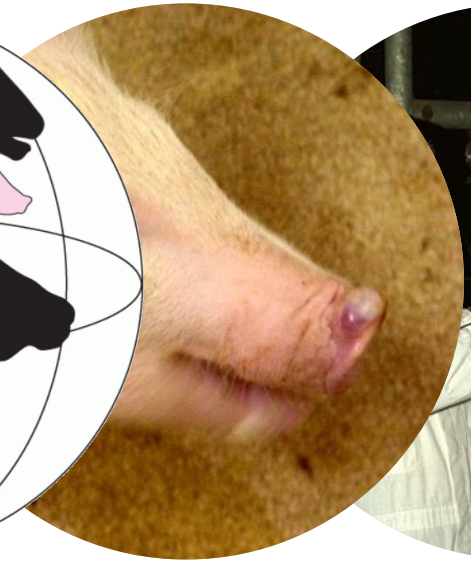
VALIDATION OF SEROLOGICAL POTENCY ESTIMATION

better estimate using continuous than dichotomised data

A. Dekker



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Type A good protection even wit… r-value or high genetic dist… red)

Why estimate homologous potency

- Main research questions:
  - is r_1-value a good predictor of the ratio between heterologous and homologous potency?
  - Are other parameter better?
- Test heterologous potency and estimate homologous
- Validation of various methods
  - Using outcome of the experiment
    - Spearmann Kaerber
    - Logistic regression
  - Estimating protection (continuous and binary)
    - Antibody titre and strain
    - Antibody titre, antigen content and dose

Data challenge experiments in Lelystad

- 447 vaccinated and challenged cattle
- 61 FMD vaccine batches
  - 16 full potency tests
- 9 different strains
  - 6 strains in full potency tests
- 3 serotypes
  - A, O and Asia1

Models to estimate protection

- Protection ~ Antibody titre + Strain

- Protection ~

  Antibody titre + Strain + Antigen concentration + Dose

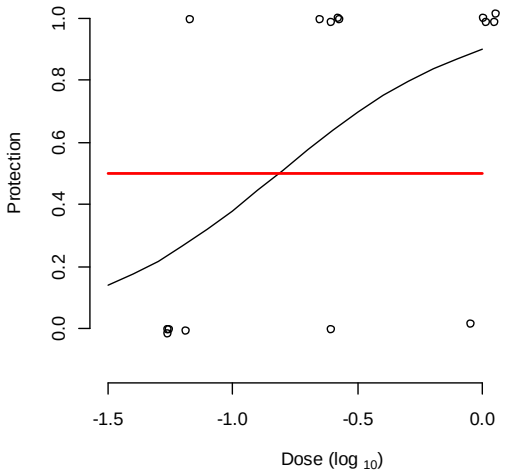
- Outcome a continuous variable between 0 and 1
- Dichotomised <0.5 not protected, ≥0.5 protected

Potency calculation

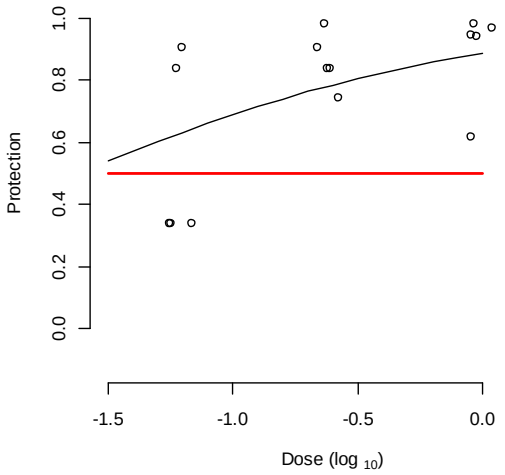
- Using outcome of the experiment
  - Spearmann Kaerber
  - Logistic regression
- Using continuous protection estimate
  - Ab + strain
  - Ab + strain + Ag + dose
- Using dichotomised protection estimate
  - Ab + strain
  - Ab + strain + Ag + dose

Example of the outcome

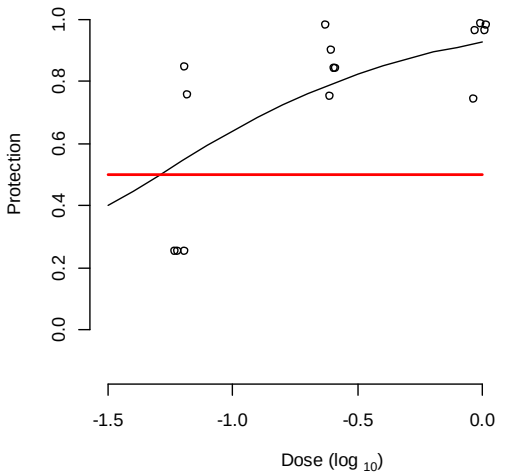
Standard logit model



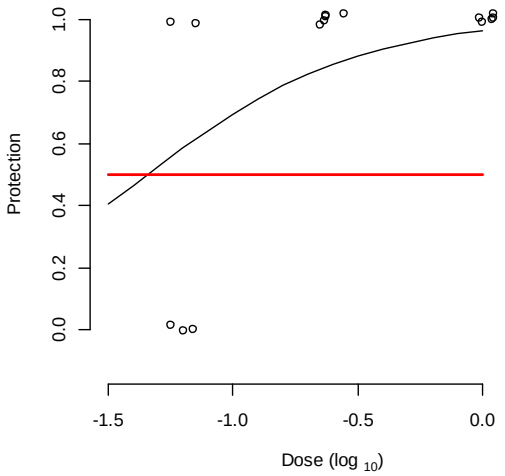
Predicted protection based on Ab



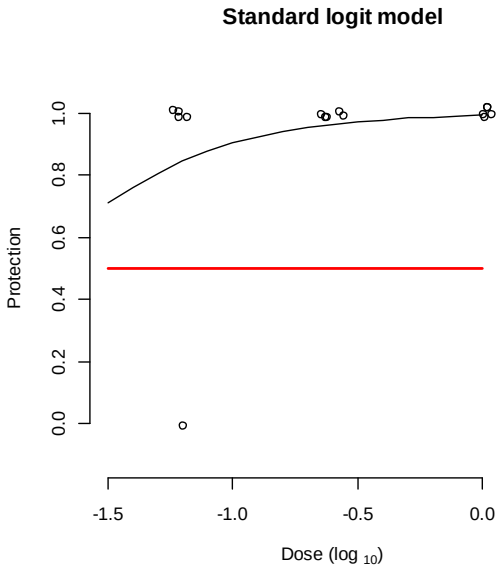
Predicted protection based on Ab, Ag and dose

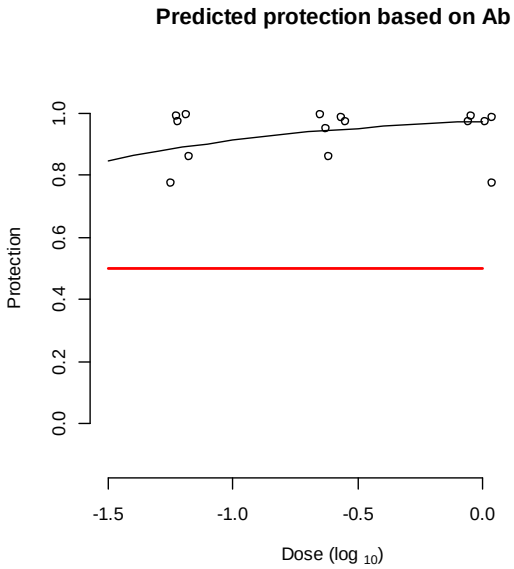


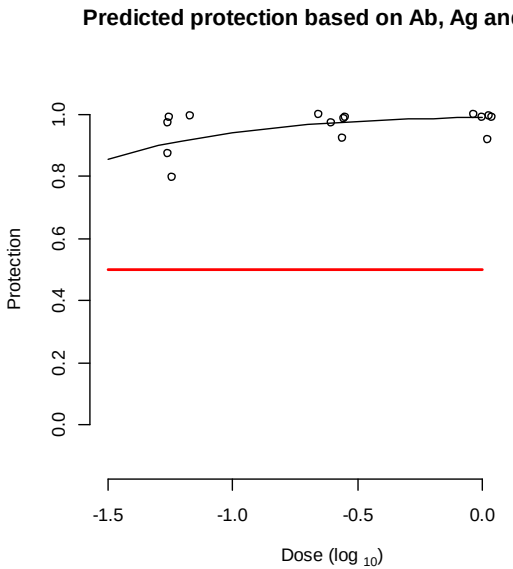
Predicted protection based on dichotomized Ab

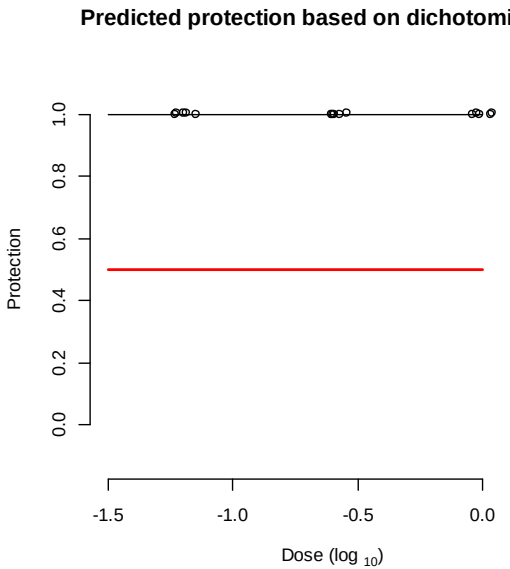


2nd example of the outcome









Correlation between outcomes

	SK	Logit	Ab	Ab,Ag,Dose	Ab dic	Ab,Ag,Dose dic
SK	1.00	0.96	0.47	0.48	0.36	0.36
Logit	0.96	1.00	0.49	0.51	0.30	0.30
Ab	0.47	0.49	1.00	0.99	0.78	0.78
Ab,Ag,Dose	0.48	0.51	0.99	1.00	0.72	0.72
Ab dic	0.36	0.30	0.78	0.72	1.00	1.00
Ab,Ag,Dose	0.36	0.30	0.78	0.72	1.00	1.00

- High correlation between methods using similar result variables
- Higher correlation between observed protection and estimate on a continuous scale

Estimates of the potency

- Potency estimates (PD_{50}/dose) of the 16 batches

	SK	Logit	Ab	Ab, Ag, Dose	Ab dic	Ab, Ag, Dose dic
Min.	2	3	17	14	7	9
1st Qu.	8	18	31	20	26	21
Median	**9**	**23**	**76**	**27**	**44**	**27**
Mean	12	47	203	69	115017443	187495
3rd Qu.	18	66	145	44	168	76
Max	24	137	1453	525	613426119	999836

Inherent variation in potency tests

- Coda tested 10 times the same vaccine
  - 4.6 to 24 PD_{50}/dose

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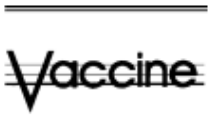
Available online at www.sciencedirect.com
ScienceDirect
Vaccine 25 (2007) 3373–3379



www.elsevier.com/locate/vaccine

European Pharmacopoeia foot-and-mouth disease vaccine potency testing in cattle: Between test variability and its consequences

N. Goris[a,*], P. Merkelbach-Peters[b], V.I. Diev[c], D. Verloo[d], V.M. Zakharov[c], H.-P. Kraft[b], K. De Clercq[a]

- 100 simulations 2 – 24 PD_{50}/dose

10 simulations	
	13.93
	8.00
	18.38
	6.06
	10.56
	13.93
	13.93
	10.56
	18.38
	6.06
Min	6.06
Max	18.38

Conclusion

- Antibody response can be used to predict protection
- Continuous predictions correlate better with observed protection and less extremes
- Estimates using vaccine dose and antigen content provide better estimates, but are often unknown
- International standardisation for relation antibody response and protection is necessary

- Is the challenge result the true gold standard? Variation in dichotomised data

Thank you for your attention

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