Commonly used study designs in public health & epidemiologic research

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Introduction to Study Designs II

**Experimental Studies:**
- Randomized Clinical/Controlled Trials (RCTs);
- Randomized Community or Field Trials;

**Observational Studies:**
- Cross-Sectional Studies;
- Case-Control Studies;
- Cohort Follow-up/Longitudinal Studies:
  - Retrospective Follow-up/Longitudinal Studies;
  - Prospective Follow-up/Longitudinal Studies;
    - Dynamic Surveillance Cohort Studies;
  - Nested Case-Control Studies;
Observational Studies: Case-Control (CC) Studies

Order of Data Collection:
• Start by defining and ascertaining data on cases and controls;
• Retrospectively (go back in time) to ascertain past exposure;

Strengths
• CC studies
  • Require smaller sample sizes and are therefore relatively quick and inexpensive;
  • Can study many exposures;
  • Are suitable for studying rare diseases;

Weaknesses
• CC studies are
  • Subject to recall bias and other problems with ascertainment of past exposures;
  • Subject to biased selection of controls;
  • Questionable temporal order of exposure and outcome;
  • Not suitable for studying rare exposures;

Cohort/Source population of cases & controls under observation

\[
\begin{array}{c}
E \quad \{ \quad b \\
\text{(Exposed)}
\end{array} \\
\{ \quad a + c \\
E^\wedge \quad \{ \quad d \\
\text{(Unexposed)}
\end{array}
\]

Past time

Outcome of Interest
Present (D=Diseased => CASES)

b+d

(CASES, D=Non-Diseased)
Outcome of Interest
Absent

Present
Observational Studies: Case-Control (CC) Studies

Relevant Study Characteristics & Key Ethical Implications:
• Observational study with NO investigator manipulation of exposure or outcome;
• Need for informed consent depends on whether the study involves interactive research activities that would not otherwise be conducted for routine health service and/or use of identifiable data, e.g. 1: interviews/tests/procedures require informed consent if not part of routine service; e.g. 2: studies which depend on record abstraction/chart review do not require informed consent if data cannot be linked back to (unlinked/blinded) from identifiers of subjects studied;
• Case-control studies may/may not be determined to be research depending on whether the study will lead to findings generalizable to any populations similar to that in which study conducted; or if generalizable to any society;
• IRB review is required if study is classified as research; some may be exempt research or non-research if conditions for determination are met;

\[
\begin{align*}
E & \left\{ \begin{array}{c}
\text{(Exposed)} \\
\text{Outcome of Interest Present (D=Diseased } \Rightarrow \text{ CASES)} \\
\end{array} \right. \\
E^\wedge & \left\{ \begin{array}{c}
\text{(Unexposed)} \\
\text{Outcome of Interest Absent (D^=Non-Diseased)} \\
\end{array} \right. \\
\end{align*}
\]
Simple Analytical Framework

Outcome of Interest
Present (D=Diseased => CASES)

Cohort/Source population of cases & controls under observation

Past time

Present time

Start at Present

Past time

Interpretation of Measure of Effect:
• Those with disease are X times more likely to have certain exposures than those without the disease;

Analytical Framework: 2 x 2 table

<table>
<thead>
<tr>
<th>D</th>
<th>D^</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>a</td>
</tr>
<tr>
<td>E^</td>
<td>c</td>
</tr>
</tbody>
</table>

Measure of Effect: Odds Ratio

• OR=Exp. Odds among cases / Exp. Odds among controls

• OR= (a / c) / (b / d) = (a . d) / (b . c)
Simple Analytical Framework

Outcome of Interest
Present (D=Diseased => CASES)

\[ \begin{array}{cc}
E & a \\
E^\wedge & c \\
\end{array} \]

Exposed

\[ \begin{array}{cc}
a + c \\
b + d \\
\end{array} \]

Unexposed

Cohort/ Source population of cases & controls under observation

Past time

Start at Present

Analytical Framework: 2 x 2 table

\[
\begin{array}{cc}
D & D^\wedge \\
E & a & b \\
E^\wedge & c & d \\
\end{array}
\]

Measure of Effect: Odds Ratio

\[
\text{OR}=\frac{\text{Exp. Odds among cases}}{\text{Exp. Odds among controls}}
\]

\[
\text{OR}= \frac{(a / c)}{(b / d)} = \frac{(a \cdot d)}{(b \cdot c)}
\]

Examples of Application of This Design:

• Case-control study examining contribution of highly active anti-retroviral therapy (HAART) for HIV to longer survival - cases are those who are deceased (or with poor survival) vs controls as those remaining alive or with long-term survival …

Potential Interpretation of Measure of Effect:

• Those with disease (deceased) are X times less or more likely to have certain exposures (HAART) than those without the disease (longer-term survivors);
Simple Analytical Framework

Outcome of Interest
Present (D=Diseased => CASES)

Exposed

Unexposed

Cohort/Source population of cases & controls under observation

Past time

Present time

Start at Present

Analytical Framework: 2 x 2 table

Measure of Effect: Odds Ratio

• OR=Exp. Odds among cases / Exp. Odds among controls

• OR= \( \frac{a}{c} / \frac{b}{d} = \frac{a \cdot d}{b \cdot c} \)

Examples of Application of This Design:
• Case-control study examining contribution of late diagnosis with HIV (diagnosed with AIDS, advanced disease) to death/poor survival - cases are those who are deceased (or with poor survival) vs controls as those remaining alive or with long-term survival.

Potential Interpretation of Measure of Effect:
• Those who died/have poor survival (cases) are are X times more likely to have certain exposures (late diagnosis/advanced disease or AIDS) than controls (those without the disease/those who remain alive/longer-term survivors);

Public Health Solution:
• Screening for HIV, early diagnosis, & timely treatment;
Observational Studies: Case-Control (CC) Studies

Simple Analytical Framework

Outcome of Interest

Present (D=Diseased => CASES)

Exposed

a

b

E

Unexposed

c

d

E^=

Past

(CASES, D=Diseased)

CONTROLS, D^=Non-Diseased)

Absent

Outcome of Interest

Present

Start at

Start at Present

Past

time

time

Analytical Framework: 2 x 2 table

D

D^=

E

a

b

E^=

c

d

Measure of Effect: Odds Ratio

• OR=Exp. Odds among cases / Exp. Odds among controls

• OR= (a / c) / (b / d) = (a . d) / (b . c)

Examples of Application of This Design:

• Case-control study examining likely source of cholera outbreak in London (1849) or Haiti (2010-2013) to cholera disease/death - cases are those who had cholera (or after signs of cholera) vs controls as those who did not have the disease.

Potential Interpretation of Measure of Effect:

• Those who had cholera/died of it (cases) are X times more likely to have certain exposures (drinking water from a contaminated source) than those without the disease;

Solution:

• London: John Snow removed pump handle from water source used by those who got sick;
• Haiti: Providing clean drinking water and wash hands;
Dr. John Snow
Epidemiology and Cholera Control