1. Introduction to Environmental Epidemiology

Introduction to Environmental Epidemiology

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2. Agenda

Agenda

- Logistics?
- Follow-up from last week
- Defining environmental epidemiology within a context of all epidemiology
- Information technology from the WHO
- Review of appropriate methods for conducting environmental epidemiology studies.
- Importance of surveillance (as a cross-cutting theme) and monitoring
- Review of methods for ascertaining complex exposures (diet and water)
- Presentations from the groups
- Assignment
3. Ignaz Semmelweis and the “Horseman on the Roof”...

Ignaz Semmelweis and the “Horseman on the Roof”

- http://www.annals.org/cgi/content/full/121/12/999

- http://mchip00.nyu.edu/lit-med/lit-med-db/webdocs/webfilms/horseman.on.the.r38-film.html

4. My Wonderful Adventure: Selected Epi Applications (1)

My Wonderful Adventure: Selected Epi Applications (1)


- 1st public health position (1979-1983) in Rhode Island (RI). Finding: resources skewed heavily towards curative medicine, geographic and specialty mal-distribution also present. $ for health care are sufficient-remedy = cap and re-allocate. Action: political defeat, grudgingly learned the wisdom of “incremental change.”
My Wonderful Adventure: Selected Epi Applications (2)

- Ph.D. Thesis (1978-1981) - With NIOSH funding evaluated the distribution of occupational mortality of RI decedents. **Finding:** Some elevations were anticipated (respiratory mortality and textile workers) while others were new and unanticipated (stomach cancer and female jewelry workers). **Action:** NIOSH, heartened by the surveillance potential of vital records, presses ahead with a national program.

My Wonderful Adventure: Selected Epi Applications (3)

- Assistant Commissioner in Massachusetts: (1983-1988) administered investigations which spanned the study of PCBs in New Bedford harbor and the cluster of childhood leukemia in Woburn.
- Life on the Hill (1988-present) Together with Richard Enander, Ph.D. characterize the autobody refinishing industry in RI. **Finding:** identify lead as a principal component in top selling body filler compounds. **Action:** lead removed from product line.
7. The Nature of Environmental Exposure

The Nature of Environmental Exposure

- Population less well defined: Why?
- Variable susceptibilities of population
- Database integrity and accuracy?
- Develop additional items through discussion

Source: www.niehs.nih.gov

7
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8. Epidemiological Triad

Epidemiological Triad (9/12/01)

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9. Two Scenarios

Two Scenarios

- Relatively high concentration of pollutants, plausible if not actual routes of exposure to human populations, chronic exposure. Examples: Superfund sites such as the two sites in Woburn, MA, Department of Energy sites and military bases in the US.
- Relatively low concentration of pollutants, less likelihood of exposure pathways to human populations, chronic exposure. Examples: Brownfield sites in the US.

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10. FACE Map

FACE Map

Woburn Massachusetts
Childhood Leukemia Cases: 1964-1986
28 cases – 16 deaths

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11. Wells G + H

Wells G + H

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12. Environmental Health Tracking

Environmental Health Tracking

- Comprehensive surveillance to support environmental disease investigation is lacking. Case in point = asthma.
- “Currently, no systems exist at the state or national level to track many of the exposures and health effects that may be related to environmental hazards, in addition, in most cases, existing environmental hazard, exposure, and disease tracking systems are not linked together.”
- Then 9/11 occurred!
13. Environmental Health Tracking (2)

Environmental Health Tracking (2)

Go to:

http://www.cdc.gov/nceh/tracking/resources.htm

14. Potential Source Areas

Potential Source Areas

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15. Soil Sampling Results

Soil Sampling Results

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16. Ground Water Sampling Results

Ground Water Sampling Results

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Potential Exposure Pathways Future Planned Use

Methodological Features of Environmental Epidemiology

- Ecologic studies
  “Homogeneity of exposure within groups is in general desirable in ecologic studies, as is heterogeneity of exposure between groups, because these conditions make it easier to detect effects of exposure.”
- Clusters
  “The first problem is determining whether the cluster really represents a high occurrence of disease.”
19. Methodological Features of Environmental Epidemiology (2)

Methodological Features of Environmental Epidemiology (2)

A second ..."problem that arises is defining the
boundaries of the area or time frame for the cluster
to be used in calculating rates."

Rothman’s negative critique of cluster investigation-
what are these attributes?

"Useful scientific data on environmental risks, on the
other hand, is more likely to be found by determining
good studies to investigate specific etiologic
hypotheses, in populations in which no clusters has
been noted."

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20. Methodological Features of Environmental Epidemiology (3)

Methodological Features of Environmental Epidemiology (3)

• Errors in measuring exposure:
  “In many epidemiologic studies, it is very difficult or
  even impossible to measure the true exposure
  exactly. Hence the observed exposure is measured
  with error (for continuous variables) or misclassified
  (for categorical variables).”

• The general presumption of nondifferential exposure
  measurement error or misclassification leading to
  bias towards the null may not hold.

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21. Take Away on Error and Misclassification (1)

Take Away on Error and Misclassification (1)

- No gold standard exists for many of the relationship being tested, hence, where does truth lie?
- Much of the work is theoretical
- The direction and/or existence of the bias depends on
  - The true error model
  - The type of data
  - The type of analysis
  - The true exposure-response relationship

22. Risk Assessment

Risk Assessment

- Risk assessment addresses:
  - Does the weight of the evidence indicate that exposure causes disease? *Hazard Identification*
  - If so, what is the quantitative dose-response relationship? *Dose - Response Assessment*
  - What does the relationship imply for regulation? *Estimates of the prevalence of exposure taken together with risk*
- Inputs include animal and human data

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23. Dose - Response Assessment Using Published Data

Dose - Response Assessment Using Published Data

- **Inputs:**
  - Linear regression of SMRs (thus we need access to cohorts)
  - Cumulative exposure estimates (emphasis on retrospective exposure)
- **Output:**
  - Unit risk estimate (URE) $\mu g/m^3$ for inhalation and is defined as an estimate of the increased cancer risk from a lifetime exposure to a concentration of one unit exposure.

24. Applying UREs for Regulatory Purposes

Applying UREs for Regulatory Purposes

- **URE** = $R_x = R_0(xB)$
  - $R_x$ = is the URE
  - $R_0$ = the background lifetime lung cancer mortality rate of 4.9% (or 0.049)
  - $X = 1 \mu g/m^3$
  - $B$ = the adjusted slope of 20.02/3.08 mg/m$^3$ or 6.5 per mg/m$^3$
25. Meta-Analysis

Meta-Analysis

- A technique which combines results across studies, usually human studies, with the goal of improving the precision of the measures of association
- Publication bias is a primary problem
- Employed as an adjunct to hazard identification

26. Components of a Meta-Analysis

Components of a Meta-Analysis

1. Define the question
2. Define the criteria for inclusion of studies
3. Find all eligible studies
4. Review the methods and results of each study
5. Summarize the results of each study in a standard format
6. Apply statistical methods to produce a summary result
27. Components of a Meta-Analysis (cont.)

Components of a Meta-Analysis (cont.)

7. Assess variation between studies (heterogeneity)
8. Review and interpret findings and report them
   From: Elwood, Mark. “Critical Appraisal of Epidemiological Studies and Clinical Trials.”

28. Controversy Between Epidemiologists - Mon Dieu!

Controversy Between Epidemiologists - Mon Dieu!

- Sander Greenland - summarize his approach
- Sydney Shapiro - summarize his concerns
29. The Problem Type

The Problem Type

- What is the summary measure of association?
- Note the impact of sample size on the width of the CI's.
- www.meta-analysis.com/ meta007.gif

30. An Example Meta-Analysis with and without Heterogeneity

An Example Meta-Analysis with and without Heterogeneity

- Width of the confidence intervals are more evident
- Application of homogeneity and heterogeneity demonstrated

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31. Etiology as a Central Concern of Epidemiology

Etiology as a Central Concern of Epidemiology

- Additional detail on John Snow and his rival William Farr
- Competing Theories of Causation
- Introduction to basic epidemiology study designs and principal sources of data
- Assessment of causation
- Assignment + announcements

32. John Snow

John Snow

- Medical doctor
- Disease detective
- More info at: http://www.ph.ucla.edu/epi/snow.html
33. William Farr

William Farr

- “Diseases are more easily prevented than cured and the first step to their prevention is the discovery of their exciting causes”

Source:
www.ph.ucla.edu/epi/snow.html

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34. Basis of Miasma Theory

Basis of Miasma Theory

Farr produced statistical evidence that the cholera was spread by polluted water, yet he long avoided this conclusion, preferring to cling to the orthodox explanation of disease propagation, which held that epidemic disease was caused by foul air (a “miasma”). Advocates of the "miasmatic" theory included Florence Nightingale and Edwin Chadwick, who expressed the view at its most extreme form in evidence to a Parliamentary Committee in 1846, claiming that:

“All smell is, if it be intense, immediate acute disease; and eventually we may say that, by depressing the system and rendering it susceptible to the action of other causes, all smell is disease.”

Parliamentary Papers, 1846 vol. 10, p.851, Chadwick’s evidence

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35. Hypothesis Formation

Hypothesis Formation

“What is cholera? Is it a fungus, an insect, a miasma, an electrical disturbance, a deficiency of ozone, a morbid off-scouring of the intestinal canal? We know nothing; we are at sea in a whirlpool of conjecture.”


36. The Broad Street Pump

The Broad Street Pump

- Important take away here is that Snow’s descriptive analysis lead to action.
- His memorial pub is close by.
- www.ph.ucla.edu/epi/snow.html

Source: www.dhss.delaware.gov/DHSS/epi/epi.html

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37. The New Pub

The New Pub

- Renamed after Snow in 1955 on the centennial of the cholera epidemic.
- The speaker = Sir Austin Bradford Hill, the author of a strikingly clear text on biostatistics

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38. Basic Epidemiologic Study Designs

Basic Epidemiologic Study Designs

- Cluster or case reports
- Ecologic
- Cross-sectional
- Cohort Studies (prospective and retrospective)
- Case-Control Studies (Nested + Pop. Based)
- Longitudinal
39. Epidemic Curves (1)

Epidemic Curves (1)

Epidemic Curve (non-propagating)

![Epidemic Curve](image)

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40. Epidemic Curves (2)

Epidemic Curves (2)

Epidemic Curve (propagating)

![Epidemic Curve](image)

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41. Natural History of a Disease

Natural History of a Disease

- The progression of signs and symptoms of the disease under study.
- Often these stages offer opportunities for prevention and or detection.
- Knowledge of natural history also informs prognosis both in the individual and for the population.

42. Epidemiological Study Designs

Epidemiological Study Designs

<table>
<thead>
<tr>
<th>Unit of Study</th>
<th>Study Design</th>
<th>Also Called</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population</td>
<td>Ecological</td>
<td>Correlational</td>
</tr>
<tr>
<td>Individuals</td>
<td>Cross-sectional</td>
<td>Prevalence</td>
</tr>
<tr>
<td>Individuals</td>
<td>Case control</td>
<td>Case-reference</td>
</tr>
<tr>
<td>Individuals</td>
<td>Cohort</td>
<td>Longitudinal, follow-up</td>
</tr>
<tr>
<td>Patients</td>
<td>Experimental studies:</td>
<td>Interventional studies</td>
</tr>
<tr>
<td></td>
<td>Randomized control trials</td>
<td>Field trials, community</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Interventional studies</td>
</tr>
</tbody>
</table>

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43. Principal Sources of Human Health Data

**Principal Sources of Human Health Data**

<table>
<thead>
<tr>
<th>Mortality data</th>
<th>Complete, accessible - relatively inexpensive</th>
<th>Accuracy of diagnosis – latency problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morbidity data</td>
<td>Minimizes latency - relatively complete</td>
<td>Comparability – nonspecificity – expensive – accessibility</td>
</tr>
<tr>
<td>Hospital discharge data</td>
<td>Timely – close to exposure</td>
<td>Competenteness – practicality – confidentiality</td>
</tr>
<tr>
<td>Reportable diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence cancer registry (MA as an example)</td>
<td>Improved quality of information – decreases latency - less costly</td>
<td>No outcome data</td>
</tr>
<tr>
<td>Follow back cancer registry (CT as an example)</td>
<td>Same as above except for cost</td>
<td>More expensive</td>
</tr>
</tbody>
</table>

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44. A Synopsis

**A Synopsis**

- *Description of the evidence*
- Exposure or intervention
- Outcome
- Study design
- Study population
- Main result
- *Non-causal explanations*
- Observation bias
- Confounding
- Chance
- *Positive features*
- Time relationship
- Strength
- Dose-response
- Consistency
- Specificity
- *Generalizability*
- Eligible population
- Source population
- Other populations
- *Comparison with other evidence*
- Consistency
- Specificity
- Plausibility
- Coherence

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Applying UREs for Regulatory Purposes

- \( U = R_x = R_0(xB) \)
  - \( R_x \) = is the URE
  - \( R_0 \) = the background lifetime lung cancer mortality rate of 4.9% (or 0.049)
  - \( X = 1 \) \( \mu g/m^3 \)
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