Pesticides: Assessing Risk and Evaluating Epidemiological Studies
A Guide for Journalists
Broader story - what pesticides are used for

In agriculture, pesticides are used to protect crops from pests and disease – without them, crop losses would double to 40-80%. Pesticides also have applications for aquatic uses as well as for horticultural and other non-food maintenance uses. The range of uses includes water system purification and paper mill systems to food storage areas and protection of household contents.

Importantly, these chemicals help farmers produce an abundant, varied, affordable supply of food. They help make nutrient-rich fresh fruits and vegetables more affordable and accessible throughout the year. In the developing world, where farmers often don’t have access to the information or the tools like pesticides to raise productivity up to 80% of the household income is spent on food. Pesticides also help increase the productivity of agricultural land so that existing natural habitats – and the biodiversity they contain – are preserved as well.

Without pesticides, about one-third of any crop would be lost to disease, infestation or predation. Locusts, rats, grasshoppers, slugs, weeds, bacteria, fungi and moulds have threatened the quality and quantity of our food supply throughout history, instigating at time pandemic illnesses, famines or unpalatable food for people to consume. It is these pests that pesticides have been created to combat.

A pesticide – and indeed many new chemicals – must undergo rigorous testing and regulatory authorisation before it can be brought onto the market. Once on the market, each product is accompanied by an information sheet describing how to handle the product safely.

However, it is understandable for people to be concerned about pesticides and any potential impact on their health, food quality and the environment. Pesticides always need to be handled responsibly and according to label instructions.

1  www.policynetwork.net/print/1049
Risk assessment process for pesticides

A product’s risk is based on the type of hazard that it poses in relationship to the likelihood of its occurrence or exposure. Consider risk as a formula:

risk = hazard x exposure

If either hazard or exposure is zero, there is no risk. Let’s be clear, it will never be possible to fully eliminate the risk involved with any product. However, it is possible to determine the likelihood of such a relationship and to minimise the risks, while maintaining the benefit that the product delivers. Assessing a product’s risk requires a systematic analysis of relevant data related to its environmental, human health and animal health impacts with estimates of how likely these exposures are to occur.

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1. Hazard identification, establishing any particular risks associated with a pesticide to determine the type, level and period of risk from exposure to a pesticide
2. Exposure assessment, determining the type, level and period of risk to certain populations from exposure to a pesticide
3. Dose response assessment, identifying the amount of pesticide absorbed by an individual from a given form of exposure
4. Risk characterisation, estimating the level and likelihood of adverse effects as well as the uncertainties or assumptions made in determining this

Risk management differs slightly from risk assessment in being the active process of determining what is an acceptable amount of risk in a particular community and which solutions offer the most benefit under these conditions. These decisions also reflect whether other viable alternatives exist and how the risk and benefits would be distributed amongst community members based on their individual values or interests.

Thus, risk managers for pesticides aim to minimise any risk associated with pesticide exposure while maximising their benefits to food production, farmers’ livelihoods and pest, disease or weed control. If the hazard is too large, or the exposure cannot be controlled, a pesticide will not be registered for use.

To the general public, a lack of information or lack of control over outcomes may increase the perceived risk of pesticide use compared to other known risks, such as driving a car or participating in an adventure sport. This may also contribute to individuals being less accepting of risks for themselves which have otherwise been deemed to be reasonable for the community at large.

This is why it is so important to conduct a robust risk assessment process on chemical products before use. These health risks can be either acute (single events), sub-chronic (repeatedly over a few weeks or months) or chronic (long-term). These risk assessments include testing over different time periods and with different dosage levels.

Based on the risk assessments, regulations have been put in place to ensure a safe and healthy food supply, without harming health or the environment, including:

- Maximum Residue Levels (MRLs): Maximum Residue Levels (MRLs) are the maximum concentration of pesticide residue likely to occur in or on food if applied according to product label instructions. MRLs are typically calculated through field trials and tests of various crops applied with pesticides. MRLs mark the authorised pesticide residue limit in food products and are set individually for each pesticide and crop. MRLs are trading standards, rather than safety limits, and serve as a check that good agricultural practice is being followed to protect human health and the environment.
- Acceptable Daily Intake (ADIs): These are derived on a scientific basis and correspond to the chronic risk. The ADI comprises the amount of potential residue that can be consumed by one person, every day of their life, without posing a risk to their health. The Maximum Residue Levels do not allow our Acceptable Daily Intake to be exceeded.
- 100-Fold Safety Factor: This is established by applying a high safety factor – typically 100 – to the “No observed adverse effect levels” (NOAELs) from long-term toxicological testing. A NOAEL is the highest dose that does not cause adverse side effects. The safety factor is designed to account for differences across species (animal to human) and within species (infants and sensitive adults).

The R&D process also continues to generate new innovations which improve the quality and range of solutions available to farmers in their work to produce and protect our food supply.
Overview of the regulatory approval process

For a pesticide to gain regulatory approval, its manufacturers must submit a registration package which contains the results of hundreds of studies, not only on health impacts but also on environmental impacts. Before a product is registered, it goes through an extensive approval process. Prior to that, it will have gone through a lengthy and costly series of tests including:

- research studies, which seek to understand the chemical and biological nature of an active ingredient (typically a molecule) and how it can be developed into a pesticide
- field trials, which assess the efficacy of a product on specific pests, weeds or diseases in a controlled environment
- toxicology and environmental studies, which analyse the safety of a product in wider biological systems and how it breaks down in plant, animal, soil and water systems
- registration process, where data dossiers are compiled for independent scrutiny of previous product tests and its viability for use in a given market

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Evaluating an epidemiological study (with checklist)

Epidemiology is the study of health and illness patterns and their causes in human populations. These studies – provided they are conducted according to the generally accepted methodology and rigour – can provide important understanding of disease causation. Public health officials and regulators refer to these studies as well as studies generated for the authorisation submission package for a new product. As a whole, these provide the evidence that public health officials and regulators can use to inform their decision-making.

At its most basic level, epidemiological studies are designed to show how exposures to a given substance may change the rate of disease in a given population, who would otherwise be assumed to experience background rates of disease.

Thus, to provide evidence for an association between a particular substance and a particular disease, an epidemiological study must not only prove a positive association between the two, but also demonstrate how other known causes have not played a role in this outcome. In other words, the study must be able to rule out other causes of the disease with a satisfactory degree of confidence.

In order to interpret and weigh the results of any epidemiological study and to determine the inevitable variations in the quality or scope of the results, the following tips may be of value:

**TIP 1:** Focus on scientific principles/"code of conduct" of the study.
You can only analyse what you have measured. Epidemiological studies should have a protocol/study plan/project description/research proposal describing how the research should be conducted and designed, and it should be made available prior to the study. The format of this protocol includes background information and study objective, which covers:
- hypothesis to be tested
- type of study
- how exposure will be measured
- type of group(s) being used for analysis
- statistical analysis
- sample size calculation

The scientific method is entirely based upon the testing of a given hypothesis, so the hypothesis to be tested is a key point to be considered. The hypothesis should be clearly stated. Other studies will be conducted to generate the hypothesis to be tested.

As with any scientific project, this protocol should be followed throughout the research process (e.g. completing a certain number of statistical analyses). If it has not been followed, the study should clearly explain how and why the researchers deviated and the implications on the results. This process should be independently peer-reviewed before the study is published or considered for other media coverage.

**TIP 2:** Look at how exposure is measured.
Don’t over-interpret weak data.

The range of exposure levels can be vast in studies and difficult to compare, and the level of exposure is not necessarily the same across the sample base. These need to be accounted for in the study analysis.

In addition, the study subjects may not be able to recall in detail the level of exposure to which they were subjected and for what length of time. It is well known that subjects suffering from a disease in general give more positive responses to queries about past exposure than healthy subjects (information bias). Others in the sample base may have moved away since the time period being researched, thus biasing the data collection, or the records with their information may not have been kept accurately. Among epidemiologists, it is widely accepted that the results of any study need replication and confirmation before any firm conclusions can be drawn, whether the study is positive or negative.
TIP 3: 
Research the context for the study.

In epidemiology, there is power in numbers. The scientific literature (accessed via PubMed) may work and to be scrutinised by journalists accordingly. If there is consistency amongst a group of studies, the association inspires more confidence in researchers; however, if there is a lack of consensus and inconsistency in the findings, this may mean that further epidemiological studies or toxicological testing may be required. Similarly, looking into the track record of the study authors can help establish what their research record is like.

TIP 4: 
Differentiate academic and journalistic uses of terms and statistics.

Popularly misunderstood study results can impact scientific progress.

For instance, scientists use the term “population-at-risk” as the population having been exposed to a substance being studied but not necessarily more at risk for developing a certain disease than the general population. Similarly, use of the word “link” by journalists can leave readers unclear about the strength or consistency of the association produced in academic studies. Therefore, a hypothesis-testing study can be recognised from its specific a priori hypothesis and rigorous methodology, following a clear, a priori determined protocol.

TIP 5: 
Recognise the difference between a hypothesis-testing and a hypothesis-generating study.

Hypothesis-testing studies carry more weight than hypothesis-generating studies.

Some studies are conducted with a specific hypothesis in mind to be tested. These are hypothesis-testing studies. Other studies lack a specific hypothesis and have a more explorative character—these are hypothesis-generating studies or “fishing expeditions.” Even if two studies, of which one is a hypothesis-testing and the other a hypothesis-generating study, have exactly the same results, they must be interpreted differently. A hypothesis-testing study is considered to carry more weight than the hypothesis-generating exercises. A hypothesis-testing study can be recognised from its specific a priori hypothesis and rigorous methodology, following a clear, a priori determined protocol.
<table>
<thead>
<tr>
<th>TYPES OF STUDIES</th>
<th>DESCRIPTION</th>
<th>ADVANTAGES</th>
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<tr>
<td><strong>COHORT STUDY</strong></td>
<td>In a cohort study, an exposed group of subjects (the “cohort”) is followed through time to observe the incidence of disease. The observed incidence is compared to the incidence in a non-exposed population.</td>
<td>The disease status cannot affect information on exposure (information bias is largely avoided). Tends to produce more reliable results and can provide multiple disease outcomes. Can be conducted retrospectively or into the future.</td>
<td>Tend to be expensive and must be conducted over a long period of time.</td>
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<td><strong>CASE-CONTROL STUDY</strong></td>
<td>Compares a group of cases with a particular disease with a group of persons without that disease, with respect to their past exposure.</td>
<td>Good for researching uncommon diseases. Can focus on a multitude of risk factors at a time. Less expensive and shorter time period than cohort studies.</td>
<td>Based on participant recall of facts; more potential for bias. Only allows for the study of one disease.</td>
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<tr>
<td><strong>CASE REPORT</strong></td>
<td>The disease status and information on past exposure.</td>
<td>Looks at a single individual and describes in detail the nature of the disease and how it may have been contracted.</td>
<td>Simple and useful for guiding direction/scope for further research. No cause and effect can be determined, and the results cannot be extrapolated. Thus, never statistically significant.</td>
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<tr>
<td><strong>CASE-REPORT DESIGN</strong></td>
<td>The population, exposure and disease are fixed while the time period is open.</td>
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<tr>
<td><strong>CROSS-SECTIONAL STUDY</strong></td>
<td>Looks at a defined population to determine possible associations between various types of exposure and disease symptoms.</td>
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<tr>
<td><strong>COHORT STUDY</strong></td>
<td>Both the specific exposure and diseases are unknown while the population and time period are fixed.</td>
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<tr>
<td><strong>ECO-ECOLOGICAL DESIGN</strong></td>
<td>Looks at a given population and compares existing data from various sources to determine whether possible associations exist between known exposure and diseases.</td>
<td>Makes use of existing population data and disease exposure information. Useful or guiding direction/scope for further research.</td>
<td>Cannot be individualised or more specifically scrutinised to eliminate possibility of bias from other factors. Has frequently resulted in later rejected conclusions.</td>
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</tbody>
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**Description of Advantages and Limitations**

- **Advantages**
  - Simple and useful for guiding direction/scope for further research.
  - Good for researching uncommon diseases.
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  - Simple and useful for guiding direction/scope for further research.
  - Makes use of existing population data and disease exposure information.

- **Limitations**
  - Tend to be expensive and must be conducted over a long period of time.
  - Based on participant recall of facts; more potential for bias.
  - No cause and effect can be determined, and the results cannot be extrapolated.
  - Cannot be individualised or more specifically scrutinised to eliminate possibility of bias from other factors.

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Epidemiology as a science and its limitations

**Benefits of Epidemiology**

These studies are helpful in identifying risk factors for disease, particularly where exposure is high and the data is consistent over time. They also help identify relationships, or correlations, between certain substances and health outcomes. Examples of this include the positive effects of folic acid in preventing spina bifida or the negative effects of smoking in contributing lung cancer.

**Limitations of Epidemiology**

Most epidemiology studies are of an observational character. While toxicologists strictly control the conditions being studied in their experiments, it would be unethical for epidemiologists to expose humans knowingly to potentially dangerous substances. Because of this, epidemiologists typically perform observational studies. In many instances the availability of records on variables, including exposed populations, exposures, disease levels or time periods, determine the type of study that can be performed and the extent to which the results may produce statistically significant results.

Epidemiologists often find it difficult to determine the level and type of exposures of the populations they study and the information on exposure is often a weak point in their studies. For most diseases, the causes are not well understood – or indeed not known at all. Also, most diseases emerge as the result of a variety of risk factors, some of which are internal/personal (e.g. genetic susceptibility, dietary habits or behaviour), while others are external/environmental (e.g. exposure to a certain substance) or lifestyle related. When the level of exposure is low, poorly defined or inconsistent amongst studies, it is difficult to interpret studies reporting weak or negative associations. Since epidemiology has an observational nature in which chance and natural variation in the presence of other risk factors can always play a role, it is generally accepted by epidemiologists that firm conclusions can only be drawn after a set of studies has been conducted, all reporting relatively consistent findings.

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**Purdue University’s Pesticides and Epidemiology: Unraveling Disease Patterns**


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For farmers, these can include fertilizers, nitrates, fuels and engine exhausts, solvents, organic and inorganic dusts, electromagnetic radiation, ultraviolet radiation, animal pathogens. http://www.ppp.purdue.edu//Pubs/ppp-43.pdf
Myths and facts about pesticides

MYTH 1:
If a disease is prevalent in a population which has been in contact with a certain exposure, there must be some association between them. No population is free of disease incidence.

Fact: Many factors can cause a disease to be prevalent in a given population including age, family history, living habits (e.g. diet, smoking). Because it is difficult, expensive or time-consuming to collect this data accurately and over time, it can easily bias or obscure the result of any study.

MYTH 2:
It is possible to grow a similar supply of affordable, varied and reliably-delivered food without the use of pesticides.

Fact: Not only would a significant proportion of food be lost, but poorer people in the developing world would have less access to varied diets, including fresh fruits and vegetables, which give them nutrients proven to defend themselves against disease.

MYTH 3:
Pesticides are not well-regulated.

Fact: Pesticides are one of the most highly regulated products in the world. For a pesticide to gain regulatory approval, a registration package must be submitted containing the results of hundreds of studies. In comparison to other products/activities such as diet bars, exercise regimens or mobile telephones, pesticides are much more robustly monitored for any potential impact on human health. In fact, during 2005-8, the average cost of discovering and registering a new crop protection product was $215 million. Over the same period, only one out of a total of 140,000 products being researched was successfully registered and sold at market.

MYTH 4:
Activist groups would have no reason to protest the use of pesticide if it were safe to be used.

Fact: Activist groups play an important role in keeping organisations accountable. However, many of these groups have objectives and funding sources which implore them to interpret scientific data in a particular way. Independently peer-reviewed scientific research should be the basis for developing and refining public health regulations.

MYTH 5:
Diseases are caused by environmental factors.

Fact: The causes of most non-infectious diseases are still not well known at best. For most chronic diseases, such as most types of cancer, the causes are not understood at all, apart from certain clearly identified lifestyle factors with a significant health impact such as cigarette smoking.

Third-party experts

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Sir Colin Berry is Emeritus Professor of Pathology at Queen Mary College, London. He is a histopathologist with experience in the regulatory toxicology of materials, pesticides and pharmaceuticals for the UK government, the European Union and the WHO and FAO. He is interested in risk evaluation and assessment and the public communication of science – he is currently a member of the ESOF 2012 Steering Committee.

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Dr. Alan Boobis is Professor of Biochemical Pharmacology and Director of the Health Protection Agency Toxicology Unit, Imperial College London. His current research interests include mechanistic toxicology, experimental carcinogenesis, and biomarker discovery using proteomics. He is a member of a number of national and international advisory committees, including the UK Committees on Carcinogenicity and on Toxicity, and EFSA Panel on Contaminants in the Food Chain. He is an Honorary Member of EUROTOX, a Fellow of the British Toxicology Society and a Fellow of the Society of Biology. He received the EUROTOX Merit Award in 2009.

DR. JOHN CLARK
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Dr. John M. Clark is currently a Professor of Environmental Toxicology & Chemistry in the Department of Veterinary & Animal Sciences at the University of Massachusetts-Amherst and directs the Massachusetts Pesticide Analysis Laboratory. He has published 158 peer-reviewed articles, 33 book chapters, and has edited seven books in the areas of pesticide mode of action, insecticide resistance and management, environmental chemistry and human exposure to pesticides. He is currently the Editor-In-Chief of Pesticide Biochemistry & Physiology. In 2007, Dr. Clark was elected as a Fellow by the American Chemical Society.

DR. HELMUT GREIM
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Dr. Helmut Greim is Chairman of the Scientific Committee on Health and Environmental Risks (SCHER) of the Health and Consumer Protection DG of the European Commission since 2004. He is also a member of the Scientific Advisory Committee on Occupational Exposure Limits (SCOEL) of the General Directorate Employment and Social Affairs of the European Commission since 1993, and a member of the Risk Assessment Committee (RAC) of the European Chemical Agency since 2007. He is the retired director of the Institute of Toxicology and Environmental Hygiene, Technical University of Munich.

Third-party experts

Sir Colin Berry, “Pesticides are Good for You” (Providence Journal, October 15, 2007)
www.policynetwork.net/print/1049

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Glossary of terms

Acceptable Daily Intake (ADI): Standards establishing the amount of any given substance, as compared to a person’s total body weight, which can be ingested daily over his lifetime without any observable health risk.

Association: A statistical association, or correlation, shows a relationship between two or more variables, however it does not necessarily imply causation.

Causation: Scientific consensus on nature of relationship whereby changes in one variable directly cause changes in another variable.

Confidence Interval: A statistical tool to indicate the reliability of an estimate.

Control: When testing a new method, process or factor against an accepted standard, the standard of comparison is known as the control.

Correlation: A statistical association, or correlation, shows a relationship between two or more variables, however it does not necessarily imply causation.

Dose-Response Relationship: The relationship between the amount of exposure to a substance and the resulting changes in an organism.

Epidemiology: The study of the causes, distribution and control of disease in populations.

Exposure: The condition of being subjected to something.

Hazard: A potential to cause harm.

Hill’s criteria: A group of criteria necessary to provide adequate evidence of a causal relationship between an incidence and a consequence.

Incidence: The number of new cases of a condition, symptom or injury that develop within a specified period of time.

Induction period: The amount of time between exposure and disease development. The longer or more variable this period, the more difficult it tends to be to determine associations.

Latency period: The amount of time between disease development and detection.

Maximum Residue Levels (MRLs): Standards which dictate the maximum expected levels of pesticide residues remaining in or on food products or animal feed products.

Odds Ratio (OR): A means of comparing whether the probability of a certain event is the same for two groups. The higher and less variance of the ratio, the stronger the likely association.

Probability: A measure of how likely it is that an event will occur.

Risk Assessment: The systematic analysis of relevant information to determine probability and severity of risks associated with a given hazard.

Risk factor: A variable associated with an increased risk that an event will occur.

Risk Management: How risk assessments are incorporated within a given social context in order to determine potential options for mitigating risks.

Sample Base: The selected population that is surveyed in a research study.

Selection Bias: A statistical error in choosing test groups for a research study.