Conclusions These findings must be interpreted with caution because any word search is dependent on the use of language, which varies between countries and language groups, and over time. Also, the affiliation field refers only to the first author. With these caveats, this historical analysis supports some anecdotal impressions about occupational epidemiology: Nordic countries, relative to their size, have made a major contribution; historically, papers have come from a small pool of countries; the large volume of papers from the USA is likely to be influential; and the trend of accelerating research output seen in the twentieth century may have stabilised.

181 ADDRESSING CONTINUOUS DATA FOR PARTICIPANTS EXCLUDED FROM TRIAL ANALYSIS: A GUIDE FOR SYSTEMATIC REVIEWERS

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Objectives To develop a framework for handling missing participant data for continuous outcomes in systematic reviews and assess its impact on risk of bias.
Methods We conducted a consultative, iterative process. We considered sources that reflect real observed outcomes in participants followed-up in individual trials included in the systematic review, and developed a range of plausible strategies that would be progressively more stringent in challenging the robustness of the pooled estimates. We applied our approach to two example systematic reviews.
Results We used 5 sources of data for imputing the means for participants with missing data: [A] the best mean score among the intervention arms of included trials, [B] the best mean score among the control arms of included trials, [C] the mean score from the control arm of the same trial, [D] the worst mean score among the intervention arms of included trials, [E] the worst mean score among the control arms of included trials. To impute SD, we used the median SD from the control arms of all included trials. Using these sources of data, we developed four progressively more stringent imputation strategies.

In the first example review, effect estimates were diminished and lost significance as the strategies became more stringent, suggesting the need to rate down confidence in estimates of effect for risk of bias. In the second review, effect estimates maintained statistical significance using even the most stringent strategy, suggesting missing data does not undermine confidence in the results. The differences are due to: [1] the size of the effect and its precision, and [2] the percentage of missing participant data.
Conclusions Our approach provides rigorous yet reasonable and relatively simple, quantitative guidance for judging the impact of risk of bias as a result of missing participant data in systematic reviews of continuous outcomes.

182 ENGLISH-SPEAKING REVIEWERS CAN CORRECTLY IDENTIFY FOREIGN-LANGUAGE ARTICLES THAT MEET ELIGIBILITY CRITERIA FOR A SYSTEMATIC REVIEW OF MANAGEMENT FOR FIBROMYALGIA

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Objective To assess whether English-speaking reviewers can identify foreign-language articles that are eligible for a systematic review of all treatments for fibromyalgia.
Methods Systematic review of AMED, CINAHL, EMBASE, MEDLINE, HealthSTAR, PsycINFO, Papers First, Proceedings First and CENTRAL, from inception of each database to April, 2011, to identify all randomised controlled trials exploring any form of therapy for fibromyalgia. All non-English language articles were identified and screened for eligibility by native-language reviewers. English-speaking reviewers screened all non-English language, guided by 10 questions, in order to identify those that were eligible for review.
Results Of 15,466 potentially eligible studies we retrieved 763 in full text, of which 133 were published in 19 non-English languages; 431 studies proved eligible of which 53 were published in languages other than English. Agreement between English and native-language reviewers for assessment of eligibility of the 133 foreign language articles was 89% and the chance-corrected agreement was substantial (kappa = 0.77). Use of a simple 4-step rule (excluding languages with only one or two articles, reviewing titles and abstracts for clear indications of eligibility, noting the lack of a clearly reported statistical analysis unless the word 'random' appears, and noting features of systematic review) preserved the highest proportion of eligible articles (96%) with the fewest number of foreign-language reviewer teams needed (n = 9).
Conclusions We identified strategies that English-speaking reviewers can implement to ameliorate the burden associated with including eligible non-English language studies in systematic reviews.

183 THE USE OF ECOLOGICAL DATA TO GENERATE HYPOTHESES ON EXOGENOUS RISK FACTORS FOR (RARE) CANCERS

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There is a public health need to balance timely generation of hypotheses with cautious causal inference. For rare cancers this is particularly challenging because standard epidemiological study designs may not be able to elucidate causal factors in an early period of emerging risks.

We have previously demonstrated that open-access databases (the GLOBOCAN 2008 resource combined with data from the United Nations Development Report and the World Bank list of Development Indicators) can be used to explore associations between potential risk factors and incidence of cancer of the brain and central nervous system at an ecological level (publication in press).

In this study we showed that the only exogenous risk factor consistently associated with higher incidence rates of cancer of the brain and central nervous system was the penetration rate of mobile/cellular telecommunications subscriptions. Furthermore,

this approach enabled evaluation of latency periods between exposure and clinical onset of the disease. For most cancers this is difficult to evaluate using standard epidemiological study designs, but this work showed that this latency period is at least 11−12 years, but probably more than 20 years.

These results showed that readily available ecological data may be underused, particularly for the study of risk factors for rare diseases and those with long latencies.

Because these analyses were done using a systematic, a priori set out statistical approach, it can be extended to other combinations of diseases and exogenous risk factors. In addition to demonstrating the methodology for cancers of the brain and central nervous system, we will show results evaluating associations between the incidence of other (rare) cancers and potential risk factors from the World Bank list of Development Indicators.

184 HANDLING MISSING PARTICIPANT DATA IN META-ANALYSIS OF DICHOTOMOUS OUTCOMES: PROPOSED GUIDELINES FOR SYSTEMATIC REVIEWS OF RANDOMISED TRIALS

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Objectives Systematic reviewers including all randomised participants in their meta-analyses need to make assumptions about the outcomes of those with missing data.

Our objective is to provide systematic review authors with guidance on dealing with participants with missing data for dichotomous outcomes.

Methods The authors conducted a systematic survey of the methodological literature regarding 'intention to treat' analysis and used an iterative process of suggesting guidance and obtaining feedback to arrive at a proposed approach.

Results We consider here participants excluded from the trial analysis for "non-adherence" but for whom data are available, and participants with missing data. Non-adherent participants excluded from the trial analysis but for whom data are available should in most instances be included in the meta-analysis, and in the arm to which they were randomised. For participants with missing data, systematic reviewers can use a range of plausible assumptions in the intervention and control arms. Extreme assumptions include 'all' or 'none' of the participants had an event, but these assumptions are not plausible. Less extreme assumptions may draw on the incidence rates within the trial (e.g., same incidence in the trial control arm) or in all trials included in the meta-analysis (e.g., highest incidence among control arms of all included trials). The primary meta-analysis may use either a complete case analysis or a plausible assumption. Sensitivity meta-analyses to test the robustness of the primary meta-analysis results should include extreme plausible assumptions. When the meta-analysis results are robust to extreme plausible assumptions, inferences are strengthened. Vulnerability to extreme plausible assumptions suggests rating down confidence in estimates of effect for risk of bias.

Conclusions This guide proposes an approach to establishing confidence in estimates of effect when systematic reviewers are faced with missing participant data in randomised trials.

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185 FOUR-YEAR FOLLOW-UP STUDY OF HEALTH HAZARDS AMONG WORKERS HANDLING ENGINEERED NANOMATERIALS

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Objectives The aim of this study was to investigate the health hazards in workers exposed to nanoparticles during manufacturing and application of nanomaterials.

Methods For this 4-year longitudinal study, we recruited 283 nanomaterial-handling workers and 213 non-exposed control workers from 15 manufacturing plants in Taiwan. Follow-up measurements were done at 6, 12, 24, 36, and 48 months. Among them, 206 nanomaterial-handling workers and 140 unexposed workers were followed up for more than twice. For each participant, a self-administered questionnaire was distributed to collect work history and personal habits after informed consent. Since there was a lack of equipment for personal sampling and summary index for mixed exposure, we adopted the control banding nanotool risk level matrix to categorise the risk level for each participant. Blood, urine and exhaled breath condensate (EBC) were collected to examine markers of cardiopulmonary injuries, lung and systemic inflammation, oxidative stress, and genotoxicity. Generalised Estimating Equation (GEE) model was applied to analyse these repeated measurements.

Results There were 108 workers in risk level 1, and 91 workers in risk level 2, and 7 in risk level 3. Although depression of antioxidant enzymes and increase of cardiovascular markers were found in the cross-sectional and early follow-up study, no significant difference was revealed between exposed workers and controls in the changes of biomarkers in this 4-year longitudinal study. The non-significant markers included lung injuries markers, cardiovascular disease markers, heart rate variability (HRV), inflammation markers, oxidative stress and lipid peroxidation markers, comet assay, pulmonary function test, and neurobehavioral function test.

Conclusions This longitudinal study suggests that there was no evidence of health hazards among nanomaterials handling workers. The preliminary survey of nanoparticle exposure level in the workplace was quite low. Such exposure level was not high enough to induce systemic health effects in nanoworkers.

186 IMPROVING THE IMPACT: NEEDS FOR AND PROGRESS IN GLOBALLY HARMONISED EPIDEMIOLOGIC STUDIES OF NANOMATERIALS WORKERS

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Epidemiological occupational health studies in the carbon black and amorphous silica industries, two classic examples of nanomaterials, were carried out in the late 1980s/mid 1990s.