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Lessons from ecological and spatial studies in relation to occupational lung disease

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Abstract

Purpose of review—The majority of epidemiological research into occupational lung disease has been advanced by study of individuals, typically in a work place setting. This review examines how recent advances in ecological and spatial study methodology and in the information held in routine databases could be used to enhance occupational health studies.

Recent findings—Ecological studies often use routinely collected data and this is becoming much more extensive and better validated with potential for increasing use in occupational health research. Improvements in computing power and statistical and geographical information systems (GIS) methodology have led to more sophisticated mapping techniques and greater use of spatial information when investigating lung diseases usually related to occupational exposures. Ecological study methodology is experiencing a radical overhaul with supplementation of group-level data with information from small-scale individual-level studies. This hybrid design can be used to reduce bias and increase power and is directly applicable to enhancement of aggregate information from job exposure matrices (JEMs).

Summary—Studies of occupational lung disease can be enhanced by incorporating methodological innovations from ecological and spatial studies.

Keywords

occupational exposure; lung diseases; occupational diseases; epidemiologic methods; geographic information systems

Introduction

The majority of epidemiological research into occupational lung disease has been advanced by study of individual cases, typically in a work place setting, with predominant study designs being cohort, case-control and cross-sectional studies.(1) Ecological studies are rarely used to study occupational lung disease – any that do may show information about occupation as a confounder rather than being the main focus of the study.(2)

Ecological studies are analytic observational studies, usually used for hypothesis generation. The unit of observation is a group of people rather than an individual⁽³⁾ where grouping may be by area of residence, distance from a factory or type of occupation; the statistical analysis in such a study usually uses rates as the outcomes of interest e.g. leukaemia incidence rates for each residential area, respiratory hospital admission rates for each distance band from factory, mesothelioma mortality rates for each occupational group. The main ecological study designs are time series and spatial studies. Time series have been most extensively used in air pollution epidemiology – rates of disease such as cardiovascular hospitalisations per day are related to air pollution concentrations in a defined area. Spatial studies use routine data on health and exposures to compare groups in different geographical areas, e.g. rates of disease in those living near certain industrial installations (or a point source) compared with those further away.

Only group-level information is available on exposures, disease and confounding factors such as smoking (or proxies thereof). Because of the bias introduced by inferring information about individuals from group-level data (the ecological fallacy),⁽⁴⁾ they are held to be a less strong study design than case-control, cohort, or randomised controlled trial study designs.

The traditional ecological study has been used in the following ways that may also be of benefit for investigation of occupational lung disease

- (i) It provides a 'first look' to indicate or identify a problem. Such studies often use existing sources of data and are therefore relatively quick and inexpensive.
- (ii) It provides corroboratory evidence of an association. This is important for conditions like work-related asthma, where practical issues often make clinical testing difficult. The recent American College of Chest Physicians consensus statement on work-related asthma⁽⁵⁾ commented on the need to use ecologic data, temporal trends and case-reports to supplement sparse randomised controlled trial evidence when making its recommendations.
- (iii) An ecological study may be the only study possible, if suitable data can only be made available at group or small area level and opportunities to study disease at individual level are limited (e.g. by political sensitivities or by cost). This may be useful for occupational studies where large industries provide the main source of occupation in an area.

Ecological studies often make use of data held on large population-based national and regional databases, such as cancer registries, hospital databases and compensation claims for occupational illness. These databases and linkages across them are becoming increasingly sophisticated. Ecological data are used extensively in spatial studies⁽⁶⁾ aided by both developments in geographical information systems (GIS) and in Bayesian statistical techniques. In addition, traditional ecological study methodology is currently undergoing a radical overhaul with implications for occupational disease analysis, most notably to improve exposure estimates using job exposure matrices (JEMs). These three areas will be discussed further below.

Most traditional statistical analyses in common usage in current medical research use techniques based on a frequentist statistical philosophy, but statistical analyses based on a Bayesian philosophy are increasingly being adopted. A discussion of statistical philosophies is beyond the scope of this review, but readers are referred to a short article by Bland & Altman(7) for an introduction to the difference between frequentist and Bayesian analyses. In brief, in a Bayesian framework, the statistical model can be specified to incorporate prior scientific knowledge or beliefs and end results are expressed as the probability of a parameter given the observed data. In a frequentist framework, the incorporation of prior scientific knowledge is less explicit than in a Bayesian statistical model and probabilities should technically be interpreted as frequencies that would be observed given a long run of repeated sampling.

Developments in routinely collected data

With the increasing computerisation of healthcare systems, many countries, regions and healthcare providers now hold large routinely collected databases going back many years. In the UK, this will soon extend to an electronic patient record (<http://www.connectingforhealth.nhs.uk/systemsandservices/nhsers>) with information from all National Health Service patient contacts from primary care to tertiary care. Some of the most detailed information is collected in Scandinavian countries,(8) with additional value from linkages across health databases. This offers a number of opportunities to investigate occupation-related lung diseases. For example, a study in Leeds, UK (9) combined hospital records, a histology database and coroner's reports to produce the first unselected population-based study of the natural history of mesothelioma.

While routine data sources are generally large, comprehensive and readily available, recent articles have examined issues in interpreting and using them, (10;11) particularly when coding versions change (e.g. from ICD-9 to ICD-10). (12)

Databases containing occupational information can be enhanced with additional information including JEMs to investigate links between potentially hazardous exposure and health outcomes. Some JEMs, such as FINJEM(13) published in 1998 have been specifically produced for use in large registry-based studies for hazard surveillance and control. FINJEM was first validated by being used to replicate the previously observed association between exposure to crystalline silica and lung cancer(14). Laakkonen(8) then investigated the cancer risks from occupational exposure to moulds and bacteria, using Finnish Census data from 1970 plus information from FINJEM, which gave information on average exposure levels to major occupational exposures in Finland since 1945. Information on alcohol and smoking were obtained from occupational averaged group-level data from national health behaviour surveys. It was concluded that occupational exposures to mould or bacteria were unlikely to be major risk factors for cancer, but an interesting reduced risk for lung cancer was seen with higher mould exposure. The authors commented this may give support to the hypothesis that bacterial endotoxins reduce the risk of lung cancer as exposure to moulds is generally concurrent with bacterial exposure.

Mapping and spatial analyses

Depending on the information collected and its validity, routine data may be employed in a number of ways e.g. aetiological studies, tracking spatial and temporal trends of disease or examining health care usage, particularly on diseases highly attributable to occupational exposure. Mapping alone can be informative – for example mapping asbestos-related disease SMRs in UK districts 1981–1999 (Figure 1) shows highest rates in the industrialised conurbation areas near London, Newcastle and Glasgow and in former ship-building centres such as Plymouth.

Hypotheses raised from mapping can be followed by analytical studies. For example, lung cancer rates and mesothelioma rates were found to be higher in former shipbuilding areas of the USA and in counties with arsenic smelters (http://dceg.cancer.gov/atlas/text2/full_txt.html).⁽¹⁷⁾ A recent update for mesothelioma⁽¹⁸⁾ using US registry data continued to show higher rates in shipyard areas on the West coast but confirmed the expected decline in the higher rates of mesothelioma in older ages.

A common problem encountered when mapping disease data is small numbers of cases where observational ‘noise’ may obscure risk patterns, particularly at fine spatial scales. This can be addressed within a hierarchical statistical model, essentially smoothing the data and providing statistical probabilities for observed relative risk (e.g. 80% probability that ‘true’ relative risk is >1 for an area). This type of modelling is usually implemented in a Bayesian statistical framework⁽¹⁹⁾ and is increasingly used in mapping of registry and other population-based data – different model specifications are available and have recently been reviewed.⁽²⁰⁾ These mapping methods are essentially conservative, with high specificity.⁽²¹⁾

Spatial studies in occupational lung disease

A further recent development is joint modelling of spatial distribution of risk for diseases that share risk factors in common – the shared component model.⁽²²⁾ This has been used in an ecological study indirectly examining the relationship between COPD mortality and coal-mining exposures in the UK.⁽²⁾ Firstly, the spatial distribution of mortality from COPD and lung cancer were jointly modelled.⁽²³⁾ This permitted adjustment of area COPD mortality risks for lung cancer mortality, using the latter as a proxy for smoking.⁽²³⁾ A subsequent ecological regression indicated higher COPD risks (adjusted for the smoking proxy) in areas with high pneumoconiosis mortality (a proxy for areas with high coal-mining related exposures), after also adjusting for deprivation, SO₂ air pollution, fruit and vegetable purchases, temperature and rainfall (paper in preparation).⁽²⁾

Where there is a cluster of a disease usually associated with occupational exposures that cannot be readily explained, a study examining the spatial clustering of such cases can result in useful hypotheses about putative environmental sources that can be examined with further analyses and follow-up studies.⁽²⁴⁾ For example, chronic beryllium disease is primarily related to occupational exposure, but residential mapping of non-occupationally acquired cases may confirm an association with a suspected industrial source⁽²⁵⁾ and help identify

the populations at risk(26) where beryllium disease should be included in the differential diagnosis of cases of sarcoidosis. Airborne exposure to asbestos was the most likely cause of a cluster of mesothelioma cases in Japan, where a spatial analysis of mesothelioma cases including dispersion from the putative factory source confirmed highest rates downwind.(27) This was combined with individual-level information to exclude occupational and other environmental sources of exposure such as from housing and road materials.

Enhancement of ecological studies by inclusion of individual level data and application to job exposure matrices

A limitation of traditional ecological studies is that they suffer from what is termed “ecological bias”(4), whereby inferences about associations between group level exposures and group level outcomes are not necessarily the same as the association between the same exposures and outcomes at the individual level. For example, the increase in rate of lung cancer in the workforce associated with, say, a doubling of the average concentration of radon in the workplace is not necessarily the same as the increase in risk of lung cancer to an individual whose occupational radon exposure is doubled. Differences between individual and group level risk estimates in ecological studies can arise for various reasons, in particular, if the exposure varies within the group. Recently, statistical methods for combining random samples of individual level data with group-level data on the same variables have been developed, which aim to alleviate ecological bias by accounting for the within-group variability in exposure. For example, exposure measurements on samples of around 50-100 individuals per group can be used to supplement aggregate exposure and outcome data, and then averages the exposure-outcome relationship over the within group exposure distribution as outlined by Prentice(28). The Hierarchical Related Regression (HRR) method of Jackson et al(29), enables individual-level exposure-response relationships to be estimated from a joint analysis of individual level and group level data on both outcomes and exposures. Extensive simulation studies have demonstrated the utility of both approaches for reducing ecological bias; HRR methods can also greatly increase power over individual level data analysis alone. HRR methods have been applied to an analysis of socio-economic predictors of limiting long term illness(29) and to investigate the relative contribution of individual and contextual socio-economic factors on risk of hospital admission for cardiovascular disease and limiting long term illness.(30;31)

The applications outlined above used area-level data to define the groups. However, other group structures can be used, for instance the people sharing the same job title. Exposure to known and suspected chemical carcinogens, endotoxins and allergens as well as to work stress, shift work, lack of physical activity and reduced/postponed parity etc. can all be estimated on an aggregate level using a JEM.(32) This matrix contains estimates of (a) the overall prevalence of exposure, and (b) the mean level of exposure among the exposed in the group, for the risk factors of interest for all distinct occupational groups.

JEMs can be combined with data from, for example, disease registers including occupation information of subjects, to carry out an ecological analysis. However, such an analysis will suffer from the same problems of bias as traditional area-level ecological studies, since

exposures are likely to vary within occupational groups. This bias could be alleviated using the methods outlined above if additional individual data were available, from, for example, a health survey including data on relevant occupational exposures and (for HRR methods) disease outcomes. Expert opinion provided by industrial hygienists and/or information from survey measurements of distribution of exposure within each JEM group could be used to provide further information on the variability of exposure within the occupational groups. Information about variability of exposure will necessarily be population specific e.g. expert opinion covering jobs in Finland is not necessarily appropriately applied to a British population. Further enhancements to JEMs can be made by adding individual-level data on non-occupational confounders such as smoking or alcohol applied to the study groupings, using data available through national surveys as used in the FINJEM study discussed earlier(8). Alternatively, enhancement data may be feasibly obtained via small-scale detailed individual-level surveys on a subset of the population under study.

We are not aware of any published examples of applications of the methods used by Prentice(28) or Jackson et al(29) discussed above to JEMs to date. However, the information necessary to enhance JEMs is often collected during JEM development. For example, Swuste in 2008(33) produced JEMs for historical asbestos exposure in the Netherlands using extensive measurements from four different databases on personal asbestos exposure measurements to provide seven categories of average exposure to asbestos using both arithmetic and geometric mean. The geometric standard deviation was also supplied in the paper. Application of the new methodologies would result in use of the published distribution (geometric mean and standard deviation)(33) being attached to the JEM category. The risk estimates for asbestosis and lung cancer could be further enhanced if information on average fibre diameter as well as mean level of exposure were available.(34) This second average (for fibre diameter) would also have a distribution attached. A similar approach could be extended to other disease areas, for example, JEMs for endotoxin exposure where exposure to geometric mean endotoxin exposure was calculated for different job titles(35) or to combinations of occupational cumulative exposures such as radon, quartz and arsenic.(36)

Conclusion

Recent enhancements in health database coverage and linkage provide new opportunities for occupational health studies. Such group-level information can be enhanced by incorporating individual-level information from other sources to reduce bias in job-exposure matrices and to provide information on confounders such as smoking. Recent advances in mapping can improve interpretation of maps where numbers of cases are small, while spatial methodology development suggests a wider role for the use of spatial analyses to examine occupational lung disease.

Annotated Reference List

- *(1). Rushton L. Occupational Causes of Chronic Obstructive Pulmonary Disease. Reviews on Environmental Health. 2007; 22(3):195–212. [PubMed: 18078004] [Comprehensive review of studies investigating various occupational exposures linked with COPD]

- * (2). Hansell AL, Aylin P, Best N. Are Annual Average Ambient Air Pollution Levels Associated with Spatial Variations in COPD Mortality in the UK? *Proc Am Thorac Soc*. 2006; 3(Abstracts Issue(April)):A46. [Abstract for an ecological regression study (paper in preparation) showing impact association of area-based pneumoconiosis mortality rates (assumed to reflect impact of coal-mining) with area-based COPD mortality rates. The latter were adjusted for cumulative smoking exposure using area-based lung cancer mortality rates as a proxy as this information is not readily available directly.]
3. Rothman, KJ.; Greenland, S. *Modern Epidemiology*. Philadelphia, PA: Lippincott-Raven Publishers; 1998.
4. Greenland S, Morgenstern H. Ecological bias, confounding and effect modification. *Int J Epidemiol*. 1989; 18:269–84. [PubMed: 2656561]
5. Tarlo SM, Balmes J, Balkissoon R, Beach J, Beckett W, Bernstein D, et al. Diagnosis and Management of Work-Related Asthma: American College of Chest Physicians Consensus Statement. *Chest*. 2008 Sep 1; 134(3_suppl):1S–41. [PubMed: 18779187]
- * (6). Elliott, P.; Wakefield, J.; Best, N.; Briggs, D. *Spatial Epidemiology. Methods and Applications*. Paperback ed, Oxford: Oxford University Press; 2001. [Recommended textbook on methodology of spatial methods]
7. Bland JM, Altman DG. Statistics notes: Bayesians and frequentists. *BMJ*. 1998 Oct 24; 317(7166): 1151–60. [PubMed: 9784463]
- ** (8). Laakkonen A, Verkasalo PK, Nevalainen A, Kauppinen T, Kyyronen P, Pukkala EI. Moulds, bacteria and cancer among Finns: an occupational cohort study. *Occup Environ Med*. 2008 Jul 1; 65(7):489–93. [PubMed: 18032534] [Ecological hypothesis-generating study using a JEM developed for use in large registry-based study to investigate potential cancer risk from occupational exposure to environmental moulds and bacteria. Study also incorporated individual-level survey information to provide likely exposure to confounders such as alcohol and smoking.]
- * (9). Chapman A, Mulrennan S, Ladd B, Muers MF. Population based epidemiology and prognosis of mesothelioma in Leeds, UK. *Thorax*. 2008 May 1; 63(5):435–9. [PubMed: 18202164] [First population-based study looking at natural history of and interventions used for mesothelioma in a UK city, combining information from three data sources, compared with cancer registry data.]
- * (10). Perez-Padilla R. Hidden Respiratory Disease-associated Deaths. *International Journal of Tuberculosis and Lung Disease*. 2008; 12(4):458–64. [PubMed: 18371275] [Study examining the impact of use of the ICD-10 coding system to estimate respiratory mortality, as >40% or respiratory-related conditions (and 5-7% of respiratory-related deaths) may be coded outside group J, the respiratory chapter.]
- * (11). Hansell AL. Lies, damned lies and mortality statistics? *Thorax*. 2006 Nov 1; 61(11):923–4. [PubMed: 17071829] [Editorial reviewing the limitations of mortality statistics.]
- * (12). Brock A, Griffiths C, Rooney C. The impact of introducing ICD-10 on respiratory mortality trends in England and Wales. *Health Statistics Quarterly*. 2006; 29(Spring 2006):9–17. [PubMed: 16523676] [Study examining the impact of changing from the ICD-9 to ICD-10 coding system on respiratory disease trends.]
13. Kauppinen T, Toikkanen J, Pukkala E. From Cross-Tabulations to Multipurpose Exposure Information Systems: A New Job-Exposure Matrix. *Am J Ind Med*. 1998; 33:409–17. [PubMed: 9513649]
14. Pukkala E, Guo J, Kyyrönen P, Lindbohm M-L, Sallmén M, Kauppinen T. National job-exposure matrix in analyses of census-based estimates of occupational cancer risk. *Scandinavian Journal of Work, Environment & Health*. 2005; 31(2):97–107.
15. Hansell, AL. *The epidemiology of chronic obstructive pulmonary disease in the UK: spatial and temporal variations*. University of London; 2004.
16. Coggon, D.; Inskip, H.; Winter, P.; Pannett, B. Occupational mortality by cause of death. Occupational health: decennial supplement. Drever, F., editor. The Registrar General's decennial supplement for England and Wales; OPCS; London: 1995. p. 62-76.
17. Devesa, SS.; Grauman, DG.; Blot, WJ.; Pennello, G.; Hoover, RN.; Fraumeni, JF Jr. Atlas of cancer mortality in the United States, 1950-94. Washington, DC, USA: US Govt Print Off; 1999. [NIH Publ No. (NIH) 99-4564]

- *(18). Teta MJ, Mink PJ, Lau E, Scurman BK, Foster ED. US mesothelioma patterns 1973-2002: indicators of change and insights into background rates. *European Journal of Cancer Prevention*. 2008; 17(6):525–34. [PubMed: 18941374] [Recent examination of US registry data confirming continued higher rates of mesothelioma in major shipyard areas of the West coast. Reassuringly rates are falling in older age groups and stable in younger age groups suggesting that exposure control measures have worked.]
- *(19). Pascutto C, Wakefield JC, Best NG, Richardson S, Bernardinelli L, Staines A, et al. Statistical issues in the analysis of disease mapping data. *Stat Med*. 2000; 19:2493–519. [PubMed: 10960868] [Statistical methodology of new Bayesian approaches to disease mapping, allowing more meaningful interpretation of maps where numbers of cases per area are sparse. Will be used for forthcoming Thames Cancer Registry maps, covering London and the south-east of the UK.]
- *(20). Best N, Richardson S, Thomson A. A comparison of Bayesian spatial models for disease mapping. *Statistical Methods in Medical Research*. 2005; 14:35–9. [PubMed: 15690999] [Examines strengths and weaknesses of the several formulations of statistical models for disease mapping.]
- ***(21). Richardson S, Thomson A, Best N, Elliott P. Interpreting Posterior Relative Risk Estimates in Disease-Mapping Studies. *Environ Health Perspect*. 2004; 112(9):1016–25. [PubMed: 15198922] [Discusses and quantifies sensitivity and specificity of Bayesian disease mapping methodology for a non-statistical audience.]
- 22. Knorr-Held L, Best NG. A shared component model for detecting joint and selective clustering of two diseases. *J R Stat Soc Ser A Stat Soc*. 2001; 164(1):73–86.
- *(23). Best N, Hansell A. Geographic variations in risk: Adjusting for unmeasured confounders through joint modeling of multiple diseases. *pidemiology*. 2009 In press. [Statistical methodology underlying reference (2), used to adjust area-based COPD mortality rates for estimated cumulative smoking exposures based on lung cancer mortality risks.]
- *(24). Hansell A. Airborne Environmental Exposure to Asbestos. *Am J Respir Crit Care Med*. 2008 Sep 15; 178(6):556–7. [PubMed: 18755931] [Discusses the usefulness of spatial studies in examining asbestos and other traditionally occupational exposures.]
- *(25). Maier LA, Martyny JW, Liang J, Rossman MD. Recent Chronic Beryllium Disease in Residents Surrounding a Beryllium Facility. *Am J Respir Crit Care Med*. 2008 May 1; 177(9):1012–7. [PubMed: 18244954] [The first report of community-acquired chronic beryllium disease since 1969. Used mapping to help outline the population at risk and in case review.]
- 26. Rossman MD. Justification for screening for chronic beryllium disease: closer to reality. *Eur Respir J*. 2008 Sep 1; 32(3):543–4. [PubMed: 18757694]
- *(27). Kurumatani N, Kumagai S. Mapping the Risk of Mesothelioma Due to Neighborhood Asbestos Exposure. *Am J Respir Crit Care Med*. 2008; 178:624–9. [PubMed: 18556631] [Spatial study examining environmental exposure to asbestos from an asbestos cement factory operating 1957-1975. Airborne spatial dispersion modelling were combined with individual-level questionnaire to exclude occupational or other environmental exposure (e.g. roads, housing material).]
- 28. Prentice RL. Aggregate data studies of disease risk factors. *Biometrika*. 1995; 82(1):113–25. [Details of a statistical model that can be used to combine samples of individual exposure data with aggregate data on health outcomes.]
- *(29). Jackson C, Best N, Richardson S. Improving ecological inference using individual-level data. *Stat Med*. 2006; 25(12):2136–59. [PubMed: 16217847] [Details of the statistical model (a Bayesian hierarchical model) that can be used to combine aggregate and individual-level data.]
- *(30). Jackson CH, Richardson S, Best NG. Studying place effects on health by synthesising individual and area-level outcomes. *Social Science & Medicine*. 2008; 67(12):1995–06. [PubMed: 18950921] [Examples of the use of the model in reference (27) combining aggregate data on cardiovascular disease hospitalisation from a national database or long-term limiting illness from the national Census with individual-level survey information.]
- *(31). Jackson C, Best N, Richardson S. Hierarchical related regression for combining aggregate and individual data in studies of socio-economic disease risk factors. *J R Stat Soc Ser A Stat Soc*. 2008; 171(1):159–78. [Example of the use of the model in reference (27) combining individual-

level and area-based measures of deprivation and examining their relative impact on risk of hospital admissions for cardiovascular disease in London.]

32. 't Mannetje A, Kromhout H. The use of occupation and industry classifications in general population studies. *Int J Epidemiol*. 2003 Jun 1; 32(3):419–28. [PubMed: 12777430]
- *(33). Swuste P, Dahhan M, Burdorf A. Linking Expert Judgement and Trends in Occupational Exposure into a Job-Exposure Matrix for Historical Exposure to Asbestos in The Netherlands. *Ann Occup Hyg*. 2008 Jul 1; 52(5):397–403. [PubMed: 18524755] [Recent JEM for asbestos exposure, including data on within-group exposure distribution that could be used in enhanced statistical analyses as described in the text.]
- *(34). Stayner L, Kuempel E, Gilbert S, Hein M, Dement J. An epidemiological study of the role of chrysotile asbestos fibre dimensions in determining respiratory disease risk in exposed workers. *Occup Environ Med*. 2008 Sep 1; 65(9):613–9. [PubMed: 18096653] [Study suggesting that exposure to thinnest asbestos fibres provides greater risk for lung cancer and asbestosis mortality. This sort of information could be used to further enhance JEMs.]
- *(35). Smit LAM, Heederik D, Doekes G, Blom C, van Zweden I, Wouters IM. Exposure-response analysis of allergy and respiratory symptoms in endotoxin-exposed adults. *Eur Respir J*. 2008 Jun 1; 31(6):1241–8. [PubMed: 18256063] [Recent study using a JEM to suggest that occupational endotoxin exposure in adulthood was associated with an increased risk of asthma-like symptoms but a reduced prevalence of hayfever.]
- *(36). Taeger D, Krahn U, Wiethege T, Ickstadt K, Johnen G, Eisenmenger A, et al. A Study on Lung Cancer Mortality Related to Radon, Quartz, and Arsenic Exposures in German Uranium Miners. *Journal of Toxicology and Environmental Health, Part A*. 2008; 71(13):859–65. [PubMed: 18569586] [Study using JEM-based estimate of exposure to three carcinogens in uranium miners, also incorporating comparisons of mortality with general population data from the WHO Mortality Database.]

Figure 1. Map of asbestos-related disease Standardised Mortality Ratios in UK districts 1981-1999 – males(15)

(Asbestos related diseases were defined as ICD9 codes 501 (asbestosis), 163 (malignant neoplasm of the pleura) and 158.8 and 158.9 (malignant neoplasm of the peritoneum) as used by Coggon et al(16))