

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.