Epidemiology Workshop

Oak Ridge Reservation
Health Effect Subcommittee

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Workshop Outline

I. What is Epidemiology and How is it Used?

II. Measures of Disease Frequency and Association

III. Measuring Exposure and Adverse Health Effects

IV. Judging a Cause-Effect Relationship

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Workshop Objectives

- **Basic epidemiology concepts.**
- **The importance of good measurement of exposure and disease.**
- **When is an epidemiologic study appropriate?**

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What is Epidemiology?

The study of the distribution and determinants of disease in populations.

(J. Last, Dictionary of Epidemiology, 1983)

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Epidemiology: The Science of Public Health

Three key aspects:

- **groups of people,**
- **measurement,**
- **comparison,**

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What Can Epidemiology Do?

- **Determine the impact of disease in groups of people.**
- **Detect changes in disease occurrence in groups of people.**
- **Measure relationships between exposure and disease.**
- **Evaluate the efficacy of health interventions and treatments.**

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What Can't Epidemiology Do?

- **Cannot tell an individual the cause of his or her disease.**
- **One study cannot prove a particular exposure caused an illness.**
- **Should not be conducted without good measurement of exposure and disease.**

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How Science Works

Every epidemiologic study and every analysis is built on a body of knowledge and is done to expand that body of knowledge

Is there a relationship between a particular exposure and a disease?

Epi Study

Animal studies

Case Reports

Epidemiologic study

Epidemiologic study

Toxicologic Models

Common Steps in Establishing a Relationship Between Exposure and Disease

- **Physician reports series of cases**
- **Descriptive analyses describe what is the problem, who is affected and where disease is occurring**
- **Analytic studies test the exposure-disease hypothesis in a study group**
- **Disease experimentally reproduced by exposure in animal studies**
- **Observation that removing exposure lowers disease**

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Measures of Disease Frequency

The most basic measure of disease frequency is a simple count of affected individuals.

However, counting is not enough!

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Why is a simple count not enough?

- 3 cases of cancer per year from a city of 1,000 people is very different than 3 cases per year from a city of 100,000 people

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So, in epidemiology we must know:

- the size of the population from which the affected individuals come, and
- the time period the information was collected.

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Basic Measure of Disease Frequency

- **Rate**
  - **an example: Incidence**

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Rate

- basic measure in epidemiology
- the frequency with which an event occurs in a group of people
- used to compare the occurrence of disease in different groups

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Example: Rates

$$\text{Rate} = \frac{\text{Number of events in a specified time period}}{\text{Average population during the time period}}$$

***the measure of time is a critical part of a rate!

Such as, the number of newly diagnosed cases of breast cancer per 100,000 women during 1999.

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Common Rates

- **<u>mortality (death) rate</u> is the number of deaths in a defined group of people during a specified time period.**

- **<u>birth rate</u> is the number of live births in a defined group of people over a specified time period.**

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Incidence

- a type of rate
- the number of new cases that develop in a group of individuals during a specific time period

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Incidence (cont.)

$$I = \frac{\text{number of new events during a period of time}}{\text{number of persons at risk during this time period}}$$

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Example: Incidence

If there were 150,00 new cases of lung cancer in the United States during 1997, the incidence rate would be:

(150,000/260,000,000) = 0.000058

0.000058 x 100,000 people

= 58 cases per 100,000 people, per year

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Measures of Association

- **How much greater the frequency of disease is in one group compared with another.**
- **Often presented in the form of a two-by-two table.**

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Two-By-Two Table

		Disease		
		Yes	No	Total
Exposure	Yes	**a**	**b**	a+b
	No	**c**	**d**	c+d
	Total	a+c	b+d	a+b+c+d

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Hypothetical Two-By-Two Table

		Lung cancer		
		Yes	No	Total
Smoking	Yes	**70**	**300**	370
	No	**15**	**700**	715
	Total		1,000	1,085

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Relative Risk (RR)

- **Measures how likely the exposed group will develop a disease compared to the unexposed group.**

$$\mathbf{RR} = \frac{\text{incidence in the exposed}}{\text{incidence in the unexposed}} = \frac{a/(a+b)}{c/(c+d)}$$

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Example: Hypothetical Study

		Lung cancer		Total
		Yes	No	
Smoking	Yes	70	300	370
	No	15	700	715
	Total	85	1,000	1,085

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$$\text{Relative Risk} = \frac{70/(70+300)}{15/(15+700)} = 9.0$$

Which means… participants who smoked were 9 times more likely to develop lung cancer than those who did not smoke.

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Interpreting Measures of Association

RR of 1.0 indicates that the occurrence of disease in the exposed an unexposed groups are identical:

- **No association observed between exposed and unexposed groups.**

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Interpreting Measures of Association (Continued)

- **RR greater than 1.0 indicates a positive association, or an increased risk among the exposed.**
- **RR less than 1.0 means that there is a decreased risk among the exposed group.**

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Standardized Mortality Ratios (SMRs)

- **the ratio of the observed number of deaths to the expected number of deaths**

- **a standard group of people is used to determine the expected number of deaths**
  - **the standard is often the US population, a state, or a county.**
  - **serves as the comparison group**

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SMRs (Continued)

Calculation:

$$\text{SMR} = \frac{\text{observed deaths}}{\text{expected deaths}}$$

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Example: Study of Smoking and Lung Cancer

Our hypothetical study found 58 lung cancer deaths between 1948 and 1963:

- **based on US population rates, we know that 42.9 cancer deaths were expected in a similar population.**

$$SMR = (58/42.9) = 1.35$$

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Example: Study of Smoking and Lung Cancer (cont.)

Our study group had a risk of cancer mortality approximately 35% greater than those in the general population.

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Measuring Exposure and Measuring Outcomes in Environmental Epidemiology

- **Contaminants in air, water, food, or soil come in contact with people through swallowing, breathing, or skin contact**

- **Once the contaminant gets in the body, it can act at that point of entry or can be distributed throughout the body where it can act upon a target organ or organs**

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Measuring Exposure

- **We can measure exposures or their surrogates along the entire path from emissions to body burden**

Types of Data	Approximation to actual exposure
1) Residence in a defined geographical area (e.g. county) of a site	Poorest
2) Residence in a geographical area in proximity to to a site where exposure is assumed	|
3) Distance <u>or</u> duration of residence	|
4) Distance <u>and</u> duration of residence	|
5) Quantified surrogate of exposure (e.g. estimate of drinking-water use	|
6) Quantified area measurements in vicinity of the residence	|
7) Quantified personal measurement	Best

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Baker D, et al., Environmental Epidemiology: A Textbook on Study Methods and Public Health Applications, 1999

What is an Outcome or Adverse Health Effect?

- **Any change in health status or body function.**
  - **Wide spectrum of effects such as wheezing, change in immune function, changes in blood chemistry, DNA adducts, adverse birth outcomes, developmental disabilities, clinical disease and death**

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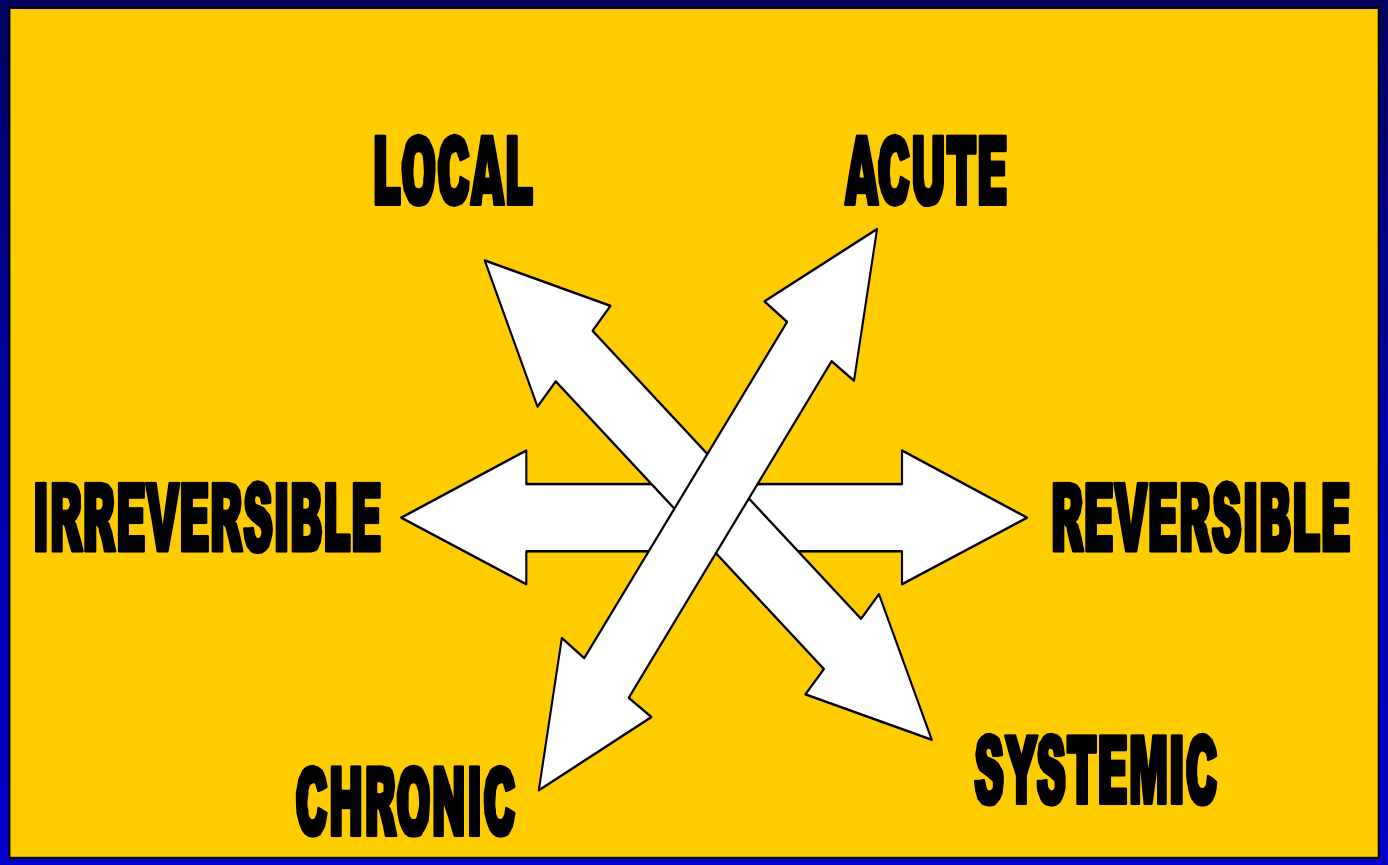
These changes can be…



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What Outcomes Do We Look For?
Biologically plausible outcomes

Contaminant → **Target Organ System**

Route of exposure

Toxicity or level → **Severity of Outcome**

Alternative explanations → **Confounding**

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Health Effects are Not Uniquely Caused by Environmental Exposures

- **25% of all pregnancies result in spontaneous abortions**
- **2% of infants are born with developmental deformities**
- **Among men, 1 in 2 will develop cancer in their lifetime (1 in 3 for women)**
- **8-10% of children have asthma**

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Cancer

- **Smoking is the leading cause of cancer in the U.S.**
  - **25% of Americans currently smoke**
- **Can be a very long time between exposure and the development of disease – many exposures over that time**
- **Cancer is not 1 disease – it is thought to be over 100 different disease in 40 anatomic sites**

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Measuring Adverse Health Effects

- **Goal: to count *all* the cases in a particular exposed group or population and compare it with cases in an unexposed group or population**

- **Where do we get this information?**

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Data Sources

- death certificates
- birth certificates
- medical exams
- hospital discharge data
- questionnaires
- disease registries
- laboratory tests or biomarkers

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Data Sources: Four Considerations

- **Severity of illness**
- **Accuracy of measuring disease-misclassification of the outcome**
- **Availability of information on confounders or other risk factors**
- **Cost and complexity and invasiveness**

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Death Certificates

- Readily available
- not all conditions of interest result in death
- considerable inaccuracy in diagnosis (error in major disease category is 25%, error within categories is 25%)
- no data on other risk factors

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Registries

- Registries of reportable diseases such as TB, cancer, birth defects.
- Cancer incidence data is available for all states.
- No information on other risk factors.
- Completeness and timeliness may be an issue.

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Medical Exams and Biologic Tests

- **Generally regarded as the "gold standard"**
- **However, physician diagnosis may vary for outcomes with no standard case definition**

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Questionnaires

- **May miss most severe outcomes**
- **Some outcomes may only be measured through a questionnaire**
- **Self-reports of illness or symptoms**

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Questionnaires, (cont.)

- **Wording or type of administration may influence responses**
- **Can collect data on other risk factors**
- **Subject to recall and response bias**

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Measuring Outcomes: Other Considerations

- **Timing and latency: especially important in chronic disease**
- **Individual variability by: age, gender, pre-existing illnesses, genetic predisposition**
- **Confounding and bias: What are alternative explanations for the exposure-disease association?**

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Summary: Measuring Health Outcomes and Exposures

- **The closer we can get to a measure of dose in the body, the more precise our exposure estimate will be.**
- **Characteristics such as age or pre-existing illness modify or determine the health effects we might see.**
- **Sources of data on health effects and exposures are varied.**

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Basic Criteria for Considering a Health Study

We need:

1. **An exposure that can be measured.**
2. **A completed pathway.**
3. **An exposed population.**
4. **A measurable effect that is plausibly related to the exposure.**

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Basic Criteria for Considering a Health Study

- **Will the epidemiologic study we are planning advance our knowledge about the relationship between exposure and disease?**

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How to Judge a Cause-Effect Relationship

You're given a paper that reports the results of a study, how do you interpret this study?

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Strength of Association

- example: Relative Risk (RR)
- the larger the risk, the more likely the relationship exists
  - less likely it is due to other factors, such as confounding

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Consistency of Findings

Has this association been seen with other studies, with other study designs, and in different groups of people?

- **If so, this strengthens the findings**

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Dose-Response Relationship

- **As exposure increases, does the risk of disease increase?**

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Time Sequence

- **the exposure MUST occur before the disease develops**

- **this is an essential criteria**

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Biologic Plausibility

- **does this make biologic sense?**
- **is there a known mechanism by which an exposure can lead to disease?**

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Biologic Plausibility (cont.)

Example: daily consumption of fatty foods increases risk of heart disease

- **there is a biologic mechanism**
- **fatty foods raises LDL cholesterol, which increases the risk of heart disease**

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In Conclusion…

- **these are not hard and fast rules (except time sequence)**
  - **there can be exceptions!**
- **These tools help us judge the scientific literature – have the authors convinced us?**

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Epidemiology is an excellent tool if used correctly!

Joseph Mangano ☮ Cancer Mortality near Oak Ridge, Tennessee

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