Scaling from challenge experiments to the field: predicted impact of vaccination on the transmission of bluetongue virus serotype 8

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Introduction

- Bluetongue (BT) is an economically important disease of ruminants caused by bluetongue virus (BTV) and transmitted by *Culicoides* biting midges.
- The most practical and effective way to protect susceptible animals against BTV infection is vaccination.
- We investigated the effects of vaccination on transmission of BTV serotype 8 (BTV-8) within and between farms, based on data from challenge experiments generated by Intervet/Schering Plough Animal Health:
  - the basic reproduction number (R_0) was used to assess the impact of vaccination within a farm; and
  - a stochastic spatial model for the spread of BTV in Great Britain (GB) was used to assess the impact of vaccination on transmission between farms.
- Both analyses allow for uncertainty in the parameters related to BTV transmission.

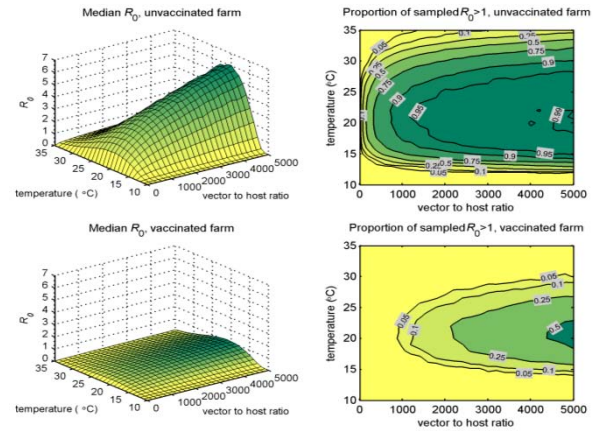
Vaccine parameters

- Estimates (95% credible limits) for the vaccine parameters are:

parameter	cattle	sheep
vaccine efficacy (%)	75 (60-85)	98 (89-100)
reduction in duration of viraemia (%)	53 (31-66)	not estimated

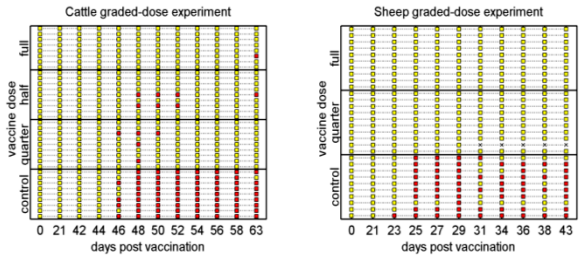
Basic reproduction number

- A temperature dependent model was used to compute the basic reproduction number (R_0) for BTV [1,2].
- Replicated Latin hypercube sampling was used to allow for uncertainty in model parameters [1]. Plausible ranges for each parameter were obtained from the literature [1], while vaccine parameters were derived from the challenge experiments.
- Comparison of R_0 in unvaccinated and vaccinated populations shows that the reduction in R_0 due to vaccination depends only on vaccine parameters.
- Based on the estimates obtained from the challenge studies, this reduction in cattle is 83% (95% CI:71-90%); in sheep it is 99.8% (95% CI: 98.9-100%).
- Allowing for uncertainty in the model parameters, R_0 exceeds one in an unvaccinated population at all but the lowest vector-to-host ratios and coolest and warmest temperatures.
- Vaccination reduces R_0 below one at all but the highest vector-to-host ratios and optimal temperatures; this is robust to uncertainty in the parameters.



Challenge experiments

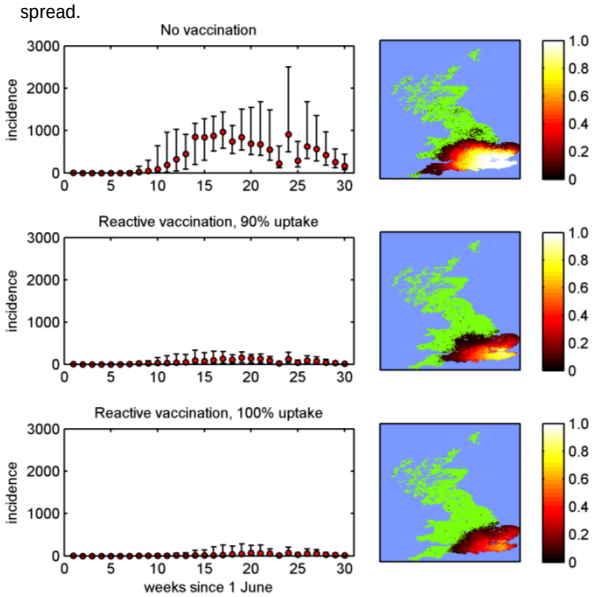
- Cattle:35 Holstein dairy calves allotted to four groups of eight or nine animals. Three groups of calves were vaccinated twice (at day 0 and 21) with Bovilis BTV8 ® using a full, half or quarter dose. A fourth group served as saline injected controls. Animals were challenged on day 42.
- Sheep: 30 sheep were allotted to three groups of ten sheep. Two groups were vaccinated at day 0 with a full or quarter dose; the third group served as saline injected controls. Animals were challenged on day 21.
- Blood samples were taken at regular intervals and the presence of virus was assessed using RT-PCR.
- The outcomes of the challenge experiments were used to estimate the vaccine efficacy (proportion of animals protected) and the reduction in the duration of viraemia in infected, vaccinated animals.



colour indicates PCR result: yellow (negative); red (positive)

Transmission between farms

- A stochastic, spatially explicit model was used to describe spread between farms in GB and the impact of vaccination [3,4].
- Three vaccination strategies were considered:
  - no vaccination
  - vaccinate 90% farms in a 50km zone around an infected premises (IP)
  - vaccinate 100% farms in a 50km zone around an IP
- Vaccination significantly reduced the incidence of disease and spatial spread.



Conclusions

- The proportional reduction in R_0 due to vaccination depends only on vaccine parameters and so will be independent of local conditions.
- From the results of the challenge experiments this reduction is predicted to be 83% and, based on parameters derived to reflect BTV-8 epidemiology in northern Europe, this is likely to be sufficient to reduce R_0 to below one.
- Vaccination was predicted to reduce significantly the incidence of disease and spatial spread in simulated BTV-8 outbreaks in GB.
- The methodology used here is ideal for assessing the impact of vaccination on transmission of diseases not amenable to experimental studies (e.g. a vector-borne disease).

References: [1] Gubbins et al. (2008) *J. R. Soc. Interface* **5**, 363-371; [2] Hartemink et al. (2009) *Epidemics* **1**, 153-161; [3] Szmaragd et al. (2009) *PLoS ONE* **4**, e7741; [4] Szmaragd et al. (2010) *PLoS ONE* **5**, e9353.