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CPH601 Chapter 3 Risk Assessment

David M. Mannino

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Risk Assessment

David M. Mannino, M.D.

Professor and Chair
Department of Preventive Medicine and Environmental Health
Director of Graduate Studies, Masters of Science in Clinical Research Design
Director, Pulmonary Epidemiology Research Laboratory
University of Kentucky College of Public Health

What is Risk Assessment

- Risk assessment is
  - Characterization of the nature and magnitude of health risks to
    - humans (e.g., residents, workers, recreational visitors)
    - ecological receptors (e.g., birds, fish, wildlife)
  - from chemical contaminants and other stressors that may be present in the environment
- Risk assessment is, to the highest extent possible, a scientific process

http://epa.gov/riskassessment/basicinformation.htm#arisk

Overview

- Risk Assessment Framework
- Hazard Identification
- Epidemiologic Methods
- Dose and Outcomes
- Human Exposure Assessment
- Health Risk Characterization
- Environmental Impact Assessment

Risk Assessment Framework

Research	Risk Assessment
Laboratory and field observations (including epidemiological studies) of adverse health effects from exposure to particular agents. ⇨	**1. Hazard Identification** (Which are the health effects that this agent can cause?)
Quantitative dose-response studies and extrapolation from high to low dose and from animals to humans. ⇨	**2. Dose-Response Assessment** (What is the relationship between dose and occurrence of health effects in humans?)
Field measurements estimating exposures in defined populations. ⇨	**3. Exposure Assessment** (What exposures are currently experienced or anticipated under different conditions?)

4. Risk Characterization
(What is estimated occurrence of the adverse effect in a given population?)

⇩

5. Risk Management
(Development, evaluation and implementation of regulatory options, aimed at risk reduction and control)

Figure 3.1 Steps in risk assessment.

Laboratory and field observations (including epidemiological studies) of adverse health effects from exposure to particular agents.

1. Hazard Identification
(Which are the health effects that this agent can cause?)

Hazard Identification

Hazard Identification

- Which are the health effects that this agent can cause?
- A qualitative description of potential health effects
- Based on
  - Toxicological studies
  - Hazard Identification in the field
  - Epidemiological studies

Hazard Identification – Toxicological studies

- Toxicokinetics
  - how the body absorbs, distributes, metabolizes, and eliminates specific chemicals
- Toxicodynamics
  - the effects that chemicals have on the human body

Hazard Identification – in the field

- Occupational settings
  - Health Hazard Evaluations (HHE)
  - Hazard audits (MSDS)
- General Environment
  - More difficult to identify specific hazards
  - Sometimes specific agent is never found

Hazard Identification - HHE

- August 1993: severe flooding and 8 cases of livestock anthrax confirmed in and around Sheyenne River valley, North Dakota
- September - October 1993: NIOSH and USDA/APHIS conducted a HHE
  - visited 14 livestock production facilities
  - conducted 18 interviews, including 7affected producers, 7 unaffected producers, and 4 veterinarians.
  - collected blood samples from 2 producers with infected livestock and 2 veterinarians with exposure to infected animals to determine anthrax antibody titer
  - collected environmental samples of soil, water, and feed to identify any remaining potential sources of infection
- No confirmed reports of human anthrax infection during the epizootic
- Producers and family members from 3 of the 7 affected farms received antibiotic therapy because of direct exposure to known or suspect anthrax-infected livestock

http://www.cdc.gov/niosh/hhe/reports/pdfs/1993-1121-2530.pdf

Hazard Identification - Epidemiological Methods

- Conducting studies
  - Sample size
  - Obtaining Data
  - Sampling the population
- Descriptive Epidemiology
  - longitudinal (often) or cross-sectional
- Ecological studies
- Analytical Epidemiology
  - Cohort Studies
  - Case Control Studies
- Interventional Epidemiology
  - Randomized Clinical Trials (or natural experiments)

Conducting Studies

- Sample size needed
  - *A priori* based on expected rates of disease in exposed/unexposed group
- Methods of obtaining data
  - Existing administrative data
  - Questionnaire administration
  - Physical examination

Conducting Studies

- Sampling the population
  - Census of population needed (sampling frame)
  - Sampling methodology
    - Simple random sample
    - Stratified random sample (used to oversample groups of special interest, i.e. minorities, the elderly)
    - Two staged sampling (frequently used in national surveys)

Hazard Identification – Epidemiological Methods

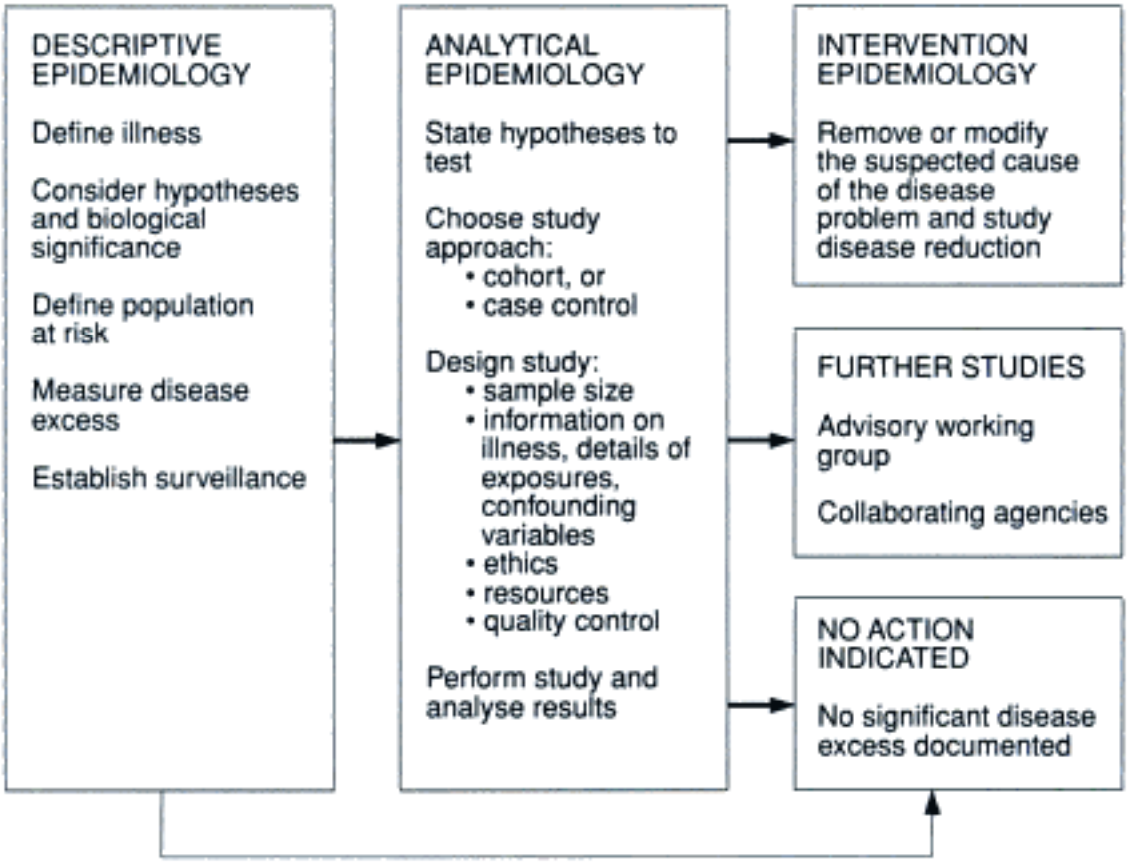


Figure 3.2 Logical development of epidemiological field investigations. From WHO, 1991a, with permission.

Descriptive Epidemiological Studies

- Historical/longitudinal studies
  - Follow a population over time
  - Examine relation between "exposure" and the development of adverse health outcomes
  - Can be done prospectively (best option) or retrospectively (historical cohort study) when adequate data are available
- Cross-sectional studies
  - snapshot of the exposure or the effects at a given time, or both
- Not trying to draw association or causality
- May establish whether possible link exists between a risk factor and an outcome –
  - compare exposure prevalence and health problem prevalence in study groups and control groups

Criteria for Causality

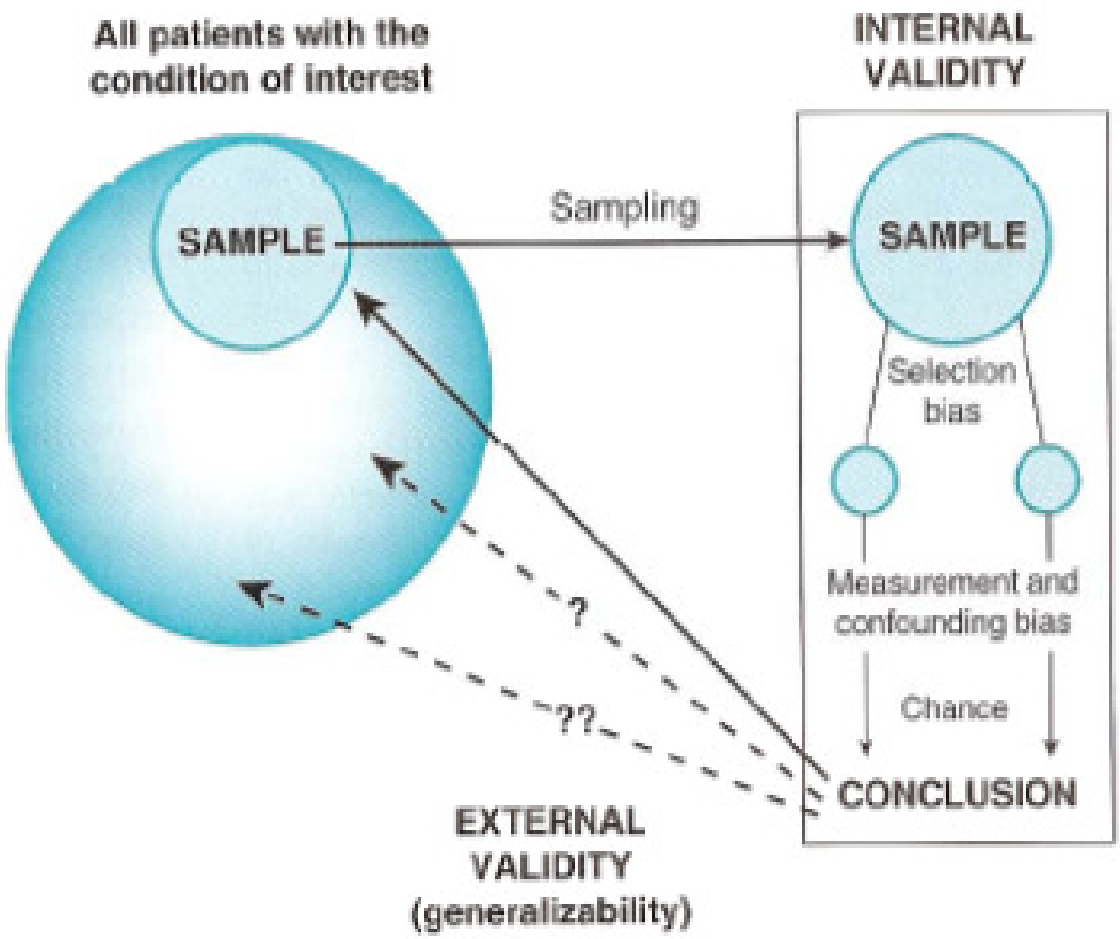
- Sir Austin Bradford Hill - guidelines
  - Strength
  - Consistency
  - Specificity
  - Temporality: time relationship
  - Biological gradient: dose-response relationship
  - Plausibility
  - Coherence
  - Experiment
  - Analogy

Table 1. Definitions of causation from the epidemiologic literature (modified from Parascandola and Weed 2001).

Definition	Main criticism
A cause is something that produces or creates an effect.	Tautological because "production" and "creation" are synonyms of "causation"
A cause is a condition without which the effect cannot occur.	Only very few diseases could then have a cause[a]
A cause is a condition with which the effect must occur.	Again, only few diseases could then have a cause[b]
A cause is made up of several components, no single one of which is sufficient of its own, which taken together must lead to the effect.	Introduces unnecessary complexity in cases of simple dose response and in cases of interaction between components
A cause is a condition that increases the probability of occurrence of the effect.	Does not distinguish between an association and a "cause"[c]
A cause is a condition that, if present, makes a difference in (the probability of) the outcome.	Is, in the strict sense, unprovable because there is only one world and one cannot observe it twice—once with and once without the condition

Kundi, EHP 2006; 114:969-974

How Do We Know Whether What We Are Seeing Is Real?

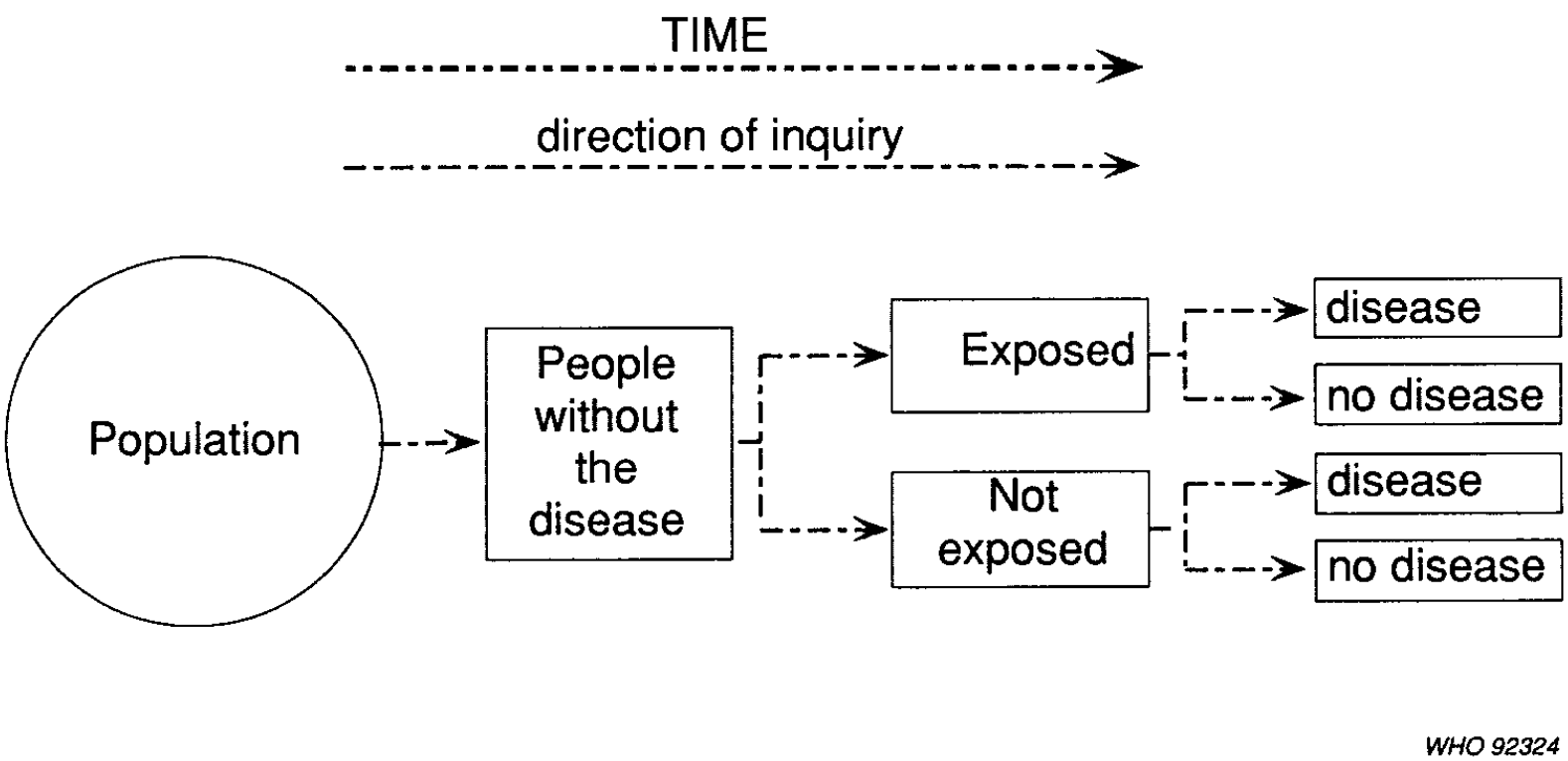


Analytical Epidemiological Studies

- Cohort studies
  - start with a population that has been exposed to the risk factor
  - then the frequencies of disease in the exposed and unexposed populations are compared as they occur over time
- Case-control studies
  - start with people who have the disease
  - then frequencies of exposure that occurred in the past in the population with the disease and the population without the disease are compared
- Be careful about *bias* and *confounders*

Analytical Epidemiological Studies – Cohort

Fig. 3.5. Design of a cohort study



Cohort – Assumptions

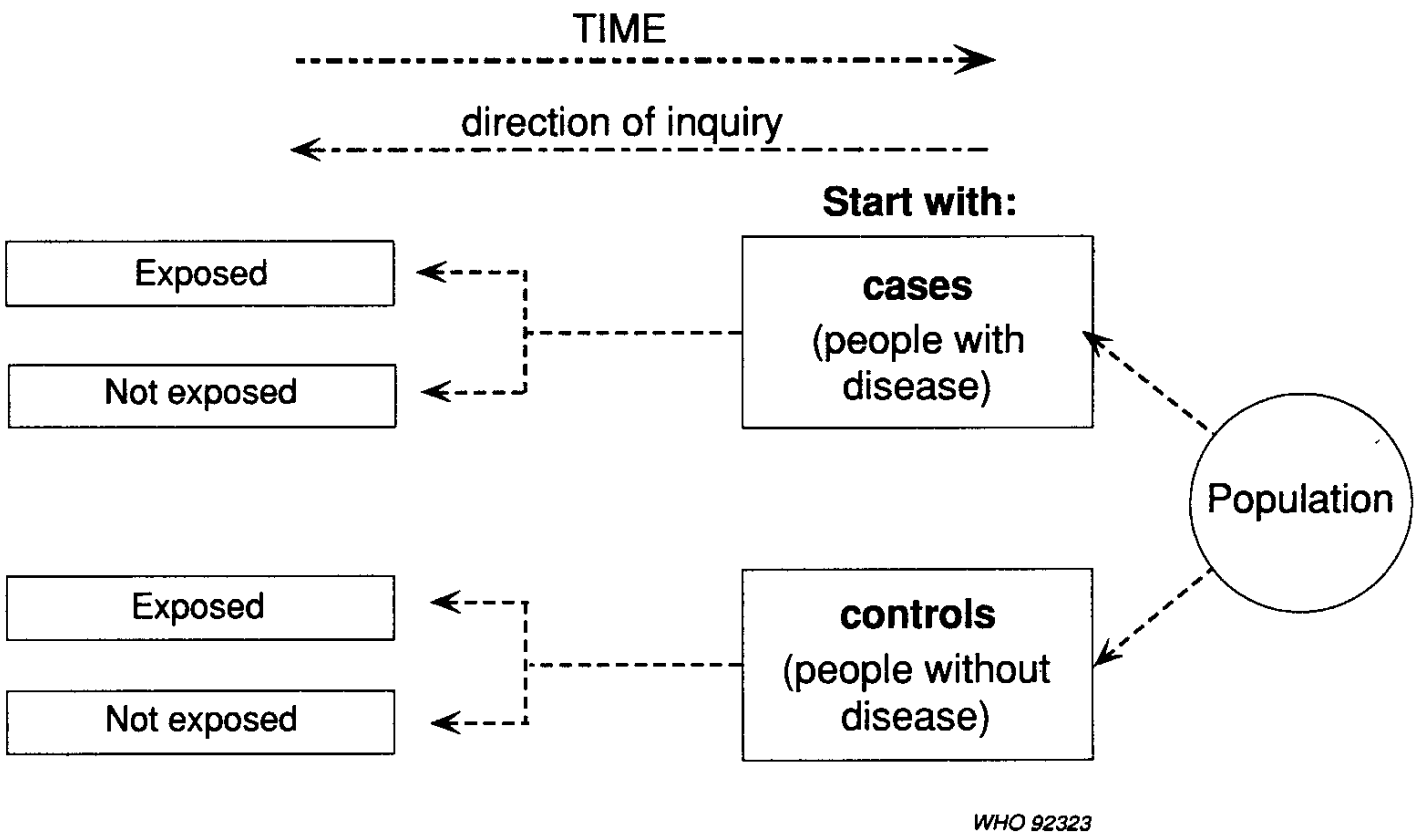
- Exposed/unexposed same
- How achieve comparability?
  - by design – choose similar subjects
    - Match by age, gender, race etc.
  - by stratification (in analysis)

Analytical Epidemiological Studies – Cohort

- Directly measure disease risks and calculate the actual population illness rate
- Allow for assessment of many competing risk factors
- Often used to study occupational disease
- Can be costly, especially if the disease under study is rare

Analytical Epidemiological Studies - Case-Control

Fig. 3.4. Design of a case-control study



Analytical Epidemiological Studies - Case-control

- Efficient way of determining whether past exposures are associated with current disease
- Accurate case definition is critical
- Some designs match cases to controls, whereas others may compare cases to the overall population sampled

Case-control – Sources of case identification

- Clinic patient rosters
- Death certificates
- Surveys
- Cancer/birth defect registries
- Use incident not prevalent cases when possible

Case-Control – Selecting cases

- Cases usually have the disease
- Define cases specifically
  - Signs/symptoms
  - Clinical exams
  - Diagnostic tests
- Err on being restrictive rather than inclusive

Case-Control – Selecting Controls

- Controls
  - underlying propensity to get disease
  - Sample of population that gave rise to cases
  - Provides info on exposure distribution in source population
- Controls should be representative of same base population
  - "would criterion" – member of control group who gets disease "would" end up as case
- Same chance of getting in sample as cases
- Sample controls independent of exposure status
  - Exposed and unexposed controls should have same probability of selection
  - Sampling fraction for exposed and unexposed parts of control group should be same
- Picking controls expensive
- Pair matching

Case-Control – Exposures

- Characteristics or events that increases or decrease the probability of disease/disability/death
- Protective and malicious exposures
- Sources of exposure information
  - In-person/telephone interview
  - Questionnaires
  - Medical/pharmacy/registry/employment/ insurance/birth/death records
  - Biological specimens - biomarkers

When to use case-control studies?

- Exposure data difficult/expensive to obtain
- Disease is rare
- Disease has long induction/latent period
- Little known about disease
- Underlying population dynamic

Interventional Epidemiology

- Test a hypothesis by modifying an exposure within the study population and examining the effect on the outcome
- Randomized Clinical Trials (or natural experiments)
- Contrast to **observational** epidemiology: examine the distribution or determinants of an outcome without any attempt to influence them

Ecologic Studies

- Look at diseases in "communities"
  - Geographical comparisons
  - Population trends over time
  - Effects of migration
- Good at generating hypotheses – but can almost never show causation

Ecological study

- Fig.1 Per-capita sugar consumption and the age-adjusted prostate cancer mortality rate in 71 countries
- Do the data support the hypothesis that increased sugar consumption is associated with increased prostate cancer mortality? YES!
- Do the data determine that sugar consumption causes prostate cancer death? NO!

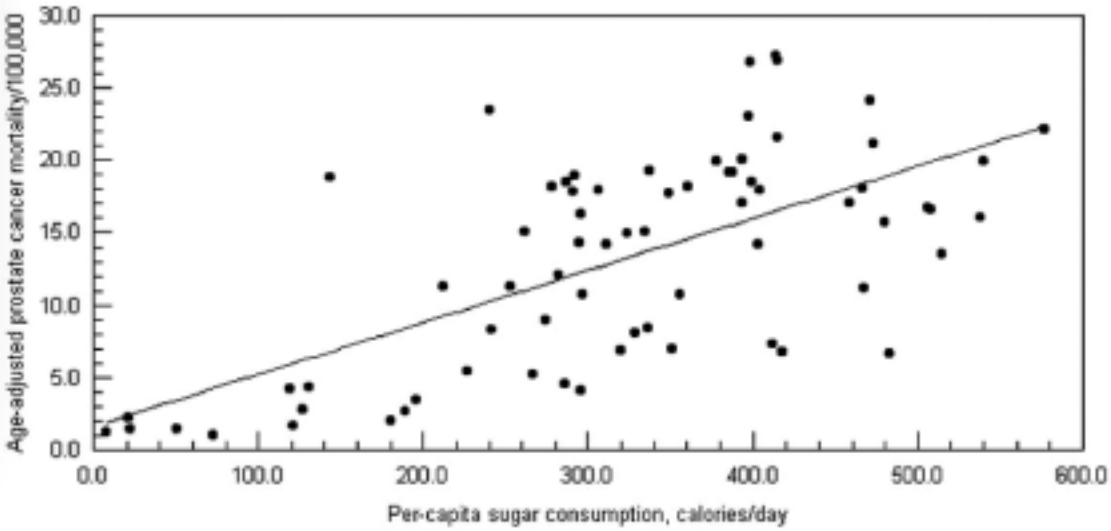


Fig. 1. Prostate cancer mortality versus sugar consumption in 71 countries.

Quantifying Risks

Analytical Epidemiological Studies – Quantifying Risks

- Relative risk in case-control
- Relative risk = # times more likely cases are to get disease than controls given exposure

	Disease	
Exposed	*Yes*	*No*
Yes	A	B
No	C	D

Relative Risk (RR)

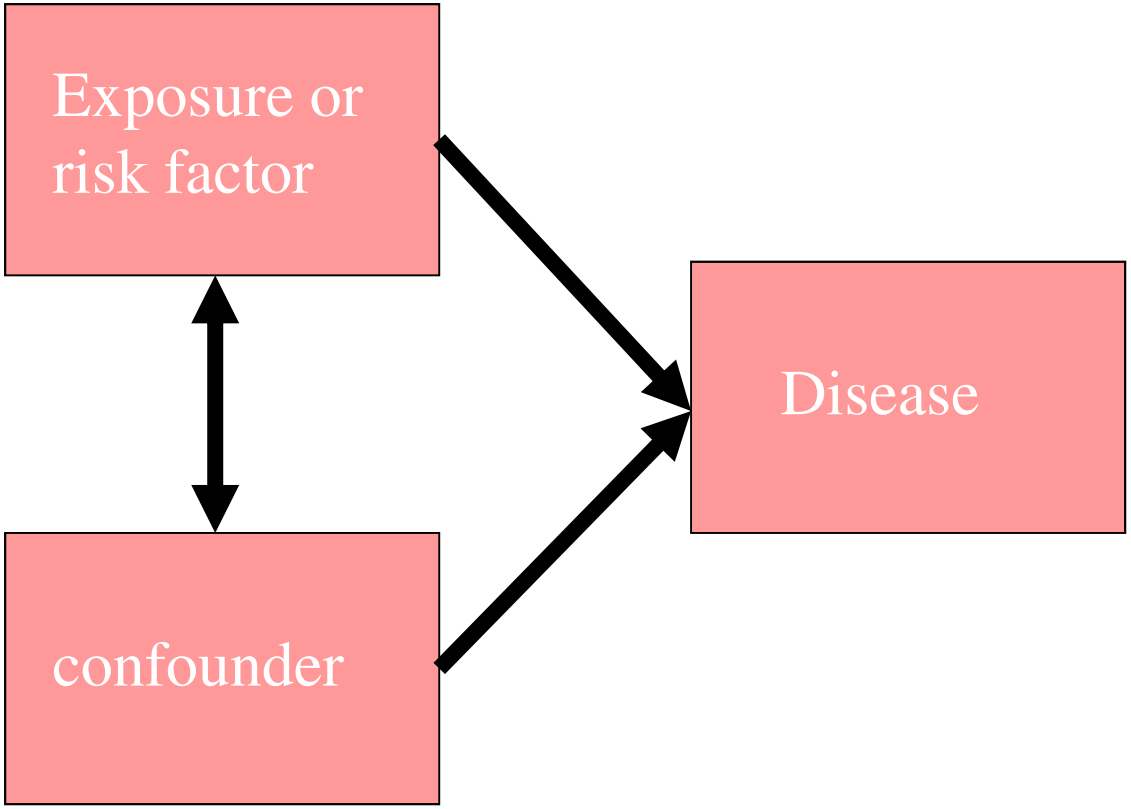
- RR = (a/a+b) / (c/c+d)
  - what does RR=3 mean?
- Meaning of magnitude of RR?
  - e.g. for cigarettes and smoking RR=10
- if RR < 1.0 → protective effect
- if RR > 1.0 → malicious effect
- Attributable Risk (rate difference)
  - a/(a+b) - c/(c+d)
  - measures potential savings

The Odds Ratio (OR)

- an estimate of relative risk
  - when cases/controls representative
  - if disease prevalence small
- if > 1.0 → increased risk
- if <1.0 → decreased risk (protective)

Confounding variables

- Factors that are NOT causal but may be associated with the exposure and the disease for other reasons



Confounding variables – Lung Cancer in Roof Workers

- Exposed to asphalt fumes during approximately 40% of their working hours
- RR varied from 1.2 to 5.0 (most between 1.2 and 1.4) in 13 epidemiological studies of roofers
- Individual asphalt or asphalt fumes exposure data were not available
- Causation??
- confounder & bias:
  - other risk factors for lung cancer, e.g. Smoking, Asbestos & Coal tar
  - the use of comparison populations that are inherently different with respect to lung cancer risk

Confounding variables - Lung Cancer in Roof Workers

- Smoking (currently): RR from 1.17 to 1.52
  - prevalence declined more steadily in the general population than among roofers
- Asbestos: RR from 1.36 to 1.78
  - exposures among roofers have declined over the past 50 years
- Coal tar: RR from 1.04 to 2.32
  - exposures among roofers have declined over the past 50 years
- Can we conclude roofers are at increased risk of lung cancer due to asphalt exposure?

Quantitative dose-response studies and extrapolation from high to low dose and from animals to humans. ⇨

2. Dose-Response Assessment (What is the relationship between dose and occurrence of health effects in humans?)

Dose-Response Relationships

Dose-Response Relationships

- Dose-response
  - Relation between the dose of a toxin and the proportion of individuals in a population developing adverse effects
- Dose-effect
  - Relation between increasing dose and worse outcome in an individual

Dose-Effect Relationships

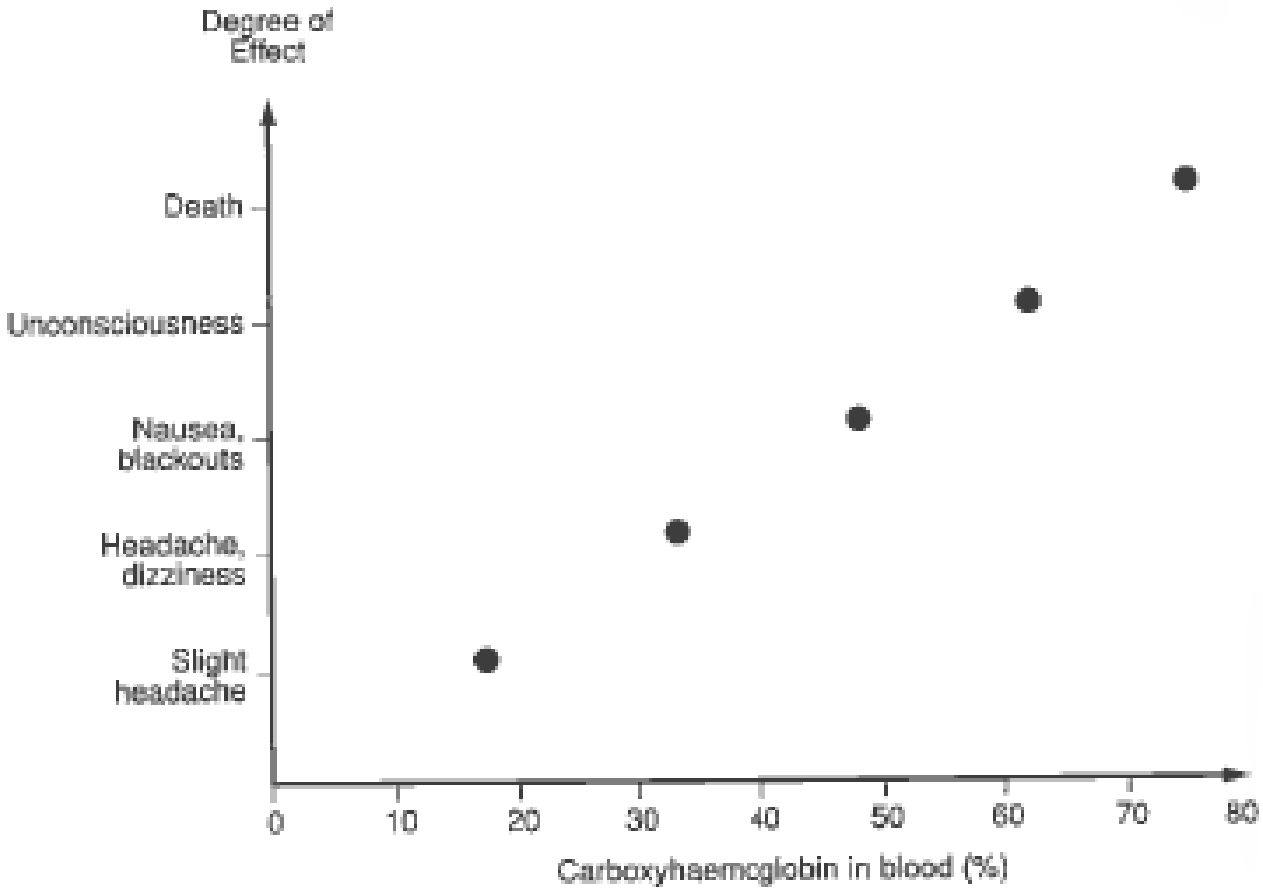
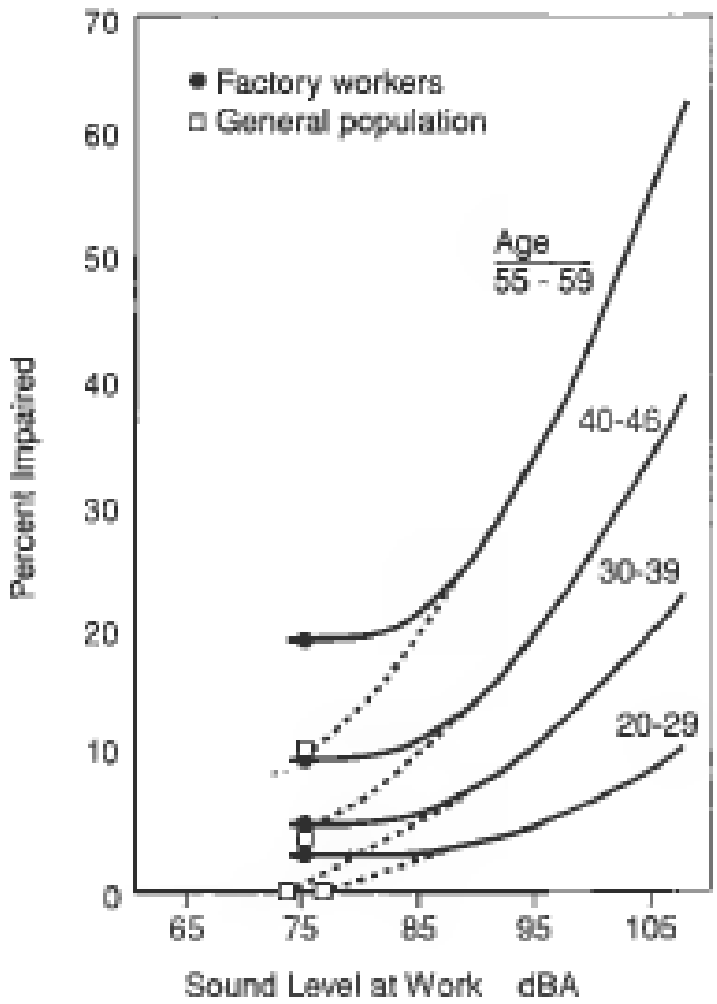
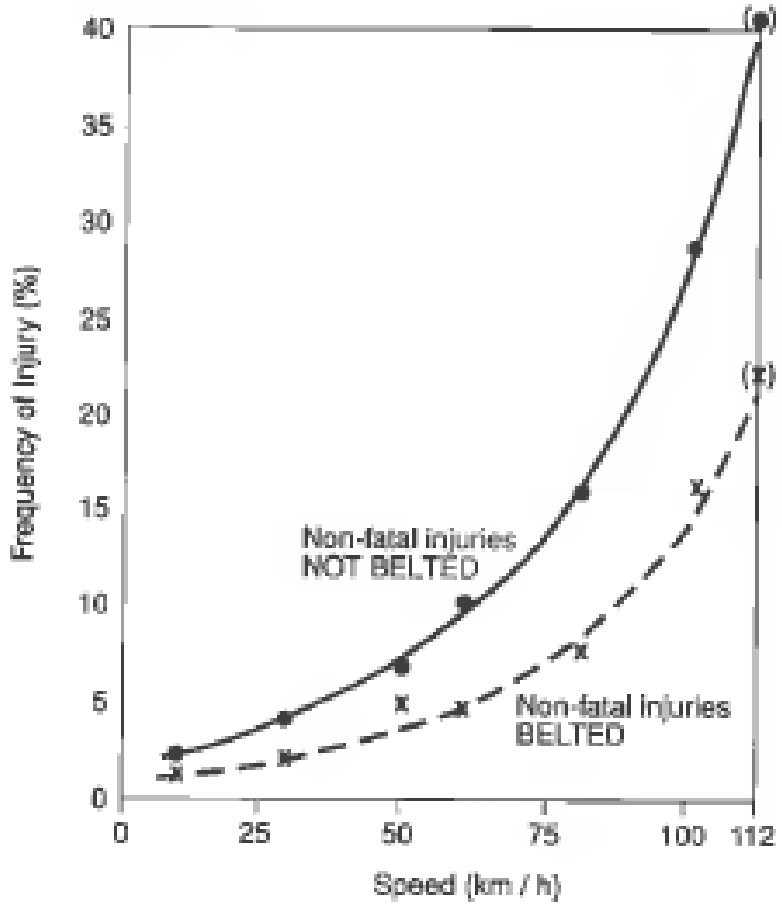


Figure 3.8 Dose–effect relationship. From Beaglehole et al., 1993, with permission.

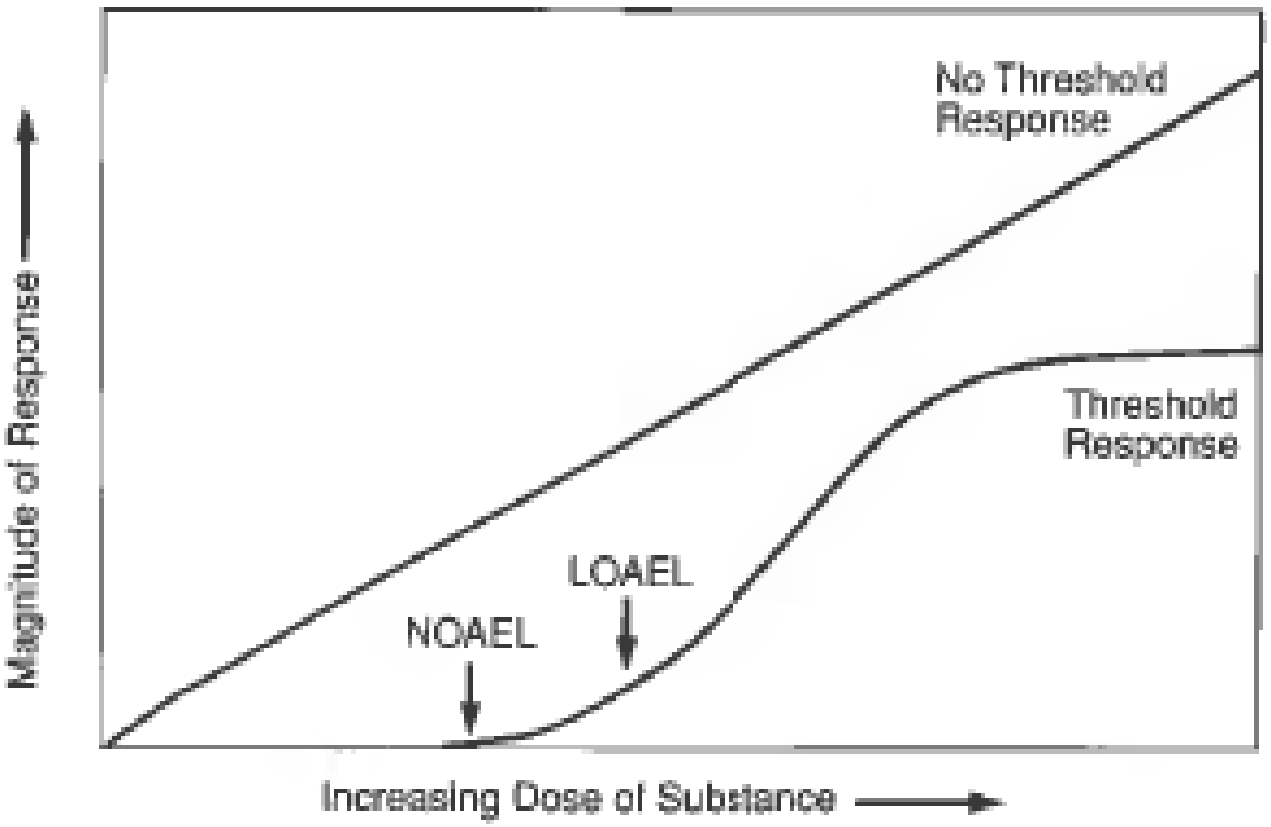
Dose-Response Relationships



Dose-Response Relationships



Dose-Response Relationships



Safety or Uncertainty Factors

- Extrapolation from experimental data to the human population
- Quality and quantity of dose-response data
- Consideration for high-risk groups:
  - infants, young children, elderly people, pregnant women and their fetuses, the nutritionally deprived, the ill, individuals with genetic disorders, and those exposed to other environmental health hazards

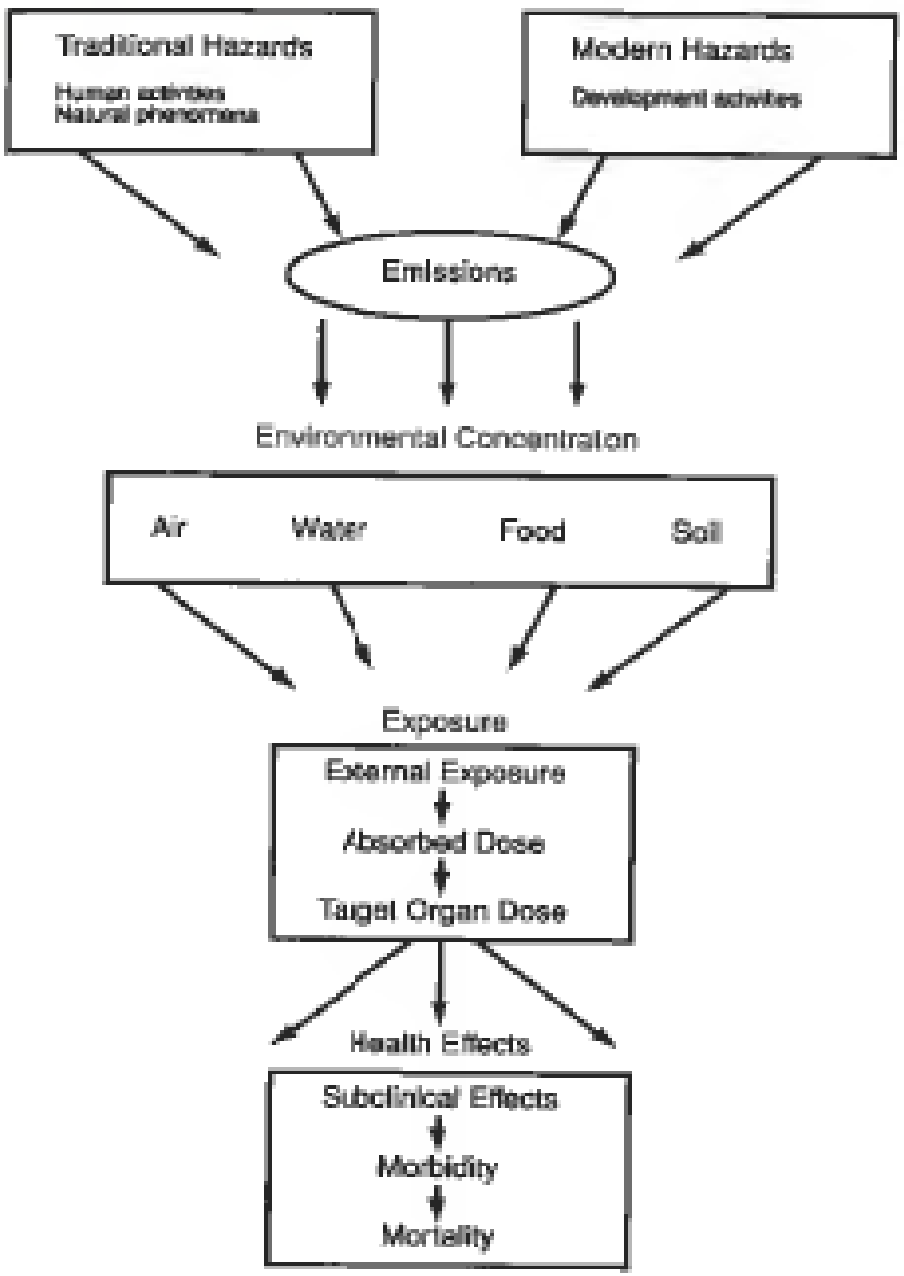
Field measurements estimating exposures in defined populations. ⇨

3. Exposure Assessment
(What exposures are currently experienced or anticipated under different conditions?)

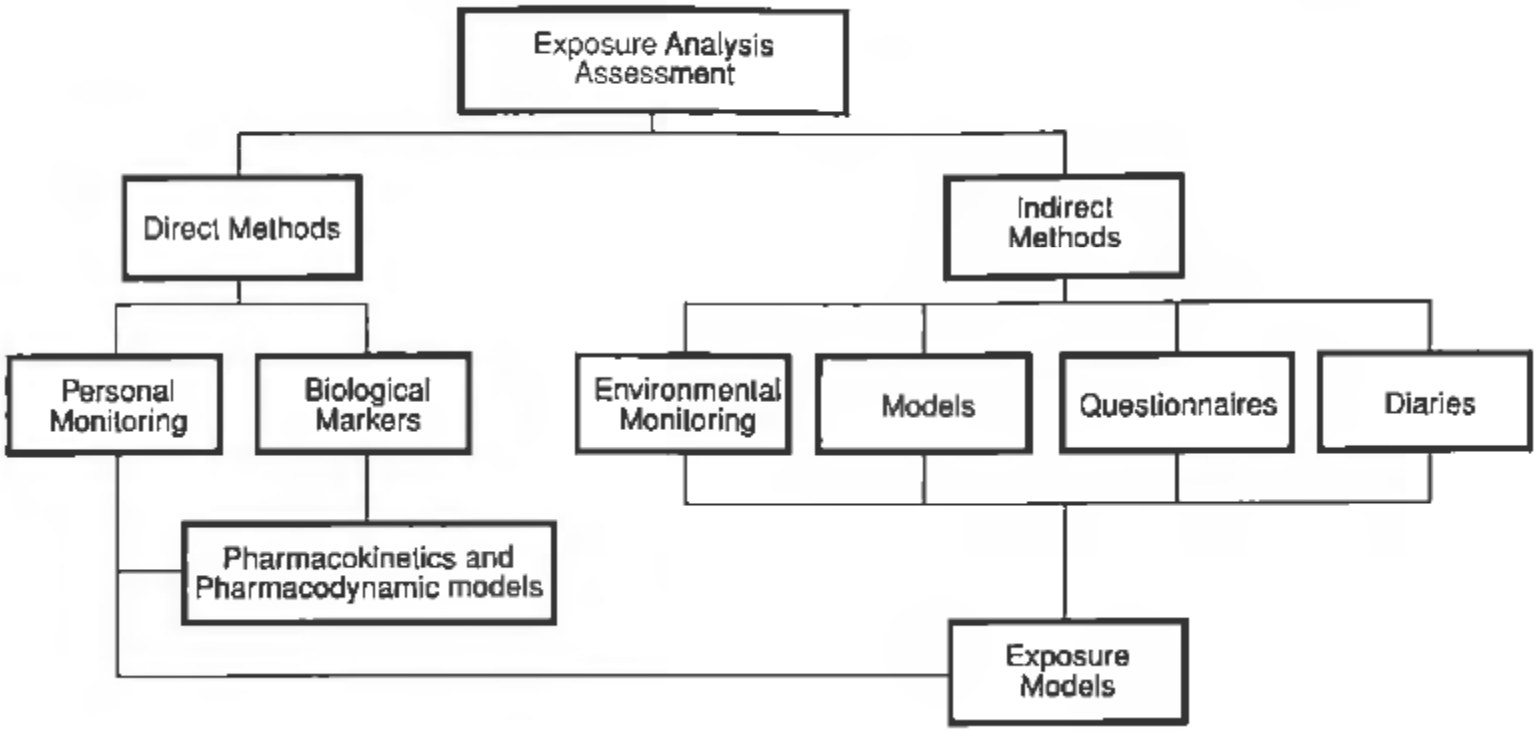
Exposure Assessment

Exposure Assessment

- Determines Dose
  - External Dose
  - Internal Dose (amount absorbed into body)
  - Biologically affective dose (amount at target organ)
- Most regulations target Exposure rather than dose



Methods of Determining Exposure



1. Hazard Identification
(Which are the health effects that this agent can cause?)

2. Dose-Response Assessment
(What is the relationship between dose and occurrence of health effects in humans?)

3. Exposure Assessment
(What exposures are currently experienced or anticipated under different conditions?)

4. Risk Characterization
(What is estimated occurrence of the adverse effect in a given population?)

⇩

5. Risk Management
(Development, evaluation and implementation of regulatory options, aimed at risk reduction and control)

Risk Characterization

Characterizing Health Risks

- Risk Characterization brings together:
  - Hazard identification
  - Dose-response assessment
  - Exposure assessment
- Estimates the health risk in the exposed population
- Four steps:
  - Exposure:
    - concentration × exposure duration
  - Dose:
    - exposure × dosimetry factors / body weight or surface area
  - Lifetime individual risk:
    - dose × NOEL or NOAEL × uncertainty factor
  - Risk in exposed population:
    - individual risk × number in exposed population (with consideration of susceptibility factors and population activities)

Environmental Health Risk Assessment

How Does Risk Assessment Work?

- What was the U.S. automobile accident mortality risk in 2008?
  - There were 6,024,000 accidents in 2007
  - 6.8 deaths per 1000 accidents ,
  - There were 301,621,000 people in the United States 01/07/07.

$$Societal\ Risk = 6\ ,024,000 \frac{accidents}{year} \times \frac{6.8}{1000} \frac{deaths}{accident} = 40,963 \frac{deaths}{year}$$

$$Individual\ Risk = \frac{40,963\ deaths / year}{301,621,000\ people} = 1.3 \times 10^{-4} \frac{deaths}{person \cdot year}$$

$$Lifetime\ Risk = 1.3 \times 10^{-4} \frac{deaths}{person \cdot year} \times 70\ years \approx 0.010 (1\ in\ 100)$$

National Highway Safety Administration Data: Actual 2007 estimate was 41,059 total fatalities.

+ EPA Risk Assessments

Where do I find EPA risk assessments?

Because risk assessments are performed all over EPA (see the EPA Organization Chart for other EPA Offices and Regions), risk assessments are produced by many of EPA's Regions and Program Offices. Here is a list of primary risk assessment sources:

- Integrated Risk Information System (IRIS) Chemical Summaries and Toxicological Reviews
  - What is IRIS?
  - What is the the IRIS Process for chemical assessment?
- National Center for Environmental Assessment (NCEA) Published Assessments
  - Agent-based risk assessments
    - Carbon Monoxide
    - Diesel Exhaust
    - Dioxin
    - Drinking Water and Disinfection By-Products
    - Lead
    - Mercury
    - Nitrogen Oxide (NOx)
    - Ozone
    - Particulate Matter
    - Pesticide Ecological Risk Assessments
    - PCBs
    - Radon in Homes
    - Secondhand Smoke (ETS)
    - Sulfur Oxide
  - Place-based risk assessments
    - Biological Assessments (Water)
    - National (Water) Assessment Database
    - Watershed and other place based risk assessments

See Tools & Guidance for a list of more resources.

http://www.epa.gov/risk_assessment/basicinformation.htm

Secondhand Smoke

The Issue
Secondhand smoke is a mixture of the smoke exhaled by smokers and the smoke given off by the burning end of a cigarette, pipe, or cigar. Secondhand smoke is also called environmental tobacco smoke (ETS), and exposure to secondhand smoke is sometimes called involuntary or passive smoking. Secondhand smoke contains more that 4,000 substances, several of which are known to cause cancer in humans or animals.

EPA has concluded that exposure to secondhand smoke can cause lung cancer. EPA estimates that exposure to secondhand smoke causes approximately 3,000 lung cancer deaths per year in nonsmokers. Secondhand smoke can also increase the risk of heart disease.

Children are particularly vulnerable to secondhand smoke because they are still developing physically and have higher breathing rates than adults. Infants and children exposed to high doses of secondhand smoke, such as those whose mothers smoke, run the greatest risk of harm from secondhand smoke. EPA estimates that up to 1 million asthmatic children have their condition worsened by exposure to secondhand smoke. Children's exposure to secondhand smoke can lead to bronchitis, pneumonia, asthma, and ear infections.

EPA Action
In 1992 EPA published its conclusion that secondhand smoke represents a serious and substantial public health risk in *The Respiratory Health Effects of Passive Smoking: Lung Cancer and Other Disorders*. EPA's conclusion that secondhand smoke causes lung cancer was based on a thorough review of all of the studies in the available literature and is supported by earlier studies by the National Research Council (NRC) and the U.S. Surgeon General who independently assessed the health effects of exposure to secondhand smoke.

EPA's report also concludes that infants and young children are especially sensitive to secondhand smoke. EPA estimates that up to 1 million asthmatic children have their condition worsened by exposure to secondhand smoke. In addition, children's exposure to secondhand smoke can lead to bronchitis, pneumonia, asthma, and ear infections.

While EPA does not have the regulatory authority to control secondhand smoke, EPA's report is expected to be of value to health professionals and policymakers in taking appropriate steps to minimize peoples' exposure to tobacco smoke in indoor environments. In cooperation with other government agencies, EPA will continue its education and outreach program to inform the public and policy makers on what to do to reduce the health risks of secondhand smoke and other indoor air pollutants.

Health in Environmental Impact Assessment

- An attempt to determine how human activities may impact human and environmental health
  - Dams
  - Mining activities
  - Industrial sites