National Collaborating Centre for Environmental Health

Centre de collaboration nationale en santé environnementale

A Primer for Evaluating the Quality of Studies on Environmental Health

Critical Appraisal of Case-Control Studies

The following queries are adapted from the *Newcastle-Ottawa Scale* (2005),[1] the Critical Appraisal Skill Programme (2006),[2] and from critical appraisals by Elwood (2007)[3] and Aschengrau and Seage III (2003)[4]

Title Page and Introduction	Examples
In what journal or other medium was the article published? (Journals with high impact factors are usually carefully peer reviewed).	The paper about pesticide risk factors for cancer appeared in *Science*, the top rated multidisciplinary journal.
Who sponsored the study and what are the authors' affiliations?	The pesticide manufacturer's association was the only sponsor of the study.
What is the context of the study and what is the investigator's motivation? Is there a convincing rationale and purpose (hypothesis) for doing the study? Is the issue clearly focussed? Did the study clearly aim to detect a beneficial or a harmful effect? There may be data quality issues with secondary analysis of data or data dredging (unplanned tests of association may yield significant results).	In a study of occupational risk factors for cancer, 200 patients with leukemia and age-matched population controls were recruited over a two year period. In the first year the questionnaire was expanded for 80 rural resident cases in total, to include more detail about occupational and residential exposure to pesticides. No relationship was found between pesticide exposure and leukemia. Some data issues: low power to detect such an association; controls were not from a rural area as were case.
Was an appropriate study design chosen to address the study question? A case-control study is typically chosen for rare outcomes.	A series of case-control studies were done to evaluate the relationship of agricultural exposure to pesticides with leukemia in adults (rare).

Study Methods	Examples
Is the case recruitment adequate, with cases defined precisely, preferably with independent validation of the case definition? Are the cases incident (new occurrences over a specified time period) or prevalent?	*Good quality*: Cases were diagnosed with leukemia after starting employment, verified by cancer clinic records. *Poor quality*: The case definition was their reply to the survey question "Have you ever had leukemia?"
Were a sufficient number of cases selected and how representative are the cases of the population, geographically and/or temporally?	*Good quality*: 100 cases were selected randomly from children living in the city and diagnosed with leukemia, at the city's cancer clinic. *Poor quality*: Cases were from a convenience sample of clinicians' offices in the province.
How were the controls selected? Were they matched, population-based or randomly selected?	*Good quality*: Controls were a random sample of children of the same grade, attending the city's schools. *Poor quality*: Controls were children diagnosed with cancer other than leukemia.
How comparable are the cases and controls?	*Good quality*: Controls were matched to cases of the same age in the same school. *Poor quality*: School children in two cities were randomly chosen as controls.
Was the exposure accurately ascertained and were measurement methods similar for both cases and controls?	*Good quality*: Cases and controls underwent a structured interview on agricultural pesticide exposures; the interviewer had no knowledge of their case or control status. *Poor quality*: Interviewers first interviewed cases using an open questionnaire format and then interviewed the controls using a structured questionnaire.
Was the typical latency of the outcome taken into account when assessing exposure? Adult cancer usually requires a latent period of 5 to 20 years from first exposure depending on the agent and dose.	*Good quality:* Initial pesticide exposures among farmers occurred over 5years prior to the incidence of leukemia. *Poor quality:* First exposure to pesticides among farmers was determined within a year of ascertainment of leukemia.

Results and Discussion	Example
How strong and precise is the association between exposure and outcome (as indicated by odds ratio and 95% CI)?	The results of the logistic regression analysis revealed that the risk of leukemia was doubled (with an odds ratio of 2.0, 95% CI 1.5-2.4) for children exposed to pesticides *in utero*.
Can confounding, systematic biases (such as information or selection bias) or random error be eliminated as alternative explanations?	The case and control children were matched by age and sex. However, there were systematic differences in the place of residence, such that the association of leukemia in children with pesticide exposure may be affected by the differences in socioeconomic status and other exposures related to residence. When interviewing the parent of the case, recall bias is another concern.
Can the study findings be generalized to other people and situations? For example, were minorities included?	The extent of pesticide exposure for the study applicators would be higher than expected among urban residents.
Can the results be applied to the local population?	The demonstration of an increased odds ratio for leukemia, associated with maternal exposure to pesticides among California residents, has applicability to local concerns.
Do the results suggest a causal association?	Apply *Hill's Guidelines for Assessing Causality*[3] (see Background on Epidemiological Studies p.5). In particular the temporal relationship between exposure and outcome should be considered, as well as consistency of the findings with other studies.

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References

1. Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. Proceedings of the 3rd symposium on systematic reviews: beyond the basics; Jul 3-5; St Catherine's College, Oxford, UK: Centre for Statistics in Medicine; 2000.
2. Public Health Resource Unit (PHRU). Critical Appraisal Skills Program (CASP). Oxford, UK: PHRU, Public Health Services; 2006. Available from: http://www.sph.nhs.uk/sph-files/casp-appraisal-tools/Qualitative%20Appraisal%20Tool.pdf.
3. Elwood M. Critical appraisal of epidemiological studies and clinical trials. 3rd ed. Oxford, UK: Oxford University Press; 2007.
4. Aschengrau A, Seage III GR. Essentials of epidemiology in public health. Sudbury, MA: Jones & Bartlett Learning; 2003.

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