Epidemiologi

Kursus forår 2004
It is more important to increase the quality of data in the collection phase than to apply sophisticated statistics

A. Bradford Hill
Epidemiologi: Definition og formål

”…the study of the distribution and determinants of disease frequency”

”…the study of the distribution and determinants of health related states or events in specified populations, and the application of this study to control of health problems”

J.M. Last, 1988; A Dictionary of Epidemiology, Oxf University Press
## Rygning & lungekræft

<table>
<thead>
<tr>
<th></th>
<th>Smokers</th>
<th>Non-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>647 (99,7%)</td>
<td>2 (0,3%)</td>
</tr>
<tr>
<td>Controls</td>
<td>633 (95,8%)</td>
<td>27 (4,2%)</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung cancer</td>
<td>41 (68,3%)</td>
<td>19 (31,7%)</td>
</tr>
<tr>
<td>Controls</td>
<td>28 (46,7%)</td>
<td>32 (53,3%)</td>
</tr>
</tbody>
</table>

Doll & Hill, BMJ, 2:739, 1950
H&B pp 45 & 90
James Lind (1716-94)

"In 1753 Lind published his classic *Treatise on the Scurvy* and dedicated it to Lord Anson, First Lord of the Admiralty, who as a commodore had sailed round the world in 1740 and knew all about the ravages of this disease. Indeed, of the 961 sailors manning his six ships, 626 were dead from scurvy by the time the fleet reached the Juan Fernandez Islands."

Lind, 1754
citeret fra Dunn, Arch Dis Child, 1997, 76, 64-5
Linds berømmte forsøg

“Two were ordered each a quart of cyder a day. Two others took twenty-five drops of elixir vitriol three times a day ... Two others took two spoonfuls of vinegar three times a day ... Two of the worst patients were put on a course of sea-water ... Two others had each two oranges and one lemon given them every day ... The two remaining patients, took ... an electary recommended by a hospital surgeon ...

The consequence was, that the most sudden and visible good effects were perceived from the use of oranges and lemons; one of those who had taken them, being at the end of six days fit for duty...”

Lind, 1754

citeret fra Dunn, Arch Dis Child, 1997, 76, 64-5
“Take for example the group of 51 districts called healthy for the sake of distinction, and here it is found that the annual mortality per cent. of boys under 5 years of age was 4·246, of girls 3·501. Turn to the district of Liverpool; the mortality of boys was 14·475, of girls 13·429. Here it is evident that some pregnant exceptional causes of death are in operation in this second city of England. What are these causes? Do they admit of removal? If they do admit of removal, is this destruction of life to be allowed to go on indefinitely? It is found that of 10,000 children born alive in Liverpool 5396 live five years, a number that in the healthy districts could be provided by 6544 annual births.”
Sygdomme kan karakteriseres

- Hvor mange?
  - Absolut/relativt
- Hvor?
- Hvornår?
- Hvem?
  - Køn, alder, etc.
- Deskriptiv epidemiologi
Fra karakteristik til årsag og anvendelse

Frequency & distribution

Determinants

Application
Kolera i London, 1854

- London uden kolera i perioden ml. 1849 & august 1854

- "The most terrible outbreak of cholera which ever occurred in this kingdom, is probably that which took place in Broad Street, Golden Square, and the adjoining streets, a few weeks ago."- John Snow, September 1854

http://www.ph.ucla.edu/epi/snow/Snowpart2_files/frame.htm
### Kolera i London, 1854

<table>
<thead>
<tr>
<th>Dato</th>
<th>Antal tilfælde</th>
</tr>
</thead>
<tbody>
<tr>
<td>28.-30. August</td>
<td>6</td>
</tr>
<tr>
<td>31. August</td>
<td>4</td>
</tr>
<tr>
<td>1.-2. September</td>
<td>79</td>
</tr>
</tbody>
</table>

Epidemi: "The occurrence of any disease whether chronic or infectious, at a greater frequency than expected" (H&B p 9)

"...I found that nearly all the deaths had taken place within a short distance of the pump."

10 deaths lived closer to another pump

5 deaths always sent to pump in Broad Street

3 deaths were children attending school near the Broad Street pump

Only 6 deaths were not users of the Broad Street pump

http://www.ph.ucla.edu/epi/snow/Snowpart2_files/frame.htm
Epidemiologi i historisk lys

- Mortalitets- og morbiditetsmønstre ændrer sig
  - ”Fra” infektionssygdomme til ”kroniske” lidelser

- Sygdomme har forskellige naturhistorier
  - Fra sygdomme med forholdsvis kort latenstid (uger til år)
  - Til sygdomme med forholdsvis lang latenstid (år til årtier)

- Ændret effekt af determinanter
  - Fra store, udtalte effekter til moderate effekter

- Fordrer løbende udvikling af ny metodologi
Epidemiologiske metoder kan bl. a. anvendes til at

• Identificere (nye) sygdomme
• Karakterisere sygdommes naturhistorie (forløb)
• Karakterisere helbredstilstanden i populationer
• Identificere årsager til sygdom
• Vurdere effektiviteten og effekten af intervention
WHO issues a global alert about cases of atypical pneumonia

“In Viet Nam the outbreak began with a single initial case who was hospitalized for treatment of severe, acute respiratory syndrome of unknown origin. He felt unwell during his journey and fell ill shortly after arrival in Hanoi from Shanghai and Hong Kong SAR, China. Following his admission to the hospital, approximately 20 hospital staff became sick with similar symptoms.”

“The signs and symptoms of the disease include initial flu-like illness (rapid onset of high fever followed by muscle aches, headache and sore throat) and most common symptoms. Early laboratory findings may include thrombocytopenia (low platelet count) and leucopenia (low white blood cell count) followed by bilateral pneumonia, in some cases progressing to acute respiratory distress requiring assisted breathing on a respirator. Some patients are recovering but some patients remain critically ill.”

Outcomes and Prognostic Factors in 267 Patients with Severe Acute Respiratory Syndrome in Hong Kong

Choi KW et al., Ann Intern Med. 2003 Nov 4;139(9):715-23
Figure 5.1 Probable cases of SARS worldwide, 7 August 2003

Forekomst af gonoré

BMJ 2002 Jun 1;324(7349):1324-7
Rekordmange er hiv-smittede

304 personer i Danmark blev sidste år konstateret hiv-smittede. Det er det højeste antal i seks år. I forhold til året før er det en stigning på 18 procent, fremgår det af en opgørelse fra Statens Serum Institut.
Fedme i Danmark

Fra Ernæringsrådet 2003: Den danske fedmeepidemi
Fedme og risiko for...

<table>
<thead>
<tr>
<th>Let øget risiko (RR=1-2)</th>
<th>Moderat øget risiko (RR=2-3)</th>
<th>Øget risiko (RR≥3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kræft</td>
<td>Hjerte-kar-sygdom</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Menstruations og hormonelle problemer</td>
<td>Blodtryksforhøjelse</td>
<td>Galdevejslidelser</td>
</tr>
<tr>
<td>PCO</td>
<td>Slidgigt</td>
<td>Dyslipidæmi</td>
</tr>
<tr>
<td>Nedsat frugtbarhed</td>
<td>Urinsyregigt</td>
<td>Insulinresistens</td>
</tr>
<tr>
<td>Lændesmerter</td>
<td></td>
<td>Åndedrætsproblemer</td>
</tr>
</tbody>
</table>

Sundhedsstyrelsen: Overvægt og Fedme
Identification of severe acute respiratory syndrome in Canada

SARS was first identified in Canada in early March 2003. We collected epidemiologic, clinical, and diagnostic data from each of the first 10 cases prospectively as they were identified. Specimens from all cases were sent to local, provincial, national, and international laboratories for studies to identify an etiologic agent.

Patients died, and five have had clinical improvement. The results of laboratory investigations were negative or not clinically significant except for the amplification of human metapneumovirus from respiratory specimens from five of six patients and from one asymptomatic contact of a patient with SARS. A novel coronavirus was isolated and amplified from respiratory specimens from five of six patients. In four cases both pathogens were isolated.

Deskriptiv og analytisk epidemiologi

Hypotese-
genererende

Epidemiologisk fokus

testende

Kasuistikken
Patientserien
Incidensopgørelse

Den økologiske undersøgelse
(korrelationsstudier)
Tværsnitsundersøgelsen

Case-kontrol studiet
Kohorte studiet
Randomiseret intervention
Forekomst af gonoré

Beral, Lancet, 25 May 1974
To forskellige situationer

Påvirkning

KOHORTEUS

CASE-KONTROLUS
Case-kontrolstudie (25. marts)

Eksponerede → Udfald

Ikke-eksponerede

Eksponerede → Rask

Ikke-eksponerede

Beaglehole et al., 1993
Kohortestudier (4. marts)

Population

Individer uden udfald

Eksponerede

Ikke-eksponerede

Rask

Udfald

Tabt

Rask

Udfald

Tabt

Beaglehole et al., 1993
• Association refers to the statistical dependence between two variables, that is, the degree to which the rate of disease in persons with a specific exposure is either higher or lower than the rate of disease among those without that exposure.

• A causal association is one in which a change in the frequency or quality of an exposure or characteristic results in a corresponding change in the frequency of the disease or outcome of interest.
## Bradford Hills kriterier

<table>
<thead>
<tr>
<th>Er associationen valid?</th>
<th>Afspejler associationen årsag og virkning?</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Er associationen tilfældig?</td>
<td>• Er associationen stærk?</td>
</tr>
<tr>
<td>• Skyldes associationen bias?</td>
<td>• Er associationen biologisk plausibel?</td>
</tr>
<tr>
<td>• Skyldes associationen konfounding?</td>
<td>• Er associationen konsistent med andre observationer?</td>
</tr>
<tr>
<td></td>
<td>• Er den tidsmæssige rækkefølge korrekt?</td>
</tr>
<tr>
<td></td>
<td>• Er der holdepunkter for en dosis-respons sammenhæng?</td>
</tr>
</tbody>
</table>

H&B 45
Beregning af studiestørrelser (OR/RR = 2)

<table>
<thead>
<tr>
<th>Kohorte undersøgelse</th>
<th>Case-kontrol undersøgelse</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1 eksponeret/ueksponeret</td>
<td>1:1 patienter/kontroller</td>
</tr>
<tr>
<td>1% sygdom i ueksponeret</td>
<td>1% eksposition i kontroller</td>
</tr>
<tr>
<td>2514 eksponeret/ueksponeret</td>
<td>2597 patienter/kontroller</td>
</tr>
<tr>
<td>5% sygdom i ueksponeret</td>
<td>5% eksposition i kontroller</td>
</tr>
<tr>
<td>474 eksponeret/ueksponeret</td>
<td>559 patienter/kontroller</td>
</tr>
<tr>
<td>15% sygdom i ueksponeret</td>
<td>15% eksposition i kontroller</td>
</tr>
<tr>
<td>133 eksponeret/ueksponeret</td>
<td>225 patienter/kontroller</td>
</tr>
</tbody>
</table>
Overvejelser ved planlægning

Design

Statistik

Problem
Data
Tid
Økonomi

Styrke
Analyse
Bias & kon
Operation.
Tag med hjem beskeder

- Epidemiologi baserer sig på den antagelse, at sygdomme har årsager, der er erkendelige.
- Der findes forskellige typer af epidemiologiske undersøgelser med hver deres styrker og svagheder.
- Statistisk association afspejler ikke nødvendigvis kausal sammenhæng, men kan skyldes tilfældigheder, bias, konfounding og kausalitet.