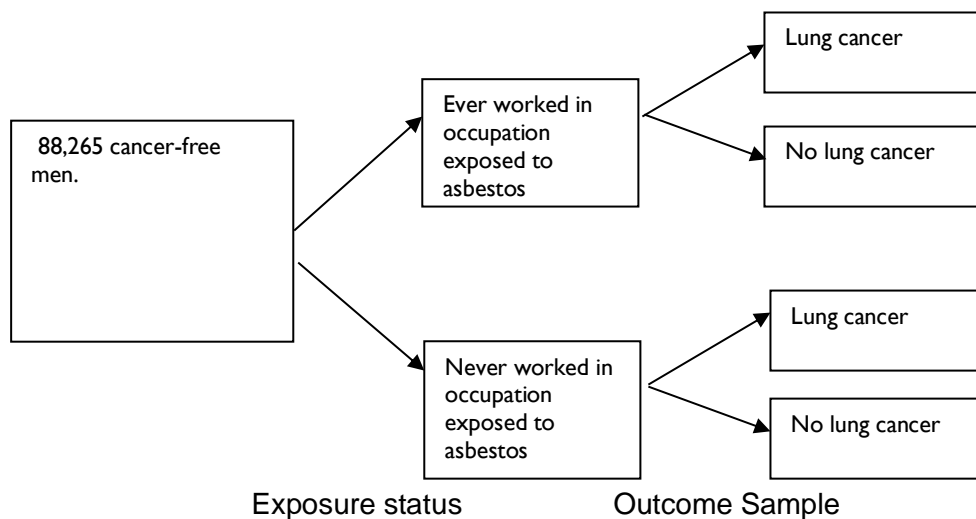


Solutions 7: Cohort studies

Section 1: European Prospective Investigation into Cancer and Nutrition (EPIC study)

Note for information: While the article used in the practical predicted a peak of mesothelioma deaths in 2011-15, this appears not to have occurred until later. The most recent data suggest the peak of mesothelioma deaths in Great Britain may have occurred around 2018 (and is predicted to decline rapidly thereafter) but this is not completely clear (see [here](#)).

Question 1a:



Question 1b: EPIC cohort participants i.e. adults from the general population who had been registered with 23 health centres in 10 European countries.

Question 2: Classification of exposure by occupational status would have been relatively crude. We can expect that some people who work in occupations where asbestos exposure is possible may not actually have been exposed. Similarly, some workers in occupations not rated as “exposed” may have received asbestos exposure. In addition, no account was taken of the amount or duration of asbestos exposure. The inaccurate assessment of asbestos exposure may have reduced the ability of the researchers to identify a link between exposure and disease (non-differential misclassification bias – covered in lecture on bias).

Question 3: People with lung cancer at baseline (i.e. prevalent cases) were excluded from the analyses because they are not “at risk” of developing the disease and so are not eligible for the study. Excluding these individuals helps ensure that the exposure preceded the onset of the disease.

Question 4:

Asbestos-associated occupation	# at-risk participants	# incident lung cancer cases over 8.4 years	Incidence risk over 8.4 years	Incidence risk ratio
Unexposed	70,877	516	0.0073	1.0 [Ref]
Exposed	17,388	187	0.0108	1.48

- a) For every 1000 men working in occupations which were associated with asbestos exposure there were 10.8 incident cases of lung cancer observed over 8.4 years.
- b) For every 1000 men working in occupations which were not associated with asbestos exposure, there were 7.3 incident cases of lung cancer observed over 8.4 years.
- c) Men who were working in occupations associated with asbestos exposure had 1.48 times the risk (48% higher risk) of getting a lung cancer diagnoses over 8.4 years, in comparison to men who were not working in occupations associated with asbestos exposure.
- d) $0.0108 - 0.0073 = 0.0035 \times 1000 = 3.5$ per 1000. Men who were working in occupations associated with asbestos exposure had 3.5 excess cases of lung cancer diagnoses per 1000 persons over 8.4 years that could be attributed to working in occupations associated with asbestos exposure.

Question 5: Population based sampling (a population-based study) increases likelihood that the study population 'represents' a general population of interest to which the causal study results may then be 'judged' to apply. It also reflects the risk of asbestos exposure among the population at large. The limitation is that asbestos is a relatively rare exposure, and so the numbers exposed will be small and this limits the statistical power to assess the association between the exposure and outcomes, particularly if the outcomes are rare.

Mesothelioma is relatively rare, and so it would be difficult to assess the association between asbestos and these conditions in a population-based cohort study.

Section 2: The effectiveness of insecticide treated bed nets in Malawi

Question 6: There was an observed incidence of 2.1 malaria infections per person-year at risk ($1909/905=2.1$). Follow-up time must correspond to the period during which malaria infections were recorded (if they occurred).

In this case, follow-up would be counted from the date of the enrolment, when monitoring for malaria infection began. Follow-up time would end at the last date of follow-up, or when the child was lost to follow-up.

Note that the units here are person-years at risk rather than person-years. This is because children who had a positive result of malaria infection by RDT would have received treatment, in this case with a drug known as Artemether Lumefantrine (AL). The researchers subtracted 10.5 days from follow-up time to account for the fact the

drug would provide some protection from a potential malaria infection while it was being metabolised (i.e. still in the body).

Question 7: With a retention rate of 85% relatively few participants were lost to follow up. This could mean that loss to follow-up would likely induce minimal selection bias in this study. However, nevertheless, if loss to follow up was substantially different between groups with different bed net use or other potential risk factors, such as age of child, and wealth group, the final result could still be affected by selection bias.

Question 8:

- Exposure: From the description it seems that ITN usage was based on caregiver reporting during the monthly study meetings, which may not be as reliable as direct observation, although this would be very challenging to do practically. [Note: According to the paper, the researchers did do a small number of household visits afterwards to validate how well reporting of ITN use matched what was being reported.]
- Outcome: Malaria infection was assessed using an RDT, which we can assume has acceptable accuracy if used in routine clinical practice. The researchers noted that there was a small risk of false positives as the RDT is an antigen test and may detect a past infection. However, this was much more practical than other diagnostics which require significant resources (e.g. blood smears). The researchers also tried to capture any infections that occurred between the monthly study visits by encouraging caregivers to attend a study clinic, so it is likely that most malaria infections were captured.

Question 9:

- The incidence rate of malaria appears to increase as the 'worse' types of bed net are used, after accounting for relevant characteristics. This study shows that ITNs continue to be effective at preventing malaria infection in this setting despite increasing insecticide resistance.
- The incidence rate of malaria appears to decrease as wealth increases, after accounting for relevant characteristics. The effect of poverty on the incidence of malaria remains pervasive even after accounting for bed net usage, highlighting the importance of equity when designing, implementing and monitoring malaria control programmes.

In order to make a judgment on the strength of evidence for these association it would be necessary to compare the precision of these estimates (i.e. the 95% confidence intervals) to see whether they overlap, which the table unfortunately does not show.