2018 AFOEM ATM EPIDEMIOLOGY SESSION

May 13th 2018

SESSION PLAN

Introduction

Quiz

Consideration of study types

Discussion

QUIZ

Question 1

A study was conducted to examine how accurately people reported their banana-eating habits before running. In the study, 250 people kept a daily on-line food and running diary. At the end of six months, they were asked whether or not they usually at one or more bananas on the day before they ran. Their self-report at the end of six months was then compared to their diary report (the diary report was accepted as the reference standard - the "truth"). The results of the study are shown in Table 1.

Table 1. Comparison of diary report and self-report of banana eating before running.

		Diary reporting		
		Bananas	***No Bananas***	***Total***
Self-report after six months	***Bananas***	*85*	*39*	*124*
	No bananas	*15*	*111*	*126*
	Total	*100*	*150*	*250*

a) What is the sensitivity of the self-report after six months?

b) What is the negative predictive value of the self-report after six months?

c) Explain in words suitable for a non-epidemiologist what the negative predictive value you calculated for the self-report after six months means (as it applies in this example, not in general).

d) According to the self-report at six months, what proportion of the 250 people eat bananas before running?

Answers for Question 1

a) Sensitivity = 85/100 = 0.85

b) NPV = 111/126 = 0.88

c) 88% of people who say they don't eat one or more bananas on the day before they run truly do not eat one or more bananas on the day before they run.

d) Apparent prevalence = 124/250 = 0.50

Question 2

The table below shows data taken from a study of an Advanced Epidemiology class. The study examined the relationship between average hours per week of preparation for class by the students and the probability of achieving a Distinction or High Distinction for the unit. Assume there were no major issues in terms of selection bias, measurement bias or confounding.

What is your interpretation of the results of the study and how confident are you in this interpretation? Please provide the reasons for your interpretation and your level of confidence.

Hours of study per week	Odds ratio[1]	95% CI
<1 hour	1.00	
1 - < 2 hours	1.12	(0.83 – 1.46)
2 - <3 hours	2.58	(2.16 – 3.01)
3 - <4 hours	1.99	(0.95 – 3.15)
4 - <5 hours	5.42	(5.03 – 5.82)
5 or more hours	9.61	(8.99 – 10.32)
Overall	3.99	(3.74 – 4.25)

1: P (trend) < 0.003

Answer for Question 2

The table provides good evidence that increasing hours of study increase likelihood of achieving a Distinction of High Distinction. The estimated average effect is that students who study for one hour or more each week have four times the likelihood of being awarded a D or HD compared to students who study for one hour or less (with the 95% CI suggesting the true effect is somewhere between 3.7 times the risk and 4.3 times the risk).

Confidence in the result is high because the odds ratio increases fairly smoothly with increasing hours of study, with such a pattern of increasing (or decreasing) risk (interpreting the odds ratio as a relative risk) expected for most true exposure response relationships. This is unlikely to be due to chance, given the probability of the trend occurring due to chance was estimated to be less than three in a thousand. The drop in odds ratio (relative to the preceding and following categories) for studying three to less than four hours is probably just due to chance, as the confidence interval for that estimate is wide, suggesting there were fewer students in this group.

In summary, the table provides good evidence that increasing hours of study per week (compared to studying for one hour or less). There is a clear dose response and the 95% confidence interval and p value strongly suggest the overall increase in risk of 300% (four times the risk in the 'exposed' compared to the 'unexposed'), and the trend of increasing performance with increasing levels of study, did not arise due to chance.

Question 3

In case-control studies, in general, only incident cases should be selected rather than prevalent cases. Why is this? In what circumstances would the inclusion of prevalent cases be unlikely to result in bias?

Answer for Question 3

The reason why incident cases should be used is that cases in a case-control study are supposed to represent the exposure experience of cases in the study base. If the probability of exposure has changed over time, cases that occurred before the study base commenced (prevalent cases) may not represent the exposure experience of cases which occur during the study base. Also, if all included cases only occur during the study base, but only surviving cases (another form of prevalent cases) are included, these surviving cases may not represent the exposure experience of all cases, as the probability of amount of exposure might be related to the severity of the disease. For example, if higher exposure leads to more severe disease, then cases with higher exposure will be more unwell and perhaps be more likely to die. Surviving cases may therefore have a lower overall exposure than all cases.

Another way of looking at this issue is to remember that the concept of a case control study is that subjects are drawn from a study base, which is defined in terms of time, person and place. Essentially, it is a cohort of people, some of whom develop the outcome and some of whom don't. In a cohort study, people have to be eligible to get the outcome when they start the study, and all people who develop the outcome should be included in the study results. If prevalent cases are used, this is not necessarily the case. Cases may have occurred prior to the study base commencing, or cases that occurred during the study but who died before the study was completed (and so were excluded) may have had a different exposure to those who didn't die. This would lead to selection bias, because a higher proportion of incident cases might be excluded from one exposure group compared to another.

Another potential issue is that diagnostic criteria or approaches might change over time, meaning that whether somebody with a given disease might be identified as a case at one time but not at another. However, this seems a much less important issue.

The above concerns wouldn't matter if the probability of exposure didn't change over time and if there was no connection between exposure and probability of death (or if diagnostic criteria didn't change over time).

The key issues are:

(i) Incident cases

- Prevalent cases mightn't represent the exposure experience of cases in the study base because:
    - Exposure might change over time and some cases occurred before the study base started
    - The fact or level of exposure might be correlated with the probability of death.

(ii) Bias unlikely

- If the likelihood or level of exposure doesn't change over time
- If the fact or level of exposure is not correlated with the probability of death.

Question 4

One commonly identified weakness of cross-sectional studies is that there is no knowledge of people who would have been in the population of interest but who aren't included in the study because they are unwell, have died, have moved away or decline to take part. In contrast, cohort studies may have a low proportion of eligible subjects who actually agree to take part in a study, but often this is not viewed as a major weakness. What are the epidemiological issues that underly these two differing assumptions about the effect on validity of the studies?

Answer for Question 4

The underlying assumptions of epidemiological studies at their simplest level is that that there are two groups that are exactly the same in all relevant ways except for one factor (the exposure or study factor). At the beginning of the study, all included subjects must not have the outcome of interest but must be able to develop it. The groups are followed over time and the incidence of the outcome (or some other measure of the outcome) is compared between the two groups. If subjects leave a group for whatever reason, this could mean the two groups are no longer directly comparable, which may introduce bias.

In a cross-sectional study, the two groups have effectively been formed some time in the past, and followed over time to the point where the study occurs. However, nothing is known about the starting groups. Subjects who are no longer in the study groups may have had a different relationship between exposure and outcome than those who remained. Therefore, studying the remaining subjects may well lead to a biased result.

In a cohort study, drop-outs occurring before the exposure groups are formed (i.e. before the study starts) do not affect the comparability of the groups IF they are comparable at the beginning of the study. The potential problem is that the drop-outs may be different to the non-drop-outs, this might differ between exposure groups, and so it might be hard to confidently produce two comparable groups. The early drop outs may have an effect on the EXTERNAL validity of the study, but this would usually not be seen as a significant weakness.

In summary, in a cross-sectional study, the drop-outs occur during the 'follow-up" period (before the cross-sectional measurement) and so can result in selection bias, whereas in a cohort study the decision to take part or not occurs before the follow-up period starts, and so should not result in selection bias IF exposure groups are comparable at the beginning of the study. This is why there is the potential for more methodological problems to arise from losses in a cross-sectional study than pre-study losses in a cohort study.

Question 5

Sometimes in a cohort study a Standardised Incidence Ratio (SIR) is calculated, comparing the rate in the cohort to the rate in a general population. In other cohort studies, the rate in the exposed subjects is compared to the rate in unexposed within the same cohort. Compare these two approaches in terms of their advantages and disadvantages. In what situations might it be appropriate or necessary to use the Standardised Incidence Ratio approach?

Answer for Question 5

<u>Comparison to the general population (SIR)</u>

Advantages:

- Usually a much larger population, thereby producing a more stable (more precise) comparison rate estimate.

Disadvantages:

- There may be important differences to the exposed population and therefore introduce selection bias
- Usually no information on important confounders (apart from age and sex) and confounding may not be well controlled.
- The outcomes may have been measured using different techniques or standards, increasing the chances of important measurement bias.
- The comparison population typically includes the exposed subjects (potentially causing a bias towards the null), but usually this effect is trivial and can be ignored.

<u>Internal comparison</u>

Advantages:

- Likely to be fairly similar to the exposed subjects, thereby decreasing the chance of important selection bias
- Likely to have some information on important confounders (in addition to age and sex), thereby increasing the chance that confounding will be well controlled.
- Information is usually collected under similar conditions, decreasing he chances of important measurement bias.
- The comparison population typically includes the exposed subjects (potentially causing a bias towards the null), but usually this effect is trivial and can be ignored.

Disadvantages:

- Usually population is fairly small, which means the comparison rate is less stable (less precise).
- The unexposed may actually have some exposure, thereby potentially biasing the result towards the null.

Might need to use standardisation because there is no internal comparison population or such a population is too small to provide stable comparison rates.