Epidemiology (5)
Measuring causal effects

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MEASURES OF CAUSAL EFFECTS

- Objectives of epidemiology
  - Measuring the effect of exposure
  - For that, only measuring disease occurrence in exposed is not enough
- The counterfactual ideal
  - To measure the effect of exposure, ideally, it's necessary to compare the disease occurrence of exposed person with the hypothetical disease occurrence if the person were not exposed in the same time period (counterfactual ideal). It's impossible. We don't have time-machine. We cannot observe people in parallel universe.
  - Thus exposed group and unexposed group with similar background are compared. To control the timing of exposure, experimentally, crossover study is possible only if the exposure has a brief effect.
    - Compare A (exposed – washout – unexposed) and B (unexposed – washout – exposed)
    - The time sequence of exposure may affect the result, so that crossover study also differs from counterfactual ideal.

Effect measures

- To achieve a valid substitution for the counterfactual experiences, several designs (incl. crossover study, randomized experiment, choosing unexposed subjects who have the same or similar risk-factor profiles for disease as the exposed subjects) are possible.
- If we can assume the comparability, the effect of exposure can be measured by the following manners.
  - Absolute differences in incidence proportions and incidence rates
    - RD (risk difference) = attributable risk
      Risk (exposed) – Risk (unexposed)
    - IRD (incidence rate difference) = attributable rate
      IR (exposed) – IR (unexposed)
  - Relative risk
    - Relative effect = (RD)/(Risk in unexposed) = RR – 1
    - RR (risk ratio) = Risk (exposed) / Risk (unexposed)
    - IRR (incidence rate ratio) = IR (exposed) / IR (unexposed)

Table 4-5. Comparison of absolute and relative effect measures

Measure	Numeric range	Dimensionality
Risk difference	[-1, +1]	None
Risk ratio	[0, ∞)	None
Incidence rate difference	(-∞, +∞)	1/time
Incidence rate ratio	[0, ∞)	None

Note: ∞ is actually division by zero when no disease occurred in unexposed group.

Examples

Table 4-6. Diarrhea during 10-day period in breastfed infants by antibody titer level			
	Low	High	Total
Diarrhea	12	7	19
No diarrhea	2	9	11
Total	14	16	30
Risk	0.86	0.44	0.63

- 0.86 = 12/14
- RD = 0.86 – 0.44 = 0.42
- RR = 0.86/0.44 = 1.96

Table 4-7. Breast cancer cases and person-years of observation for women with TB, repeatedly exposed to multiple X-ray and unexposed			
	Exposed	Unexposed	Total
BC cases	41	15	56
Person-yr	28010	19017	47027
Rate (/10000 yr)	14.6	7.9	11.9

- 14.6 = 41/28010x10000
- IRD = 14.6/10000 (yr^{-1}) – 7.9/10000 (yr^{-1}) = 6.7/10000 (yr^{-1})
- IRR = 14.6/7.9 = 1.86

Relation between RR and IRR

- If risk remains less than about 0.20, for short time periods,
  RR = R(E)/R(U) = {IR(E) x time}/{IR(U) x time} = IR(E)/IR(U) = IRR
- For longer time periods, RR becomes different from IRR.
  - In the case of table 4-6, maximum possible R(E) cannot exceed 1, when R(U) is 0.44, RR must be less than 1/0.44 = 2.3 (1.96 << 2.3).
  - IR has no such restraint. In table 4-6, we can back calculate IR(E) and IR(U) from risk-data.
    - $14 \times (1 - IR(E))^{10} = 2 \rightarrow 1 - (2/14)^{0.1} = 0.1768\ldots = IR(E)$
    - $16 \times (1 - IR(U))^{10} = 9 \rightarrow 1 - (9/16)^{0.1} = 0.0559\ldots = IR(U)$
    - IRR = IR(E)/IR(U) = 3.16… (whereas the text says 3.4)
- For very shorter time periods, RR shrinks along with the length of the time interval: myocardial infarction risk in the next 10 seconds is almost zero.

Attributable fraction

Table 4-8. 1 yr disease risk for E and U			
	U	E	Total
Disease	900	500	1400
No disease	89100	9500	98600
Total	90000	10000	100000
Risk	0.01	0.05	0.014

Table 4-9. 1 yr disease risk for 3 level exposure				
	None	Low E	High E	Total
D	100	1200	1200	2500
No D	9900	58800	28800	97500
Total	10000	60000	30000	100000
Risk	0.01	0.02	0.04	0.025
RR	1	2	4	
Prop. in cases	0.04	0.48	0.48	

- RD = R(E) – R(U)
- Attributable fraction (AF) = RD/R(E) = {R(E) – R(U)}/R(E) = 1 – 1/RR
- The proportion of the disease burden among exposed people that is caused by the exposure
- In Table 4-8, AF=(0.05-0.01)/0.05=4/5=0.8 (80%)
- Among 1400 cases, 500 were exposed, the proportion was 500/1400 = 0.357. Overall AF for the population is 0.357x0.8=0.286
- Otherwise, 500x0.8=400 are attributable to exposure. 400/1400=0.286
- Total AF = $\sum (AF_i \times P_i)$
- In Table 4-9, total AF = 0 + {(2-1)/2}x0.48 + {(4-1)/4}x0.48 = 0.24+0.36 = 0.60
- Otherwise, {0 + 1200x(2-1)/2 + 1200x(4-1)/4}/2500 = 0.6