Exploring New Frontiers in Occupational Epidemiology: The Hunter Community Study (HCS) from Australia

Derek R. SMITH1*, John ATTIA2 and Mark McEVOY2

1WorkCover New South Wales Research Centre of Excellence, Faculty of Health, University of Newcastle, Ourimbah, New South Wales 2258, Australia
2Centre for Clinical Epidemiology and Biostatistics, Faculty of Health, University of Newcastle, Newcastle, Australia

Received March 20, 2009 and accepted September 9, 2009

Abstract: This article describes a pioneering longitudinal investigation from Australia known as the Hunter Community Study (HCS). The HCS investigates retired and near-retired persons randomly selected in a regional area on the heavily populated east coast. As it collects detailed survey, clinical, and biological measures, the HCS is more comprehensive than most other research of this nature. The HCS also has significant occupational implications at an international level, being one of the first Australian studies to take a full, lifetime occupational history linked to job exposures. Longitudinal cohort studies with exposure assessment, such as the HCS offer epidemiologists around the world a clear opportunity for examining and evaluating the long-term risks of employment across a variety of workplace settings. It is only with detailed datasets that continuing progress can be made in elucidating mechanisms of occupational disease causation in the new millennium.

Key words: Cohort studies, Epidemiology, Occupational, Exposure, Australia

Background

Occupational epidemiology has roots in classical medicine and can trace its origins at least as far back as Lind’s 18th century intervention with citrus fruits to help prevent scurvy among sailors in the British Navy1). Although various workplace diseases and their sequelae have been described since antiquity2), Percivall Pott’s 1775 treatise on scrotal cancer among chimney sweeps is generally believed to be one of the first identifications of causal links between occupation and malignancy3). A 1950s investigation of bladder cancer in the British chemical industry by Case and colleagues4) is often regarded as the archetypal historical cohort study. Longitudinal cohort studies now form the backbone of modern occupational epidemiology, and have served a particularly important role in the identification of various carcinogens and other workplace hazards with long lag times. Large community-based cohort studies have also been important in this discipline. Perhaps one of the most famous has been the Framingham Heart Study from the United States (US), which began in 1948, which was followed up by the Framingham Offspring Study in 1971, and most recently, a third-generation cohort in 20025). In Western Australia, a similar longitudinal cohort study has been conducted in the town of Busselton since 1966, otherwise known as the Busselton Health Study6).

Gender specific health issues represent an important consideration in modern occupational health and are particularly relevant in workplaces where the majority of staff are female8). Various longitudinal cohort studies have targeted the nursing profession. The US Nurses’ Health Study (US-NHS) for example, initially comprised a mailed survey of 121,700 women in 1976 to examine relationships between the use of oral contraceptives, cigarette smoking and the risk of major illnesses9). It maintained a high follow-up rate and remains one of the most...
detailed long-term studies of diet and major illnesses\textsuperscript{10}. A similar investigation, the Japan Nurses’ Health Study (JNHS) was initiated in 2001 to investigate the effects of various lifestyle factors and healthcare habits on the health of Japanese women\textsuperscript{11}. Almost 50,000 women responded to the baseline survey, with a 6-year entry period and a proposed 10-yr follow up\textsuperscript{12}. In Australia, the Nurses and Midwives e-Cohort Study (NMeCS) has been running since 2006, although response rates have thus far been very low\textsuperscript{13}. Aside from the US-NHS, JNHS and the NMeCS, various other cohort studies have also focussed exclusively on women. The Women’s Health Initiative (WHI) is a US-based study of approximately 64,500 women that commenced in 1992\textsuperscript{14}. The Million Women Study (MWS) is a population-based cohort study of around 800,000 women aged 50–64 yr from the United Kingdom (UK) that began in 1996\textsuperscript{15}).

The Hunter Community Study

In 2004–05, a pioneering longitudinal investigation was commenced in Australia, known as the Hunter Community Study (HCS). The HCS aims to investigate retired and near-retired persons and has just completed its baseline phase by sampling over 3,000 older Australians aged 55–85, randomly selected from electoral rolls in a regional area on the heavily populated east coast. As it collects detailed survey, clinical, and biological measures, the HCS is more comprehensive than most other Australian cohort studies. Main features of the HCS are summarised in Table 1.

Occupational exposure assessment

The HCS has significant occupational implications from both an Australian and international context, being one of the first Australian studies to take a full, lifetime occupational history linked to job exposures. Exposure assessment is well-known to represent a challenge for occupational epidemiology\textsuperscript{16}, partly because exposure itself is a complex, time-varying concept that must be summarized before it can be useful for exposure-response modelling\textsuperscript{17}. New risks in occupational health are also becoming more difficult to detect due to ever-decreasing exposure levels, as well as confounding due to multiple exposures in the modern workplace\textsuperscript{18}. Although it may be possible to collect retrospective exposure data from large organizations, this is often not cost-effective when considering only a relatively small number of target substances\textsuperscript{19}. Nevertheless, exposure-response analyses do play a critical role in the evaluation of etiological relevance of both chemical and physical exposures\textsuperscript{20}.

Job exposure matrices

For these reasons, the first computerised job-exposure matrices were introduced into occupational epidemiology during the 1970s, and have since been continually refined. In 1991 researchers using the Finnish Cancer Registry (FCR) database found that job-exposure matrices were the only feasible method for analysing the large FCR dataset by occupational exposure, thereby leading to the development of the Finnish Job-Exposure Matrix (FINJEM)\textsuperscript{21}. Data is supplemented with information on the labour force and with professional judgements\textsuperscript{22}. FINJEM is able to provide quantitative information on exposure prevalence, levels, and numbers of exposed persons by period, agent and occupation\textsuperscript{23}.

Control of potential bias

Aside from collecting the data itself, issues of confounding and bias are also important to consider in all studies involving occupational epidemiology\textsuperscript{24}. For these reasons, aside from documenting general demographic items such as age and gender, the HCS also records a full lifetime history of both tobacco and alcohol consumption among participants. These factors represent an important consideration within occupational epidemiology, and have long been debated as a potential source of bias. Smoking habits are well-known to vary by occupation\textsuperscript{25}, and the two are often substantially confounded\textsuperscript{26}. Similar to inherent workplace risks, smoking rates also vary widely by occupation in Australia, making it essential that smoking data is also considered when analysing HCS data. In 1989–90 for example, although roughly one-third of all Australian workers smoked, this rate varied considerably.

Table 1. Key components of the Hunter Community Study (HCS)

<table>
<thead>
<tr>
<th>Component</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full lifetime occupational history linked to a job-exposure matrix (FINJEM)</td>
</tr>
<tr>
<td>Full lifetime history of tobacco smoking and alcohol consumption</td>
</tr>
<tr>
<td>Sensory measures including vision, hearing, smell, vibration and balance</td>
</tr>
<tr>
<td>Measures of spirituality, religion and attendance at places of worship</td>
</tr>
<tr>
<td>Collection of biological samples, including whole blood, plasma, serum and whole cells</td>
</tr>
<tr>
<td>Routine analysis of electrolytes, full blood count, cholesterol, liver function, fasting glucose and fibrinogen</td>
</tr>
<tr>
<td>Self-reported and individual pedometry results for measuring physical activity</td>
</tr>
<tr>
<td>Linkage with various local, state and national health databases</td>
</tr>
</tbody>
</table>
by occupation and would also change over time\textsuperscript{27}. By 2004–05, approximately one-quarter of employed Australians were smoking, but again this varied widely, with over half of male cleaners being regular smokers, but less than 3\% of female science, building and engineering professionals doing so\textsuperscript{28}. Alcohol consumption represents another lifestyle variable that should also be collected during epidemiological investigations in the workplace\textsuperscript{29}.

**Healthy ageing**

Longer life expectancies, lower birth rates and delayed retirement are all impacting on contemporary workforce demographics\textsuperscript{30}. An ageing workforce offers various new challenges for occupational epidemiology, and one that some have suggested may actually need more of a geriatric perspective\textsuperscript{31}. One main focus of the HCS is healthy ageing, including post-retirement, and for these reasons it was deemed important to ensure that sensory measures such as vision, hearing, vibration and balance are carefully investigated. Of particular interest to occupational epidemiologists is the inclusion of tests of olfaction in the HCS. Given that olfactory neurons represent some of the most exposed nerve cells in the body, being in constant, direct contact with air and particulate matter, it has been suggested that changes in olfaction can be the harbinger of neurotoxic exposures\textsuperscript{32}.

**Physical activity**

Physical activity is another factor that plays a key role in healthy ageing. In terms of its overall contribution to the burden of disease for example, physical activity has been recognised as Australia’s second most important area for risk-factor reduction, after tobacco\textsuperscript{33}. On the other hand, the health benefits of physical activity have been shown to be at least as great as treating hypertension or cholesterol reduction\textsuperscript{34}. For these reasons, the HCS issues a personal pedometer to measure physical activity levels among each member of the cohort. In recent years there has also been increasing scientific interest in the potential relationships between spirituality, religion and health\textsuperscript{35}. The HCS therefore includes measures of spirituality, religion and attendance at places of worship; one of the first Australian cohort studies to have done so.

**Biological measurements**

Apart from collecting detailed demographic and workplace information, the field of epidemiology also has a long history of using biological samples and measurements in its research\textsuperscript{36}. Biological sampling comprises another important facet of the HCS, with common biochemistry including electrolytes, full blood count, cholesterol, liver function, fasting glucose and fibrinogen, being routinely undertaken as part of the study’s clinical component. Additionally, samples of whole blood, plasma, serum and whole cells are also frozen for future use, a provision that only recent cohorts have included. The US NHS for example, although beginning in 1976, did not receive funding to collect biological samples until 1989\textsuperscript{10}. Biological sampling at baseline, therefore, represents another significant advantage of the HCS.

**Genetic biomarkers**

Multifaceted epidemiologic research with the potential to identify genetic biomarkers can be seen as a continuum between basic sciences, clinical, occupational and public health practice\textsuperscript{36}. As such, the examination of genetic biomarkers enabled by collecting biologicals has become an important issue for occupational epidemiology in recent years, for a variety of reasons. Firstly, there are the biomarkers of susceptibility, the genetic variants known as polymorphisms within enzymes that metabolise environmental exposures. These enzymes are present either in the cytochrome P450 system that comprises phase I metabolism (i.e. making the toxin electrophilic), or in the common phase II enzymes that make the toxin soluble for excretion (e.g. glutathione-S-transferase or N-acetyltransferase)\textsuperscript{37}. The net result is that an individual has either an increased or decreased ability to detoxify exposures, and hence, a comparatively lesser or greater likelihood of toxicity, respectively. Secondly, there are the biomarkers of exposure, for example adducts that reflect the reaction of a toxin with a protein or with DNA\textsuperscript{38}.

Thirdly, there are the biomarkers of genetic damage; which represent the toxin’s footprint, having had a detectably damaging effect on DNA. These include single or double-stranded DNA breaks detected using the COMET assay, DNA base mismatch, micronuclei, sister chromatid exchanges, and cytogenetic abnormalities\textsuperscript{39}. Detection of the latter 3 biomarkers usually requires analysis of whole viable cells, not just isolated DNA. As such, it is particularly novel that the HCS stores whole cells in DMSO to enable the future testing of these cellular biomarkers, a feature that is relatively uncommon among most other cohorts with stored biologicals. It is interesting for environmental epidemiologists to consider that some DNA changes acquired in such a manner may be subsequently transmitted to future generations\textsuperscript{40}, particularly if the mutations occurs in germ cells. Indeed, this has already been hypothesised by certain authors as a possible explanation for childhood leukaemia\textsuperscript{41}.

**Multiple physiological measures**

The benefits of measuring occupational and environmental exposure biomarkers of internal dose and biologically effective dose may be further enhanced if they are
measured along with biomarkers of biological effects such as inflammation, reactive oxygen species, lipid peroxidation and cellular damage. In its current form, the HCS already collects inflammatory marker information in the form of fibrinogen levels and leukocyte counts, with future plans to measure high sensitivity C-reactive protein (hsCRP) and cytokines such as interleukin-6 (IL-6) as more sensitive markers of systemic inflammation. The HCS also has the potential to measure occupational and environmental exposures such as volatile organic compounds and transition metals. Overall, as a result of these measurements, the HCS can provide a comprehensive picture of occupational and environmental exposures by combining information provided by FINJEM with biomarker information obtained from stored biological samples.

Data linkage
A final pioneering facet of the HCS cohort is its linkage with various local, state and national health databases. Record linkage as a concept aims to bring together records derived from different sources but relating to the same person\(^42\). It is known to be an invaluable tool for epidemiological research, particularly in studies involving cancer incidence among different occupational groups\(^43\). Occupational cancer research which utilises record linkage has been particularly successful in countries and regions with national cancer registries and personal identification numbers, such as Denmark, Finland, Norway, Iceland and Sweden\(^44\). Record linkage has also been successfully used in various Australian studies\(^42, 45, 46\).

Conclusion
Occupational health research as a distinct science depends on vast and sophisticated databases of epidemiological information in order to inform decisions and make conclusions based on causation\(^47\). When disease epidemiology was in its infancy most occupational exposure levels were relatively high, although with time many exposures have been markedly reduced, making the detection of increasingly subtle risks a growing priority. Longitudinal cohort studies with exposure assessment, such as the HCS, therefore offer epidemiologists around the world a clear opportunity for examining and evaluating the long term risks of employment across a variety of workplace settings. It is only with detailed datasets such as those provided by the HCS, that continuing progress can be made in elucidating mechanisms of disease causation in the new millennium.

Acknowledgements
The Hunter Community Study research team includes: Wayne Smith, Catherine D’Este, Mark McEvoy, Roseanne Peel, John Attia, Julie Byles, Janine Duke, Ben Ewald, Stephen Hancock, David Henry, Peter Schofield and Rodney Scott. The team gratefully acknowledges the work of many other clinic nurses and data collectors, as well as the many participants who freely gave their time.

Financial support for the study was gratefully provided by the Vincent Fairfax Family Foundation, the University of Newcastle Strategic Initiative Fund and the University of Newcastle Braun Fellowship.

References


