

VALIDATION OF SEROLOGICAL POTENCY ESTIMATION

better estimate using continuous than dichotomised data

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Type A good protection even with low value or high genetic diversity (red)

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High potency heterologous challenge virus
K.E. Brehm^a, N. Kumar^a, H. ...

Comparison of immune responses after intra-typic heterologous and homologous vaccination against foot-and-mouth disease virus infection in ...
P.L. Eblé^{a,*}, M.G.M. de Bruijn^a, F. van Hemert-Kl...
Contents lists available at ScienceDirect
Vaccine
journal homepage: www.elsevier.com/locate/vaccine

Vaccination against foot and mouth virus transmission in groups of ...
K. Orsel^{a,*}, A. Dekker^b, A. Bouma^a, J.A. Stegeman^a, ...

Efficacy of a high potency O₁ Manisa foot-and-mouth disease vaccine in cattle against heterologous challenge with a field virus from the O/ME-SA/Ind-2001 lineage collected in North Africa
Emma Fishbourne^a, Anna B. Ludi^{a,*}, Ginette Wilsden^a, Pip Hamblin^a, Bob Statham^a, Abdelghani Bin-Tarbiliana Brocchi^b, Santina Grazioli^b, Aldo Dekker^c, Phaedra Eblé^c, Donald P. King^a

< PD₅₀

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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
 - Spearman 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

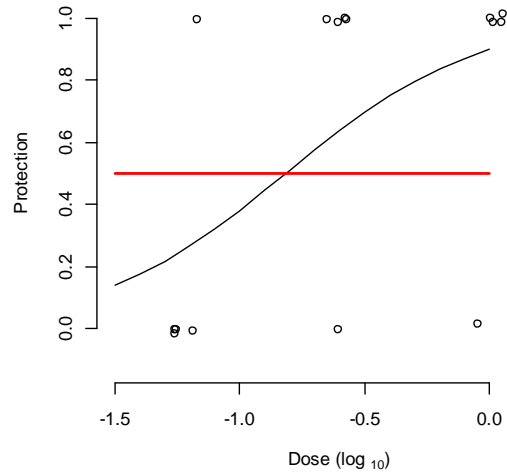
- Protection \sim Antibody titre + Strain
- Protection \sim
Antibody titre + Strain + Antigen concentration + Dose
- Outcome a continuous variable between 0 and 1
- Dichotomised <0.5 not protected, ≥ 0.5 protected

Potency calculation

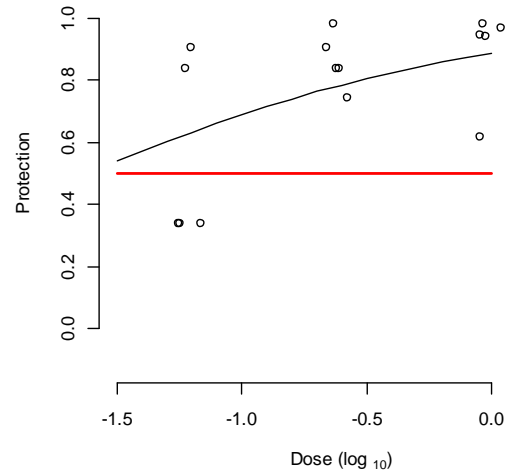
- Using outcome of the experiment
 - Spearman Kaerber
 - Logistic regression
- Using continuous protection estimate
 - Ab + strain
 - Ab + strain + Ag + dose
- Using dichotomised protection estimate
 - Ab + strain
 - Ab + strain + Ag + dose

Example of the outcome

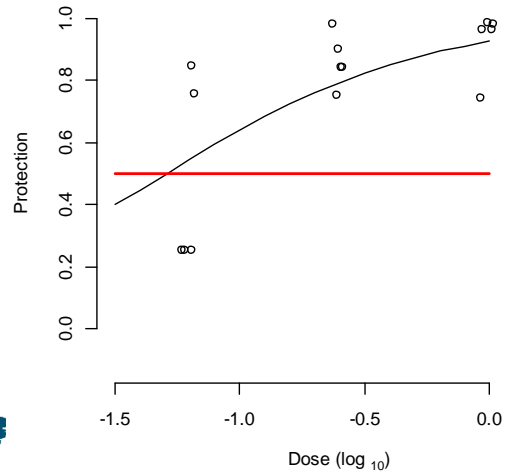
Standard logit model



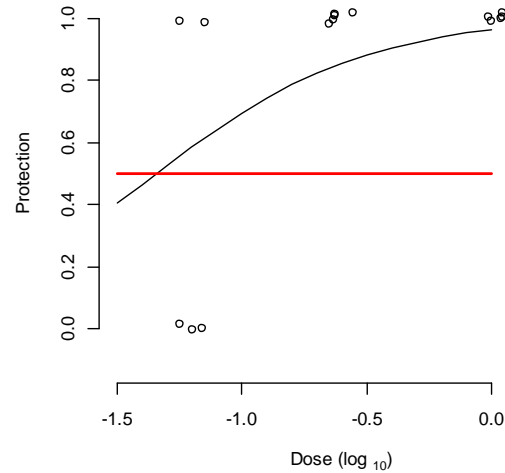
Predicted protection based on Ab



Predicted protection based on Ab, Ag and dose

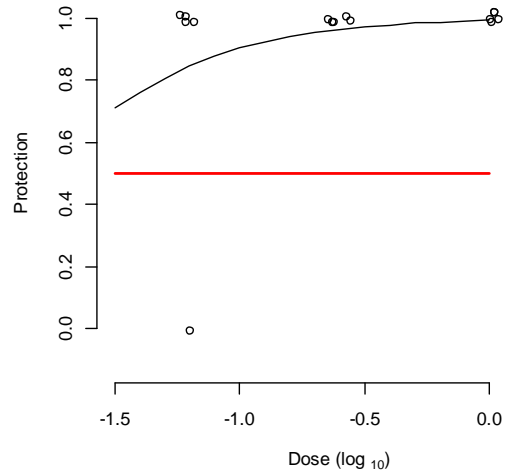


Predicted protection based on dichotomized Ab

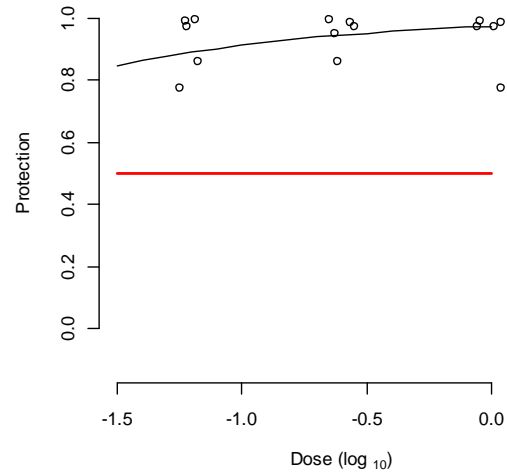


2nd example of the outcome

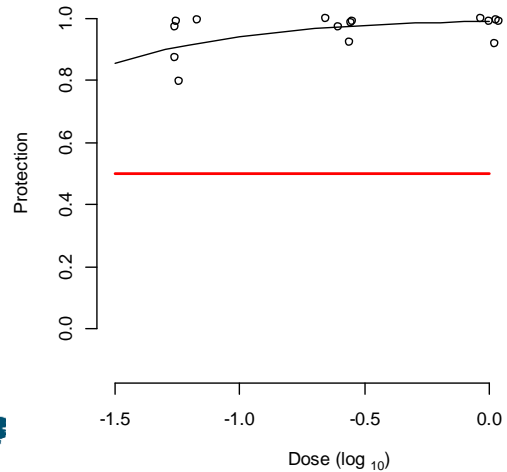
Standard logit model



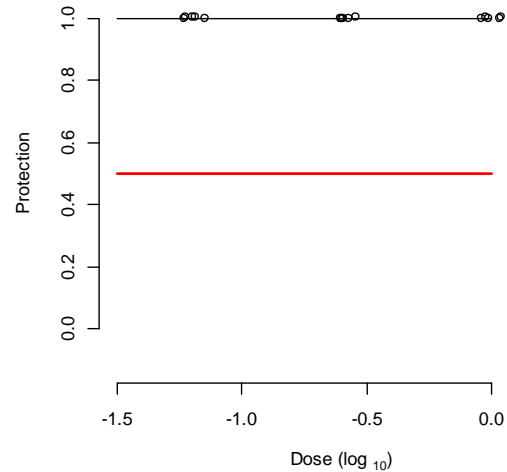
Predicted protection based on Ab



Predicted protection based on Ab, Ag and dose



Predicted protection based on dichotomized Ab



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 dic	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
1 st Qu.	8	18	31	20	26	21
Median	9	23	76	27	44	27
Mean	12	47	203	69	115017443	187495
3 rd 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 PD₅₀/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

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

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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