Study Design Issues on HAP assessment

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Study Designs

why now?

- Informs how, when, and how frequently measurements will be performed
- Useful to keep in mind throughout the Development process of proposals and study plans
- Extends beyond just HAP and EHS into broader issues
- No study design is perfect

(but, early attention leads to better studies)
Study population, source population, target population

- The group studied
- The group from whom the study population is drawn
- The group to whom inferences will be made
What makes a study useful?

- Addresses a relevant and significant research question
- Results in the study population are generalizable (external validity)
- The study population is sufficiently large to address the research question
- **The study design is appropriate**
- The study results are not (too) affected by bias (internal validity)
Study Design - Basics

- First: experimental or observational
  - Experimental: investigator manipulates exposure
  - Observational: investigator studies exposures as they occur
- Second: if experimental,
  - Was exposure assigned at random?
- Third: if observational,
  - What is the underlying design?
Basics of study design

- **Experimental**
  - RCT (randomization to treatment and control)
  - Other interventions

- **Observational (individual level)**
  - Cohort
  - Case-control (and other case-based sampling)
  - Cross-sectional

- **Observational (population level)**
Types of Study Design

- Disease Clusters
- Ecological
- Cross-sectional
- Retrospective Cohort
- Case Control
- Prospective Cohort
- Experimental Studies

Descriptive → Analytic
EXPERIMENTAL
(Randomized study)

OBSERVATIONAL
(Non-Experimental Randomized) Study

POPULATION

RANDOMLY ALLOCATED

EXPOSED

D+

D-

NOT EXPOSED

D+

D-

POPULATION

NON-RANDOMLY ALLOCATED

(e.g., self-selected)

EXPOSED

D+

D-

NOT EXPOSED

D+

D-
Why Randomize?

- So that group assignment does not depend on participant characteristics
  - Assure comparability on potential confounding and modifying factors
  - Assure comparability on any “unknown” factors

- Caution: Systematic and haphazard assessment is not the same as randomization
What is your research question?

Do you have an intervention?

What are you comparing?

How long will the study take?

What type of data will you collect? How often?

What’s your budget?
The Question (Hypothesis)

Does use of an clean (e.g., LPG) stove reduce

- The risk of chronic obstructive pulmonary disease in adult women?
- The risk of mortality in under-five children?
Cross-sectional

Group I
Traditional Stove

Group II
LPG Stove

Measurements made at the same time
May show an association • Difficult to establish causality
Cross-sectional

- Identify groups and take measurements
- Can occur quickly and relatively inexpensively
- Can study several outcomes
- Good for hypothesis generation
- Yields prevalence
- Does not establish sequence of events

Issues with bias
Case Control

Compare individuals with a specific disease (cases) to those without the disease (controls)

Useful for rare conditions
Case Control

Unexposed

Exposed

Unexposed

Exposed

People without Disease

CONTROLS

People with Disease

CASERS

Investigation starts here

Time
Control Selection

Useful to think of the "study base", i.e., the underlying population that gave rise to the cases. The assumption is that individuals in the study base are representative of the same basic experiences.

Controls should be at risk of developing the disease and represent the same underlying population which gave rise to the cases. Often match on age, sex, ethnicity, and other demographic / SES variables.
Case Control

What might you look for?

Where would you want controls to come from?
Case Control

- Useful for rare diseases
- Can study multiple exposures at a time
- Relatively inexpensive, short duration
- Very difficult to "reconstruct" historical exposures
- Selecting controls can be very challenging
Cohort Studies

Define a group of people and follow them through time to observe disease occurrence in relation to exposure

"Cohort" was the Roman term for a group of soldiers that marched into battle together
Prospective

Population

People without Disease

Exposed

Unexposed

Time + Direction of Inquiry

Investigation starts here
Prospective

- Identify cohort and follow through time
- Collect data on exposures and disease
- “Gold standard” of observational studies
- Expensive, logistically intensive, and lengthy
- Difficult for rare diseases
Retrospective

Population

People without Disease

Exposed

Unexposed

Information needs start here

Investigation starts here

Time
Retrospective

- Define a historical cohort
- Trace mortality to present time
- Reconstruct exposure status from logs
- Quick, cheap, multi-cause, common in occupational epi
- Difficult to reconstruct historical exposures
Experimental

- Investigator controls predictor variable (an intervention)
- Controls for influence of confounding variables
- Key features: Manipulation, Control Group, and Randomization
- Considered by many as the "gold standard" of study designs
Randomized Control Trials

- Produce strongest evidence for cause + effect
- Costly in time and money
- Somewhat narrow research questions
- Customizing interventions can limit generalizability
- Ethical concerns
- Potential for observation / inclusion in a study inducing changes in behavior (known as the Hawthorne Effect)
- Placebo Effect
## Hierarchy of Evidence

### Table: Validity Hierarchy

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<tr>
<th>Study Design</th>
<th>Strengths</th>
<th>Weaknesses</th>
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<td>Randomized controlled trials</td>
<td>• High internal validity</td>
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<td>• Reduced risk of confounding variables</td>
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<td>• Cannot infer causality</td>
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ELEMENTS IN THE DESIGN OF RANDOMIZED CLINICAL TRIALS

1. Selection of subjects
   - Representativeness
   - Generalizability, external validity
Evaluating an Intervention
HAP STUDY DESIGNS
Three Main Study Designs

- Cross Sectional
- Before + After
- Before + After with control

In this case, we are evaluating the impact of an intervention on household air pollution.
Cross-sectional

Group I
Traditional Stove

Group II
LPG Stove

Measurements made at the same time
May show an association • Difficult to establish causality
Cross-sectional

Measurements made at the same time
May show an association • Difficult to establish causality

Requires least amount of planning
Requires no household-level follow-up

Needs a large sample size
Before and After

Participating Homes
*Traditional Stoves*

Participating Homes
*Intervention Stoves*

Time 0

3 months later
Before and After

Small sample size

Uses same household before and after, controlling for many household-level covariates

Requires several months of follow-up

Changes in air pollution may result from other factors — changes in fuel, seasonality, etc
Before and After with Control

Participating Homes
- Traditional Stoves

Participating Homes
- Intervention Stoves

Control Homes

Time 0
3 months later
Before and After

- Separately quantifies the impact of external factors from that of the stove
- Requires a large total sample size
- Requires holding back an intervention from some households (control group), which poses ethical and political concerns
- Difficult to match controls to participants
- Controls may obtain intervention(s) independent of the study
Questions?
A primer on sample size calculations
**Power**
the likelihood a study will detect an effect when there is an effect to be detected. In our examples, this would be the chance of detecting a difference in household air pollution due to an intervention when there really was a difference.

**p-value**
fundamentally the percentage error rate of stating there is an effect when there is in fact no effect. For example, in testing interventions in a before-and-after design, where the improved stove does not really result in reduced HAP, if \( p < 0.05 \), there is a 5% chance of thinking the intervention reduces HAP.

**Detectable Difference**
The magnitude of difference (in HAP, for our case) that will be detectable with statistical significance.

Assume 80% power and a p-value of 5%
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| | Before and After with Control | COV of measurements [2] |  |
| | 0.1 | 0.2 | 0.3 | 0.4 | 0.5 | 0.6 | 0.7 | 0.8 | 0.9 | 1  | 1.1 | 1.2 | 1.3 |
| 10% | 31  | 126 | 283 | 502 | 785 | 1130| 1538| 2009| 2543| 3140| 3799| 4521| 5306|
| 20% | 8   | 31  | 71  | 126 | 196 | 283 | 385 | 502 | 636 | 785 | 950 | 1130| 1326|
| 30% | 3   | 14  | 31  | 56  | 87  | 126 | 171 | 223 | 283 | 349 | 422 | 502 | 590 |
| 40% | 2   | 8   | 18  | 31  | 49  | 71  | 96  | 126 | 159 | 196 | 237 | 283 | 332 |
| 50% | 1   | 5   | 11  | 20  | 31  | 45  | 62  | 80  | 102 | 126 | 152 | 181 | 212 |
| 60% | 1   | 3   | 8   | 14  | 22  | 31  | 43  | 56  | 71  | 87  | 106 | 126 | 147 |
| 70% | 1   | 3   | 6   | 10  | 16  | 23  | 31  | 41  | 52  | 64  | 78  | 92  | 108 |
| 80% | 0   | 2   | 4   | 8   | 12  | 18  | 24  | 31  | 40  | 49  | 59  | 71  | 83  |
| 90% | 0   | 2   | 3   | 6   | 10  | 14  | 19  | 25  | 31  | 39  | 47  | 56  | 66  |
| 100%| 0   | 1   | 3   | 5   | 8   | 11  | 15  | 20  | 25  | 31  | 38  | 45  | 53  |
Choosing a CoV + Detectable Difference

The CoV is often high in these settings. Use available literature and preliminary measurements to help decide on an appropriate CoV.

Altering the detectable difference can have a big impact on sample size; however, choosing a larger detectable difference may invalidate your results.

Recommend oversampling by 20-30% to account for any unpredictable events in the field.
Essence of Trial Design

- **Experimentation vs. Observation:**
  - Experimentation: “exposure” is under the control of the researcher; exposure is an intervention
  - Observation: exposure is merely observed by the researcher