Introduction to epidemiology in health economics

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Epidemiology

Definition epidemiology

- Study distribution and determinants of health-related states or events
- In populations
- And the application hereof to the control of health problems

The epidemiologic approach

- Defining a case
- Measuring disease frequency and describing patterns
- Comparing disease frequency and measuring associations

Uses of epidemiology

1. Nature of the study
2. Description of health status of populations

Uses of epidemiology

Epidemiology in Public Health

Tasks:
- Public Health surveillance
- Field investigation
- Analytic studies
- Evaluation
- Linkages
- Policy development

Tasks:

Epidemiology and health economics

- Evaluation of health care interventions by cost-effectiveness analysis in randomized controlled trials
- Example: What is the most efficient approach to reducing malaria infections: indoor residual spraying or mosquito nets?

Epidemiology and clinical decision making (1)

- Epidemiology focuses on populations, while clinical sciences focus on individual patients.
- Clinical epidemiology is the science of making predictions about individual patients, using strong scientific methods for studies of groups of patients to ensure that the predictions are accurate.
- Focus of clinical epidemiology:
  - Diagnosis: Assessing the value of clinical tests
  - Treatment: Assessing the value of clinical interventions

Epidemiology and clinical decision making (2)

- Clinical epidemiology is used as an aid to clinical decision making.
- Clinical decision making combines clinical expertise, patient concerns, health economics and evidence from clinical epidemiology to arrive at diagnosis and treatment recommendations.
- Results from epidemiological studies can be – amongst information on other factors – lead to the compilation of clinical guidelines for medical professionals.

Costs and outcomes of a health care intervention

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>A  Changes in health status</td>
<td>D  Health care resources</td>
</tr>
<tr>
<td>B  Production gains</td>
<td>E  Non-health resources</td>
</tr>
<tr>
<td>C  Process utility or disutility</td>
<td>F  Burden of care on household</td>
</tr>
<tr>
<td>G  Patient’s time</td>
<td></td>
</tr>
</tbody>
</table>

Epidemiology and clinical decision making (3)

Another term that is used: Evidence-based medicine is the application of clinical epidemiology to the care of patients:
- Formulating specific clinical questions
- Finding the best available research evidence
- Judging whether the information is strong enough to base clinical decisions on
- Actually using this information in the care of patients

Criteria for causation

» Temporal relation
» Plausibility
» Consistency
» Strength (association)
» Dose-response relationship
» Reversibility
» Study design
» Judging the evidence

Epidemiological study designs

Overview of study types

- Observational studies
  - Descriptive studies
  - Analytical studies
- Experimental studies (intervention studies)

Descriptive studies

» Case reports/series
» Cross-sectional surveys (prevalence)

Case report/series

O’Connor PM, et al.
Costs of vision impairment in childhood and youth: diary case studies.
Cross-sectional surveys

Roy AN, Smith M.
Prevalence and cost of insomnia in a state Medicaid fee-for-service population based on diagnostic codes and prescription utilization.

Cross-sectional comparative studies: design

- Time
- Disease status?
- Exposure status?
- Compare prevalence of disease between different exposures

Example cross-sectional comparative study (1)

- Time
- Diarrhea (past month)?
- Water source?
- Compare prevalence of diarrhea between different water sources

Example cross-sectional comparative study (2)

Wang W, et al.
How do type 2 diabetes mellitus-related chronic complications impact direct medical cost in four major cities of urban China?

Analytical studies

- Cross-sectional comparative studies
- Case-control studies (case-reference)
- Cohort studies (follow-up, incidence)

Cross-sectional studies

Advantages
- Relatively quick and inexpensive
- Can be used as an initial exploration of a hypothesis

Disadvantages
- Temporal relationship often problematic
- Generally not suitable for rare diseases, rare exposures or diseases of short duration
- Cannot estimate incidence rate of a disease
Case-control studies: design

Comparison of exposed and non-exposed cases


Selection of cases

The definition of a case needs to be very specific:

- Within what period of time will a patient qualify as a case?
- Is the case definition well defined (including exclusion criteria)?
- Incident versus prevalent cases

Selection of controls

- Sample from source population cases
- Population versus hospital controls
- How many controls for each case? 1-4

When is a case-control study appropriate?

When to use case-control study design:

- Low frequency of outcomes (rare disease)
- Unethical to do randomization (or impractical)
- Low budget (relatively inexpensive)
- Quick results needed
- Multiple potential causes of disease

Measurement of exposure

- Cases and controls must be assessed for exposure in the same way
- Direct questioning, biochemical measurements, established recording system
- Be aware of (recall) bias

Example case-control study (1)

Children < 5 years with diarrhea
- Used suspected water source
- Used other water sources

Children < 5 years without diarrhea (with acute respiratory infections)
- Used suspected water source
- Used other water sources

Children < 5 years
- Used suspected water source
- Used other water sources
Example case-control study (2)

Lurie IZ, et al.
Differences in medical care expenditures for adults with depression compared to adults with major chronic conditions.

Cohort studies: design

![Diagram]

Defining study population

- Must be disease free at start
- Internal comparison group
  - For common exposures
  - Representative or not necessary but exposed and unexposed groups must be comparable
- External comparison group
  - Often used for rare exposures, e.g., industrial
  - Beware of healthy worker effect or other selection biases

Measurement of exposure

- Interviews/questionnaires
- Existing records
- Physical examination
- Biological specimens
- Environmental measurements
  
  (comparable for all study participants)

Outcome measurement

- Questionnaires, records (e.g., hospital discharge/disease registries/death certificates), periodic health examinations
- Procedures must be applied equally to all study participants to avoid bias
- Try to avoid Loss To Follow-Up (LTFU) as selection bias might be introduced: various contact details, financial compensation ...

Cohort studies: Advantages

- Can look at many different outcomes
- Valuable for rare exposures
- Exposure measured before outcome (temporal relationship clear)
- Exposure can be measured accurately (if prospectively)
- Can calculate incidence of disease and relative risk
Cohort studies: Disadvantages

- Not suitable for rare diseases/diseases with a long latent period
- Loss to follow-up can be a problem
- Expensive: prospective versus retrospective

Example cohort study (1)

Children < 5 years using suspected water source

- diarrhoea
- no diarrhoea

Compare cumulative incidence rates

Example cohort study (2)

Clay FJ, et al.
Bio-psychosocial determinants of time lost from work following non life threatening acute orthopaedic trauma.

Experimental studies

- Randomized Controlled Trials (Clinical trials) incl. Cluster RCTs
- Non-RCT (e.g. before-after)

RCT: design

- Eligibility criteria
- Randomisation
- Concealed treatment allocation
- Blinding
- Intention-to-treat analysis
Randomisation/Concealed treatment allocation

Blinding in RCT

Person observing outcome after the intervention should be unaware of treatment a participant received

The participant should also be blinded to the treatment received

Allocation concealment

Intention to treat analysis

ITT: once randomised, always randomised
Follow-up and case ascertainment continues regardless of:
- Adherence
- Change in regimen
- Ineligibility after randomisation

Per protocol analysis

Limitations of RCTs

Expensive/long term commitment

Restrictive enrollment criteria
- Exclude chronically ill, women, children and minorities
- "Efficacy" may not represent "effectiveness"
  - Efficacy results from a RCT setting
  - Effectiveness results from real world setting

RCTs are unethical when the outcome is adverse event

Example RCT

Aspler A, et al.
Impact of treatment completion, intolerance and adverse events on health system costs in a randomised trial of 4 months rifampin or 9 months isoniazid for latent TB.

Cluster randomized controlled trial

Randomization unit is a group of people (a cluster)

For RCT involving a group policy/intervention which impacts on individual patients/persons

Logistical easier

Must take clustering into account for sample size calculation and adjust for clustering in analysis
Example Cluster RCT

Tun-Lin W, et al.
Reducing costs and operational constraints of dengue vector control by targeting productive breeding places: a multi-country non-inferiority cluster randomized trial.

Non-randomised experimental studies

- Before – after studies
  - Easier to implement than RCT
  - Not sure whether change is due to secular change or to intervention

Overview

Did investigator assign exposure? | Experimental Random allocation? | RCT | Non-RCT
--- | --- | --- | ---
Yes | Yes | Yes | Yes
No | No | No | No

Morbidity frequency measures

- Population at risk
- Prevalence = no. of cases at a specified point in time
- Incidence = no. of new cases arising in a given period

Prevalence rate

\[ P = \frac{\text{Number of people with the disease or the condition at a specified time}}{\text{Number of people in the population at risk at the specified time}} \times 10^n \]
Factors influencing P

- Severity of illness
- Duration of illness
- Number of new cases (incidence)
- Diagnosis and treatment

\[ P \text{: Helpful in assessing the need for health care and the planning of health services} \]

Cumulative incidence rate or risk

\[ CI = \frac{\text{Number of people who get a disease during a specified period}}{\text{Number of people free of the disease in the population at risk at the beginning of the period}} \times 10^n \]

Risk of getting the disease

Example CI (1)

Age-specific incidence rates for laboratory-confirmed, cryptococcal diseases.


Example CI (2)

Sileri P, et al.
Adhesions are common and costly after open pouch surgery.

Aim:
We aimed to review the incidence of adhesive SBO-related complications after open pouch surgery and to model the potential financial impact of a laparoscopic approach purely as an adhesion prevention strategy.
Example P and CI

Primary school, 100 pupils.
First day new term: 9 children with a cold
Over the next week: another 7 children developed a cold

P = ?
CI = ?

Example P and CI

Primary school, 100 pupils.
First day new term: 9 children with a cold
Over the next week: another 7 children developed a cold

P = 9/100 or 9% at the first day of the new term
CI = 7/91 or 7.7% in a week (population free of disease = 100 – 9 = 91)

Incidence rate

\[ I = \frac{\text{Number of people who develop disease during a specified period}}{\text{Sum of the length of time during which each person in the population is at risk (or: average number of people in the population)}} \times 10^n \]

Example incidence rate

Prospective study of hormonal contraception and women’s risk of HIV infection in South Africa

Results:
During the 5010 person-years of follow-up, 111 incident HIV infections were observed (HIV incidence, 2.2 infections/100 person-years).

Mortality frequency measures (1)

Crude mortality rate (death rate) =

\[ \frac{\text{Number of deaths in a specified period}}{\text{Average total population during that period}} \times 10^n \]

Example death rate

Crude death rate for all the countries of the world in 2007 (per 1000 per year). Derived from: http://myfundi.co.za/e/Mortality_rate
Example death rate (2)

Hayashida K, et al.
Difference in lifetime medical expenditures between male smokers and non-smokers.

Results:
Smokers had a higher mortality rate, shorter life expectancy, and generally higher annual medical expenditures than non-smokers.

Example QALY

Al-Ruzzeh S, et al.
Economic evaluation of coronary artery bypass grafting surgery with and without cardiopulmonary bypass: cost-effectiveness and quality-adjusted life years in a randomized controlled trial.

Example DALY

Luz PM, et al.
Disability adjusted life years lost to dengue in Brazil.

Mortality frequency measures (2)

» Cause-specific mortality rate
» Age-specific mortality rate
» Infant or Child mortality rate
» Maternal mortality rate
» Sex-specific mortality rate
» Race-specific mortality rate
» Years of potential life lost
» Life expectancy (free from disability)
» QALYs and DALYs lost

Measures of association

Comparing disease occurrence

» Absolute:
  - Risk difference
  - Others [e.g., attributable fraction (exposed), population attributable risk]

» Relative:
  - Relative risk/risk ratio
  - Odds ratio
Risk difference

Risk difference = Risk exposed – Risk unexposed

Example:

Those going into the forest have a malaria incidence rate of 10/1000 per month; those who do not have a malaria incidence rate of 1/1000 per month. The risk difference is 10/1000 – 1/1000 or 9/1000.

Value of the RR

Note:

1. The risk of disease is greater in those with the risk factor and those without is less.
2. If the risk factor is associated with the condition under study.
3. If not clear whether the disease is due to the risk factor or another, then the risk factor can be tested for association using a chi-square test of association.
4. If AR is less than 10 or both AR and RR is less than 200, then the numbers are too small to analyze or reduce a certain problem.

Example outbreak cohort study

<table>
<thead>
<tr>
<th>Food</th>
<th>Total</th>
<th>Number ill</th>
<th>Total</th>
<th>Number ill</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot chicken</td>
<td>343</td>
<td>156</td>
<td>251</td>
<td>74</td>
</tr>
<tr>
<td>Potato fries</td>
<td>422</td>
<td>184</td>
<td>152</td>
<td>46</td>
</tr>
<tr>
<td>Cold chicken</td>
<td>202</td>
<td>155</td>
<td>372</td>
<td>75</td>
</tr>
</tbody>
</table>

Relative Risk

RR = Risk exposed / Risk unexposed

<table>
<thead>
<tr>
<th>Presence of the risk factor</th>
<th>Presence of the problem</th>
<th>Risk of developing illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>Risk exposed</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>Risk unexposed</td>
</tr>
</tbody>
</table>

RR versus Risk difference

<table>
<thead>
<tr>
<th>Incidence (%)</th>
<th>Population A</th>
<th>Population B</th>
</tr>
</thead>
<tbody>
<tr>
<td>In exposed</td>
<td>40</td>
<td>90</td>
</tr>
<tr>
<td>In non-exposed</td>
<td>10</td>
<td>60</td>
</tr>
<tr>
<td>Risk difference (%)</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>RR</td>
<td>4.0</td>
<td>1.5</td>
</tr>
</tbody>
</table>

Example outbreak cohort study

<table>
<thead>
<tr>
<th>Food</th>
<th>Total</th>
<th>Number ill</th>
<th>Total</th>
<th>Number ill</th>
<th>AR (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hot chicken</td>
<td>343</td>
<td>45</td>
<td>231</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>Potato fries</td>
<td>422</td>
<td>44</td>
<td>152</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Cold chicken</td>
<td>202</td>
<td>77</td>
<td>372</td>
<td>25</td>
<td></td>
</tr>
</tbody>
</table>
### Example RR

Clay FJ, et al.

Bio-psychosocial determinants of time lost from work following non life threatening acute orthopaedic trauma.


**Results:**

The participant reported reason for return to work "to fill the day" was a significant predictor of earlier RTW (RR 2.41 [95% CI 1.35-4.30]) …

### Example outbreak case-control study

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Cases</th>
<th>Controls</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>3</td>
<td>7</td>
<td>10</td>
</tr>
<tr>
<td>No</td>
<td>25</td>
<td>49</td>
<td>74</td>
</tr>
<tr>
<td>Total</td>
<td>28</td>
<td>56</td>
<td>84</td>
</tr>
</tbody>
</table>

### Odds ratio

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Cases</th>
<th>Controls</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>a</td>
<td>b</td>
<td>a+b</td>
</tr>
<tr>
<td>Absent</td>
<td>c</td>
<td>d</td>
<td>c+d</td>
</tr>
<tr>
<td>Total</td>
<td>a+c</td>
<td>b+d</td>
<td>a+b+c+d</td>
</tr>
</tbody>
</table>

\[
\text{Odds ratio} = \frac{a \times d}{b \times c}
\]

- **Hospital**
  - Cases exposed: 3 (11%)
  - Controls exposed: 7 (13%)
  - Odds ratio: 0.8
  - P-value: 1.0

- **Butcher store**
  - Cases exposed: 12 (44%)
  - Controls exposed: 54 (10%)
  - Odds ratio: 3.5
  - P-value: 0.03

- **Grocery store**
  - Cases exposed: 25 (93%)
  - Controls exposed: 54 (52%)
  - Odds ratio: 11.6
  - P-value: <0.01

### Example OR

Friedman AL, et al.

Early clinical and economic outcomes of patients undergoing living donor nephrectomy in the United States.


**Results:**

Independent predictors of donor complications included older age (odds ratio [OR] 1.01), male sex (OR 1.19) …
OR and RR

Table 3: OR, Exposure and Disease in a Hypothetical Population of Adult Females

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Disease</th>
<th>OR</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>No</td>
<td>1.0</td>
<td>0.71-1.38</td>
<td>0.56</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>0.6</td>
<td>0.37-0.97</td>
<td>0.01</td>
</tr>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>3.0</td>
<td>1.6-5.6</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

**Example: Calculating Odds Ratio**

OR = (a*d) / (b*c) = 3.0

Notes: OR = odds ratio, CI = confidence interval. The OR is a measure of the association between the exposure and the outcome. A value greater than 1 indicates a positive association, while a value less than 1 indicates a negative association. A value of 1 indicates no association.

**OR** and **RR**


Questions? Additional information?

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