Lecture 3: Frequency

How do we measure disease, define risks, and then make use of this information?

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Objectives - Concepts

1. Understand the concept of uncertainty, probability and odds
2. Measures of disease frequency
   - Prevalence
   - Incidence
     - Cumulative incidence
     - Incidence density (the concept of person-time)
3. Relationship between incidence, duration & prevalence
4. Risk estimates and their uses

Objectives - Skills

1. Convert probability to odds and vice versa
2. Define, calculate and interpret prevalence, cumulative incidence, and incidence density
3. Define, calculate and interpret "risk estimates"
   - RR, RRR, ARR, NNT, OR, PAR, PARF
Measuring Disease and Defining Risks

- Clinicians are required to know or make estimates of many things:
  - The occurrence of disease in a population
  - The "risk" of developing a disease or an outcome (prognosis)
  - The risks and benefits of a proposed treatment

- This skill requires an understanding of:
  - Measures of disease frequency
    - Proportions and odds
    - Prevalence and incidence rates
    - Risk (relative and absolute)

Uncertainty

- Medicine isn't an exact science, uncertainty is ever present

- Uncertainty can be expressed either:
  - Qualitatively using terms like 'possible', 'likely', 'unlikely'
    - Study: Docs asked to assign prob to commonly used words:
      - 'Possible' ranged from 0.19-0.50
      - 'Unlikely' ranged from 0.01-0.05
  - Quantitatively using probabilities (P)
    - Advantage: explicit interpretation, exactness
    - Disadvantage: may force one to be more exact than justified

Probability vs. Odds

Probability (P) or "risk" of having an event
Odds = ratio of the probability of having an event to the probability of not having the event or P / (1-P)

Example: 1 out of 5 patients suffer a stroke,.....

- P = 1/5 = 0.2 or 20%
- Odds = (P) / (1-P)
- Odds = 0.2 / 0.8 or 1:4 or "one to four"
**Relationship between Prob. and odds**

Probability and odds are more alike the lower the absolute P (risk).

<table>
<thead>
<tr>
<th>Probability</th>
<th>Odds</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.90</td>
<td>1</td>
</tr>
<tr>
<td>0.80</td>
<td>5</td>
</tr>
<tr>
<td>0.70</td>
<td>10</td>
</tr>
<tr>
<td>0.60</td>
<td>15</td>
</tr>
<tr>
<td>0.50</td>
<td>20</td>
</tr>
<tr>
<td>0.40</td>
<td>30</td>
</tr>
<tr>
<td>0.30</td>
<td>50</td>
</tr>
<tr>
<td>0.20</td>
<td>100</td>
</tr>
<tr>
<td>0.10</td>
<td>1.5</td>
</tr>
<tr>
<td>0.01</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- Prob = Odds/1 + Odds
- Odds = Prob/1 - Prob

Example:

Prob = 2/(1 + 2) = 0.667

Odds = 0.667/1.667 = 0.40

Odds = 0.667/0.33 = 2

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**Measures of disease frequency**

**Prevalence**

Define: the proportion of a defined group or population that has a clinical condition or outcome at a given point in time.

- Prevalence = Number of cases observed at time t / Total number of individuals at time t
  - ranges from 0 to 1 (it's a proportion), but usually referred to as a rate and is often shown as a %

Example:

- Of 100 patients hospitalized with stroke, 10 had ICH
- Prevalence of ICH among hospitalized stroke patients = 10%

The prevalence rate answers the question:

- What fraction of the group is affected at this moment in time?

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**Measures of disease frequency**

**Incidence Rates**

- A special type of proportion that includes a specific time period and population-at-risk

- Numerator = the number of newly affected individuals occurring over a specified time period

- Denominator = the population-at-risk over the same time period

- There are two types of incidence rates.......

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Cumulative Incidence Rate (CIR)

- A measure of "average risk"
  - CIR answers the question: "what is the probability or chance that an individual develops the outcome over time?"

- Also referred to as the "risk" or "event rate"

- Common risks or CIR's
  - 5-year breast cancer survival rate
    - 94% (for local stage), 18% (for distant stage)
  - Case-fatality rate
    - 23% of newborns with bloody D and fever die (e.g., Akin)
  - In-hospital case-fatality (mortality) rate
    - 5% of hospitalized patients die at hospital X
  - Attack rate
    - 25% of passengers on a cruise ship got VSO

- Must be accompanied by a specified time period to be interpretable - because the CIR must increase with time
  - 7-day CIR of stroke following TIA + 10% e.g.,
  - 90-day CIR of stroke following TIA + 10% e.g.,
Incidence Density Rate (IDR)

Cell: the speed at which a defined at-risk group or population develops a new clinical condition or outcome over a given time period.

- IDR = Number of newly diagnosed individuals
  Sum of time periods for all disease-free individuals
- Denominator is "person-time" or "population time"
- A measure of the instantaneous force or speed of disease
- IDR ranges from 0 to infinity (it is not a proportion)
- Dimension = per unit time or the reciprocal of time (time⁻¹)

The Concept of "person-time"

- The sum of the disease-free time experienced by individuals at risk in the population
- Concept: 100 people followed for 6 months have same person-time experience as 50 people followed for a year.
  - 100 x 0.5 = 50 person-years
  - 50 x 1.0 = 50 person-years
- How to calculate? (add up disease-free time)
  - 100 subjects followed for 6 months
  - 1 new case develops in every 6 months (i.e., 2 times)
  - Person time is the sum of disease-free days for each month (1 time: 6)
  - IDR = 100 x 0.5 = 50 x 66.67 = 333.33 person-months
  - IDR = 55.66 person-months or 8.34 per 1,000 person months
- Person time can be measured in whatever scale that makes the most sense i.e., person-days, person-weeks, person-months, person-years (PY)

Incidence Density Rate (IDR)

- A measure of the "speed" that disease is occurring
- IDR answers the question: "At what rate are new cases of disease occurring in the population?"

Common IDR's

- Mortality rate (Vital Statistics)
  - Lung CA mortality rate = 50 per 100,000 PY
  - Breast CA mortality rate = 15 per 100,000 PY

- Disease Incidence Rates
  - IDR of neonatal diarrhea = 283 per 1,000 child weeks
  - Disease specific IDR rates
    - Calculated for specific sub-sets defined by age, gender or race
      - Black Male: Lung CA incidence rate = 122 per 100,000 PY
      - White Female: Lung CA incidence rate = 43 per 100,000 PY
Concept of the Prevalence "Pool"

New cases (Incidence) → Recovery rate → Death rate

Relationship between Prevalence and Incidence

• Prevalence is a function of:
  • the incidence of the condition, and
  • the average duration of the condition
    – duration is influenced in turn by the recovery rate and mortality rate
• \[ \text{Prev} = \text{Incidence} \times \text{Duration} \]
• This relationship explains why....
  • Arthritis is common ("prevalent") in the elderly
  • Rickets is rare.
  • Influenza is only common during epidemics.

Measures of Effect

- Presentation and Interpretation of Information on Risk

  • Information on the effect of a treatment can be presented in several different ways
  • Relative Risk (RR)
  • Relative Risk Reduction (RRR)
  • Absolute Risk Reduction (ARR)
  • NNT (Number needed to treat)

• The way risk information is presented can have a profound effect on clinical decisions (both on part of patients and doctors)

Metadata 2 Images, Dept. of
Epidemiology, Brock Univ.
The 2 x 2 Table – Clinical Intervention Study (RCT)

<table>
<thead>
<tr>
<th>Intervention (t)</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment Group</td>
<td>a</td>
<td>b</td>
</tr>
<tr>
<td>Control (placebo) (c)</td>
<td>c</td>
<td>d</td>
</tr>
</tbody>
</table>

Risk_a = a / a + b
Risk_c = c / c + d

(Risk = CIR)

Example – RCT of Endoscopic Ligation vs. Endoscopic Sclerotherapy For Bleeding Esophageal Varices (Stiegmann, NEJM, 1992)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Death</th>
<th>Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligation (t)</td>
<td>18</td>
<td>46</td>
</tr>
<tr>
<td>Treatment Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sclerotherapy (c)</td>
<td>29</td>
<td>36</td>
</tr>
</tbody>
</table>

Risk_a = 18 / 64 = 0.28
Risk_c = 29 / 65 = 0.45

Risk_a and Risk_c are the risks of death in the treatment and control groups, respectively. Risk_c is often referred to as the baseline risk.

Relative Risk (RR) – RCT’s

- Definition: The relative probability (or risk) of the event in the treatment group compared to the control group
  - RR = Risk_t / Risk_c
  - RR = 0.28 / 0.45 = 0.62
- Clinical interpretation (RCT):
  - "the death rate after ligation/treatment is 0.62 times lower than the death rate after sclerotherapy treatment"
  - A measure of the efficacy of a treatment
  - Null value = 1.0.
  - RR < 1.0 = decreased risk (beneficial treatment)
  - RR > 1.0 = increased risk (harmful treatment)
  - Not a very useful measure of the clinical impact of treatment (need ARR)
Relative Risk Reduction (RRR)

- **Defn:** The proportion of the baseline risk that is removed by therapy
- **RRR = 1 – RR**
- **RRR = 1 - 0.62 = 0.38 or 38%**
- **Clinical interpretation:** "The death rate is 38% lower after ligation treatment compared to sclerotherapy treatment."
- Indicates by how much in relative terms the event rate is decreased.
- Also calculated as the ARR divided by the baseline risk
  
\[
  \text{ARR/Risk} = \frac{0.45-0.28}{0.45} = 38%
\]
- Null value = 0

Absolute Risk Reduction (ARR)

- **Defn:** The difference in absolute risk (or probability of events) between the control and treatment group
- **ARR = Riskc - Riskt**
- **ARR = 0.45 - 0.28 = 0.17**
- **Clinical interpretation:** "The absolute risk of death is 17% lower with ligation treatment compared to sclerotherapy treatment."
- A simple and direct measure of the impact of treatment
- Also called the risk difference (RD) or attributable risk
- The ARR depends on the background baseline risk which can vary markedly from one population to another
- Null value = 0

Constant RRR (0.33) but varying ARR due to different baseline risks
The Number Needed To Treat (NNT)

- Definition: The number of patients who would need to be treated to prevent an adverse event
- NNT = 1 / ARR
  NNT = 1 / 0.17 = 5.9 (or 6)

- Clinical interpretation (RCT)
  - "for every 6 patients who received fentanyl intravenously rather than an i-site infusion, one death is prevented"
  - A very useful clinical measure because it is more interpretable than the ARR and it conveys the impact of a clinical intervention
  - NNT for primary stroke prevention for statins = 10,000 a year
  - NNT for secondary stroke prevention for statins = 57 a year
- NNT depends on the efficacy of the intervention (= RRR) and the underlying baseline risk

Effect of Base-line Risk and Relative Risk Reduction on NNT

<table>
<thead>
<tr>
<th>Baseline Risk (%)</th>
<th>Relative Risk Reduction (RRR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>0.25</td>
</tr>
<tr>
<td>60</td>
<td>3</td>
</tr>
<tr>
<td>30</td>
<td>7</td>
</tr>
<tr>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>5</td>
<td>40</td>
</tr>
<tr>
<td>1</td>
<td>200</td>
</tr>
</tbody>
</table>
| 0.1               | 2000 | 4000 | 5000 | 10000

How information is conveyed (RRR, ARR or NNT) makes a difference!

- Drug effects are perceived to be much more favourable when they are presented as RRRs rather than ARRs
- See article by Skolbekken in the course pack.
- Pay attention to how data on the effects of drugs are framed in advertisements.

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Relative Risk (RR) – Cohort studies

- In cohort studies, RR is also used to measure the magnitude of association between an exposure (risk factor) and an outcome (See lecture 8).
- Definition: The relative probability (or risk) of disease in the exposed group compared to the non-exposed group.
- Example: Smoking and Lung CA.
  - RR of Lung CA death in heavy smokers = 4.17 per 1,000 person-years
  - RR of Lung CA death in non-smokers = 0.17 per 1,000 person-years
  - RR = $\frac{RR_{SM}}{RR_{NC}} = \frac{4.17}{0.17} = 24.5$
- Clinical interpretation (cohort):
  - "The risk of dying of lung CA is about 25 times higher in lifetime heavy smokers compared to lifetime non-smokers."
- Not a very useful measure of the impact of the risk factor in the population (need PARF)

Other important effect measures not covered in this lecture

- Odds ratio (OR)
  - See course notes, plus will be covered in the lecture 9 on case-control studies.

- Population attributable risk (PAR)
  - (See course notes)

- Population attributable risk fraction (PARF)
  - (See course notes)