Making Sense of Population Studies

Q&A with Sir Colin Berry, M.D., Ph.D., D.Sc.

Epidemiology is the study of diseases in human or animal populations, specifically how, when and where they occur. Epidemiologists try to determine which factors are associated with diseases and which ones may protect people or animals against them. Sir Colin Barry, emeritus professor of pathology, Queen Mary University of London, explains how to make sense of population studies, especially when it comes to pesticides and health.

Why are population studies important and how do they help shape public health policy?
Epidemiological studies can help assess the health risks of environmental factors, such as exposure to chemicals. Unlike laboratory experiments, studies of human populations provide evidence under real world conditions with actual people. However, studies reporting associations between measures of population health and exposure to hazardous environmental factors are difficult to interpret. Therefore, risk assessment must include careful evaluation of all existing evidence.

Robust epidemiological evidence led to the discovery that cigarette smoking is a causal factor for lung cancer and made clear that some occupational exposures (vinyl chloride, asbestos), certain viruses and bacteria (hepatitis viruses, EBV and *H. pylori)* and various forms of radiation contribute to the development of cancer. Clearly, population studies can lead to important public health recommendations. However, they can also create confusion and result in inappropriate advice or use of resources if not done well. False positive responses may be produced by inadequate study design, poor performance of a test or inappropriate evaluation of data.

What makes a quality, well designed population study?
First, authors should have the appropriate mix of scientific expertise and experience without conflicts of interest. Research codes of conduct call for scientists to be reliable, impartial, independent, honest, objective and open. Any scientific study must be based on a testable hypothesis that can be verified or falsified. It should be based on a detailed protocol and scientific methods accessible to others with publishable results. Moreover, it should be replicable, which is why the protocol must be clear and recorded and results must be peer-reviewed for credibility.

Fundamentally, a population study may reveal an association, but it cannot identify a causal mechanism. Conclusions about an association or cause must be carefully weighed against all information as well as consider confounding factors and prior evidence in the scientific literature.

Moreover, any epidemiological study should explain how its features (e.g., assessments of bias, confounding, exposure response) were accounted for and how non-epidemiological sources of

evidence contributed to findings. If an environmental hazard is associated with several health effects, it should be assessed separately for each one. The chart below lists good practices at each step of research.

How can a non-scientist determine if a population study is credible?

Asking a series of questions can be very informative. First, was the study published in a peer-reviewed scientific journal? Do the authors have relevant expertise? How large was the sample size and over what period of time was the study carried out? Most importantly, in terms of conclusions, is there any other way of explaining the facts or any other answer that is equally or more likely to cause the effect? This inquisitive caution should be applied before drawing conclusions that contribute little to the advancement of public safety and may cause unnecessary concern to many.

Any assessment of chemicals, such as pesticides, must include their identity, molecular structure, class and physicochemical properties, mode(s) of action, results of relevant laboratory or animal toxicity tests, anticipated use(s) and potential for human exposure, and relevant toxicological data. The latter require careful interpretation as the extrapolation of rodent studies to hypothetical human impact must consider dosage and the practice of continuous feeding, which are often orders of magnitude greater than any likely human exposure.

How have poorly designed or confounding population studies confused the public about health issues?

Concerns about the quality and reproducibility of scientific papers have emphasised the uncertainty of observations in biological sciences. Compounding this problem are the impacts on public health policy, such as the International Association on the Research of Cancer (IARC) process of hazard identification related to cancer. What is the value of a system that does not clearly identify its methodology for defining a hazard and which does not provide realistic estimates of risk?

One must question the scientific integrity and societal value of studies that simply identify potential human health hazards without assessing exposure and thereby, risk. In many fields, such as oncology, “false positives” may cause considerable anxiety and lead to behavior that is detrimental to public health. The recent IARC listing of the widely used weed killer glyphosate as a “probable cause of cancer” served little purpose other than unduly alarming the public. Flaws in the IARC process have been discussed elsewhere and by many scientists.

Regarding population studies on pesticides, how can consumers tell the difference between junk science and legitimate research?

A chemical, such as a specific type of pesticide, cannot simply be classified as “dangerous” or “safe;” it always depends on the typical amount or dose to which someone is exposed and for

how long that exposure lasts. The effects of a chemical will change with different exposures, so that below a certain dose it may be harmless or beneficial and at a higher dose it may be toxic. *Botulinus* toxin (botox) eases facial worry lines, it may cause serious worry if it gets into your stomach.

Exposure to common chemicals, such as pesticide residues, are often expressed in “parts per million” (ppm) or “parts per billion” (ppb). One ppb is equivalent to one grain of sugar in an Olympic swimming pool. A chemical that is toxic in gram or milligram amounts may not be dangerous at these lower levels of exposure. It’s worth remembering that exposure to a highly hazardous chemical does not necessarily make it a risk, especially if it is handled responsibly.

Pesticides have been associated with health issues in studies that do not always assess other possible causes of observed effects or which are not reproduceable. Confounding factors may be evident (say smoking) in which case they will be accounted for in the study or they may be hidden (perhaps in the genetic make-up of the study population) or simply unrecognized. Where there are multiple and conflicting studies, special forms of analysis are needed. Reproducibility is essential to prove scientific rigor and avoid misleading results.

Responsible Epidemiologic Research Practice

Study element	Recommendation
1a. The study group	The first step in any epidemiologic study is to establish a study group and the responsibilities and accountabilities of its members.
1b. Meaningful research question	The first task of the study group is to define the aim of the study or specific hypothesis to be tested. Include a systematic review of the literature if applicable
1c. Research protocol/grant proposal	Every epidemiologic study, with the aim of publishing the results, should be based on a detailed research protocol describing the study. The level of detail is such that another research group is able to carry out the study as intended with the protocol in hand. Once finalized, it is required that the study protocol is ultimately made public, either by placing it on a publicly accessible website or by uploading it in an appropriate studies register
1d. Grant submission	Be frank about your project and do not promise more than you can deliver
1e. Ethical review	Review by appropriate committee
2a. Human volunteers protection	The conduct of the epidemiologic study should be carried out in accordance with the study protocol and by adhering to the Declaration of Helsinki
2b. Data collection	The data collection process is a vital element of any study and therefore should be documented in detail. Include a digital log
2c. Statistical analysis	The statistical analysis should be conducted according to the protocol.
2d. Report preparation	The report must be an accurate balanced and concise reflection of the conducted study taking into account existing guidelines, and it should describe its limitations and deviations from the protocol
3a. Manuscript submission	A scientific study is only completed when all its results are properly reported and when the study has been well documented and archived Any protocoled study must be published
3b. Contacts with journalists	The study and its results should be presented to journalists in a reliable and balanced manner, without making the results appear to be more (or less) than they really are.
3c. Data archiving and sharing	Once the report is in a final form, the study group must ensure that the raw data files and the final data set used for the statistical analysis are securely stored, protecting privacy of subjects and accompanied by a fully explanatory data description or code book. Data sharing in principle is encouraged and should be the norm because reuse of data makes research more cost-effective.
3d. Document archiving	Throughout the study execution, but also after the study has been finalized, and the study group is accountable for its work.

Source: Netherlands Epidemiological Society, *Journal of Clinical Epidemiology* 100 (2018) 111-119.

References:

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