

Practical 2: Confounding and Effect Modification for Effect Measures in Cohort and Case-Control Studies

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Advanced Statistical Methods in Epidemiology

Cohort Studies

The BELCAP Study - Background:

- ▶ Dental epidemiological study
- ▶ A prospective study of schoolchildren from an urban area of Belo Horizonte, Brazil
- ▶ The Belo Horizonte caries prevention (BELCAP) study
- ▶ The aim of the study was to compare different methods to prevent caries

Details:

- ▶ Children selected were all 7 years old and from a similar socio-economic background
- ▶ Interventions:
 - ▶ Control (3),
 - ▶ Oral health education (1),
 - ▶ Enrichment of the school diet with rice bran (4),
 - ▶ Mouthwash (5),
 - ▶ Oral hygiene (6),
 - ▶ All four methods together (2)
- ▶ Interventions were cluster randomised to 6 different schools

questions:

Calculate the

- ▶ **crude** relative risk
- ▶ and **Mantel-Haenszel** relative risk (adjusting for initial dental status)

event is IMPROVEMENT (DMFT at begin of study **larger** than DMFT at the end of study), so that we are considering relative risk for improvement of dental status with and without adjusting for dental status at begin of study

Cohort study on risk of developing a respiratory disease

Swan (1986) gives the following data from a study of infant respiratory disease. The numbers show the proportion of children developing bronchitis or pneumonia in their first year of life by sex and type of feeding.

Table: Numbers are: number with bronchitis or pneumonia / at risk

	type of feeding		
Sex	Bottle only	Breast +supplement	Breast only
Boys	77/458	19/147	47/494
Girls	48/384	16/127	31/464

- ▶ what could be the risk/preventive factor here?
- ▶ what could be a confounder?

Survival Analysis on the S.S. Titanic

At 2.20 a.m. on the morning of April 15th 1912 the unsinkable S.S. Titanic sank in the North Atlantic Ocean with the loss of nearly 1500 lives. The Titanic represented the state of the art in the shipping technology of its day. It was 852 ft long, displaced 52,310 tons, and was equipped with a system of sealed bulkheads which were believed to render the vessel unsinkable. While on its maiden voyage the Titanic struck an iceberg producing a 300 ft long gash in its side and flooding five bulkheads. In the three hours after the ship struck the iceberg, the Titanics bulkheads gradually filled with water and it sank before a rescue ship, the S.S. Carpathia, could reach it. Two-thirds of the Titanics complement of passengers and crew went to the bottom with it.

Survival Analysis on the S.S. Titanic

Table: numbers are: survivors/non-survivors

	class traveled			
Sex	First	Second	Third	Crew
M	57/118	14/154	75/387	192/670
W/C	146/4	104/13	103/141	20/3

- ▶ provide evidence that the risk for surviving was considerably lower for men than for woman and children (W/C)!
- ▶ provide an analysis for the survival risk of the people based on their class traveled! Use gender as a potential confounder!

Survival Analysis on the S.S. Titanic

An inquiry investigating the sinking of the ship was held by Lord Mersey in 1912, also called the Mersey inquiry. It was suggested in this investigation that the low survival rate of the third class was due to the fact that a large proportion of the third class travelers were emigrants and 'that their lack of English prevented them from following the crew's instructions'. The following table carries information on survival rates by nationality. Use these data to provide evidence that the above claim cannot be sustained. This analysis is more difficult since, for example, a simple comparison of British and non-British travelers – even if adjusted for gender – will not suffice since, if these risks are comparable one might argue that a selection process took place in the sense that those with good knowledge of English language had higher chances of survival whereas, if the risk for survival for British nationals turned out to be higher, this could be taken as reasons for the validity of the above claim. Hence a comparison with the Irish nationals is helpful who are native English speakers and many of them traveled in third class.

Survival Analysis on the S.S. Titanic

Table: numbers are: survivors/non-survivors

	nationality		
Sex	British	Non-British	Irish
M	17/114	60/240	8/41
W/C	22/30	48/68	32/32

Case-Control Studies

Source Investigations

During January 1984 six cases of legionnaires' disease were reported to the health authority in Reading, UK, all of whom became ill between 15 and 19 December 1983 (Anderson *et al.* 1985). This cluster suggested a point source outbreak. A local search was then conducted to discover whether there had been any other legionnaires' disease with onsets within the same 5 days. General practitioners and hospital physicians were asked to consider recent referrals and report any possible cases for further consideration, whilst hospital discharge and autopsy records were reviewed and outpatient X-rays were checked for possible cases, so far un-diagnosed.

Source Investigations

The result was that 13 cases were detected in all. The cases had no obvious factor in common, such as all working in the same place, so that no clear source of the legionella bacterium was apparent. However, all cases had visited Reading town centre just before their illness.

A case-control study was mounted to compare exposure between the cases and a selected set of 36 people without the disease (the controls). Cases and controls were compared by the number who had visited each of six designated parts of Reading town centre, just prior to the outbreak. Results are given in the Table below.

Source Investigations

In this investigation the case-control approach is the only one possible. Speed of hypothesis testing was of paramount importance since further infections could lead to deaths. Cohort studies of legionnaires' disease will, in any cases, be impractical because of the rare nature of the disease (only 558 cases were reported in England and Wales in the four years prior to the Reading outbreak), despite the common presence of the bacterium in many natural and human-made water supplies. Hence extremely large samples would be required.

Source Investigations

Number of people visiting parts of Reading town center in the 2 weeks preceding the onset of legionnaires' disease

Aread of Reading	Cases	Controls
Abbey Square	9	19
Butts Centre	12	21
Forbury Gardens	3	6
Minster Street	9	21
South Street	4	9
Railway Station	3	9
Overall	13	36

Task: Identify the spatial source of contamination by using the tool of a case-control study and by computing the ORs with 95% CI!

Riskfactor for caries

In a case-control of risk factors for dental caries McMahon *et al.* (1993) present data relating to age of child, age of mother and whether or not the child has dental caries, as shown below. Caries is defined here as a minimum of four decayed, missing or filled teeth.

Age of mother (in yrs)	Age of child (months)					
	< 36		36-47		≥ 48	
	Caries	Control	Car.	Contr.	Car.	Contr.
< 25	1	1	1	5	8	9
25-34	4	16	18	67	46	113
≥ 35	1	2	3	14	10	35

Task: Calculate the *crude* and *Mantel-Haenszel* odds ratio for caries of the child using a suitable reference group! Which age-variable is considered to be the confounder here?