

Interpretation and Validation of Diagnostic Tests in Veterinary Science

Background

This workshop builds on the pre-ISVEE XI workshop of the same name that was held in Cairns, Australia in 2006. Instructors were Ian Gardner, Nils Toft and Axel Colling. The 3-day workshop had 23 participants from Denmark, US, New Zealand, Mexico, Ireland, The Netherlands, Sweden and Australia. The Cairns workshop covered the basic principles of test validation and an introduction to latent class analysis.

This time the focus is on interpretation and validation of diagnostic tests in veterinary science. We will provide detailed coverage of validation alternatives in the absence of a perfect reference (gold) standard. In response to feedback from the 2006 course, participants will be given the opportunity for 'hands-on' analysis during afternoon practical sessions.

Course instructors

Mark Stevenson (The University of Melbourne), Simon Firestone (The University of Melbourne), Geoff Jones and Cord Heuer (Massey University), Ian Gardner (The University of Prince Edward Island) and Axel Colling (The Australian Animal Health Laboratory/CSIRO). All instructors are members of the OIE Collaborating Center in Test Validation Science for the Asia-Pacific region.

Course topics

- Epidemiological and statistical issues related to validation of tests;
- Application of tests for screening, diagnosis and surveillance including use of multiple tests;
- Validation strategies that consider individual animal and herd diagnosis, allowing for the presence or absence of a perfect reference (gold) standard including hands-on methodology of latent class test evaluation when a gold standard is not available; and
- Principles of quality control and quality assurance to monitor assay validity including aspects of measurement uncertainty.

Learning outcomes:

At the end of the workshop, participants will be able to:

1. Define accuracy and precision as they relate to diagnostic tests.
2. Interpret measures of precision for quantitative test results, calculate and interpret kappa for categorical test results.
3. Estimate diagnostic sensitivity and specificity (and their confidence intervals) based on all members or subsets of a defined study population.
4. Determine the sample size to estimate sensitivity and specificity for confidence intervals of predefined width.
5. Define predictive values and describe the factors that influence them.
6. Know how to use and interpret multiple test results in series or parallel.
7. Define and explain the impact of correlated test results (e.g. tests that are not conditionally independent) on diagnostic test interpretation.
8. Know how to select an appropriate cut-off for declaring a test result positive.
9. Understand the principles to estimate sensitivity and specificity when no perfect reference (gold) standard exists.

10. Describe the key principles of latent class analysis, when one is asked to provide an estimate of diagnostic sensitivity and specificity in the absence of a gold standard and perform a latent class evaluation of diagnostic tests using OpenBUGS software.
11. Understand the key principles to be considered when asked to plan verification experiments and comparison studies after a diagnostic test has been changed.
12. Understand and describe the selection and analysis of samples for internal and external quality control purposes.
13. Understand and apply principles of measurement uncertainty in veterinary diagnostic validation science.

Background and skills of participants

The target audience for this workshop is epidemiologists, science researchers, laboratory diagnosticians, and other interested laboratory diagnostic scientists who develop, validate and apply diagnostic tests for different purposes and epidemiological settings. Postgraduate training in quantitative epidemiology or a related discipline is desirable, but not essential.

Workshop participants are requested to use their own laptops.

Software

Medcalc (<https://www.medcalc.org/>): ROC curves, likelihood ratios, and other calculations when there is a perfect reference standard.

OpenBUGs (<http://www.openbugs.net/w/FrontPage>): Bayesian modeling of sensitivity and specificity in the absence of a perfect reference standard.

R (<https://www.r-project.org/>) driven by RStudio (<https://www.rstudio.com/>): R code will be made available for most calculations and examples, with RShiny online tools available for some of the basics (see <http://fvas.unimelb.edu.au/research/projects/veterinary-epidemiology-melbourne/resources>). Those unfamiliar with R but wishing to make most use of this should complete the tutorial R for Reproducible Scientific Analyses (<http://swcarpentry.github.io/r-novice-gapminder/>).

Outlook

A follow-up workshop on use of Bayesian latent class models for prevalence estimation, hierarchical models for estimation of sensitivity and specificity, ROC curves for continuous test results and logistic regression modeling where outcomes are measured by imperfect tests is in the planning phase and will be offered in Victoria, Australia in 2019.

Contact information

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Program

Day 1

Time	Instructor	Format	Details
0830 - 0900			Registration.
0900 - 0945	IG/MS/CH/AC	Lecture	Diagnostic tests --- background and motivating examples.
0945 - 1030	MS/AC/SF	Lecture	Quantifying diagnostic test performance 1 (Se, Sp, PPV, NPV).
1030 - 1100			Morning tea.
1100 - 1200	MS/SF	Lecture	Quantifying diagnostic test performance 2 (likelihood ratios).
1200 - 1300			Lunch.
1300 - 1430	IG/SF	Practical	Quantifying diagnostic test performance 1 (MedCalc hands-on).
1430 - 1500			Afternoon tea.
1500 - 1600	AC/SF	Practical	Verification and comparison of diagnostic tests/ Use of quality control samples and Measurement Uncertainty (MU) with practical examples.

Day 2

Time	Instructor	Format	Details
0900 - 0945	IG	Lecture	Critical appraisal of papers that assess diagnostic test performance.
0945 - 1030	MS/CH	Lecture	Multiple test strategies.
1030 - 1100			Morning tea.
1100 - 1200	MS/CH	Lecture	Apparent prevalence and true prevalence.
1200 - 1300			Lunch.
1300 - 1430	MS/CH	Practical	Multiple test strategies
1430 - 1500			Afternoon tea.
1500 - 1600	MS/CH	Practical	Apparent prevalence and true prevalence.

Day 3

Time	Instructor	Format	Details
0900 – 0945	IG	Lecture	Estimation of diagnostic Se and Sp in the absence of a gold standard 1.
0945 – 1030	GJ	Lecture	Estimation of diagnostic Se and Sp in the absence of a gold standard 2.
1030 – 1100			Morning tea.
1100 – 1200	GJ	Lecture	Estimation of diagnostic Se and Sp in the absence of a gold standard 3.
1200 – 1300			Lunch.
1300 – 1430	GJ/SF	Practical	Latent class analysis 1 (OpenBugs hands-on).
1430 – 1500			Afternoon tea.
1500 – 1600	GJ/SF	Practical	Latent class analysis 2 (OpenBugs hands-on).

Mark Stevenson

Qualifications: BVSc (Syd), MVSc (Syd), PhD (Massey), MANZCVSc (Dairy Cattle Medicine)

Positions held: 2014 to present: Professor, Veterinary Epidemiology (One Health), Faculty of Veterinary and Agriculture Science (FVAS), University of Melbourne

2007 to 2014: Associate Professor, Veterinary Epidemiology, Massey University

2002 to 2007: Senior Lecturer, Veterinary Epidemiology, Massey University

1998 to 2002: PhD student, Massey University

1995 to 1998: Lecturer, Dairy Cattle and Swine Health, Massey University

1986 to 1995: Private veterinary practice, New South Wales, Australia

Expertise: Biostatistics and epidemiological research design. Quantitative epidemiology and infectious disease modelling. Applied (field) epidemiology – outbreak investigation, surveillance and response.

Teaching and capacity development in epidemiology, biostatistics, outbreak investigation and response and emergency management. Spatial epidemiology. Development of veterinary services and public health capacity in developing countries.

Simon Firestone

Qualifications: BVSc (Melb), MAppEpi (ANU), PhD (Syd), MANZCVSc (Epidemiology)

Positions held: 2015 to present: Senior Lecturer in Veterinary Epidemiology and Public Health, FVAS University of Melbourne

2011 to 2015: Lecturer in Veterinary Epidemiology and Public Health, FVAS

2009 to 2012: PhD student, University of Sydney

2008: Regional Coordinator South-East Asia, Veterinaires sans Frontieres Canada

2006 to 2007: Short-term Professional Epidemiologist, WHO Cambodia and Indonesia

Country Offices, Communicable Disease Surveillance and Response

2004 to 2006: Masters student, Australian National University

2001 to 2004: Veterinarian, mixed practice in Australia, the United Kingdom and Thailand

Expertise: Bayesian latent class modelling for diagnostic test evaluation. Quantitative epidemiology and infectious disease modelling. Applied (field) epidemiology outbreak investigation, surveillance and response. Teaching and capacity development in epidemiology, biostatistics, outbreak investigation and response and emergency management. Development of veterinary services and public health capacity in developing countries.

Ian Gardner

Qualifications: BVSc (Syd), MPVM (UC Davis), PhD (UC Davis)

Positions held: 2011 to present Professor of Epidemiology and Canada Excellence Research Chair (Aquatic Epidemiology), University of Prince Edward Island (UPEI), Canada

1998 to 2011 Professor of Epidemiology, University of California, Davis (UCD)

1994 to 1998 Associate Professor, Epidemiology and Animal Health Management (UCD)

1988 to 1993 Assistant Professor, Epidemiology and Animal Health Management (UCD)

1987 to 1988 Special Veterinary Officer (Pig Health), Department of Agriculture, Orange, New South Wales, Australia.

1975 to 1985 Veterinary Officer, Department of Agriculture, Orange, NSW

Expertise: Surveillance, aquatic and terrestrial epidemiology, aquatic disease control and prevention, farmed and wild fish populations. Developing methods to assess disease risk in terrestrial and aquatic food animals. These methods have been used in global veterinary and public health activities, and have influenced policies at the United States Department of Agriculture and the World Organisation for Animal Health. “Most cited researcher” with more than 300 peer-reviewed scientific publications in leading journals, such as *Preventive Veterinary Medicine*, *American Veterinary Medical Association*, and *Veterinary Pathology*.

Geoff Jones

Qualifications: BA (Oxf), PGCE (Exe), MSc (Sheffield), PhD (Calif. Davis)

Positions held: 2011 to present: Associate Professor, Statistics, Massey University

2000 to 2010 Senior Lecturer, Statistics, Massey University
1997 to 2000 Lecturer, Statistics, Massey University
1996 to 1997 Postdoctoral Researcher, University of California, Davis, USA
1993 to 1996 Research Assistant, University of California, Davis, USA
1991 to 1993 Senior Lecturer, Statistics, University of the West of England, Bristol, UK
1988 to 1990 Tutor in Quantitative Methods, MARA College of Higher Education, Seremban, Malaysia
1986 to 1988 Lecturer in Statistics, MARA Junior Science College, Seremban, Malaysia
Expertise: Modelling and analysis of diagnostic test data. Bayesian applications in epidemiology.
Fellow of the Royal Statistical Society, 1991. Member, American Statistical Association, 1996.

Cord Heuer

Qualifications: BVM (Hannover), Dr. med. vet. (Hannover), MSc (Guelph), PhD (Utrecht)

Positions held:

2013 to present: Professor, Veterinary Epidemiology, Massey University
2005 to 2013: Associate Professor, Veterinary Epidemiology, Massey University
2001 to 2005: Senior Lecturer, Veterinary Epidemiology, Massey University
1996 to 2001: Short term consultant for overseas development (Kenya, Pakistan)
1992 to 1996: Short term consultant for overseas development (Mongolia, Thailand, Pakistan, Syria, Kenya, Uganda, Malawi)
1988 to 1990: Team Leader of the Central Rangelands Development Project Veterinary Component (GTZ, Somalia)
1986 to 1987: Project Desk Officer at GTZ: Technical, financial and administrative services for livestock projects.
1981 to 1985: Technical Advisor to the Department of Livestock Production and Artificial Insemination, Government of Punjab (Lahore, Pakistan)
1978: Private veterinary practice, Germany
Expertise: Epidemiological methods and application to animal health research with a special interest in ruminant research (sheep pneumonia, cattle reproduction, mastitis, lameness), public health, mathematical modelling of infectious disease and related pathogens (*Mycobacterium avium* ss. paratuberculosis, bovine virus diarrhoea, *C. fetus* subsp. *venerealis*, *Leptospira* spp., *Neospora caninum*). Leading research programmes in John's disease, human and animal leptospirosis and bovine viral diarrhoea.

Axel Colling

Qualifications: BVSc (Ludwig-Maximilian University, LMU), Dr.med.vet. (LMU)

Positions held: 2003 to present: Diagnostic Veterinary Scientist, Australian Animal Health Laboratory (AAHL), CSIRO

1997 to 2002: External Quality Assurance Co-ordinator, FAO/IAEA Seibersdorf Laboratories
1995 to 1997: Technical Officer, Joint FAO/IAEA Division, Vienna, Austria
1993 to 1994: Consultant for Joint FAO/IAEA Division Trypanosomosis control project (Tanzania/Zanzibar) and Rinderpest (Sudan) project; German Development Service (DED): Rinderpest eradication campaign, Sudan; German Agency for Technical Cooperation (GTZ), Trypanosomosis control project, Cote d'Ivoire.
1990 to 1993: Veterinarian, Private Practice, Bad Honnef, Germany.

Expertise: Development and validation of diagnostic tests for infectious animal diseases when samples from infected animals are scarce. Development of standards and templates of practical use for test validation, certification and registration for national and international regulatory bodies. Application and extension of validation parameters and methods for new test platforms and reagents such as Next Generation Sequencing and Multiplex technologies and for zoonotic emerging pathogens in humans and animals. Use of internal and external quality control to establish quality systems based on ISO 17025 and laboratory accreditation.