R_0 ESTIMATION FROM HORIZONTAL TRANSMISSION EXPERIMENTS

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Mathematical modelling is a useful tool in addressing questions in veterinary epidemiology. It can be used to evaluate measures taken to stop transmission of infections[1] or to quantify the necessary surveillance program[2]. To make these models as trustworthy as possible, it is valuable to estimate parameters of infection transmission from real data. These could be field data, from endemic diseases by following herds or from epidemic diseases by collecting data during outbreaks[1,3]. Infection transmission parameters could also be obtained experimentally in transmission experiments.

Transmission experiments are experiments in which some individual animals in a group of animals are infected. Subsequently it is measured how many of the non-infected animals get infected during the experiment. Transmission experiments can be used to test effectiveness of certain measures, e.g. vaccination, in reducing transmission of pathogens between hosts[4,5]. Another goal of transmission experiments could be estimating transmission parameters. Becker[6] describes the martingale method to estimate R_0 and that estimate has been modified by De Jong & Kimman[4]. R_0 is the basic reproduction ratio and is defined as the expected number of secondary infections caused by 1 infectious individual in a susceptible population. Some experiments reveal a lot more data than used in this martingale calculation. In this presentation another way of estimating R_0 will be presented that makes better use of the data.

Data structuring

In the transmission experiments used as an example, 10 pigs are placed in one pen and 5 of these pigs have been inoculated with Classical Swine Fever Virus (CSFV) at the start of the experiment. Subsequently every two or three days in the first three weeks and once a week for another three weeks blood samples have been taken. With leukocyte fraction of these blood samples virus isolations have been done, to see whether the tested animal was viraemic at that moment. We assumed that animals were infectious when viraemic, resulting in an infection diagram as in table 1. Reckoning with a latent (infected but not yet infectious) period of 5 days, for all time intervals sets of numbers of susceptible (S) and infectious (I) animals, together with the number of new cases (C) could be made (Table 1).

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	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
i	-		-		-		-		-		-		-		-							+				
i	-		-		-		+		+		+		+		-							-				
i	-		-		-		-		-		-		-		-							+				
i	-		-		-		+		+		+		+		-							+				
i	-		-		-		+		+		+		+		+							+				
c	-		-		-		-		-		-		-		-							+				
c	-		-		-		-		-		-		-		-							+				
c	-		-		-		-		-		-		+		+							+				
c	-		-		-		-		-		-		-		+							+				
c	-		-		-		-		-		-		+		+							+				

(a)

	0-5	*5-7*	*7-9*	*9-16*
S	7	7	5	4
I*Δt	0.5	5.5	6	31
C	0	2	1	4

(b)

Table 1: (a) infection diagram of a transmission experiment. i = inoculated animal; c = contact animal; + = positive sample; - = negative sample; empty = no sample; grey shading = period in which the animal has been infected. In two inoculated animals inoculation was not successfull. (b) Four distinct time intervals could be distinguished in which susceptible animals were subject to infectivity, denoted as I*Δt

Estimation of R_0

Estimation of b

It is assumed that the rate of getting infected of a susceptible animal is $\beta \cdot I/N$. This makes the probability of escaping infection within a time interval $e^{-\beta \cdot I \cdot \Delta t/N}$. This results in the probability of getting C out of S infections:

$$p = \binom{S}{C} \left(1 - e^{-b \cdot I \cdot \Delta t / N}\right)^{C} \left(e^{-b \cdot I \cdot \Delta t / N}\right)^{S-C}$$

Multiplying these probabilities for all observed *n* time intervals results in the likelihood expression:

$$likelihood = \prod_{k=1}^{n} \binom{S_k}{C_k} \left(1 - e^{-b \cdot (I \cdot \Delta t)_k / N}\right)^{C_k} \left(e^{-b \cdot (I \cdot \Delta t)_k / N}\right)^{S_k - C_k}$$

Maximizing this likelihood for β results in the maximum likelihood estimator (MLE) for β. For calculating the variance of this estimator, it is assumed that β is lognormally distributed with a variance of logβ of $(d^2 likelihood/d(\log\beta)^2)^{-1}$.

Estimation of a

It is assumed that the recovery rate of an infectious animal is α. This makes that the infectious periods T are exponentially distributed with parameter α. Recovery rate α is estimated with a generalized linear model using GenStat®:

$$E(X) = \alpha T$$

X = 0, if at the end of the observation period infectiousness was not ended yet, otherwise X = 1. Estimation was done with a log link function and a Poisson distribution.

Estimation of R_0

R_0 was estimated using the estimators of β and α:

$$R_0 = \beta/\alpha$$

A confidence interval could be constructed using the variances of log β and log α:

$$Var(\log R_0) = Var(\log \beta) + Var(\log \alpha)$$

Results

In the series of experiments which the above experiment is part of, β was estimated 0.44 and α was estimated 0.065, resulting in an R_0 of 6.8. The 95% confidence interval of R_0 was {3.6, 12.7}.

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