

Practical 7: Cohort studies

Objectives

At the end of the practical students should be able to:

- Calculate and interpret incidence measures
- Interpret measures of relative risk
- Discuss that measurement of exposure precedes occurrence and measurement of outcome in a cohort study
- Explain the need for large numbers and long follow-up time in a cohort study (especially for rare diseases), and the potential impact of loss to follow-up
- Discuss the value of cohort studies for studying rare exposures

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

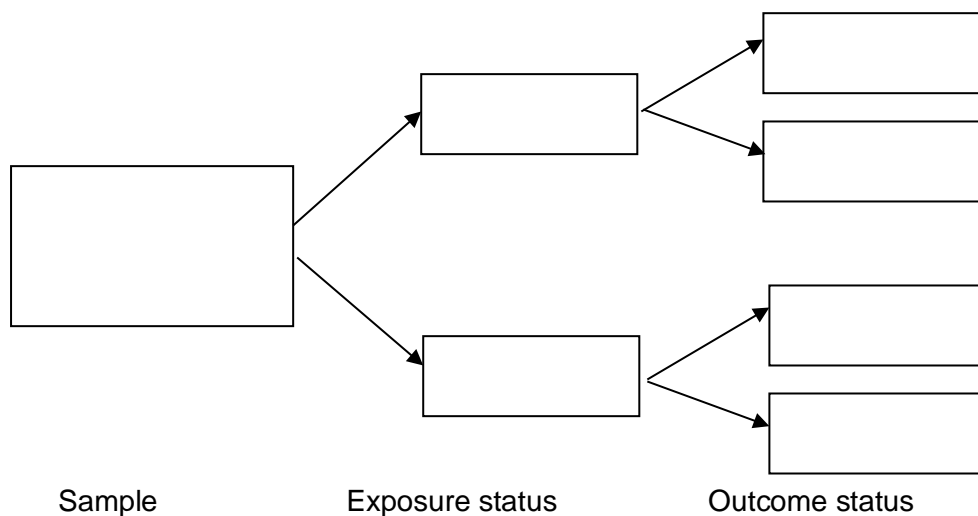
The health risks of asbestos exposure have been known for many years. Asbestos exposure is associated with a range of cancers, particularly of the lungs and the pleura (mesothelioma). Mesothelioma is very rare. Asbestos exposure may also cause non-cancer lung disease such as asbestosis.

EPIC is a multi-centre prospective cohort study of adults from the general population conducted in 23 health centres in 10 European countries¹. At recruitment, participants filled in a questionnaire providing detailed information on many risk factors, including occupational history. Participants were defined as “exposed” to asbestos if they had worked in an occupation defined by labour experts as being at risk of asbestos exposure.

For these analyses, 88,265 cancer-free men were followed for an average of 8.4 years and information was collected about incident lung cancer during follow-up, which was the “outcome” in this study.

Question 1a:

Fill in the study design framework below.



Question 1b: What was the study population that this sample was drawn from?

Question 2: Do you think that defining people as “exposed” to asbestos based on job title provided an adequate measure of occupational asbestos exposure?

Question 3: Having lung cancer was an exclusion criterion for study participation. Why?

Table 1: Incidence risk of lung cancer among men in the EPIC study

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		1.0 [Ref]
Exposed	17,388	187		

Question 4: Complete table 1 and interpret the figures you calculated:

1. Incidence risk of lung cancer among men exposed to asbestos
2. Incidence risk of lung cancer among men not exposed to asbestos
3. Incidence risk ratio for the association between asbestos exposure and lung cancer. Use ‘unexposed’ as the reference group.
4. Incidence risk difference.

Question 5:

- a) What were the strengths and limitations of using a population-based cohort (rather than an occupational-based cohort) for assessing the association between asbestos exposure and lung cancer risk?
- b) Would it have been sensible to investigate the association between asbestos and a specific form of lung cancer (e.g. mesothelioma) with a population-based cohort study design?

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

Insecticide treated bed-nets (ITNs) are a major strategy used for the control of malaria. However, there is concern that increasing levels of resistance to the insecticide applied to ITNs may compromise this strategy, which relies on a ‘community’ effect of many ITNs to kill large numbers of mosquitos. In this cohort study by Lindblade et al (2015), researchers aimed to assess the effectiveness of ITNs to prevent malaria infection in children in a region of Malawi known to have moderate insecticide resistance².

Children aged 6 to 59 months were recruited from six villages in a rural area of Liwonde district that had recently participated in a mass distribution of ITNs. During the study period, caregivers were asked to bring enrolled children to a monthly study meeting and (if ever unwell) to a study clinic, where they were assessed for malaria infection use a routine diagnostic known as a *rapid diagnostic test* (RDT), and their recent use of ITNs was recorded.

In the analysis of this cohort, there had been 1,909 infections with *Plasmodium falciparum* malaria among 1,199 children followed up over a total of 905 person-years at risk (PYAR). A total of 1,018 children (85%) enrolled in the cohort had completed one year of follow-up.

Question 6: Calculate the incidence of observed malaria infections amongst this cohort, stating the units. For each participant, when would follow-up time begin and end?

Question 7: Was loss to follow-up a potential source of bias in this study?

Question 8: Comment on the accuracy of the exposure and outcome assessments within this cohort.

The researchers were interested in which characteristics increased the incidence of malaria amongst the enrolled children. Within the cohort, the incidence rates were computed using a statistical model that adjusted for a number of relevant characteristics (Table 2). The table shows the incidence of malaria by bed-net usage and wealth (assessed by asset index).

Table 2. Predictors of malaria incidence amongst participants in the cohort study (adapted from Lindblade et al (2015), [table 3](#)).

Characteristic	Incidence rate (Infections per person year) *
Bed net usage	
Insecticide-treated bed net	1.7
Non-treated bed net	2.0
No bed net	2.6
Household wealth	
Poorest	2.3
Middle	2.2
Least poor	1.8

*Adjusted for age, baseline malaria infection, bed net usage, wealth, caregiver education, altitude, ITN density, prevalence of malaria infection, season.

Question 9: Describe and interpret the association between the type of (i) bed net used and (ii) wealth, and the incidence of malaria infection.

References:

1. Menvielle G, Boshuizen H, Kunst AE, Vineis P, Dalton SO, Bergmann MM, et al. Occupational exposures contribute to educational inequalities in lung cancer incidence among men: Evidence from the EPIC prospective cohort study. *Int J Cancer*, 126(8):1928-35 (2010).
2. Lindblade KA, Mwandama D, Mzilahowa T, Stenhardt L, Gimnig J, Shah M, Bauleni A, Wong J, Wiegand R, Howell P, Zoya J, Chipwanya J and Mthanga D. A cohort study of the effectiveness of insecticide-treated bed nets to prevent malaria in an area of moderate pyrethroid resistance, Malawi. *Malaria J* 14, 31 (2015).