# How Epidemiologic Studies are Used for Setting Air Pollution Standards

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# Areas Covered

- ❖OEHHA's Role in Air Quality Standards (AQS) Setting for Criteria Pollutants
- ❖OEHHA's previous history with $SO_2$
- ❖Study Types Used for Recommendations
- ❖Epidemiologic Study Designs Relevant to $SO_2$
- ❖Evaluating Quality of Air Pollution Epidemiologic Studies

# OEHHA's Role in AQS Setting for Criteria Pollutants

- OEHHA tasked to create health-based recommendations for air quality standards: legal definition of clean air
- Standards have:
  - Pollutant definition
  - Concentration
  - Averaging time
  - Monitoring method
  - Form of the standard
- Based solely on health considerations

# OEHHA's Previous History with SO2

- CA Standard last revised 1994
  - 24 hr: 40 ppb
  - 1 hr: 250 ppb
- Reviewed for adequacy of child protection in 2000 (California Senate Bill 25)
  - CA 1-hr standard was not adequate to protect all members of the community.
- US EPA standard revised August 2010
  - 1 hr: 75 ppb

# Study Types Used for Recommendations

- Controlled human exposure studies
- Animal toxicology studies
- Epidemiology studies

# Controlled Human Exposure Studies

Exposures of human volunteers in a laboratory setting

- **Advantages**
  - Precise measures of exposure and response
- **Limitations**
  - Few studies on more vulnerable populations
  - Small sample size and researcher-defined doses
  - Cannot predict effects of chronic exposures

# Animal Studies

- **Advantages**
  - Higher doses
  - More endpoints (higher severity)
- **Limitations**
  - Effects seen in animal models may be more difficult to extrapolate to human health effects

# Epidemiologic Studies

**Observational, not experimental**

- **Advantages**
  - Evaluate exposures and responses of free-living populations over a wide range of individuals, behaviors, and subgroups, including susceptible individuals
  - Examine both short and long-term exposures
- **Limitations**
  - Difficult to determine specific exposure averaging time
  - Need to account for other factors, particularly co-pollutants (e.g., PM, $NO_2$, $O_3$, CO, PAHs)
  - Exposures limited to real-world doses

# Epidemiologic Study Designs Relevant to $SO_2$

1. Cohort (prospective & retrospective)
2. Case-control
3. Time-series
4. Cross-sectional
5. Ecologic

# Study Design #1: Cohort

- Follows a group of people with and without a common exposure over time and identifies those who develop a disease during the follow-up period
  - Exposed and unexposed may be selected from same population or separate, but must be comparable with respect to other exposures
- Prospective - Study begins in present and follows subjects over time
- Retrospective – Study begins in past and follows subjects over time
  - Use information collected on past exposures and disease

# Study Design #1: Cohort (cont)

- Birth cohort studies follow pregnancies from conception to miscarriage, stillbirth or birth
- Windows of exposure in birth studies
  - During follow-up period there may be some periods when the fetus is most susceptible to effects of exposure
    - Month of pregnancy
    - Trimester of pregnancy
- Exposures may be determined separately for each window of exposure

# Study Design #1: Cohort Examples of $SO_2$ Studies

- Prospective
  - Xu et al., 1995 (preterm birth)
- Retrospective
  - Dejmek et al., 2000 (male reproduction)

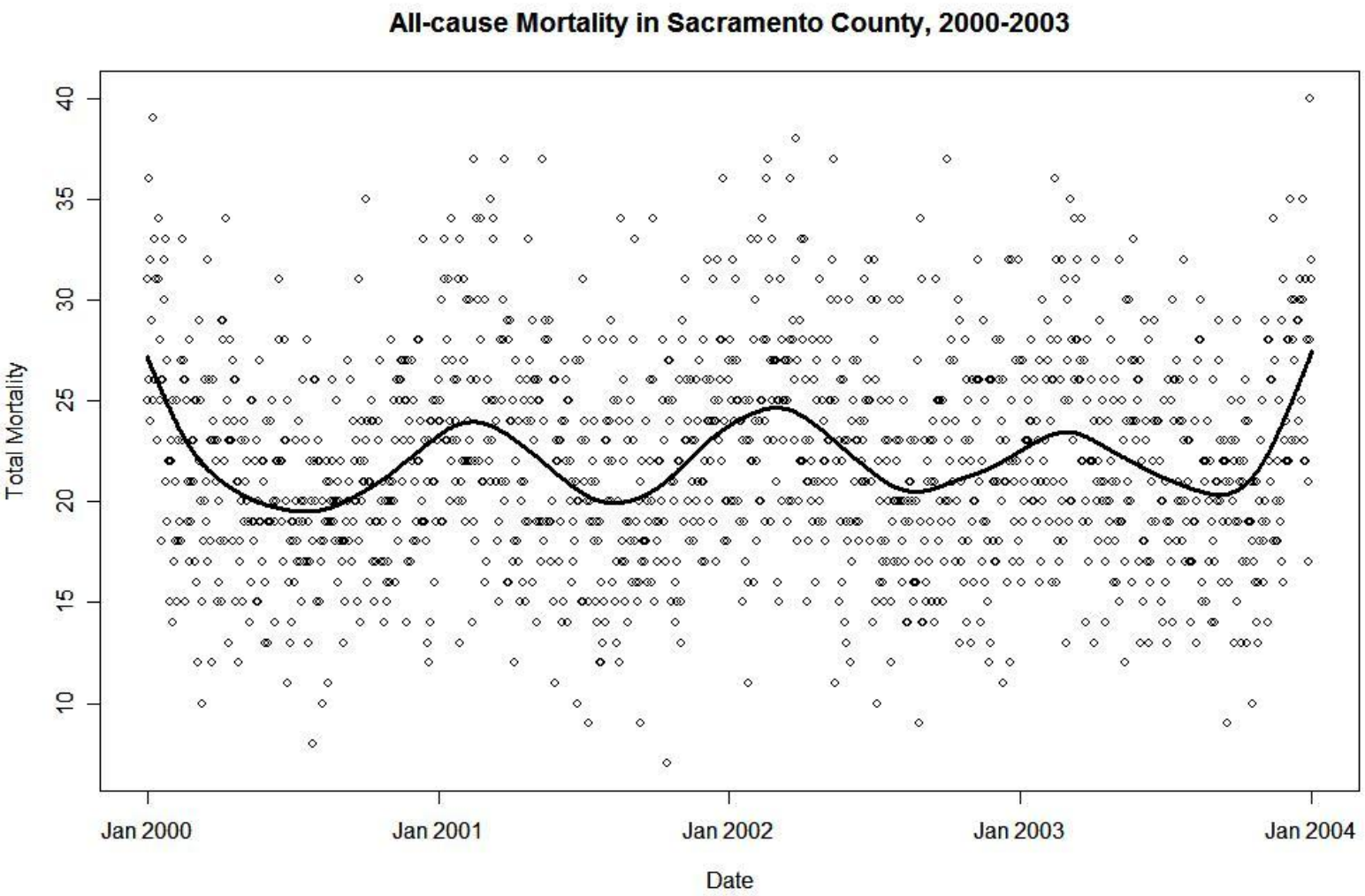
# Study Design #2: Case-control

- Subjects with a particular disease are identified first (cases)
- Control subjects come from the same population as cases but do not have the disease
- The exposure of interest is then measured in both cases and controls
- Controls are often matched to cases on factors that may be associated with both disease and exposure of interest
- Good for studying rare diseases where you would have to study too many people with the cohort design

# Study Design #3: Time-Series

- Examines association over time in one area between daily changes in pollution and daily counts of outcome (e.g., mortality or preterm birth)
- Individual-level variables like smoking and body mass index do not change appreciably from day to day so these factors do not need to be controlled.
- The few variables that vary daily with both pollution and health can be added to the model (e.g., weather, day of week). Season can be controlled by adding a smooth for time.
- Example of $SO_2$ Study
  - Sagiv et al., 2004 (preterm birth)

# Mortality and Time with Smooth



# Study Design #4: Cross-sectional

- Also called survey or prevalence study
- Study population selected from a single target population by random sampling
- Measures individuals' exposure and disease at one point in time
- Example of $SO_2$ Study
  - Robbins et al., 1999 (sperm aneuploidy)

# Study Design #5: Ecologic

- Most often used to compare disease rates in separate geographic areas with different exposure composition
- No individual level data is gathered
- On a group level you know the number of exposed and the number of cases, but you do not know which individuals were exposed

# Evaluating Quality of Air Pollution Epidemiologic Studies

- Exposure Assessment
- Confounding
- Multiple Comparisons

# Exposure Assessment

- Personal monitoring
  - Best because it introduces the least amount of exposure misclassification
  - But this is expensive and necessitates small studies.
- Ambient air pollution monitoring: How to minimize bias from exposure misclassification
  - Inverse distance weighting (distance between monitor and subject's residence used to adjust exposure),
  - Only including subjects within a certain distance of the monitor.
- Misclassification leads to bias toward to the null when non-differential (underestimates of risk)
  - The likelihood of exposure misclassification is not affected by the disease status.

# Confounders

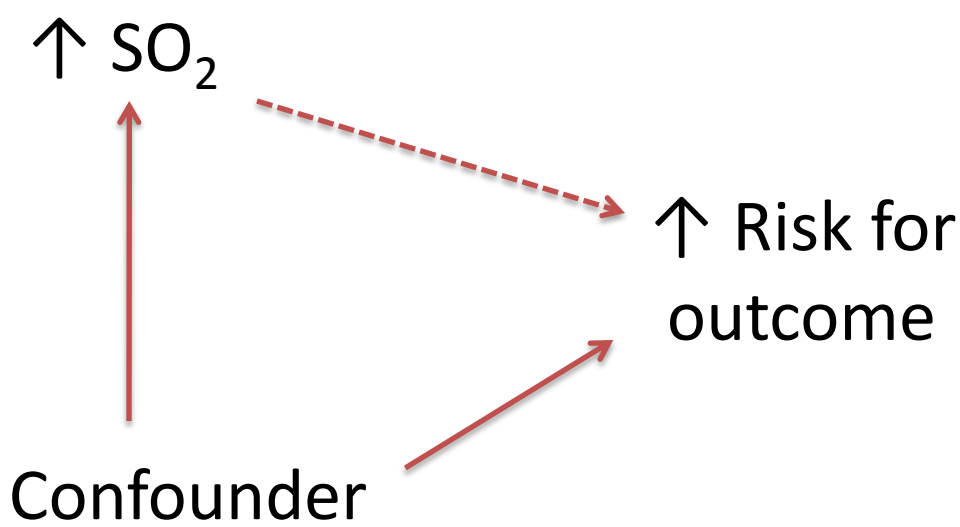
- Factors (other air pollutants, lifestyle factors, demographic characteristics, etc.) that can distort the relationship between the exposure and the outcome
  - Associated with both the exposure & outcome
  - Must not be a necessary intermediate step in causal pathway between the exposure and the outcome

# Possible Associations of $SO_2$ with Health Outcomes

## Direct Causal Effect

↑ $SO_2$ → ↑ Risk for outcome

## Confounding



# Methods for adjusting for confounders

- Adding a term in the model for the potential confounder
- Matching the exposed and unexposed subjects on the potential confounder
- Stratify the analysis by the potential confounder

# Multiple Comparison

- Statistical adjustment for multiple comparisons
  - Reduces the error of finding a false association
  - Increases the error of NOT finding a true association
  - Rothman (Epidemiology, 1990) does not recommend adjusting
- We generally look at the body of evidence across human and animal studies
  - If we see similar effects across studies, then we are more certain that chance alone does not explain the results

# Individual Air Pollutants Regulated by US EPA and CA

California Environmental Protection Agency

- A number of common air pollutants, referred to as "criteria air pollutants" are regulated by US EPA and California
- Air quality standards are constructed from comprehensive reviews of the relevant epidemiological and experimental studies
- Epidemiological studies can be instrumental in determining harmful levels of a given pollutant