

Epidemiology in medical practice

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Some snippets from the research & evaluation methods list proposed by the RCGP on the knowledge and skills required for evidence-based practice

the epidemiology perspective

- A quantitative approach to disease and its causation
- Studying and comparing populations and groups
- Observing the distribution of disease patterns
- Assessing the effects of different determinants
- Examining methods for optimising disease control and its strategies

Epidemiological sources

■ Routine statistics

(available, cheaper, wide coverage, but incomplete, inaccurate, late and limited)

■ Surveys

(expensive, time-consuming, involve smaller numbers, but quality control methods and limitations of data known, can cover other subject areas not covered routinely)

The evidence from epidemiology: source 1: ROUTINE STATISTICS

- Mortality and morbidity statistics
- Hospital inpatient statistics and enquiry (HIPE); Hospital Activity Analysis; Hospital Episode Statistics
- Primary Health Care and General Practice morbidity
- Notifications
- Registers

The evidence from epidemiology: source 2: SURVEYS

- **Descriptive studies** – measuring frequency of occurrence of disease (or characteristics)
- **Analytic studies** – testing hypothesis about determinants of disease in individuals and populations
- **Experimental studies** – testing such hypothesis by showing whether the frequency of a disease may be affected by altering exposure to a suspected cause

Analytical studies 1: Case-Control studies

- Comparison of people with the disease and normal people, showing that the suspected cause occurs more frequently among those with the disease than those without it

- Quick, inexpensive, cannot measure incidence and useful for rare diseases

But: exposure determined *after* disease occurrence; strongly affected by CONFOUNDING factors and problems in selection of controls and ascertainment (dissimilar quality of information among cases and controls)

Analytical studies 2: Cohort studies

- Comparison of people exposed to the suspected cause and those not exposed, showing that a greater proportion of people develop the disease among the exposed group than among the non-exposed.
 - Incidence and relative risk may be measured directly; cases evolve during the study. Overall less inherent bias than case-control method.

But: expensive; time consuming when prospective; not useful for rare diseases

Measures of Disease Frequency: Incidence and Prevalence

- Prevalence (or prevalence proportion)

P.P. = $\frac{\text{no. of subjects having the disease}}{\text{total no. of subjects}}$ at a point in time

- Incidence rate

I.R. = $\frac{\text{no. of disease onsets}}{\text{person-time at risk}}$ over a defined period of time

- Incidence proportion (or cumulative incidence)

I.P. = $\frac{\text{no. of subjects who get the disease during a period}}{\text{no. of subjects at risk at the beginning of the period}}$

Attributable Risk or Effect

(the disease attributable to the exposure)

- Measures the difference between the incidence (or prevalence) in the exposed and that in the unexposed

e.g In a study of infant mortality and maternal smoking, the proportion of babies who died in the 1st year of life was 0.030 in smokers and 0.020 in non-smokers. The Risk difference of 0.010 reflects the absolute effect of the exposure that is, maternal smoking (of 15+ daily) increased the risk of infant death by 10 per 1,000 babies

Relative risk 1 *(or Risk Ratio)*

The Relative Risk represents the increased (or decreased) risk of a disease due to a particular exposure. It reflects the strength of a suspected cause.

Denoted as:

$$\text{R.R.} = \frac{\text{Incidence in the exposed}}{\text{Incidence in the unexposed}}$$

0.030/0.020 in example of infant death and maternal smoking = 1.5

Also known as *incidence ratio*.

The *prevalence ratio* may also be calculated as a *measure of relative effect*

Relative risk 2

Relative Risk or Risk Ratio (sometimes also called Hazard Ratio or even Odds Ratio in certain circumstances)

If X% of people exposed to a putative cause suffer a certain effect and Y% not exposed to the cause (or alternatively, the general population) suffer the same effect, the RR is X/Y . If the effect is “bad”, then a RR greater than unity denotes a “bad” cause, while an RR less than unity suggests beneficial cause.

A Relative Risk of exactly 1 (= unity) suggests that there is no correlation.

but watch for the confidence intervals – if they include 1, not significant and could go either way; if very wide, poor power possibly due to small numbers

Relative risk 3

- 1. Even where there is no correlation, the RR is never exactly unity, since both X and Y are estimates of statistical variates, so the question arises as to how much deviation from unity should be acceptable as significant.
- 2. X and Y, while inherently unrelated, might be correlated through a third factor, or indeed many others (for example, *age*). Sometimes such **confounding factors** might be known (or thought to be known) and (sometimes dubious) attempts are made to allow for them. Where they are not known they cannot be compensated for, by definition.
- 3. Sometimes **biases** are inherent in the method of measurement employed.
- 4. Statistical results are often subjected to a chain of manipulations and selections which (whether designed to or not) can increase the deviation of the RR from unity.
- 5. Publication bias can give the impression of average RRs greater than 1.5 when there is no effect at all.

Relative risk 4

- For these reasons most scientists (which includes scientifically inclined epidemiologists) take a fairly rigorous view of RR values. In observational studies, they will not normally accept an RR of less than 3 as significant and **never** an RR of less than 2. Likewise, for a putative beneficial effect, they **never** accept an RR of greater than 0.5. Sometimes epidemiologists choose to dismiss such caution as an invention of destructive sceptics, but this is not the case. For example:
 - *In epidemiologic research, increases in risk of less than 100 percent are considered small and are usually difficult to interpret. Such increases may be due to chance, statistical bias, or the effects of confounding factors that are sometimes not evident .*
[Source: National Cancer Institute, Press Release, October 26, 1994.]
 - This strict view of RRs may be relaxed somewhat in special circumstances; for example in a fully randomised double blind trial, as opposed to an observational study, which produces a result with a high level of significance.

Hazard Ratios 1

Time-to-event curves analyzed by Cox proportional hazards regression are commonly used to describe the outcome of drug studies. This methodology has the advantage of using all available information, including patients who fail to complete the trial, such as in cancer chemotherapy or human immunodeficiency virus antiviral treatment studies.

The goal of treatment in such studies may be to prevent the development of a complication, for example, *Pneumocystis carinii* pneumonia, and to describe the likelihood of this complication's developing in the treatment group compared to the control group. **The hazard ratio describes the relative risk of the complication based on comparison of event rates.**

Hazard Ratios 2

Hazard ratios have also been used to describe the outcome of therapeutic trials where the question is to what extent treatment can shorten the duration of the illness. However, the hazard ratio, a type of relative risk, does not always accurately portray the degree of abbreviation of the illness that occurred. In these circumstances, time-based parameters available from the time-to-event curve, such as the ratio of the median times of the placebo and drug groups, should be used to describe the magnitude of the benefit to the patient. The difference between hazard-based and time-based measures is analogous to the odds of winning a race and the margin of victory. The hazard ratio is the odds of a patient's healing faster under treatment but does not convey any information about how much faster this event may occur.

Hazard Ratio 3

The clinical outcomes of a safety trial for oral contraceptives are shown in Table 2 below.

There were 8506 participants in the Estrogen + Progestin group, and 8102 participants in the placebo group. The data in the table shows that the treatment increased and decreased certain health risks for the group of participants who were in the Estrogen + Progestin group.

For health risks that have a Hazard Ratio greater than one, it means that the chances of getting that health risk increased with the treatment.

For health risks that have a Hazard Ratio less than one, it means that the chances of getting that health risk decreased with the treatment.

Hazard ratio 4

TABLE 2 Hazard Ratio: <1 Helped, >1 Harmed, 1 no change

Table 2. Clinical Outcomes by Randomization Assignment*

Outcomes	No. of Patients (Annualized %)		Hazard Ratio	Nominal 95% CI	Adjusted 95% CI
	Estrogen + Progestin (n = 8506)	Placebo (n = 8102)			
Follow-up time, mean (SD), mo	62.2 (16.1)	61.2 (15.0)	NA	NA	NA
Cardiovascular disease†					
CHD	164 (0.37)	122 (0.30)	1.29	1.02-1.63	0.85-1.97
CHD death	33 (0.07)	26 (0.06)	1.18	0.70-1.97	0.47-2.98
Nonfatal MI	133 (0.30)	96 (0.23)	1.32	1.02-1.72	0.82-2.13
CABG/PTCA	183 (0.42)	171 (0.41)	1.04	0.84-1.28	0.71-1.51
Stroke	127 (0.29)	85 (0.21)	1.41	1.07-1.85	0.86-2.31
Fatal	16 (0.04)	13 (0.03)	1.20	0.58-2.50	0.32-4.49
Nonfatal	94 (0.21)	59 (0.14)	1.50	1.08-2.08	0.83-2.70
Venous thromboembolic disease	151 (0.34)	67 (0.16)	2.11	1.58-2.82	1.26-3.55
Deep vein thrombosis	115 (0.26)	52 (0.13)	2.07	1.49-2.87	1.14-3.74
Pulmonary embolism	70 (0.16)	31 (0.08)	2.13	1.39-3.25	0.99-4.56
Total cardiovascular disease	694 (1.57)	546 (1.32)	1.22	1.09-1.36	1.00-1.49
Cancer					
Invasive breast	166 (0.38)	124 (0.30)	1.26	1.00-1.59	0.83-1.92
Endometrial	22 (0.05)	25 (0.06)	0.83	0.47-1.47	0.29-2.32
Colorectal	45 (0.10)	67 (0.16)	0.63	0.43-0.92	0.32-1.24
Total	502 (1.14)	458 (1.11)	1.03	0.90-1.17	0.86-1.22
Fractures					
Hip	44 (0.10)	62 (0.15)	0.66	0.45-0.98	0.33-1.33
Vertebral	41 (0.09)	60 (0.15)	0.66	0.44-0.98	0.32-1.34
Other osteoporotic‡	579 (1.31)	701 (1.70)	0.77	0.69-0.86	0.63-0.94
Total	650 (1.47)	788 (1.91)	0.76	0.69-0.85	0.63-0.92
Death					
Due to other causes	165 (0.37)	166 (0.40)	0.92	0.74-1.14	0.62-1.35
Total	231 (0.52)	218 (0.53)	0.98	0.82-1.18	0.70-1.37
Global index§	751 (1.70)	623 (1.51)	1.15	1.03-1.28	0.95-1.39

*CI indicates confidence interval; NA, not applicable; CHD, coronary heart disease; MI, myocardial infarction; CABG, coronary artery bypass grafting; and PTCA, percutaneous transluminal coronary angioplasty.

†CHD includes acute MI requiring hospitalization, silent MI determined from serial electrocardiograms, and coronary death. There were 8 silent MIs. Total cardiovascular disease is limited to events during hospitalization except venous thromboembolic disease reported after January 1, 2000.

‡Other osteoporotic fractures include all fractures other than chest/sternum, skull/face, fingers, toes, and cervical vertebrae, as well as hip and vertebral fractures reported separately.

§The global index represents the first event for each participant from among the following types: CHD, stroke, pulmonary embolism, breast cancer, endometrial cancer, colorectal cancer, hip fracture, and death due to other causes.

Calculating and using number needed to treat

Some physicians use another measure of risk and benefit, the **number needed to treat** (NNT), in considering the consequences of treating or not treating.

The **NNT** is the number of patients to whom a clinician would need to administer a particular treatment for one to benefit from it.

If, for example, the NNT for a treatment is 10, the practitioner would have to give the treatment to 10 patients for each to have a 1 in 10 chance of being a beneficiary.

NNT - NNH

If the absolute risk reduction from a treatment is large, you need to treat only a small number of patients to observe a benefit in at least some of them. Conversely, if the absolute risk reduction is small, you must treat many people to observe a benefit in just a few.

An analogous calculation to the one used to determine the NNT can be used to determine the number of patients who would have to be treated for 1 patient to experience an adverse event. This is the **number needed to harm (NNH)**.

Tools of Measurement: the questionnaire

(one of several tools of measurement)

Interview method versus postal survey

Problems with interview method:

No anonymity; much higher costs (training, site, mobility required); non-random error by interviewer

Advantages of interview method:

Probing possible; higher response; greater length possible

Problems with postal survey method:

Response often worse; must be short ; send back cost-time-bother; reliance on mail; varying educational levels and illiteracy

Advantages of postal survey method:

Safeguards anonymity; cheaper; quicker; less bias; can touch on sensitive areas (politics, income, sexual habits)

Exclusion criteria

Exclude:

- persons living in the area but not fulfilling case or control definition e.g. not lived in area for adequate time; wrong age range; etc
- Persons too sick to respond
- Possible confounders – relationship with exposure being studied e.g smokers in a coffee and IHD study
- Persons sick before start of study

Pilot studies

- Mimicking proposed field work on a small scale to assess viability beforehand

- Can test:

 - response rate*

 - clarity of questions; types of answers*

 - logistical problems, costs*

 - data flow, storage and analysis*

IMPORTANT: Need to allow time after Pilot, *before fieldwork* to implement necessary changes from lessons learnt

A Valid screening tool

- *Valid* - One which measures what it sets out to measure
- For a tool to be valid, it must have high sensitivity and high specificity

Validity indices

Sensitivity: proportion of true positives, correctly identified ($a/a+c$)

(must be high when false negatives serious e.g. screening for cancer)

Specificity: proportion of true negatives, correctly identified ($d/b+d$)

(must be high to reduce undue anxiety, wasteful expensive investigation)

Positive Predictive Value: likelihood that a person with a positive test has the disease ($a/a+b$)

Negative Predictive Value: likelihood that a person with a negative test has not got the disease ($d/c+d$)

Testing Validity

Screening Test	Reference Positive	Test Negative	
Positive	True Positives correctly identified (a)	False Positives (b)	Total Positives by screening (a+b)
Negative	False Negatives (c)	True Negatives correctly identified (d)	Total Negatives by screening (c+d)
	Total True Positives (a+c)	Total True Negatives (b+d)	Grand Total (a+b+c+d)

e.g. testing a glucose strip vs. oral GTT

<i>Glucose strips</i>	<i>Oral Glucose</i>	<i>Tolerance Test</i>	
	+	--	All
+	7 (a)	1 (b)	8 (a+b)
--	3 (c)	89 (d)	92 (c+d)
All	10 (a+c)	90 (b+d)	100 (a+b+c+d)

Sensitivity = $7/10 = 70\%$ (of all positives, how many identified?)

Specificity = $89/90 = 98.9\%$ (of all negatives, how many identified?)

**Positive predictive value = $7/7+1 = 7/8 = 87.5\%$
(how likely is a test positive truly positive?)**

**Negative predictive value = $89/89+3 = 89/92 = 96.7\%$
(how likely is a test negative truly negative?)**

An association is more likely to be causal if it is:

- Strong
- Graded
- Independent (of possible confounders)
- Consistent
- Reversible
- Plausible

Reference

- Epidemiology in Medical Practice. 5th Edition. ,Barker, Cooper and Rose. Churchill Livingstone.