Modelling the population dynamics of *E. coli* VTEC in a calf cohort

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Introduction

•Intimin-positive Verocytotoxigenic *Escherichia coli* (VTEC) are often isolated from patients with Haemolytic Urinary Syndrome (HUS).

•Cattle carrying Verocytotoxigenic *Escherichia coli* (VTEC), including serogroup O157, are regarded as a major reservoir of infection for humans.

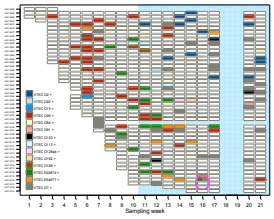
•Although it is not known whether non-O157 VTEC found in cattle are harmful to humans, cattle/calves might be a potential reservoir for those harmful pathogens.

• Thus, it is important to understand the characteristics of VTEC within cattle populations.

•Faecal samples were taken once a week from 49 newly-born calves on Scottish Highland beef farm for 21 weeks.

•13 serogroups of VTEC were isolated and identified by PCR and DNA hybridisation.

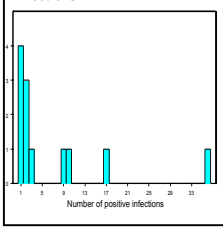
•85 samples with single identified serogroups, 23 samples with unknown identity, 1 sample with multiple serogroups is circled by ◯



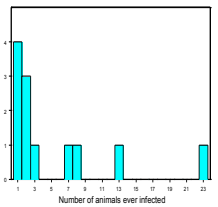
•For our modelling purpose, only data during the first 17 weeks were used, therefore only 12 serogroups were observed.

•For each serogroup, we define 3 quantities to characterise the data:

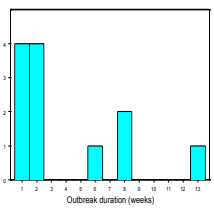
Number of positive infections



Number of animals ever infected



Outbreak duration



Aims

•To construct models that can best describe the observed data and answer the following questions:

•Are there transmission processes within the cohort?

•Are all serogroups similar or different?

•Estimate the average and maximum possible number of serogroups circulating in the calf cohort.

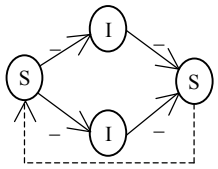
•Estimate the number of multiple infections.

Models

•A stochastic Susceptible-Infected-Susceptible (SIS) process for each serogroup:

Susceptible calves can acquire infections either via transmission (_) or environment routes (_).

Infected calves return to susceptible status via the recovery route (_).



A sampling process is also implemented to take samples from the SIS process. Assuming no interaction between serogroups, and with the basic SIS process described above, we construct 2 models:

•Homogenous model:
12 independent SIS processes with no variation in the epidemiological parameters (e.g. _, _, _) between serogroups.

•Heterogeneous model:
Heterogeneity can be introduced in one of the three epidemiological parameters (e.g. _, _, _). The model is the same as above but allows for different serogroups having different values for the same parameter.

•Maximum likelihood method is used to estimate epidemiological parameters:
stochastic models are simulated to construct a joint probability space in the number of positive infections, number of animals ever infected and outbreak duration. The best parameter set/model is the one that most likely to produce results similar to the data.

Results

•For the homogenous model, the best parameters are:

transmission (_): 0.004 (0.002-0.01)
environment (_): 0.001 (0.001-0.003)
recovery (_): 0.2 (0.1-0.5)

95% confidence interval for the transmission parameter (_) excludes 0, therefore suggests transmission of *E. coli* VTEC within the cohort. 70% (48-83%) of infections occur via transmission between animals (_) while 30% (17-52%) via environment route (_):

However, homogenous model fails to explain the variation in outbreak duration among the serogroups.

•Model with heterogeneity in the recovery rate (_) is significantly better than the homogenous model and other heterogeneous models, therefore variation in the rate at which serogroups are lost from infected animals might be important.

Transmission is still important as 95% confidence interval for the transmission parameter (_: 0.004 (0.002-0.006)) still excludes 0. However, 57% (28-75%) of infections are now from transmission while 43% (25-72%) are from environment.

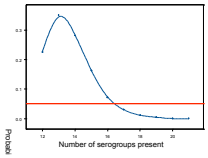
The heterogeneous model suggests that 4 serogroups have a low recovery rate (_: 0.2) , 8 serogroups have a higher recovery rate (_: 1.0), and the model can account for the variation in outbreak duration.

Discussions: answers to earlier questions

•In some simulations, infection is there but not detected with the sampling frame (i.e. zero observations). 50,000 simple SIS processes are simulated and divided into groups of 12, 13, 14, 15, 16 etc. We then calculate the probability of observing 12 serogroups per group.

On average, 13/14 serogroups must be present in the calf cohort to observe 12 serogroups.

At 0.05 level, in order to observe 12 serogroups, the max number of serogroups present in the calf cohort is about 17.



•No interaction is assumed between serogroups, therefore multiple infection may occur within individual calves. Using the methodology as described above and superimpose 50,000 SIS realisations in groups of 14, we then determine the the number of serogroups per sample.

Out of 570 samples:

Serogroups	Data	Model
0	484 (84%)	461 (81%, 70-91%)
1	85 (15%)	96 (17%, 9-25%)
2	1 (0.2%)	12 (2%, 0-5%)
3	0	1 (0.2%,0-1%)
≥4	0	0

Thus, the model predicts more samples with multiple infections, and the discrepancy between data and model may be due to:

•PCR/DNA hybridisation technique may not allow 2 serogroups or more to be detected in the same sample.

•at one given time, *E.coli* VTEC are predominated by a single serogroup (i.e. the assumption of independent infections is wrong).

Conclusions

•Variation in the rate at which serogroups are lost from infected animals is important.

•Models suggest *E. coli* VTEC transmission (50-70% of infections) between calves in this particular cohort.

•The average number of serogroups circulating (to observe 12) in this cohort is 13 to 14.

•The max possible number of serogroups is about 17 (to observe 12).

•Expectation of more samples with multiple serogroups.

Future directions

•Apply the same methodology to other data sets and ask how robust our conclusion is.

•Look for evidence of interactions between serogroups and implement that in future models.

Acknowledgements

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