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CPH601 Chapter 3 Risk Assessment

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Risk Assessment

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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**

- Laboratory and field observations (including epidemiological studies) of adverse health effects from exposure to particular agents.
- Quantitative dose-response studies and extrapolation from high to low dose and from animals to humans.
- Field measurements estimating exposures in defined populations.

**Risk Assessment**

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)

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

- 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 7 affected 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

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>
<thead>
<tr>
<th>Definition</th>
<th>Main criticism</th>
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<tr>
<td>A cause is something that produces or creates an effect.</td>
<td>Tautological because “production” and “creation” are synonyms of “causation”</td>
</tr>
<tr>
<td>A cause is a condition without which the effect cannot occur.</td>
<td>Only very few diseases could then have a cause&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>A cause is a condition with which the effect must occur.</td>
<td>Again, only few diseases could then have a cause&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>A cause is made up of several components, no single one of which is</td>
<td>Introduces unnecessary complexity in cases of simple dose response and in</td>
</tr>
<tr>
<td>sufficient of its own, which taken together must lead to the effect.</td>
<td>cases of interaction between components</td>
</tr>
<tr>
<td>A cause is a condition that increases the probability of occurrence of the</td>
<td>Does not distinguish between an association and a “cause”&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>effect.</td>
<td></td>
</tr>
<tr>
<td>A cause is a condition that, if present, makes a difference in (the</td>
<td>Is, in the strict sense, unprovable because there is only one world and one</td>
</tr>
<tr>
<td>probability of) the outcome.</td>
<td>cannot observe it twice—once with and once without the condition</td>
</tr>
</tbody>
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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*
Fig. 3.5. Design of a cohort study

TIME

direction of inquiry

Population

People without the disease

Exposed

Not exposed

disease

no disease

disease

no disease
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

- **TIME**
- **direction of inquiry**

Start with:

- **cases**
  - (people with disease)

- **controls**
  - (people without disease)

Exposed
Not exposed
Exposed
Not exposed
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!
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
<table>
<thead>
<tr>
<th>Exposed</th>
<th>Disease</th>
<th></th>
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<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>A</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>B</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>D</td>
</tr>
</tbody>
</table>
Relative Risk (RR)

- **RR** = \( \frac{a}{a+b} \) / \( \frac{c}{c+d} \)
  - 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)**
- \( \frac{a}{a+b} - \frac{c}{c+d} \)
  - measures potential savings
The Odds Ratio (OR)

- an estimate of relative risk
  - when cases/controls representative
  - if disease prevalence small
- if $> 1.0 \rightarrow$ increased risk
- if $< 1.0 \rightarrow$ 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

[Graph showing dose-response relationships between sound level at work (dB) and percent impaired, with different age groups indicated.]
Dose-Response Relationships
Dose-Response Relationships

- NOAEL
- LOAEL
- No Threshold Response
- Threshold Response

Magnitude of Response vs. Increasing Dose of Substance
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
Exposure Assessment

Field measurements estimating exposures in defined populations.

3. Exposure Assessment

(What exposures are currently experienced or anticipated under different conditions?)
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

- Exposure Analysis Assessment
  - Direct Methods
    - Personal Monitoring
      - Pharmacokinetics and Pharmacodynamic models
    - Biological Markers
  - Indirect Methods
    - Environmental Monitoring
    - Models
    - Questionnaires
    - Diaries
    - Exposure Models
1. Hazard Identification
(Which are the health effects that this agent can cause?)

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(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)
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.

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

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

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

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 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 than 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