved in this project relates to the investigation of past and current workers' health status and medical history. In particular, the planned matching of employee name to cancer registry data will require approval of the ethics committee of each registry that is to be approached, and University ethics approval will be required to allow interviewing of persons with cancer. Consent for registry matching will be required from current employees. However, it will be argued (and has been accepted previously by the ethics committees) that it will not be possible or practical to gain this permission (because of out of date or unknown contact details) for past employees, and it can be reasonably argued that the investigation is being done for public benefit. It is reasonable to expect that an ethics committee will grant access on the basis of that public benefit without requiring individual consent of the past employees. In addition, In keeping with ethics committee recommendations from a recent similar study, letters will be sent from the Faculty to all past employees informing them of the study and inviting them to contact the project leader if they would like to discuss the project.

CONFLICT OF INTEREST

There are no known conflicts of interest in connection with this project.

CONFIDENTIAL INFORMATION AND EXISTING INTELLECTUAL PROPERTY

It is not expected that the confidential information will be used for the project or included in the project report. No pre-existing intellectual property is expected to be introduced by the respondent.

TIMEFRAME

The main impediment to the project is the work required to gain access to cancer registry information. As mentioned earlier in this submission, obtaining ethics approval is typically a long and drawn-out process. It is not unusual for a requirement for several iterations of an ethics document before it is approved, and the ethics committees typically meet only every few months. Since permissions will be required from 10 ethics committees, it is typical for there to be between six and 12 months between when the application is first submitted and the data are finally received. Therefore, it is to be expected that the project will not be completed until towards the end of 2008 or early 2009. Although this time frame seems very long, it is not possible for the project team to significantly influence this, apart from making timely submissions to the ethics committees.

Therefore, the project will be conducted in two overlapping phases. This is the approach being taken in the National Gallery project on which the project team is currently working, and seems to have worked well. Phase 1 will be the review of past and present workplace exposures and work practices. Phase 2 will cover the cancer registry matching, comparison to Australian data and review of literature on occupational causes of the identified cancers. Both phases will start concurrently, but an interim report, covering Phase 1, will be submitted in the first half of 2008. The final report, which will cover Phase 2 and include the Phase 1 interim report, will be submitted as soon as possible after the results are received by the cancer registry. It is not possible at this stage to be definitive as to when this will be, as this is primarily dependent on cancer registry processes rather than the study team but it will almost certainly not be until the last quarter of 2008.