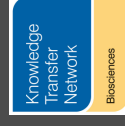


# Capturing variation in infectivity from binary disease data

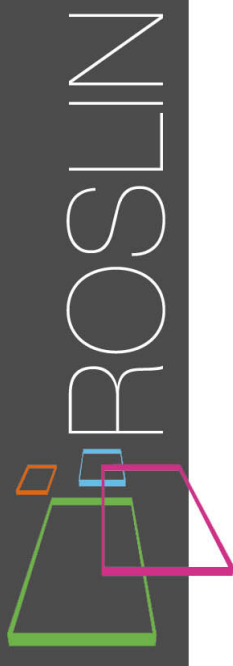
D. Lipschutz-Powell<sup>[1]</sup>, J.A. Woolliams<sup>[1]</sup>, P. Bijma<sup>[2]</sup> and A. Doeschl-Wilson<sup>[1]</sup>

<sup>[1]</sup> The Roslin Institute and Royal (Dick) School of Veterinary Studies, University of Edinburgh, Easter Bush, Midlothian EH25 9RG, UK

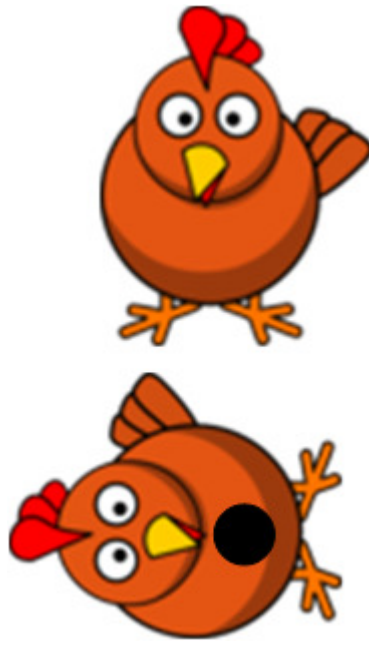
<sup>[2]</sup> Animal Breeding and Genomics Centre, Wageningen University, Wageningen, Netherlands



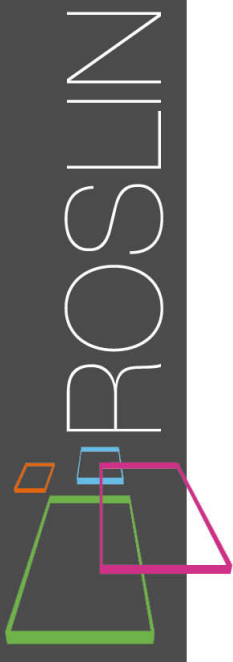
# Introduction



- Genetic analyses of disease data often show low heritabilities.
  - Caused by missing variation in infectivity?
- Infectivity = propensity of transmitting infection upon contact with a susceptible individual
- Evidence on impact of super-spreaders from e.g. SARS (Shen et al., 2004).
- Difficult to measure directly
- Observed in group-mates
- Infectivity is an associative effect.



# Associative effects



- Classically,  $P_i = A_i + E_i$  (Falconer and MacKay, 1996).
- Associative effect: phenotypes of other individuals which affect the analysed trait
- Part of associative effect may be additive genetic and therefore subject to selection.

$$\begin{aligned} P_i &= A_{D,i} + E_{D,i} + \sum_{j=1}^{n-1} P_{S,j} & j \neq i \\ &= A_{D,i} + E_{D,i} + \sum_{j=1}^{n-1} (A_{S,j} + E_{S,j}) \end{aligned} \quad (\text{Griffing, 1967})$$

# Associative effects



<b>Variance</b>	<b>Expected</b>	<b>Conventional</b>	<b>Associative</b>
Susceptibility	20.39	18.28	19.55
Infectivity	9.20	/	3.87

Values scaled by  $10^3$

(Lipschutz-Powell et al., Proc. WCGALP 2010 & under review)

- Developed for static traits

# Hypothesis



The accuracy and impact of an associative effects model, when used to analyse binary disease data, may be improved by extending it to allow for dynamics of disease.

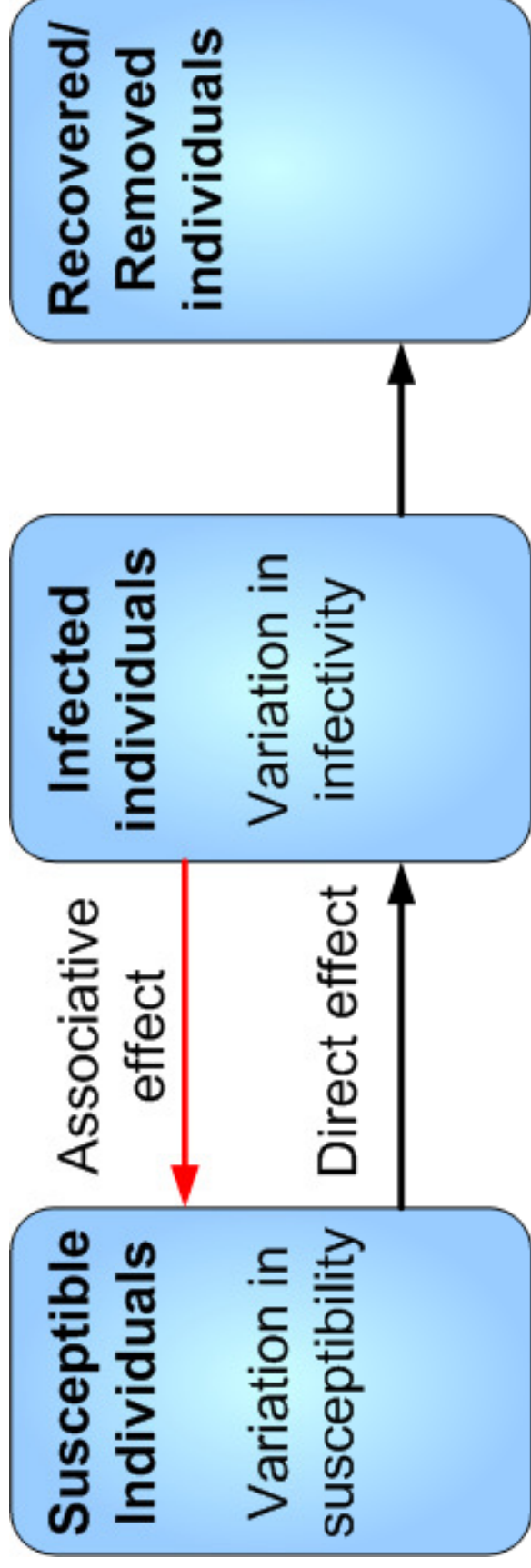


# Materials & Method

# Disease Data



Simulation of epidemic using a stochastic model



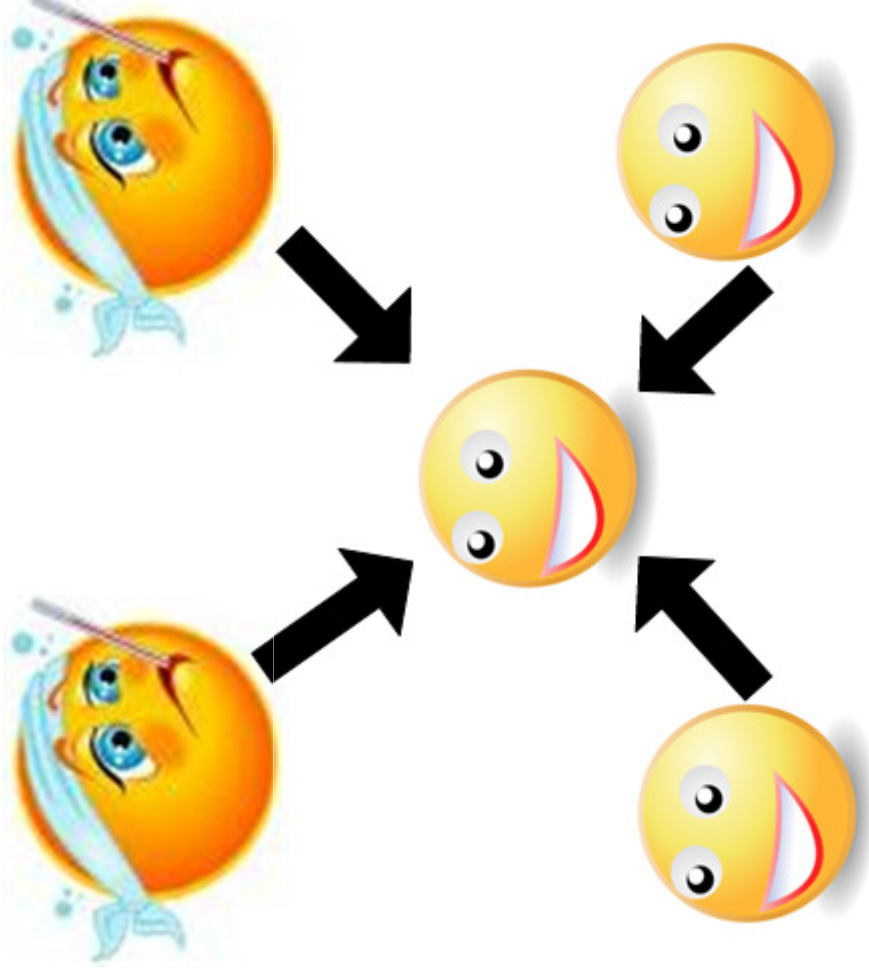
Assumed infectivity and susceptibility independent

# Method - Analyses



- All genetic analyses were carried out using ASReml (Gilmour 2006)

Standard model

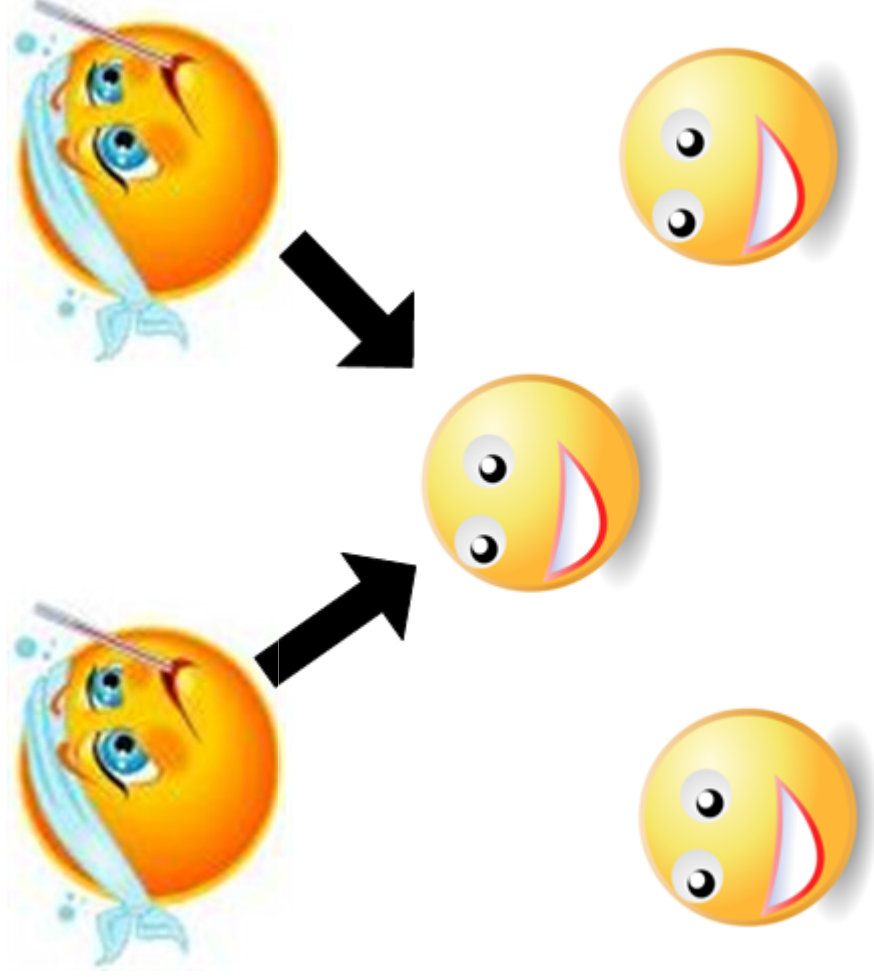




# Method - Analyses



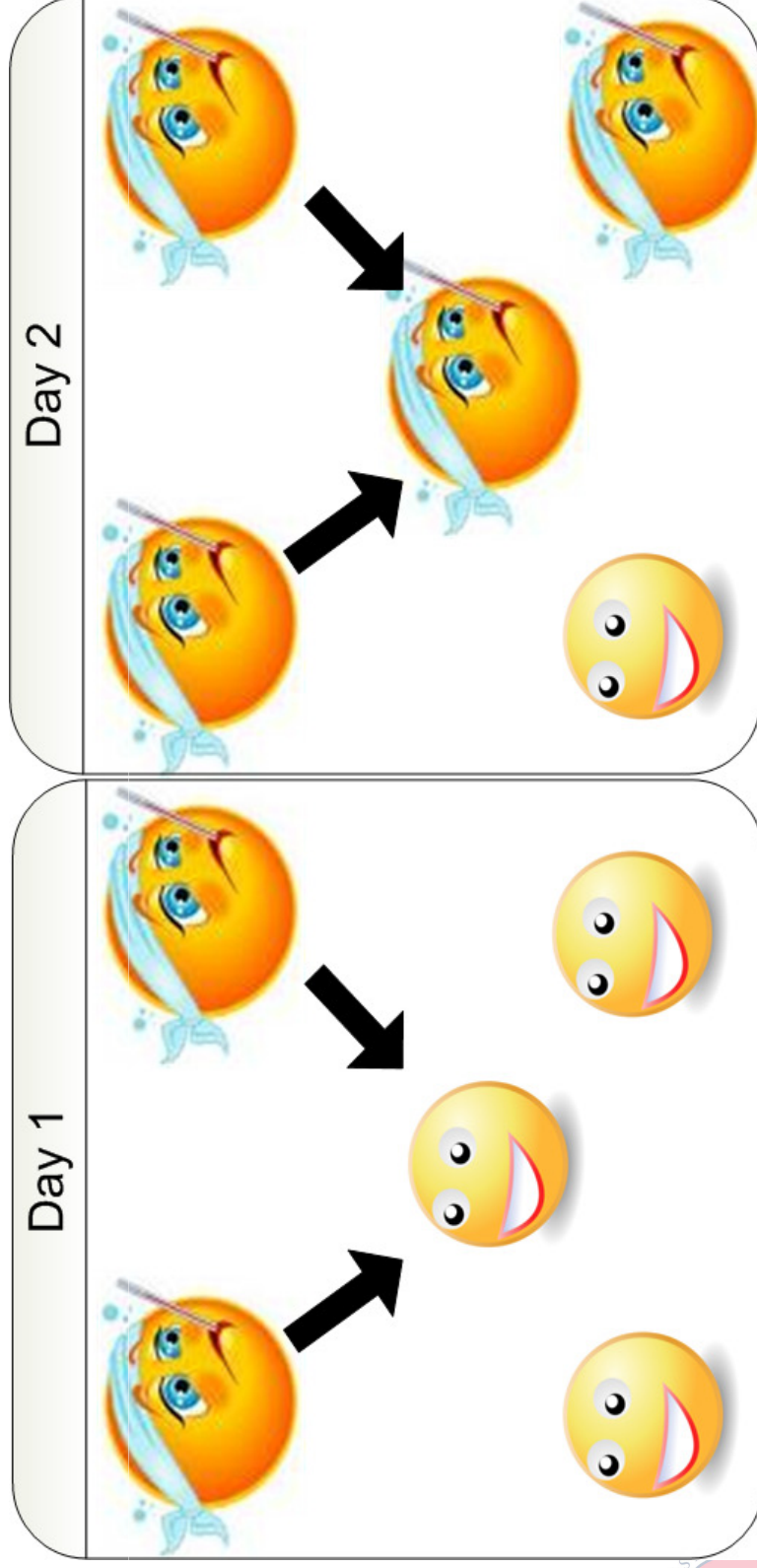
Case model



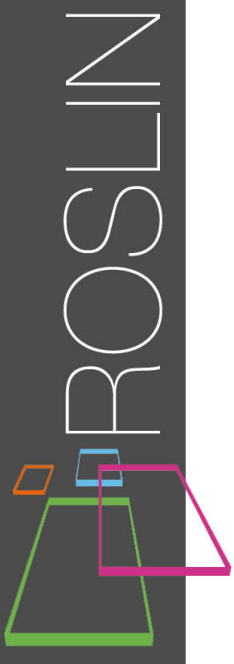
# Method - Analyses



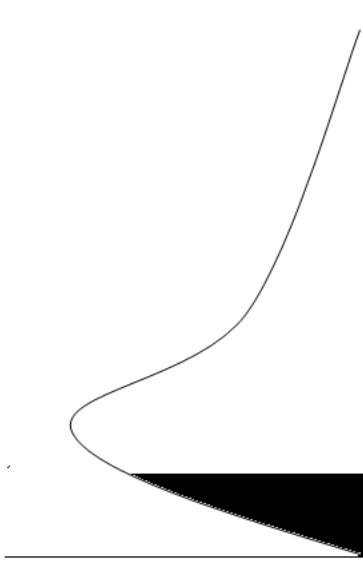
## Case-ordered model



# Model Evaluation



- Accuracy:
  - correlation between estimated breeding values (EBV) and susceptibility & infectivity
- Impact:
  - Mean susceptibility & infectivity
  - Risk and severity of outbreaks
  - Basic reproduction number  $R_0$
  - Selected subpopulations



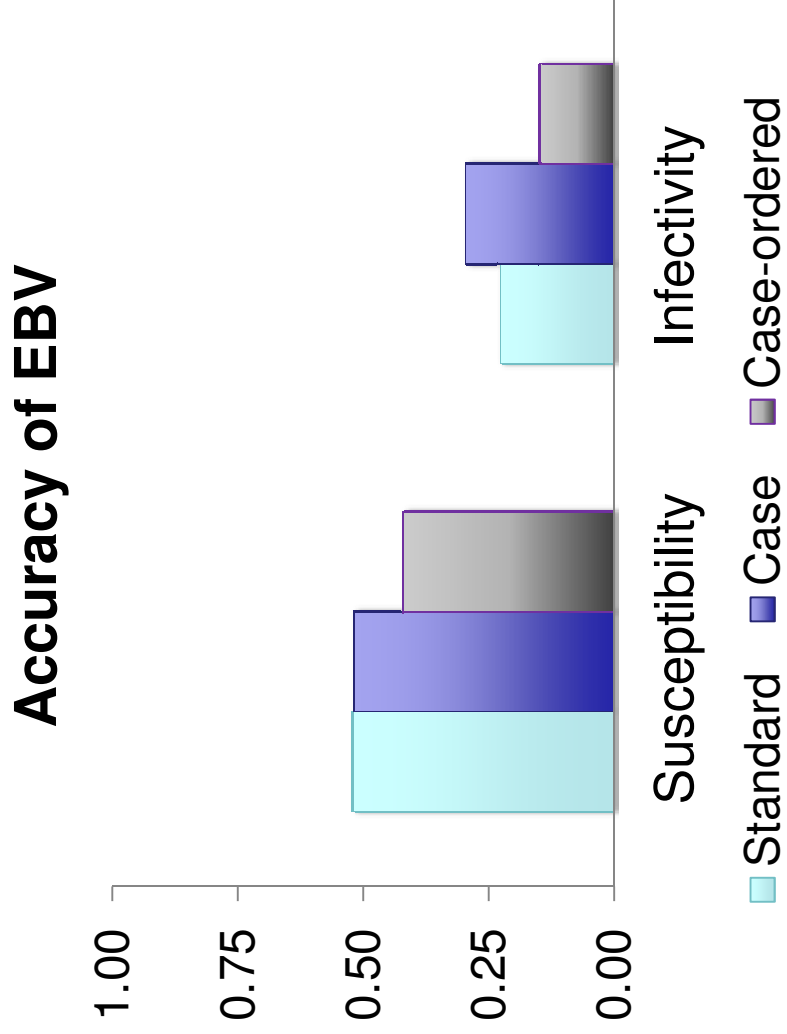


# Results

# Results – Accuracy



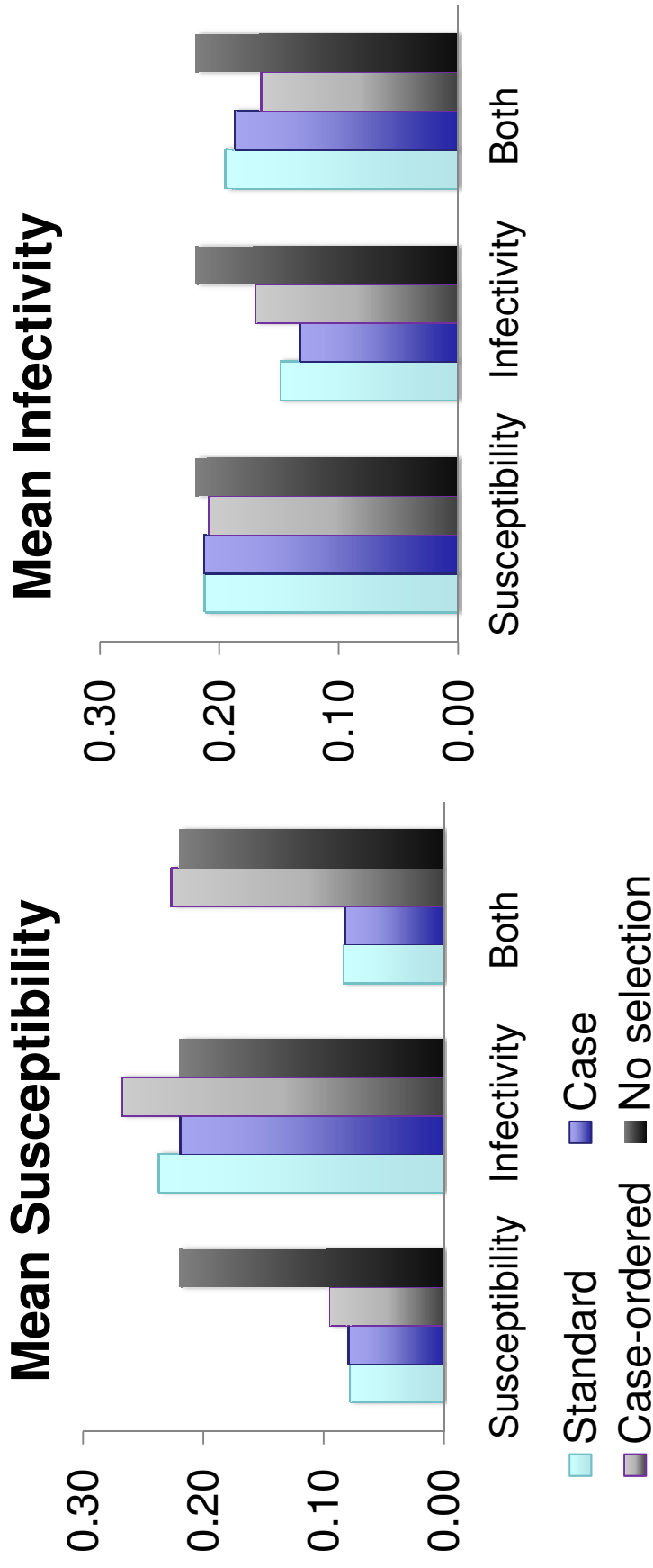
# PROSLIN



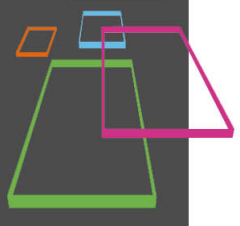
# Results – Impact on TBV



# ROSLIN

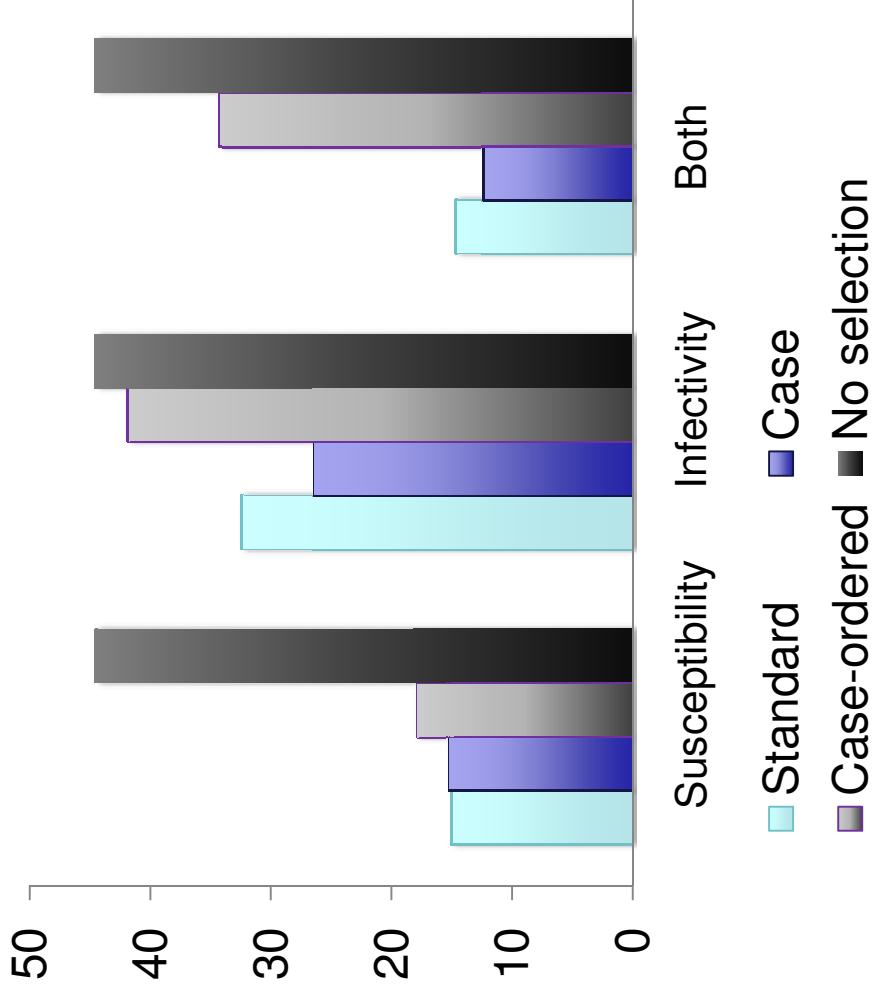


# Results – Impact on $R_0$

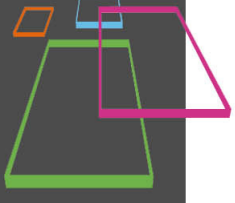


# PROSLIN

## Basic Reproduction Number



# Conclusion



- Associative effects models capture variation in infectivity
- Infection dynamics are important
- Trade-off between verisimilitude and accuracy & impact
- Future studies should concentrate on interaction between susceptibility and infectivity
- Overall case model provides best estimates



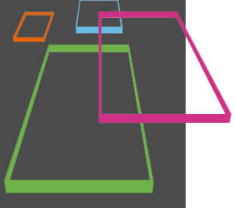
# Thank you!



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**Any questions?**



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