Legal, Ethical, and Policy Aspects of Epidemiologic Investigations

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Section A

Introduction
Learning Objectives

- Explain the general mechanisms by which the findings of epidemiologic studies impact public policy
- Discuss the elements of risk assessment
- State the difference between the epidemiologic definition and the legal definition of causality
- Describe some current issues related to data confidentiality and privacy
Epi in the News

- Bird Flu
  - Surveillance
  - Modeling
  - Interventions
- Vioxx (NSAIDs)
  - Marketed by Merck
  - Increases risk of coronary artery disease
  - Epi data influences legal decisions
Can epidemiological evidence establish causation?
  − In an individual?
  − In Vioxx users generally?

What level of certainty can be reached?
Roles

- Should epidemiologists serve as experts?
  - For the defense?
  - For plaintiffs?
- Are there ethical concerns?
- Should they be paid? how much?

*English-language publications only

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Sex, Racial Differences in the Management of Acute MI

1994–2002

Reperfusion therapy
Use of aspirin
Use of beta-blockers
Coronary angiography

White men
White women
Black men
Black women

Sex, Racial Differences in the Management of Acute MI

**Conclusion:**

- Although the reasons for these differences are unknown, their persistence emphasizes the need for a continued search for explanations so that inequities in clinical care may be eliminated

Some Paths from Epi to Policy

- Diverse
- Personal ➔ Societal
- Specific ➔ General
- Regulatory
- Non-regulatory
- Litigation
Impact of Epi — Today

- Food choices
- Obesity
- Air quality
- Exercise habits
- Medications
- Medical care
- Surveillance (bioterrorism)
From Data to Decision to Action

Data
↓
Inference
↓
Synthesis
↓
Evaluation
↓
Decision
↓
Action
Hypothesis

Study design

Funding

Study conduct

Publication

Policy utilization

Policy
## What Is the Role of Epidemiology in This Schema?

<table>
<thead>
<tr>
<th>Epidemiologic evidence</th>
<th>Epidemiologists</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evidence for causal inference</td>
<td>Carry out and report research</td>
</tr>
<tr>
<td>Hypothesis generation</td>
<td>Participate in evidence synthesis and evaluation</td>
</tr>
<tr>
<td>Program evaluation</td>
<td>Become decision makers</td>
</tr>
</tbody>
</table>
What Do Epidemiologists Publish?

American Journal of EPIDEMIOLOGY
Volume 162 Number 4 August 15, 2005
www.aje.oupjournals.org

HUMAN GENOME EPIDEMIOLOGY (HuGE) COMMENTARIES
297 Genomic Epidemiology of Complex Disease: The Need for an Electronic Evidence-based Approach to Research Synthesis. Michael B. Bracken

META-ANALYSIS
305 Large Meta-Analysis Establishes the ACE Insertion-Deletion Polymorphism as a Marker of Alzheimer's Disease. Donald J. Luchsinger, Mario Corrêa-Broga, Donald R. Warden, A. David Smith, Kristel Steegers, Jonathan A. Prince, Corneila M. van Duijn, and Patrick G. Kahoe

ORIGINAL CONTRIBUTIONS
318 Statins and Prostate Cancer Risk: A Case-Control Study. Jack Alan Shannon, Salome Tswodaros, Mark Garzotto, Tomasz M. Beier, Rhianna Derenick, Amy Palma, and Paige E. Harris
334 The Effect of Trihalomethane and Haloacetic Acid Exposure on Fetal Growth in a Maryland County. Chad K. Porter, Shannon D. Putnam, Katherine L. Hunting, and Mark R. Riddle
Lung Cancer and Indoor Pollution from Heating and Cooking with Solid Fuels

The IARC International Multicentre Case-Control Study in Eastern/Central Europe and the United Kingdom

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2 International Agency for Research on Cancer, Lyon, France.
3 Public and Environmental Health Research Unit, London School of Hygiene and Tropical Medicine, London, United Kingdom.
4 Institute of Carcinogenesis, Cancer Research Center, Moscow, Russia.
5 Department of Epidemiology, The Nifor Institute of Occupational Medicine, Lodz, Poland.
6 National Institute of Environmental Health, Budapest, Hungary.
7 Department of Occupational Health, Specialized State Health Institute, Banska Bystrica, Slovakia.
8 Royal Castle Lung Cancer Research Programme, University of Liverpool, Liverpool, United Kingdom.
9 Institute of Hygiene, Public Health, Health Services, and Management, Bucharest, Romania.
10 Institute of Hygiene and Epidemiology, First Faculty of Medicine, Charles University, Prague, Czech Republic.
11 Department of Cancer Epidemiology and Genetics, Masaryk Memorial Cancer Institute, Brno, Czech Republic.
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13 Current affiliation: Centre for Public Health Research, Massey University, Wellington, New Zealand.

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Exposure to fuel-burning from cooking and heating has not been studied in Europe, where lung cancer rates are high. And many residents have had a long tradition of burning coal and unprocessed biomass. Study subjects included 2,861 cases and 3,118 controls recruited during 1998-2002 in the Czech Republic, Hungary, Poland, Romania, Russia, Slovakia, and the United Kingdom. The odds ratio of lung cancer associated with solid fuel use was 1.22 (95% confidence interval CI: 1.04, 1.44) for cooking or heating, 1.27 (95% CI: 0.99, 1.60) for solid fuel only for cooking, and 1.24 (95% CI: 1.05, 1.47) for solid fuels used for both cooking and heating. Risk increased relative to the percentage of time that solid fuel was used for cooking (P < 0.0001), while no risk increase was detected for solid fuel used for heating. The odds ratio of lung cancer in whole-life users of solid cooking fuel was 1.80 (95% CI: 1.35, 2.40). Switching to nonsolid fuels resulted in a decrease in risk. The odds ratio for the longest duration of time since switching was 0.76 (95% CI: 0.63, 0.92). These data suggest a modest increased risk of lung cancer related to solid-fuel use for cooking rather than heating.

The Effect of Trihalomethane and Haloacetic Acid Exposure on Fetal Growth in a Maryland County

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As water flows from treatment plants to the tap, chlorine, used to disinfect surface water meant for residential use, reacts with residual organic and inorganic matter, creating chlorine disinfection by-products. In recent years, these by-products have been scrutinized as a potential reproductive and developmental hazard. This study examined whether exposure to the four total trihalomethanes or the five haloacetic acids (two major subgroups of chlorine disinfection by-products) was related to an increased risk of intrauterine growth retardation in four regions of a Maryland county from 1998 to 2002. Maternal exposure to each by-product was evaluated for each trimester as well as over the entire pregnancy. The authors were not able to demonstrate any consistent, statistically significant effect on intrauterine growth retardation associated with any of the chlorine disinfection by-products, nor did they find any indication of a dose-response relation. However, they did find some potential for a slightly elevated risk of intrauterine growth retardation during the second and third trimesters for both total trihalomethanes and five haloacetic acids when comparing increasing quintiles of exposure to constituents of total trihalomethanes and five haloacetic acids.
Section B

Epi to Policy: Setting Standards
Figure 2. Current NAAQS Review Process

1. Hypothesis: PM increases mortality (1990s)
   
2. NMMAPS (1996)
   
3. Funding (1996)
   
   
5. Publication (2000)
   
The New England Journal of Medicine


JONATHAN M. SAMET, M.D., FRANCESCA DOMINICI, PH.D., FRANK C. CURRIERO, PH.D., IVAN COURSAC, M.S., AND SCOTT L. ZEGER, PH.D.

ABSTRACT

STUDIES showing that current levels of air pollution in the cities of many developed and developing countries are associated with increased rates of mortality and morbidity have heightened concern that air pollution continues to pose a threat to public health. The evidence suggests...
Increase in Deaths from All Causes for Each Increase in PM10 of 10 μg/m³ (%)

The epidemiologic evidence that levels of particulate matter are associated with the risk of mortality and morbidity has prompted the promulgation of a new standard for PM$_{2.5}$ in the United States and a rethinking of guidelines for particulate matter in Europe. Our analyses provide evidence that particulate air pollution continues to have an adverse effect on the public’s health and strengthen the rationale for limiting levels of respirable particles in outdoor air.
Ozone and Short-term Mortality in 95 US Urban Communities, 1987-2000

Michelle L. Bell, PhD
Aidan McDermott, PhD
Scott L. Zeger, PhD
Jonathan M. Samet, MD
Francesca Dominici, PhD

Exposure to tropospheric ozone is widespread in the United States, occurring also outside southern California, where ozone formation was first recognized. Short-term exposure to ozone has been linked to adverse health effects, including increased rates of hospital admissions and emergency department visits, exacerbation of chronic respiratory conditions (eg, asthma), and decreased lung function. Numerous time-series studies have addressed the relationship between ozone levels and mortality counts on short-term intervals of 1 or a few days, including some studies involving multiple locations; however, their findings have been inconsistent. Interpretation of this evidence is constrained by the limited range of locations included in these reports, the variability of meth-

Context Ozone has been associated with various adverse health effects, including increased rates of hospital admissions and exacerbation of respiratory illnesses. Although numerous time-series studies have estimated associations between day-to-day variation in ozone levels and mortality counts, results have been inconclusive.

Objective To investigate whether short-term (daily and weekly) exposure to ambient ozone is associated with mortality in the United States.

Design and Setting Using analytical methods and databases developed for the National Morbidity, Mortality, and Air Pollution Study, we estimated a national average relative rate of mortality associated with short-term exposure to ambient ozone for 95 large US urban communities from 1987-2000. We used distributed-lag models for estimating community-specific relative rates of mortality adjusted for time-varying confounders (particulate matter, weather, seasonality, and long-term trends) and hierarchical models for combining relative rates across communities to estimate a national average relative rate, taking into account spatial heterogeneity.

Main Outcome Measure Daily counts of total non-injury-related mortality and cardiovascular and respiratory mortality in 95 large US communities during a 14-year period.

Results A 10-ppb increase in the previous week’s ozone was associated with a 0.52% increase in daily mortality (95% posterior interval [PI], 0.27%-0.77%) and a 0.54% increase in cardiovascular and respiratory mortality (95% PI, 0.31%-0.98%). Effect estimates for aggregate ozone during the previous week were larger than for models considering only a single day’s exposure. Results were robust to adjustment for particulate matter, weather, seasonality, and long-term trends.

Conclusions These results indicate a statistically significant association between short-term changes in ozone and mortality on average for 95 large US urban communities, which include about 40% of the total US population. The findings indicate that this widespread pollutant adversely affects public health.

Benefits and Costs of the Clean Air Act

Final Report to Congress on Benefits and Costs of the Clean Air Act, 1990 to 2010

EPA 410-R-99-001

Final Report to Congress on Benefits and Costs of the Clean Air Act, 1970 to 1990

EPA 410-R-97-002

Throughout the history of the Clean Air Act, questions have been raised as to whether the health and environmental benefits of air pollution control justify the costs incurred by industry, taxpayers, and consumers. While the benefits and costs of individual programs and standards continue to be addressed through narrowly-focused regulatory analyses, there has never been a comprehensive, long-term, scientifically valid and reliable study which answered the broader question:
Colorado Plateau During the Uranium Boom
Lung Cancer Mortality

<table>
<thead>
<tr>
<th>Follow-Up Cutoff Date</th>
<th>Observed/Expected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1959</td>
<td>6/3</td>
</tr>
<tr>
<td>1962</td>
<td>15/4.2</td>
</tr>
<tr>
<td>1967</td>
<td>62/10</td>
</tr>
<tr>
<td>1974</td>
<td>144/29.8</td>
</tr>
<tr>
<td>1977</td>
<td>185/38.4</td>
</tr>
</tbody>
</table>
Original Radiation Exposure Compensation Act

- Compensates miners who worked in five states, 1947–1971
- For nonsmokers with lung cancer, eligible if 200 or more WLM
- For smokers with lung cancer, eligible if 300+ WLM if <45 yrs or 500+ WLM at any age
- This act does not address the real problem
Radiation Exposure Compensation Act Amendments

An Act

To amend the Radiation Exposure Compensation Act, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

[*1] SECTION 1. SHORT TITLE.

This Act may be cited as the "Radiation Exposure Compensation Act Amendments of 2000".

[*2] SEC. 2. FINDINGS.
Policy Matters for Epidemiologists

- Is there a risk?
  - Is the level of risk acceptable?
- What level of exposure is “safe”?
- How big is the problem?
  - For the population?
  - For the individual?
- Who is affected?
- What determines the exposure?
  - What exposures are “healthy”?
- How effective are the alternative approaches for reducing exposure?
Tools for Using Epidemiologic Data

- Techniques for summarizing evidence
  - Meta-analysis
  - Pooled analysis
  - Other review methods
  - Expert review
- Guidelines for evidence evaluation
- Risk assessment
  - Integrative method for summarizing all relevant lines of evidence
Questions of Cause Cause Calls for Action

- Does workplace exposure to ETS cause lung cancer?
- Does EMF cause brain tumors?
- Does HPV cause cervical cancer?
“The statement that an exposure ‘causes’ a disease in humans represents a serious claim, but one that carries with it the possibility of prevention. Causal determinants may also carry substantial economic implications for society and for those who might be held responsible for the exposure or for achieving its prevention.”

— Surgeon General’s Report, 2004
The Case for Action

Finally, in passing from association to causation I believe in ‘real life’ we should have to consider what flows from that decision. On scientific ground we should do no such thing....But in another and more practical sense we may surely ask what is involved in our decision. In occupational medicine our object is usually to take action. If this be operative cause and that be deleterious effect, then we shall wish to intervene to abolish or reduce death or disease.
Epidemiology and the Law

- Epidemiology is concerned with causes of disease in groups, not for individuals.
- Criteria for causality have been developed for exposure-disease associations in groups, not for individuals.
IN THE CIRCUIT COURT OF THE ELEVENTH JUDICIAL CIRCUIT IN AND FOR DADE COUNTY, FLA

GENERAL JURISDICTION DIVISION

HOWARD A. ENGLE, M.D., et al., Plaintiffs

v.

R.J. REYNOLDS TOBACCO COMPANY, et al., Defendants

Case No. 94-08273 CA-22

VERDICT FORM FOR PHASE 1

We, the jury return the following Verdict:
Smoking Cigarettes

Does smoking cigarettes cause one or more of the following diseases or medical conditions?

Aortic aneurysm  Yes ___ No ___

Asthmatic bronchitis (as related to COPD)  Yes ___ No ___

Bladder cancer  Yes ___ No ___

Cerebrovascular disease (including stroke)  Yes ___ No ___

Cervical cancer  Yes ___ No ___

COPD (including emphysema)  Yes ___ No ___

Coronary heart disease  Yes ___ No ___

Esophageal (throat) cancer  Yes ___ No ___

Infertility  Yes ___ No ___
Criteria for Causality

- **Epidemiology:** Plausibility, consistency, temporality, strength, dose-response

- **Law:** “Preponderance of evidence” or “more likely than not”
“The culprit is an environment which promotes behaviors that cause obesity.”

Neighborhoods and schools

Modes of transportation

Local food availability

Food advertising

Governmental policies

Epidemiologists and Public Policy

- Consultants
- Witnesses
- Testifiers
- Policy makers
- Advocates
Engaging in Policy as an Epidemiologist

- **Pros**
  - Responsibility of public health scientists
  - Assure impact of research
  - Challenging
  - Rewarding
  - Make friends

- **Cons**
  - Treacherous, non-science ground
  - Time-consuming
  - Often unfunded
  - Perceived/real conflicts of interest
  - Make enemies
### Frequency of Policy Statements

<table>
<thead>
<tr>
<th>Policy Statement</th>
<th>AJE</th>
<th>AE</th>
<th>E</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>63 (26.7%)</td>
<td>12 (30%)</td>
<td>5 (8.3%)</td>
<td>80 (23.8%)</td>
</tr>
<tr>
<td>Clinical practice</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Public health practice</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Corporate policy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regulatory—legislative</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arena not defined</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
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</tbody>
</table>

Some Issues Arising in the Practice of Epidemiology

- Regulatory implications
- Legal consequences
- The epidemiologist as consultant
- The epidemiologist as policy maker
- Advocacy
- Privacy
- Confidentiality
- Use of biologic samples
- Conflict of interest
- Informed consent
Backlash against Epidemiology

- Motivation: the powerful societal consequences of epidemiologic research
- Guidelines for epidemiologic studies
- Calls for “sound science”
- Accusations of “junk science”
- The standard raps
  - Observational
  - Not good for “weak effects”
  - Cannot control other factors
All scientific work is incomplete—whether it be observational or experimental. All scientific work is liable to be upset or modified by advancing knowledge. That does not confer upon us a freedom to ignore the knowledge we already have, or to postpone the action that it appears to