

Meeting 8: Observation studies 1

Reading

- Cameron A (1999) Survey Toolbox, available from [http://www.ausvet.com.au/resources/LiveToolbox\(en\).pdf](http://www.ausvet.com.au/resources/LiveToolbox(en).pdf) Part 1 Chapter 2 'General Principles of Animal Disease Surveillance' pp 11-36, Part II 'Survey design and analysis' Chapters 7,8,9 pp 143-189.
- Thrusfield 2nd Edn pp 221-224 or 3rd Edn pp 266-288 (Observational Studies).
- Thrusfield 2nd Edn pp 178-191 or 3rd Edn pp 228-246 (Surveys)
- Dohoo Chapter 7 'Introduction to observational studies' pp 139-146
- Baldock FC. (1998) What constitutes freedom from disease in livestock? AVJ 76: 544-545.

Presentations

1. Types of observational studies (including strengths and weaknesses)
2. Discuss the circumstances when a cross sectional study is most appropriate, the key design features and the statistics that can be calculated.
3. 'Is Vitamin D intake associated with the risk of Multiple Sclerosis?'. One member of the group should **briefly** research MS – occurrence, hypothesised risk factors etc and bring their findings to the session (5 minutes worth). At the meeting members of the group allocate themselves to different study types (cross-sectional, case-control, cohort and intervention/clinical trial) and discuss how they would conduct a trial examining this question using their nominated design. The design should include exposure and outcome and concentrate on the strengths and weaknesses of their study type.

Exercises

1. Work two (or more) of the example examination questions below.
2. Select two (or more) of the following papers
 - Schouten J et al (2004) Prevalence estimation and risk factors for Escherichia coli O157 on Dutch dairy farms. Prev Vet Med 64:49 - 61.
 - Jackson R et al (2004) Survey of the seroprevalence of brucellosis in ruminants in Kosovo. Veterinary Record 154(24):747 - 751.
 - Cole FL et al. (2004) Prevalence and demographic characteristics of exertional rhabdomyolysis in horses in Australia. Veterinary Record 155: 625-630.
 - Garner MG et al. (1997) A national serological survey to verify Australia's freedom from porcine reproductive and respiratory syndrome. AVJ 75: 596-600.
 - Small L and Pinch DS. (2003) Survey for hydatidosis in cattle bred in the northern region of the Northern Territory of Australia. AVJ 81: 355-358.

Discuss the design and conduct of these studies

Example examination questions

1. Describe the circumstances where collection of data on disease occurrence from an abattoir would be appropriate. What are the limitations of this method? (2005 oral)
2. Write brief notes on selection of subjects for a cross sectional study (2005 written)
3. *Babesia gibsoni* has recently been found in Pit Bull terriers in Victoria. However little is known about its distribution or prevalence in Australia. You have been asked to design a study to identify the prevalence of *Babesia gibsoni* in the Australian dog population.

What type of study would you use and what are the strengths and weaknesses of your chosen study design? Describe the study design, including study objectives, hypothesis, unit of interest, reference and study populations.

What sampling methods would you use and how would you select your sample size?

Discuss possible means of data collection and the advantages and disadvantages of alternative sources of data.

Describe any potential biases and how you may control these.

Discuss how you would analyse and interpret the results.(2003 written)

4. Canine coronavirus is becoming an agent of concern to small animal practitioners. In particular there is some controversy regarding the prevalence of seropositive dogs and the role that the virus may play in canine gastroenteritis. As a consultant epidemiologist you have been asked to design and carry out a cross-sectional study to investigate these problems. Describe how you would proceed with planning the study, including discussion of important factors affecting study design. (2002 written)
5. *Salmonella enteritidis* (SE) is a common cause of food poisoning in many countries, with the main source of infection being raw or partly cooked eggs and egg products. For example human illness from SE positive eggs in the United States is now approximately 637 000 cases per year. SE in chickens causes a silent systemic infection that can be detected by both bacteriological and serological techniques. Prevalence of infection in naturally infected commercial layers has been found to be very low.

The Australian and New Zealand egg industries are thought to be free of SE infection and relatively few human cases occur in either country compared to overseas. No human cases of SE due to consumption of Australian or New Zealand eggs have been reported. You have been engaged by the egg industry in your country (Australia or New Zealand) to plan an epidemiological study to demonstrate freedom from SE. Describe how you would proceed with this project and discuss the key issues affecting study design.

6. A pharmaceutical company has commissioned you as an epidemiologist to identify the major health issues associated with pet dogs in NZ/Australia to help them review the direction of the R & D program. You have one year in which to complete the project and a generous, although not unlimited budget available to you.

Describe how you would go about fulfilling this task, giving details of:

- a. The different sources of information on dog health that you might use (25%)
- b. The way in which you would collect data from these sources (50%)

- c. The strengths and weaknesses of each with respect to data quality and ease with which the information can be collected (25%)
7. Infectious bovine rhinotracheitis (IBR) is a viral infection of cattle that is endemic in Australian herds. The virus occurs worldwide, but strains overseas appear to be more pathogenic and have been subject to eradication programs in some countries. Although we now that IBR occurs in Australia, and that Australian strains are less pathogenic than overseas strains, we know very little about the prevalence or distribution. You have been asked to design a survey to estimate the prevalence of IBR infected herds in the country. Describe how you would proceed with designing such a survey and discuss factors that influence your decisions at each major step of the design.

Additional reading/resources

- Epidemiological Skills in Animal Health, PGFVS Proceedings 143; pp 39-47 (Investigation methods), pp 49-55 (surveys), pp 57-64 (observational studies and measures of association) pp 111-119 (monitoring), pp 151-158 (survey design), pp 337-351 (using existing data sources), pp 353-361 (monitoring and surveillance).
- East IJ et al (2004) Survey for the presence of White Spot Syndrome Virus in Australian crustaceans. AVJ 82:4, 236-239.
- Black PF et al (2001) Serological examination for evidence of infection with Hendra and Nipah viruses in Queensland piggeries. AVJ 79:6, 424-426.

Meeting 9: Observational studies 2

Reading

- Dohoo Chapter 8 'Cohort Studies', pp 151-162, Chapter 9 'Case-Control Studies', pp 163-175 and Chapter 10 'Hybrid Study Designs' pp 177-184.
- Thrusfield, 2nd Edn, pp 220-223 or 3rd Edn, pp 266-269 (Observational studies)
- Stevenson MA (2005). Introduction to Veterinary Epidemiology: 227.407 Study Guide. Massey University, Palmerston North, New Zealand. pp 24 – 32.
- Schlesselman, J., 1982, Case-Control Studies Design, Conduct, Analysis. Oxford University Press, New York.

Presentations

1. Advantages and disadvantages of case-control studies.
2. Advantages and disadvantages of retrospective and prospective cohort studies.
3. Hybrid study designs (for example, nested case-control studies).

Exercises

Critically appraise a selection of the following papers. What are the positive and negative features of the study design used in each study?

- Chesterton, R., Pfeiffer, D., Morris, R., Tanner, C. (1989) Environmental and behavioural factors affecting the prevalence of foot lameness in New Zealand dairy herds - a case-control study. *NZ Vet J* 37: 135 - 142.
- Johansen C, Boise J, McLaughlin J, Olsen J (2001). Cellular telephones and cancer --- a nationwide cohort study in Denmark. *Journal of the National Cancer Institute*, 93: 203 - 237.
- Muscat JE, Malkin MG, Thompson S, Shore RE, Stellman SD, McRee D et al. (2000). Handheld cellular telephone use and risk of brain cancer. *Journal of the American Medical Association*, 284: 3001 - 3007.
- Parsonnet J, Friedman GD, Vandersteen DP, Chang Y, Vogelmann JH, Orentreich N, Sibley RK (1991). *Helicobacter pylori* infection and the risk of gastric-carcinoma. *New England Journal of Medicine*, 325(16): 1127 - 1131.
- Neilen M (1989) Twinning in dairy cattle: a study of risk factors and effects. *Theriogenology* 32(5):845-861.
- Steenholdt C and Hernandez J (2004) Risk factors for umbilical hernia in Holstein heifers during the first two months after birth. *JAVMA* 224(9):1487-1490.
- Wilesmith JW et al (1997) A cohort study to examine maternally associated risk factors for bovine spongiform encephalopathy. *Veterinary Record*, 141: 239-243.
- Healy AM et al (2004) A paired case-control study of risk factors for scrapie in Irish sheep flocks. *Prev Vet Med* 64: 73-83.

Example examination questions

1. Write brief notes to demonstrate your understanding of case-control studies (2001 written).
2. A veterinary practitioner asks you for epidemiological advice about an apparent problem amongst Huntaway dogs (a breed of sheep dog). On the basis of dogs presented to his clinic the practitioner suspects that Huntaways have a higher incidence of hip dysplasia (HD). This concern is of some importance as many sheep dogs in New Zealand are Huntaways. How would you advise this veterinarian to go about determining if Huntaways are, in fact, at greater risk than other breeds of dog of being affected by HD? (2000 written)
3. Crohn's disease is a disease of humans with many similarities to Johne's disease in ruminants. It is a chronic inflammatory condition of the intestines that is histologically similar to Johne's disease. Mycobacterium paratuberculosis has also been isolated from some cases of Crohn's disease, but this is not a consistent finding. There is increasing concern that exposure to M. paratuberculosis is a cause of Crohn's disease, but existing evidence for causality is limited. There is particular concern about risks to people exposed to dairy cattle infected with M. paratuberculosis.

You are part of a research team of epidemiologists which has been asked to investigate this issue on an epidemiological, rather than bacteriological basis, focussing on risks to people exposed to infected dairy cattle. You have reasonable resources at your disposal. Describe how you would proceed (1999 written)

Additional reading/resources

Kelsey, J., Thompson, W., Evans, A., (1986). *Methods in Observational Epidemiology*. Oxford University Press, New York. pp 77 – 147 and pp 148 – 186.

Meeting 10: Intervention studies

Reading

- Dohoo Chapter 11 (controlled trials) Chapter 2 (sampling, sample size)
- Thrusfield 2nd Edn or 3rd Edn, Chapter 16 (clinical trials)
- Committee for Proprietary Medicinal Products (CPMP). 2000. Points to consider on switching between superiority and non-inferiority. Available: <http://www.emea.eu.int/pdfs/human/ewp/048299en.pdf>
- CONSORT statement: Revised recommendations for improving the quality of reports of parallel group randomised trials 2001. Available: <http://www.consort-statement.org/Statement/revisedstatement.htm>

Presentations

1. Key considerations in designing an intervention study
2. Outcome measures: compare non-inferiority, superiority and equivalence trials; discuss power, p-values and confidence intervals when interpreting results.
3. Vaccine trials: vaccine efficacy, herd immunity, unit of interest, atomistic and ecological fallacies
4. Control of biases (randomisation, blinding)

Exercises

1. Read and assess the following papers (or any other recent papers you may find). You can use the CONSORT checklist to help with this:
 - Dias PT, Alders RG, Fringe R and Mata BV. Laboratory and Field Trials with Thermostable Live Newcastle Disease Vaccines in Mozambique. Available: [http://www.aciar.gov.au/web.nsf/att/JFRN-6BN93R/\\$file/pr103chapter19.pdf](http://www.aciar.gov.au/web.nsf/att/JFRN-6BN93R/$file/pr103chapter19.pdf)
 - Cusack PMV (2004) Effect of mass medication with antibiotics at feedlot entry on the health and growth rate of cattle destined for the Australian domestic market. AVJ, 82:154-156.
 - Williamson JH, Woolford MW and Day AM (1995) The prophylactic effect of a dry-cow antibiotic against *Streptococcus uberis*. NZVJ, 43: 228-234.
 - Karpathy RC, Firth GA and Tannock GA (2003) Field evaluations of safety and efficacy of an Australian Marek's disease vaccine. AVJ 81: 222-225.
1. Work through as a group one of the following exam questions.

Example examination questions

1. A new genetically engineered vaccine has recently been developed for infectious bronchitis virus in poultry. This vaccine can be applied to individuals as day-old chicks or as a mass vaccination. It has undergone extensive laboratory evaluation and the developers are now ready to commence field trials under commercial conditions. You have been asked to design a field study to evaluate the efficacy of the vaccine in preventing mortalities and production losses in commercial broiler enterprises. Describe how you would proceed (2001 written).
2. A live avirulent *Toxoplasma* vaccine is very effective in preventing *Toxoplasma* abortions in sheep. *Toxoplasma gondii* is closely related to *Neospora caninum*, so it is possible that the live *Toxoplasma* vaccine would be efficacious against *Neospora* abortions in cattle. This hypothesis requires investigation and a field trial is desired. Describe how you could investigate the efficacy of the sheep *Toxoplasma* vaccine in preventing bovine *Neospora* abortions using a field trial approach (2000 written).
3. You are a consultant to a veterinary pharmaceutical company that is about to try and register a new product for the treatment of osteoarthritis in dogs. The new product is a different formulation of the same active ingredient as an existing product already on the market. Accordingly, the company wants registration on the basis that the two products are equally effective. A clinical trial is required and a number of veterinary practises in Australia are available to assist. Describe in detail the study or studies that you would recommend in this situation (1999 written).
4. Write brief notes, using examples, to demonstrate your understanding of matching in clinical trials (1995 written).

Additional reading/resources

- Jones B, Jarvis P, Lewis JA and Ebbutt AF (1996) Trials to assess equivalence: the importance of rigorous methods. *BMJ*, 313: 36-39 (Available by searching www.bmj.com/)
- Beller EM, GebSKI V and Keech AC (2002) Randomisation in clinical trials. *MJA*, 177: 565-567. Available: http://www.mja.com.au/public/issues/177_10_181102/bel10697_fm.html
- Altman DG and Bland JM (1995) Absence of evidence is not evidence of absence. *BMJ*, 311: 485. Available: <http://bmj.bmjournals.com/cgi/content/full/311/7003/485>
- Dohoo IR and Thomas FC (1989) Clinical trials in veterinary medicine *Can Vet J*, 30: 291-303.
- Baldock C (1991) New Approaches to disease investigation. An update on clinical trials. *Dairy Medicine and Production*, Proceedings 161, Postgraduate Committee in Veterinary Science, University of Sydney, p.423-437.
- Hedges J et al (2001) A longitudinal field trial of the effect of biotin on lameness in dairy cows. *J Dairy Science* 84:1969-1975.