Chapter 5

Quantification of the effect of control strategies on classical swine fever epidemics

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Abstract

Emergency vaccination during an epidemic of Classical Swine Fever Virus (CSFV) has become a serious option because of the ethical problems of strategies with massive culling and the availability of a marker vaccine that reduces virus transmission. Here we present a model of between-herd CSFV transmission, which quantifies the effect of control strategies with and without vaccination. We estimate the model parameters from data of the Dutch CSFV epidemic of 1997/1998. With the model, a set of control strategies is compared, consisting of five control measures in several combinations. Consequently, the following general requirements of successful strategies can be formulated. First, to achieve extinction of a CSFV epidemic, transmission through transport should be prevented and the indirect virus transmission, i.e. all transmission not through animal contacts, should at least be halved, either by vaccination or by culling of the susceptible pig population. Second, to minimise the size and duration of an epidemic, the extinction requirements should be met quickly and indirect virus transmission should be reduced by far more than a half. Although the origin of the model parameters let the requirements in fact be only applicable for the southeastern part of the Netherlands, it is argued that epidemics in other areas will not need stricter control strategies.

5.1. Introduction

Classical swine fever (CSF) is a viral disease of swine (Taylor, 1995). The entry of classical swine fever virus (CSFV) into populations of non-vaccinated domestic pigs can cause large epidemics. Nonetheless, the domestic pig population of the European Union (EU) is not preventively vaccinated against CSFV, because importing countries do not accept vaccinated pigs (Anonymous, 1980). They consider vaccinated pigs as infected, which is due to the fact that most antibody tests react positively in vaccinated animals. This problem was to be solved with the E\textsuperscript{ns}-antibody ELISA, designed to be used with the E2 subunit marker vaccine which only evokes antibodies against the E2 subunit and not against E\textsuperscript{ns}. However, the E\textsuperscript{ns} ELISA has a sensitivity of only 75% (Depner et al., 2001).

In 1997, a CSFV entry into the Netherlands led to a large epidemic (hereafter called the Dutch CSFV epidemic), which lasted 1.5 years and in which 429 herds were infected (Elbers et al., 1999). In part the epidemic was so large and long-lasting because the initial set of control measures, as prescribed by the EU, was insufficient to bring the basic reproduction ratio between herds, $R_0$, to a value below
1. Additional control measures appeared necessary, among which preventive slaughter of herds with traced contacts with infected herds or in close vicinity of infected herds (Stegeman et al., 1999b). Preventive slaughter, however, has major disadvantages, because the killing of healthy pigs, if not for consumption, is economically and ethically undesirable (Terpstra et al., 2000).

Future introductions of CSFV should therefore be followed by an alternative control strategy, without preventive killing but with the effect of reducing $R_0$ sufficiently to end the epidemic quickly. A future strategy might include emergency vaccination, e.g. with an E2 subunit vaccine, which reduces the basic reproduction ratio between individual pigs to below 1 (Bouma et al., 2000; Chapter 3). Vaccination of the entire pig population will therefore certainly lead to extinction of a CSF epidemic. However, the economic consequences might be far-reaching since importing countries will not resume import of live pigs and pig products as long as the entire population is not CSFV-free. If importing countries do not accept a sensitivity of 75% to prove virus-freedom, all vaccinated animals will have to be removed before resuming export. If sufficiently effective, it would be preferable to use strategies with only partial vaccination, e.g. only vaccination of fattening pigs. These could already be replaced by unvaccinated piglets before the end of the epidemic.

Considerations like these make it desirable to know the requirements of a good control strategy. To determine these requirements, the effects of various control strategies should be quantified. Nielen et al. (1999) and Mangen et al. (2001) studied the epidemiological and economic effects of a number of control strategies, in part defined by the reaction of trading partners — whether they will or will not import vaccinated pigs. In both these studies, simulation models with a very detailed structure were used. The models, for example, were spatially explicit and simulated every single contact between farms. The approach enabled the authors to make detailed economic analyses, but leads to questions regarding the reliability of the exact outcomes since many parameter values had to be chosen without data. Moreover, a general insight into the requirements of a good control strategy cannot be obtained. This points out the need for a quantitative analysis of control strategies with reliable parameter estimates from epidemic data.

In this paper, we present a mathematical model of CSFV transmission between pig herds. We use the model to link data on CSFV transmission and assumptions on the effect of control measures. In section 2, the model structure is presented. In section 3, the model is used to construct likelihood functions, which are used to estimate the model parameters from data of the 1997/1998 CSFV epidemic in the Netherlands. Section 4 describes how five control measures are incorporated into the model. In section 5, the estimated parameters are used to quantify the effects of the
five control measures, which are applied in all possible combinations. From the analysis, general requirements for good control strategies are deduced. Finally, in section 6 the results are interpreted and discussed in relation to previous publications, model assumptions, and the future of CSFV control.

5.2. Model structure

The model describes the transmission of CSFV between pig herds in the Netherlands. In the basic model, the set of EU control measures is applied, as was applied in the first ten weeks of the Dutch CSFV epidemic (Stegeman et al., 1999b). The most important control measures are the culling of infected herds, a transport prohibition, the tracing and testing of infectious contacts, and the implementation of hygiene measures and surveillance in the affected area. In the basic model, however, the complete transport prohibition is relaxed and animal transport from multiplier to finishing herds and from finishing herds to the slaughterhouse is permitted. This relaxation causes heterogeneity in the contact pattern, and therefore two herd types are distinguished in the model, multiplier herds and finishing herds. Multiplier herds contain sows and produce 23 piglets per sow per year (Siva software, 2001), which are transported to the finishing herds at an age of ten weeks. This leads to a piglet to sow ratio of $(23 \cdot 10 : 7) : 365 = 1610 : 365$ within multiplier herds. The pigs remain 100 days on the finishing herds, until slaughter.

The virus transmission between pig herds is modelled as a branching process of infected herds, which means that the number of available susceptible herds to be infected is not limiting. Immediately after infection, virus spreads within the herd. The herd gives rise to new infected herds by a Poisson process with a variable rate proportional to the number of infectious animals within the herd. The infection process stops when infection of the herd is detected, as detection is immediately followed by culling of the herd. Although virus entry into a herd can result in a minor outbreak, only major outbreaks within herds are modelled since these are the most important for further virus transmission between herds. For an overview of all model parameters, variables, and functions, see Appendix 5A.

5.2.1. Within-herd transmission

Virus transmission within a herd starts with one infectious pig, immediately after infection of the herd. We assume that this is followed by a linear birth-death process (Cox and Miller, 1965) of infected pigs, independent of herd type. In
epidemiological terms, birth would be equivalent to infection and death to recovery. The linear birth-death process is described by

\[ \frac{dp_i(t)}{dt} = \mu p_i(t) \] (5.1.1)

\[ \frac{dp_i(t)}{dt} = -(\lambda + \mu)p_i(t) + 2\mu p_{i+1}(t) \] (5.1.2)

\[ \frac{dp_i(t)}{dt} = -(\lambda + \mu)p_i(t) + (i-1)\lambda\mu p_{i-1}(t) + (i+1)\mu p_{i+1}(t), \text{ if } i \geq 2 \] (5.1.3)

in which \( p_i(t) \) is the probability of having \( i \) infectious pigs at time \( t \), \( \lambda \) is the per capita infection rate and \( \mu \) is the recovery rate (Cox and Miller, 1965).

The solution to this set of differential equations with initial conditions \( p_1(0) = 1 \) and \( p_i(0) = 0 \forall i \neq 1 \) is given by (after Cox and Miller (1965), p. 166)

\[ p_0(t) = \frac{\exp(\lambda t) - 1}{\mu \exp(\mu t) - 1} \] (5.2.1)

\[ p_i(t) = (1 - p_0(t))(1 - \mu p_i(t))(\mu p_i(t))^{-1}, \] (5.2.2)

in which \( r = \lambda - \mu \), the mean exponential growth rate of the number of infectious pigs, and \( R = \lambda/\mu \), the basic reproduction ratio between animals. In the model, \( R \) is assumed to exceed 1 (and hence, \( r > 0 \)), otherwise no major outbreaks can occur within herds.

We now define the stochastic variable \( I(t) \) as the number of infected animals at time \( t \) since infection of the herd and conditioned on non-extinction, as the model only takes major outbreaks in herds into account:

\[ P(I(t) = i) = \frac{p_i(t)}{1 - p_0(t)} = (1 - \mu p_0(t))(\mu p_0(t))^{-1}. \] (5.3)

\(^1\) Throughout the paper, upper case letters denote stochastic variables, whereas lower case letters denote parameters or ordinary variables. Note that \( r \) and \( R \) are two different model parameters.
By letting $t \to \infty$, a continuous approximation to the discrete distribution for $I(t)$ can be made (see Appendix 5B):

$$I(t) = H \exp(rt), \text{ in which}$$

$$H \equiv \text{pdf}(h) = \frac{R-1}{R} \exp\left(-\frac{R-1}{R}h\right).$$

The approximation (5.4) is used instead of the real solution (5.2) to keep the model more manageable. In short, the within-herd transmission of CSFV is described by a deterministic exponential curve of which the height is random and has an exponential distribution.

5.2.2. Herd detection

Infected herds can be detected at any time after they are infected. Detection of infected herds takes place by a Poisson process with an increasing rate $\alpha = aH \exp(rt)$. The first realisation is the detection time. Parameter $\alpha$ is the detection rate per infectious pig. After detection of a herd, it is immediately culled and cannot give rise to new infected herds anymore.

5.2.3. Between-herd transmission: indirect contacts

Each infectious herd can transmit the virus to susceptible herds via indirect contacts, i.e. all potentially infectious contacts except transport of infectious pigs. Transmission takes place by a Poisson process, thereby giving rise to new infectious herds with increasing transmission rates $\beta_f I(t) = \beta_f H \exp(rt)$ for infecting finishing herds and $\beta_m I(t) = \beta_m H \exp(rt)$ for infecting multiplier herds, where $t$ is the time since infection of the infectious (source) herd. The type of source herd is assumed irrelevant. Parameters $\beta_f$ and $\beta_m$ are the transmission rates per infectious pig per indirect contact per day. The sum $\beta_{ind} = \beta_f + \beta_m$ is the total rate by which an infectious animal in an infectious herd gives rise to new infectious herds through indirect contacts.
5.2.4. Between-herd transmission: transport contacts

Infectious herds can also transmit virus through transport of live pigs. In the model, this mode of transmission is restricted to multiplier herds infecting finishing herds. For simplicity, the assumption is made that this occurs analogously to the indirect-contact transmission, viz. by a Poisson process with rate \( \beta_p I(t) = \beta_p H \exp(rt) \), in which \( \beta_p \) is the transmission rate per infectious pig for transport contacts.

5.3. Parameter estimations

The described model contains six parameters: (1) \( r \), the exponential growth parameter for the number of infectious pigs on a farm; (2) \( R \), the basic reproduction ratio between animals on a farm, which describes the height of the exponential infectious curve within farms. The pair \((r, R)\) is a reparametrisation of the parameter pair \((\lambda, \mu)\) of the within-herd transmission model: \( r = \lambda - \mu \) and \( R = \lambda/\mu \); (3) \( \alpha \), the detection parameter, which denotes the rate of herd detection per infectious pig on a farm; (4) \( \beta_{ind} \), the between-herd transmission parameter that denotes the rate at which one infectious pig infects other herds by indirect herd contacts. The indirect transmission is split into two types, for the transmission to finishing herds and to multiplier herds, which are denoted by the parameters \( \beta_f \) and \( \beta_m \), respectively. The values of \( \beta_f \) and \( \beta_m \) can be derived from their sum \( \beta_{ind} \) and from their ratio: (5) the \( \beta_f: \beta_m \) ratio, which determines the division of \( \beta_{ind} \) into \( \beta_f \) and \( \beta_m \); (6) \( \beta_r \), the between-herd transmission parameter for transport contacts.

5.3.1. Methods

5.3.1.1. Estimation of \( r, R, \alpha \), and \( \beta_{ind} \)

The first four parameters \( r, R, \alpha \), and \( \beta_{ind} \) have been estimated simultaneously by using data from the 1997/1998 epidemic in the Netherlands under the assumption that the data had arisen according to the described mathematical model. From the data, three stochastic processes could be distinguished and the log-likelihood functions \( L_1(r, R) \), \( L_2(r, R, \alpha) \), and \( L_3(r, R, \alpha, \beta_{ind}) \) for these processes were formulated. The sum of these log-likelihood functions \( L(r, R, \alpha, \beta_{ind}) = L_1(r, R) + L_2(r, R, \alpha) + L_3(r, R, \alpha, \beta_{ind}) \) has been maximised numerically in Mathematica® (Wolfram, 1999) for the four parameters simultaneously to obtain the maximum likelihood estimates.
The combined likelihood function has also been used to derive a distribution of the estimators. Since $\alpha$ and $\beta_{\text{infd}}$ are positive by definition and $r$ must be positive to enable within-herd transmission, it was assumed that the estimators for $r$, $\alpha$, and $\beta_{\text{infd}}$ were lognormally distributed. Since $R > 1$ to enable within herd transmission, it was assumed that the estimator for $R^{-1}$ was lognormally distributed. A covariance matrix for $\log r$, $\log (R^{-1})$, $\log \alpha$, and $\log \beta_{\text{infd}}$ was obtained numerically in Mathematica® (Wolfram, 1999) by calculating

$$\text{var} = \begin{pmatrix}
\frac{\partial^2 \mathcal{L}}{\partial \log r^2} & \cdots & \frac{\partial^2 \mathcal{L}}{\partial \log r \partial \log \beta_{\text{infd}}} \\
\frac{\partial^2 \mathcal{L}}{\partial \log r \partial \log (R^{-1})} & \ddots & \vdots \\
\frac{\partial^2 \mathcal{L}}{\partial \log r \partial \log \alpha} & \ddots & \vdots \\
\frac{\partial^2 \mathcal{L}}{\partial \log r \partial \log \beta_{\text{infd}}} & \cdots & \frac{\partial^2 \mathcal{L}}{\partial \log \beta_{\text{infd}}^2}
\end{pmatrix}^{-1} \quad (5.5)$$

The goodness-of-fit of the model to the parameters has been tested for each likelihood equation separately, by calculation of the Pearson $\chi^2$ statistic

$$\chi^2 = \sum_{i=1}^n \left( \frac{y_i - E(Y_i)}{\text{var}(E(Y_i))} \right)^2 \quad \text{in which } n \text{ is the number of records, } y_i \text{ the } i\text{th observation, } E(Y_i) \text{ the expected value of the } i\text{th observation, and } \text{var}(E(Y_i)) \text{ the estimated variance of the } i\text{th observation. The statistic is } \chi^2 \text{-distributed with } n - p \text{ degrees of freedom, where } p \text{ is the number of parameters estimated with the regarded likelihood equation.}$$

5.3.1.2. Log-likelihood function $L_1(r, R)$

The first log-likelihood function described the detection of infected animals in a random sample of animals as a function of time since infection of the herd. The function provided information on the within-herd transmission parameters $r$ and $R$.

$^2$ Note that a basic reproduction ratio larger than 1 implies a net exponential increase: $R > 1 \Leftrightarrow r > 0$ (Diekmann and Heesterbeek, 2000).
Table 5.1. The dataset for $L_{t}(r,R)$. Each row represents the record of one herd.

<table>
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<th>$t_{det}$ (days)</th>
<th>$n_{det}$</th>
<th>$n_{tot}$</th>
<th>$n_{pos}$</th>
<th>$E(N_{pos})$</th>
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<td>321</td>
<td>42</td>
<td>6</td>
<td>6.70</td>
</tr>
</tbody>
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- $a$ The time interval between infection and detection
- $b$ The number of animals in the herd
- $c$ The number of tested samples
- $d$ The number of positive samples
- $e$ The expected number of positive samples according to the model and the parameter estimates.
Of a set of 82 herds of the 1997/1998 epidemic of CSF in the Netherlands, the exact day of virus introduction is known from tracing (Stegeman et al., 1999b). Of this set of herds, those 32 finishing herds were selected, in which blood samples from animals throughout the herd had been taken to test for seroconversion. Of each of these herds, the known data were: the time between infection and detection \( t_{det} \), the total number of animals \( n_{tot} \), the number of sampled and tested animals \( n_{test} \), and the number of animals tested seropositive \( n_{pos} \) (Table 5.1).

We assumed a perfect serological test with a sensitivity and a specificity of 1. Then, for each record, the number of seropositive animals \( n_{pos} \) was a realisation of a random draw of \( n_{test} \) animals out of a population of \( n_{tot} \) animals with \( N_{ser} \) true seropositives; the stochastic variable \( N_{pos} \) was therefore hypergeometrically distributed:

\[
P(N_{pos} = n_{pos}) = \sum_{n_{ser} = n_{pos}}^{n_{ser} + n_{tot} - n_{pos}} \binom{n_{ser}}{n_{pos}} \binom{n_{test} - n_{pos}}{n_{test} - n_{pos}} \binom{n_{tot} - n_{test}}{n_{tot} - n_{test}} P(N_{ser} = n_{ser})
\]

The number of true seropositives \( N_{ser} \), of which the distribution had to be determined to use equation (5.6), was the accumulated number of animals infected 18.45 days before \( t_{det} \), 18.45 days being the average time until seropositivity of an individual animal (Stegeman et al., 1999b). The number of true seropositives \( N_{ser} \) consisted of the number of animals that had been infected at rate \( \lambda(t) \) by within-herd transmission plus the number of initially infected animals, which was the height \( H \) of the infectious curve at the time of infection of the herd:

\[
N_{ser} = H + \int_0^{t_{det}} \lambda(t) \exp(-r(t_{det} - 18.45)) dt = \frac{R}{R-1} H \exp(r(t_{det} - 18.45)).
\]

Eq. (5.7) was used to derive the probability \( P(N_{ser} = n_{ser}) \), by approximating the continuous exponential distribution for \( N_{ser} \) by a discrete geometrical distribution:

\[
P(N_{ser} = n_{ser}) = P(N_{ser} \leq n_{ser}) = \left[ \frac{n_{ser}}{R} \right] \left[ \frac{n_{ser} + 1}{R + 1} \right] \left( \frac{R-1}{R} \exp(-r(t_{det} - 18.45)) \right) \]
in which \( \frac{R-1}{R} \exp\left(\frac{R-1}{R} h\right) \) is the probability density function (pdf) for the height of the infectious curve \( H \), and \( \pi_0 = 1 - \left(\exp\left(\frac{R-1}{R}\right)\right)^2 \exp(-r(t_{det} - 18.45)) \). By taking the logarithm of Eq. (5.6) and summing over all 32 observations, the function \( L_1(r, R) \) was obtained.

5.3.1.3. Log-likelihood function \( L_2(r, R, \alpha) \)

The second log-likelihood function described the detection of infected herds. It mainly provided information on the detection parameter \( \alpha \). However, as detection depends on the within-herd dynamics, also the within-herd transmission parameters \( r \) and \( R \) were involved.

For 82 of the 429 herds of the Dutch CSF epidemic, the day of virus introduction is known. We used the interval in days between infection and detection as the detection times \( t_{det} \) of these 82 herds (Stegeman et al., 1999b):

\[
10(2\times), 12, 13, 14(3\times), 16(3\times), 18(3\times), 20(4\times), 21(2\times), 22(3\times), 23, 24(3\times), 25(2\times),
26(2\times), 27(2\times), 28, 29(6\times), 30(4\times), 33(3\times), 34(2\times), 35, 36, 37(2\times), 38(4\times), 39,
41(2\times), 42(6\times), 43, 44, 45, 47(2\times), 48(3\times), 49(2\times), 50, 51, 52, 55, 56, 57(2\times)
\]

The detection times were considered as random draws from a probability distribution of the stochastic variable \( T_{det} \), which could be expressed in terms of the parameters \( r, R, \) and \( \alpha \) and became, integrated over all possible values of \( H \):

\[
\text{pdf}(t_{det}) = \int_0^{\frac{\alpha}{r}} \frac{ah \exp\left(r t_{det} - \frac{ah}{r} (\exp(r t_{det}) - 1)\right)}{R-1} \exp\left(-\frac{R-1}{R} h\right) dh
\]

\[
= \frac{\alpha R^{-1} \exp(r t_{det})}{\frac{\alpha}{r} \exp(r t_{det}) - \frac{\alpha}{r} + \frac{R-1}{R} \frac{\alpha}{r}}
\]

(5.9)
In Eq. (5.9), $a_\text{h} \text{exp}(r t_{\text{det}})$ is the detection rate at time $t_{\text{det}}$, 
$\text{exp}(-a_\text{h}(\text{exp}(r t_{\text{det}})-1)/r)$ is the
probability that the herd has not been detected until $t_{\text{det}}$, 
and $\frac{R-1}{R} \text{exp}\left(-\frac{R-1}{R} h\right)$ is
the pdf for $H$. By summing the logarithm of Eq. (5.9)
over the 82 observations, the function $L_2(r, R, \alpha)$ was
acquired.

5.3.1.4. Log-likelihood
function $L_3(r, R, \alpha, \beta_{\text{ind}})$

The third log-likelihood function described the CSFV transmission between herds. Although it mainly provided information on transmission parameter $\beta_{\text{ind}}$, also the parameters $r$, $R$, and $\alpha$ were included, since these parameters together determine the average number of infectious animals within an infectious herd.

After the first detection of the Dutch CSFV epidemic, the compulsory set of EU measures came into force for 10 weeks. Of each week, the number of infectious herds $j$ and the number of new infections $c$ had been reconstructed by Stegeman et al. (1999a) (Table 5.2). According to the model, the numbers of new infections per week $C$ were regarded as random draws from Poisson distributions of which the parameters depended on the number of infectious herds $j$ and on $r$, $R$, $\alpha$, and $\beta_{\text{ind}}$.

$$E(C) = \beta_{\text{ind}} \nu(r, R, \alpha) j.$$ \hspace{1cm} (5.10)

Since $\beta_{\text{ind}}$ is the average number of herds infected per infectious animal per day, the function $\nu(r, R, \alpha)$ had to convert one infectious herd into a number of infectious ‘animal days’. Therefore, $\nu(r, R, \alpha)$ is the expected number of infectious ‘animal days’ per herd divided by the expected number of weeks from infection to detection of a herd.

Table 5.2. The dataset for $L_3(r, R, \alpha, \beta_{\text{ind}})$. Each row represents the record of one week.

<table>
<thead>
<tr>
<th>$j$</th>
<th>$c$</th>
<th>$E(C)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>22.9</td>
<td>9</td>
<td>8.4</td>
</tr>
<tr>
<td>27.2</td>
<td>16</td>
<td>10.0</td>
</tr>
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<td>30.3</td>
<td>10</td>
<td>11.2</td>
</tr>
<tr>
<td>35.9</td>
<td>12</td>
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<td>15.2</td>
</tr>
<tr>
<td>50.1</td>
<td>17</td>
<td>18.5</td>
</tr>
<tr>
<td>55.6</td>
<td>20</td>
<td>20.5</td>
</tr>
<tr>
<td>59.0</td>
<td>20</td>
<td>21.8</td>
</tr>
<tr>
<td>67.5</td>
<td>27</td>
<td>24.9</td>
</tr>
<tr>
<td>68.6</td>
<td>26</td>
<td>25.3</td>
</tr>
</tbody>
</table>

* The average number of infectious herds
* The number of new infections
* The expected number of new infections according to the model and the parameter estimates.
\[ \nu(r, R, \alpha) = \frac{E(\# \text{ infectious animal days} | r, R, \alpha)}{E(\# \text{ infectious weeks} | r, R, \alpha)}. \] (5.11)

In Eq. (5.11), the numerator is equal to

\[ E(\# \text{ infectious animal days}) = \int_0^\infty h \exp\left( rt - \frac{ah}{r} (\exp(rt) - 1) \right) dh \frac{R - 1}{R} \exp\left( -\frac{R - 1}{R} h \right) dh, \]

where \( h \exp(rt) \) is the infectiousness at time \( t \), \( \exp\left( -\frac{ah}{r} (\exp(rt) - 1) \right) \) the probability that the herd has not been detected at time \( t \), and \( \frac{R - 1}{R} \exp\left( -\frac{R - 1}{R} h \right) \) the pdf for \( H \).

In Eq. (5.11), the denominator, i.e. the expected number of weeks that a herd is infectious, is

\[ E(\# \text{ infectious weeks}) = \int_0^\infty \int_0^\infty \frac{1}{7} E(\text{length of infectious period in days}) \]

\[ = \int_0^\infty \alpha h \exp\left( rt - \frac{ah}{r} (\exp(rt) - 1) \right) dt \frac{R - 1}{R} \exp\left( -\frac{R - 1}{R} h \right) dh \]

\[ = \int_0^\infty \alpha \frac{R - 1}{R} \exp(rt) \left( \frac{\alpha}{r} (\exp(rt) - 1) + \frac{R - 1}{R} \right) dt, \] (5.12)

in which \( \alpha h \exp\left( rt - \frac{ah}{r} (\exp(rt) - 1) \right) \) is the pdf for the detection time and \( \frac{R - 1}{R} \exp\left( -\frac{R - 1}{R} h \right) \) the pdf for \( H \). The division by 7 is to convert the expected number of days to the expected number of weeks.

This results in the probability of observing \( c \) new cases in a week being
Effect of control strategies

\[ P(C = c) = \frac{(\beta_{\text{ind}} v(r, R, \alpha))^c}{c!} \exp(-\beta_{\text{ind}} v(r, R, \alpha)) . \]  

(5.13)

Summing the logarithms of Eq. (5.13) over the ten weekly intervals resulted in the function \( L_3(r, R, \alpha, \beta_{\text{ind}}) \).

5.3.1.5. The ratio \( \beta_f : \beta_m \)

The fifth model parameter is the ratio \( \beta_f : \beta_m \), which is the ratio by which infectious herds of both types infect finishing and multiplier herds, respectively. For estimation of the ratio, the 429 infected herds of the Dutch CSFV epidemic were subdivided into three groups, according to the ratio of finishing pigs and sows in the herds. In a perfectly closed herd that does not sell or buy piglets, the ratio between the number of finishing pigs (each sow produces 23 piglets a year, which are all living as a finishing pig for 100 days) and the number of sows (each living 365 days a year) would be \( 23 \cdot 100/365 \approx 6.3 \). Therefore, the groups were subdivided as follows: net piglet producers (finishing pig to sow ratio < 5.0), net piglet receivers (finishing pig to sow ratio > 7.5), and a third group (finishing pig to sow ratio between 5.0 and 7.5, breeding herds which supply gilts to herds with sows, and herds with unknown animal numbers). The third group is likely to have very few transport contacts, since only transport of piglets to finishing herds is permitted. Because infected third-group herds do not infect other herds by transport, just like the finishing herds, the third group has been included in the receiver group to determine the \( \beta_f : \beta_m \) ratio.

5.3.1.6. The parameter \( \beta_r \)

The parameter \( \beta_r \) is the parameter for transmission through transport contacts. It is derived by first calculating the mean number of finishing herds that are infected by one infectious multiplier herd through transport, \( \sigma_r \). Subsequently, the parameter \( \beta_r \) is chosen such that the mean number of infections through transport per herd according to the model will also be \( \sigma_r \).

The mean transport frequency of piglets from multiplier herds to finishing herds is approximately \( 32/365 \approx 1/11.4 \) (one transport every 11.4 days) (Mangen, 2002). By assuming an average transmission probability of \( \pm 0.8 \), the frequency of transmission through transport becomes \( 1/14 \), thus once in two weeks. The expected number of contact infections due to transport of infectious pigs, \( \sigma_r \), then becomes:
\[ \sigma_v = \frac{1}{14} E(\text{length of herd's infectious period in days}) \]

\[ = \frac{1}{14} \int_0^\infty \frac{\alpha t R^{-1} \exp(\alpha t) \exp(\beta t)}{R \left[ \frac{\exp(\alpha t) - 1}{R} + \frac{R - 1}{R} \right]} \, dt , \tag{5.14} \]

which was already derived in Eq. (5.12), apart from the division by 14.

In the model, the rate of transmission through transport is assumed to be proportional to the number of infectious animals at the infectious multiplier herd, i.e. equal to \( \beta_v I(t) = \beta_v H \exp(\alpha t) \). Therefore, with the expected total number of contact infections through transport being \( \sigma_v \), \( \beta_v \) is equal to \( \beta_v = \alpha \sigma_v \).

### 5.3.2. Results

The estimates for \( \log r \), \( \log(R-1) \), \( \log \alpha \), and \( \log \beta_{\text{int}} \) were \(-2.0\), \(0.60\), \(-6.7\), and \(-6.2\) respectively. The covariance matrix of the estimators of these parameters was:

\[
\begin{pmatrix}
0.0078 & 0.021 & -0.019 & -0.019 \\
0.021 & 0.17 & -0.0094 & -0.010 \\
-0.019 & -0.0094 & 0.097 & 0.089 \\
-0.019 & -0.010 & 0.089 & 0.089
\end{pmatrix}
\tag{5.16}
\]

Transformed to the original model parameters, the point estimates with 95% confidence intervals are listed in Table 5.3. Table 5.3 also shows the means and 95% confidence intervals of \( \beta_v \). The 95% confidence limits of \( \beta_v \) are the 250th and 9751st value of the ordered range of 10,000 determined \( \beta_v \)s with parameters randomly drawn from the above distribution of \( \log r \), \( \log(R-1) \), \( \log \alpha \), and \( \log \beta_{\text{int}} \). To get an idea of the level of between-herd transmission with the estimated parameters, we have calculated the basic reproduction ratio between herds \( R_h \) as the largest eigenvalue of the next-generation matrix (Diekmann and Heesterbeek, 2000):
Effect of control strategies

In matrix (5.17), \( \varphi_{tr} = 1 \) if transport is permitted and \( \varphi_{tr} = 0 \) if not. The estimated \( R_h \) with and without transport are given in Table 5.3. The \( R_h \) without transport, i.e. the largest eigenvalue of (5.17), is equal to \( \beta_{ind} / \alpha \). Therefore, the variance of \( \log R_h \) can be derived from the covariance matrix (5.16): \( \text{var}(\log R_h) = \text{var}(\log \beta_{ind}) + \text{var}(\log \alpha) - 2\text{covar}(\log \beta_{ind}, \log \alpha) \). The 95% CI for \( R_h \) with transport has been determined as for \( \beta_{tr} \).

Subsequently, a \( \chi^2 \) goodness-of-fit test was carried out for the three likelihood functions. All \( E(N_{pos, i}) \) for \( L_1(r, R) \) and \( E(C_i) \) for \( L_2(r, R, \alpha, \beta_{ind}) \) are given in Tables 5.1 and 5.2, respectively. The \( E(T_{det, i}) \) for \( L_3(r, R, \alpha, \beta_{ind}) \) were equal for all \( i \): 32.0. The one-sided test results are \( P = 0.26 \) (\( \chi^2 = 34.5 \); d.f. = 30) for \( L_1 \), \( P = 0.55 \) (\( \chi^2 = 76.6 \); d.f. = 79) for \( L_2 \), and \( P = 0.55 \) (\( \chi^2 = 4.97 \); d.f. = 6) for \( L_3 \). Thus, the model cannot be rejected.

Finally, the division of the 429 infected herds of the Dutch CSF epidemic into groups resulted in 231 net piglet producers, 105 net piglet receivers, and 93 rest herds. By inclusion of the rest herds in the net piglet receiver group, a \( \beta_f/\beta_m \) ratio of approximately 1:1 is retrieved. The ratio 1:1 was used for the model calculations.

Table 5.3. The estimates and 95% confidence intervals of the model parameters and the basic reproduction ratios.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>( r )</td>
<td>0.13</td>
<td>0.11 - 0.16</td>
</tr>
<tr>
<td>( R )</td>
<td>2.8</td>
<td>1.8 – 5.1</td>
</tr>
<tr>
<td>( \alpha )</td>
<td>0.0013</td>
<td>0.00068 - 0.0023</td>
</tr>
<tr>
<td>( \beta_{ind} )</td>
<td>0.0021</td>
<td>0.0012 - 0.0038</td>
</tr>
<tr>
<td>( \beta_{tr} )</td>
<td>0.0029</td>
<td>0.0016 - 0.0050 a</td>
</tr>
<tr>
<td>( R_h ) without transport</td>
<td>1.7</td>
<td>1.4 - 2.0</td>
</tr>
<tr>
<td>( R_h ) with transport</td>
<td>2.5</td>
<td>2.1 - 2.8 a</td>
</tr>
</tbody>
</table>

a These 95% CIs have been approximated by drawing 10,000 times from the parameter estimator distribution and determining \( \beta_{tr} \) and \( R_h \) for each parameter set. The 250th and 9751st values of the ordered ranges were the limits of the confidence intervals.

\[
\begin{pmatrix}
\beta_f \\
\beta_{tr} \\
\alpha
\end{pmatrix} = \begin{pmatrix}
\beta_f \\
\beta_{tr} + \beta_{tr} \varphi_{tr} \\
\alpha
\end{pmatrix}
\] (5.17)
5.4. Control scenarios

The effects of five different control measures have been investigated with the described model, as well as all relevant combinations of these measures:

(A) Total transport prohibition
(B) Killing of young piglets (in combination with a breeding ban)
(C) Vaccination of all piglets (not sows) at multiplier herds, followed by recurrent vaccination of newborn piglets
(D) Single vaccination of all pigs at finishing herds
(E) Vaccination of piglets on arrival at finishing herds

Tested control scenarios consist of combinations of these measures and are indicated by codes referring to the above list, e.g. scenario AD holds a transport prohibition and a single vaccination of finishing herds. All tested scenarios are listed in Table 5.4. Missing letter combinations code for scenarios that are impossible, for example, all scenarios with control measures (A) and (E) together. To distinguish single control measures from control scenarios, the measures are always put between brackets, so (A) refers to a measure and A to a scenario.

The effect of control scenarios is modelled by multiplication of the transmission rate parameters $\beta_m$, $\beta_f$, and $\beta_{tr}$ by the functions $\phi_m(t)$, $\phi_f(t)$, and $\phi_{tr}(t)$, respectively. For each control scenario, the functions $\phi(t)$ are different. The control scenarios start at $t = 0$. Assumptions for the functions $\phi(t)$ are

1. Animals vaccinated at $t = 0$ are instantaneously protected, i.e. not susceptible. Although in reality the vaccine significantly reduces transmission only after 2 weeks (Bouma et al., 2000), that is already sufficient to reduce the size of within-herd outbreaks even if the herd is infected just after vaccination. Protected animals cannot be infected, so the transmission rate for indirect infectious contacts is multiplied by the fraction of unvaccinated animals on the farm, which denotes the probability that the first animal to be infected is unvaccinated.

2. On a multiplier herd, the piglet to sow ratio is 1610:365, as noted before. This means that, if there are no susceptible piglets present, $\phi_m(t) = 365/(1610+365) = 365/1975$. When control measure (C) is applied, the vaccine is not assumed to protect at once, because vaccination is an ongoing process, which results in the continuous presence of yet insufficiently protected pigs. Hence, it is assumed that piglets are protected by vaccination from the age of four weeks onwards, namely, vaccination at two weeks of age plus two weeks for the vaccine to start its effect. Then, $\phi_m(t) = (365+1610\cdot4/10)/1975 = 1009/1975$. 

96
Table 5.4. The functions $\phi(t)$ for each of the tested scenarios; time $t$ is measured in days and $t = 0$ is defined as the initiation of the control scenarios.

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Time interval</th>
<th>$\phi(t)$</th>
<th>$\phi_e(t)$</th>
<th>$\phi_d(t)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABCD</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>ABC</td>
<td>$t &gt; 0$</td>
<td>1</td>
<td>365/1975</td>
<td>0</td>
</tr>
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<td>ABD</td>
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<td>$t &gt; 0$</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>ACD</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>1009/1975</td>
<td>0</td>
</tr>
<tr>
<td>AC</td>
<td>$t &gt; 0$</td>
<td>1</td>
<td>1009/1975</td>
<td>0</td>
</tr>
<tr>
<td>AD</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>A</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>BCD</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>CD</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>1009/1975</td>
<td>0</td>
</tr>
<tr>
<td>DE</td>
<td>$t &gt; 0$</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>none</td>
<td>$t &gt; 0$</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>BC</td>
<td>$0 &lt; t \leq 100$</td>
<td>$1 - t/100$</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 100$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>BDE</td>
<td>$0 &lt; t \leq 70$</td>
<td>0</td>
<td>$1 - 23t/1975$</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 70$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
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<td>BD</td>
<td>$0 &lt; t \leq 70$</td>
<td>$t/100$</td>
<td>$1 - 23t/1975$</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$70 &lt; t \leq 100$</td>
<td>0.7</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$100 &lt; t \leq 170$</td>
<td>$1.7 - t/100$</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 170$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>BE</td>
<td>$0 &lt; t \leq 70$</td>
<td>$1 - t/100$</td>
<td>$1 - 23t/1975$</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$70 &lt; t \leq 100$</td>
<td>$1 - t/100$</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 100$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>$0 &lt; t \leq 70$</td>
<td>1</td>
<td>$1 - 23t/1975$</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$70 &lt; t \leq 170$</td>
<td>$1.7 - t/100$</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 170$</td>
<td>0</td>
<td>365/1975</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>$0 &lt; t \leq 100$</td>
<td>$1 - t/100$</td>
<td>1009/1975</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 100$</td>
<td>0</td>
<td>1009/1975</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>$0 &lt; t \leq 100$</td>
<td>$t/100$</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 100$</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>E</td>
<td>$0 &lt; t \leq 100$</td>
<td>$1 - t/100$</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>$t &gt; 100$</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

(3) Transmission through transport contacts is only prevented if there is no transport at all or if the transported piglets have been vaccinated at the multiplier herd. In all other cases transport of pigs from infected multiplier herds leads to major outbreaks in finishing herds with normal within-herd transmission rates.
Vaccination does not affect virus transmission within herds, because in most cases the vaccinated and unvaccinated animals on a farm are separated (they are housed within weight classes, which are approximate age classes, which in most cases denote the vaccination status).

The functions $\phi(t)$ for all tested control scenarios are listed in Table 5.4. As can be seen from Table 5.4, for some control scenarios, all $\phi(t)$ remain constant from $t = 0$. For other scenarios, however, one or more functions had to be subdivided into time intervals, to account for the changing situation due to transport. For example, scenario B starts with a completely susceptible population, but in 70 days all piglets are removed from the multiplier herds and in another 100 days the finishing herds are emptied as well. Therefore, $\phi_m(t)$ decreases linearly from 1 to $365/1975$ within 70 days; $\phi_tr(t) = 1$ until $t = 70$ and then becomes 0; and $\phi_f(t)$ first remains 1 for 70 days and then decreases linearly from 1 to 0 within 100 days.

5.5. Model analysis

5.5.1. Methods

5.5.1.1. Probability of extinction

A common measure to characterise transmission of an infectious agent in a population of herds would be the basic reproduction ratio between herds $R_h$, the expected number of herds infected by one infectious herd in a population of susceptible herds. An $R_h < 1$ ascertains extinction of the infection, whereas an $R_h > 1$ denotes the possibility of major epidemics (Diekmann and Heesterbeek, 2000). For some of the scenarios, however, $R_h$ is not a constant value in the initial stage since one of the functions $\phi(t)$ changes with time. Therefore, we chose to determine the probability of extinction of an epidemic. The probability of extinction is directly related to the threshold property of $R_h$, since extinction will occur with probability 1 if in a control scenario $R_h$ eventually reaches a constant value $< 1$.

The probability of extinction heavily depends on the epidemic situation at the time a control scenario is implemented, viz. on the number of undetected infected herds present in the population, the types of the infected herds (multiplier or finishing herds), and how much the infection has already spread in the herds. Regarding the progression of infection in infectious herds, we always assume that the herds have been infected at $t = 0$, implying that the entire infectious period still has to be completed. As for the initial numbers and types of infectious herds, the
probability of extinction has to be calculated only with one finishing herd or one multiplier herd as a starting condition. Subsequently, the probabilities of extinction for all other starting conditions can be calculated, because the model is a branching process: if the probability of extinction starting with one multiplier herd is \( z_m \) and the probability starting with one finishing herd is \( z_f \), then the probability of extinction starting with \( x \) multiplier herds and \( y \) finishing herds will be \( z_m^x z_f^y \).

For determination of the probabilities of extinction \( z_f \) and \( z_m \), two types of control scenario could be distinguished. The first type comprised all scenarios with constant functions \( \phi(t) \), which were the scenarios ABCD, ABC, ABD, AB, ACD, AC, AD, A, BCD, CD, and DE (Table 5.4). For these control scenarios, \( R_h \) could be calculated as the largest eigenvalue of the next-generation matrix (Diekmann and Heesterbeek, 2000):

\[
\begin{pmatrix}
\beta_f \varphi_f(t) & \beta_f \varphi_f(t) + \beta_m \varphi_m(t) \\
\beta_m \varphi_m(t) & \beta_m \varphi_m(t)
\end{pmatrix}
\]

(5.18)

Matrix (5.18) is a more general form of matrix (5.17), in which \( \varphi(t) = \varphi_m(t) = 1 \). If \( R_h < 1 \), then both \( z_f \) and \( z_m \) were equal to 1. If, on the other hand, \( R_h > 1 \), then it was possible to determine the probability of extinction with a method based on the properties of branching processes. In Appendix 5C, the following set of recursive equations is derived, from which \( z_f \) and \( z_m \) could be solved numerically:

\[
z_f = \frac{1}{1 - \frac{\beta'_f}{\alpha} (z_f - 1) - \frac{\beta'_m}{\alpha} (z_m - 1)}
\]

(5.19.1)

\[
z_m = \frac{1}{1 - \frac{\beta'_f + \beta'_m}{\alpha} (z_f - 1) - \frac{\beta'_m}{\alpha} (z_m - 1)}
\]

(5.19.2)

In Eq. (5.19), \( \beta'_f = \phi_f(t) \beta_f \), \( \beta'_w = \phi_w(t) \beta_m \), and \( \beta'_w = \phi_w(t) \beta_w \). For the point estimates of \( z_f \) and \( z_m \), the point estimates of \( \beta_{ind} \) and \( \alpha \) were used. Confidence intervals for \( z_f \) and \( z_m \) were determined by drawing 1000 times from the distribution of parameter estimators and determining \( z_f \) and \( z_m \) for each set of parameters. The 25th and 976th value of the ordered range denote the limits of the 95% confidence interval.
Chapter 5

The second type of control scenario had at least one of the functions $\varphi(t)$ not constant. However, all functions $\varphi(t)$ in the long run did reach a constant value, so all control scenarios ultimately reached a constant $R_\infty$. According to the ultimate constant $R_\infty$, the second type could be divided into two subtypes. The first subtype consisted of all control scenarios where $R_\infty$ becomes smaller than 1. Control scenarios BC, BDE, BD, BE, B, and C were of this subtype, for which $z_f = z_m = 1$. The second subtype comprised the scenarios where $R_\infty$ ultimately exceeded 1 — scenarios D and E. For these scenarios, $z_f$ and $z_m$ had to be determined by 1000 repeated continuous time stochastic simulations (see Appendix 5D) with the model parameters set at their estimate. Starting with one finishing or multiplier herd, each simulation continued until either extinction or until a generation with at least 21 infectious herds was reached, the latter outcome indicating a major outbreak. Further, to get some insight into the variation of these $z_f$ and $z_m$ values due to uncertainty about the model parameters, for each of 1000 random draws from the distribution of the parameter estimators, 25 model simulations were executed from which $z_f$ or $z_m$ was estimated. The variance of these estimates was calculated from the simulation results and consists of two parts (Rao, 1973) [for notational convenience, we define $\vartheta = (r, R, \alpha, \beta_{\text{ind}})^T$]:

\[
\text{var}_\vartheta(Z_f, \vartheta) = \text{var}_\vartheta[E(Z_f, \vartheta)] + E_\vartheta[\text{var}(Z_f, \vartheta)],
\]

in which $Z_f(\vartheta)$ is the estimator of $z_f$ as a function of $\vartheta$. The expected conditional variance in the second right-hand side (RHS) term reflects the variation due to stochastic effects and was equal to $z_f(1-z_f)/25$. It could be approximated by $f_z(1-f_z)/25$, in which $f_z$ is the average $\hat{z}_f(\vartheta)$. The variance of the conditional expectation in the first RHS term reflects the uncertainty about the model parameter estimates and was estimated by subtracting the expected variance from the observed variance by rewriting (5.20) as:

\[
\hat{\text{var}}_\vartheta[E(Z_f, \vartheta)] = \sum_\gamma \frac{(\hat{z}_f - z_f(\vartheta))^2}{1000} - z_f(1-z_f)/25.
\]

By assuming a normal distribution of the conditional expected value, an approximate confidence interval for $z_f$ was obtained, which may serve to indicate the effect of the uncertainty about the model parameter estimates. A confidence interval for $z_m$ was determined analogously.
5.5.1.2. Duration and size of the epidemic

Although the probability of extinction is very useful in deciding which control strategies are insufficient, it does not distinguish between the scenarios in which extinction will be reached. Therefore, all scenarios with \( z_f = z_m = 1 \) were compared with respect to the duration and the size of the epidemic, i.e. the number of herds ultimately infected. The comparison was done by continuous time stochastic simulations of epidemics. Both duration and size of the epidemic largely depend on the situation at the time the control measures are implemented, as did the probability of extinction. The duration starting with one infectious herd, however, cannot so easily be extrapolated to situations with more infectious herds. Hence, we simulated with three starting conditions: one infectious finishing herd, one infectious multiplier herd, and five of both types of herds. The expected size of the epidemic is easier to extrapolate to other starting conditions, since this will always be a multiplication factor with respect to the initial number of infectious herds. Thus, the size of the epidemic has only been determined for the starting condition with five infectious herds of both types.

Simulations were performed as described in Appendix 5D. For each scenario and starting condition, 1000 simulations were done in which each simulation used another set of model parameters, randomly drawn from the distribution of the estimators. Of the 1000 simulations, the median time to extinction and the median size of the epidemic were determined together with the 95% interval by taking the 25th and 976th value of the ordered ranges of times and sizes.

5.5.1.3. Further model investigations

Finally, we made some plots to explore the sensitivity of the model outcomes for the four model parameters \( r, R, \alpha, \) and \( \beta_{\text{inh}} \) and for the calculated \( R_h \) (largest eigenvalue of matrix (5.18)); to explore the correlation between calculated outcomes \( z_f \) and \( z_m \); and to explore the correlation between the size and duration of the simulated epidemics.

The variation in extinction times and epidemic sizes, as obtained with the simulations, is a combination of variation due to random effects of the stochastic simulation and variation due to uncertainty about the parameter values. The sensitivity plots were used to distinguish between these two sources of variation. If the variation is mainly due to random effects, no relation between the parameters and the outcomes can be observed. In that case, more precise estimates of the parameters will not help to better predict the effectiveness of the control measures.
If, on the other hand, the model outcomes are related to the parameter values, better estimates can improve the predictions.

5.5.2. Results

Table 5.5 shows the estimated probabilities of extinction and the 95% confidence intervals for all tested scenarios. By comparison of the effectiveness of the strategies, we can come up with two conditions that have to be met to ensure extinction. First, virus transmission through transport should be prevented. This can be achieved by a transport prohibition (control measure (A)), by a breeding prohibition (control measure (B)), or by recurrent vaccination of multiplier herds (control measure (C)). Second, at least half of the indirect transmission should be prevented. This can be observed from comparing the effective scenario AD, in which the indirect transmission is reduced by 50%, and the ineffective scenario ABC, in which the indirect transmission is still present for 59%. The second
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Condition can also be explained from the estimate of $R_h$ without transport, of which the upper limit of the 95% confidence interval is 2.0. Reducing the indirect transmission by a half results in an upper confidence limit of 1.0, which leads to extinction. Prevention of transmission can be accomplished by a breeding prohibition (control measure (B)), or by vaccination (control measures (C), (D), and (E)).

There are three possibilities of satisfying both conditions at the same time, namely, both control measures (A) and (D), only control measure (B), or only control measure (C). It is important to note that the second condition is met by control measures (B) and (C) because of the permit to transport pigs: the susceptible finishing pigs are either not replaced at all (in case of (B)), or replaced only by vaccinated pigs (in case of (C)). Consequently, if a transport prohibition is added as a control measure, the scenarios become less effective (compare scenarios ABC vs. BC, AB vs. B, and AC vs. C). This can be resolved by vaccinating the finishing herds.

For scenario 'none', Figure 5.1a shows the sensitivity plots of $z_f$ and $z_m$ against parameters $r$, $R$, $\beta_{ind}$, $\alpha$, and $R_h$ using the 1000 simulations for determining the confidence intervals for $z_f$ and $z_m$. For all other scenarios with $z_f$ and $z_m$ smaller than 1, the sensitivity plots look similarly and are therefore not shown. It appears that $R_h$ is the major determinant for both $z_f$ and $z_m$. This is not very surprising, since the terms of the next-generation matrix (5.18), which determines $R_h$, also appear in the equations for $z_f$ and $z_m$ (5.19). Figure 5.1b shows a high correlation between the calculated $z_f$ and $z_m$.

Table 5.6 shows the results of the simulations of the scenarios with certain extinction: the durations and sizes of the epidemics. In some of the simulations with scenario AD, the random draw of the model parameters led to an $R_h$ above 1. If during such a simulation the number of infected herds grew so large that the probability of a major epidemic exceeded 95%, the simulation was stopped and duration and size of the epidemic were set to infinity. This happened in two of the 1000 simulations starting with one infectious herd and in seven of the 1000 simulations starting with ten infectious herds.

Close examination of the results in Table 5.6 reveals that there are two ways in which the effectiveness of a scenario can be improved. The first way is by a more severe reduction of indirect transmission between herds. This can best be seen by comparing the scenarios ABCD, ACD, and ABD. These all have constant functions $\varphi(t)$, but differ in the value of $\varphi_m(t)$, so they differ in the level of indirect transmission. $R_h$ for these three scenarios is 0.16 for ABCD, 0.43 for ACD, and 0.85 for ABD. By comparison of the results in Table 5.6, it appears that a lower $R_h$
Figure 5.1. Investigation of $z_f$ and $z_m$ with respect to the distribution of the model parameters. Each dot represents one of 1000 draws from the parameter distribution.

(a) The sensitivity plots of $z_m$ (top row) and $z_f$ (bottom row) against the four transformed parameters $\log r$, $\log(R-1)$, $\log\alpha$, and $\log\beta_{\text{ind}}$, and against the derived parameter $\log R_h$.

(b) The plot of the correlation between $z_m$ and $z_f$. 
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strongly reduces both duration and size. The second way to improve a scenario is by reaching the maximal reduction in indirect and direct transmission earlier. This is illustrated by comparing the scenarios ABCD, BDE, BE, and BD, which reach the same $R_h = 0.16$ after 0, 70, 100, and 170 days respectively. The expected duration and size increase in the same order, as seen in Table 5.6.

For scenario AD, the sensitivity of the duration and size for the model parameters $r$, $R$, $\beta_{ind}$, $\alpha$, and $R_h$ is shown in Figure 5.2a. The sensitivity plots are representative for all other scenarios. None of the parameters seem to determine the duration and size of the epidemic, although $R_h$ is of importance as noted after comparison of the scenarios ABCD, ACD, and ABD above. Apparently, within the estimated range of $R_h$, stochasticity is the main source of variation in both duration and size. Figure 5.2b shows a clear correlation between size and duration of the simulated epidemics with scenario AD.

5.6. Discussion

We presented a mathematical model for the transmission of CSFV between pig herds. We showed that the model structure was in accordance with available data of

<table>
<thead>
<tr>
<th>Scenario</th>
<th>duration (days)</th>
<th>size (herds)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 f. a</td>
<td>1 m. b</td>
</tr>
<tr>
<td>ABCD</td>
<td>32</td>
<td>8 - 92</td>
</tr>
<tr>
<td>ABD</td>
<td>38</td>
<td>6 - 442</td>
</tr>
<tr>
<td>ACD</td>
<td>35</td>
<td>7 - 151</td>
</tr>
<tr>
<td>AD</td>
<td>38</td>
<td>6 - 442</td>
</tr>
<tr>
<td>BCD</td>
<td>32</td>
<td>8 - 92</td>
</tr>
<tr>
<td>BC</td>
<td>39</td>
<td>9 - 129</td>
</tr>
<tr>
<td>BDE</td>
<td>38</td>
<td>7 - 158</td>
</tr>
<tr>
<td>BD</td>
<td>43</td>
<td>6 - 215</td>
</tr>
<tr>
<td>BE</td>
<td>41</td>
<td>7 - 181</td>
</tr>
<tr>
<td>B</td>
<td>63</td>
<td>8 - 230</td>
</tr>
<tr>
<td>CD</td>
<td>35</td>
<td>7 - 151</td>
</tr>
<tr>
<td>C</td>
<td>46</td>
<td>7 - 197</td>
</tr>
</tbody>
</table>

a The initial situation of only one infected finishing herd
b The initial situation of only one infected multiplier herd
c The initial situation of five infected finishing herds and five infected multiplier herds
Figure 5.2. Investigation of the epidemic size and duration with respect to the distribution of the model parameters. Each dot represents one of 1000 stochastic simulations, each with a different set of model parameters, randomly drawn from their distribution. Each simulation started with five infected finishing herds and five infected multiplier herds. (a) The sensitivity plots of the duration (top row) and epidemic size (bottom row) against the four transformed parameters $\log r$, $\log (R-1)$, $\log \alpha$, and $\log \beta_{\text{ind}}$, and against the derived parameter $\log R_h$. (b) The plot of the correlation between duration and epidemic size.
the Dutch CSFV epidemic and we used the data to estimate the model parameters. With the model we were able to predict the effects of several scenarios for the control of CSFV epidemics. Two general conditions for extinction of CSFV epidemics could be derived and two criteria for improving the effectiveness of a scenario were discerned. Finally, the sensitivity analyses showed that the only parameter of real importance is $R_0$, which is mainly determined by the quotient of $\beta_{ind}$ and $\alpha$. A better estimate of $R_0$, however, will hardly improve the model predictions, as most of the uncertainty in outcome lies in the stochasticity of the epidemic process.

The conditions for extinction of an epidemic are (1) prevention of transmission through pig transports and (2) reduction of indirect virus transmission by at least 50%. A striking result was that a transport prohibition can have a negative effect on the effectiveness of a scenario compared to the same scenario without transport prohibition (scenarios ABC vs. BC, AB vs. B, and AC vs. C). That is because the second condition for extinction is met by scenarios BC, B, and C through removal of the susceptible pigs in the finishing herds, which is prevented by a transport prohibition. Permitting transport can be beneficial in another way as well, since it will ‘wash out’ the tracks of small outbreaks on the farms. These small outbreaks, which are not incorporated into the model but which will certainly arise during an epidemic, can lead to problems at the end of the epidemic, when an area has to be declared free of CSFV by a large-scale serological screening. Detection of minor outbreaks in a screening will lengthen the duration of trading and export limitations and increase the costs of the epidemic.

Two criteria for improving the effectiveness of CSFV control were distinguished. The first was a stricter reduction of indirect transmission, which leads to a decrease in $R_0$. If $R_0$ is only just below 1, as with scenario ABD, the number of infected herds in the next generations will decrease slowly and it will take many generations before extinction is established. A more profound reduction in $R_0$ will decrease the number of generations and, as a result, the epidemic will take less time and affect fewer herds. The second criterion was a quicker reduction of transmission, which leads to a low $R_0$ earlier after start of the control strategy. If effectiveness is somehow delayed, as with scenario BDE, where transmission via transport is blocked only from 70 days, the first one or two generations of infected herds will still appear under a regime with $R_0 > 1$. A quicker reduction of $R_0$ will lead to considerably less infected herds, and hence an earlier extinction of the epidemic. The effect of quick action was also observed in the simulation study of Mangen et al. (2001), where it appeared that a delay in implementing control measures of 20 days could almost double the number of detected herds.
The sensitivity analysis showed that the only parameter of real importance is $R_h$. This parameter largely determines the probability of extinction as can be seen in Figure 5.1. As for the duration and size of the epidemic, $R_h$ is of minor effect within its estimated range, although an increase in both duration and size is expected with higher $R_h$. Here, the stochastic effects determine the major part of the variation. The fact that $r$ and $R$ seem to be of no importance for the model outcomes does not mean that they have been entirely useless. Incorporating within-herd dynamics made it possible to do more reliable parameter estimations — otherwise the data would not fit to the model — and that also increased the reliability of the parameter values that do matter, namely, $\beta_{\text{ind}}$ and $\alpha$.

Since the parameter estimations are all based on the data of the Dutch CSFV epidemic in the southeastern part of the Netherlands, the model results in fact only account for that specific region. It is a very pig-dense area with relatively many multiplier herds. A lower pig density will probably reduce the value of $\beta_{\text{ind}}$, although the extent of this reduction will depend on the density-dependence of the contacts implicitly incorporated in $\beta_{\text{ind}}$. A lower multiplier herd fraction will lead to relatively fewer infected multiplier herds, which are most infectious if transport is allowed. In conclusion, if a control scenario comes out positive in this model, it will be effective in most other areas as well.

The within-herd exponential growth parameter $r$ was estimated to be 0.13 (95% CI 0.11-0.16). Stegeman et al. (1999a) estimated $r$ from 7 breeding herds of the same set of 82 herds we used and came up with an estimate of 0.11 (0.06-0.16), which is in reasonable agreement. When the parameter $\mu$ of the within herd transmission model (Eq. (5.1)) is calculated from the estimates of $r$ and $R$, it is possible to estimate the mean generation time of the within herd transmission as $0.5\mu^{-1} = 6.8$ days. The generation time can be compared to generation times estimated from transmission experiments with CSFV (Chapters 2, 3, 4), which are equal to the estimated latent period — the period an animal is infected but not yet infectious — plus half of the average infectious period. This results in generation times of 10.9 and 9.2 (weaner and adult pig groups of Chapter 2, respectively), and of 13.9 and 8.2 (3 months and 6 months old groups of Chapter 4, respectively; values of $\mu$ not presented in the paper). These are slightly higher than the estimate in this paper, but still reasonably close, considering the rough simplification of the within-herd transmission in our model.

The basic reproduction ratio between herds $R_0$ was estimated to be 1.7 without transport contacts (95% CI 1.4-2.0). This is in fact an estimate for $R_0$ in the first ten weeks of the Dutch CSFV epidemic. Stegeman et al. (1999b) estimated $R_0$ in the same period at 1.3. The difference can be completely attributed for by the different
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estimate of the mean duration of the infectious period, which is proportional to \( R_0 \). If calculated by Eq. (5.9), the infectious period in our model is 32 days, which is equal to the mean duration of the 82 herds in the dataset of the second log-likelihood function. Stegeman et al. (1999b) estimated the average infectious period at 25 days, from a dataset that for a major part contains infectious period lengths estimated from serological data.

An important aspect of our model compared to most existing models for CSF epidemics is its relatively simple structure (cf. Jalvingh et al., 1999; Mangen et al., 2001; Nielen et al., 1999). Only six parameters are included, of which five were directly estimated with data of the Dutch CSF epidemic and one (\( \beta_t \)) was related to the average transport frequency. The simplicity enabled us to generalise the model outcomes and come up with requirements for good control strategies. Besides, it provided the opportunity to point out parameters for which more precise estimates are needed. Because the parameters could be estimated from data of a previous epidemic, we can be confident that the quantitative results are reliable. Nevertheless, two assumptions need further attention.

First, a branching process model as presented in this paper does not take the susceptible herds into account. This means that there is an implicit assumption of unlimited availability of susceptible herds. Hence, effects like local depletion or other spatial heterogeneities are not included. Because of the lack of spatial structure, some control measures cannot be incorporated into the model easily; for example, preventive slaughter or vaccination within short distance of infected herds. These control measures can only be incorporated by modelling their effect on the indirect between-herd transmission through adjustment of the functions \( \varphi(t) \). The effects should then be estimated from data of previous epidemics. Lack of spatial structure also leads to the implicit assumption that all control measures are implemented in a large enough area. Escape of virus from the area would be the start of a new epidemic in terms of our model.

The second major assumption is the reduction of the population structure into two herd types, multiplier herds and finishing herds. This is by far not as detailed as the true diversity in herd types, ignoring the existence of mixed herds (with sows and finishers), breeding farms (supplying gilts for the multiplier herds), and artificial insemination stations. The reason to include herd diversity in a model would be the different epidemiological impact of different herd types. Regarding within-herd virus transmission, experiments have shown different transmission rates between weaner and slaughter pigs (Chapter 2). The sensitivity analyses in this paper, however, show that both parameters involved in within-herd transmission, \( r \) and \( R \), appear to be of hardly any importance in determining the model outcomes (Fig. 5.1 and 5.2). It is, therefore, not expected that breaking down the population into herd
types with different within-herd transmission parameters would change the model results. As far as between-herd transmission is concerned, different herd types would be included to account for heterogeneity in the contact pattern. In the model, we included two herd types since we wanted to account for the possibility to relax the transport prohibition and allow transport of piglets to finishing herds and of finishing pigs to the slaughterhouse. As a result of the division into two herd types, a $\beta_f:\beta_m$ ratio had to be determined. This was complicated by the diversity in herd types in the data set, which consisted for about a quarter of mixed and breeding herds. Because the herd type is only important for the rate at which the herd itself causes new infections, and not for the type of herd it is infected by, the rest group could simply be included in the finishing herds group. This led to a $\beta_f:\beta_m$ ratio of 1:1.

The political decision to use a specific control strategy will not only depend on its epidemiological effectiveness. Other major roles will be played by the economic effectiveness and the public opinion. Regarding the economic effectiveness, costs of an epidemic are of course related to its duration and to the number of infected herds, but in addition other costs can result from implementing specific control measures. Especially if these control measures are related to export, the costs can become high (Mangen et al., 2001). An important aspect of export-related costs is the acceptance of vaccinated pigs by importing countries. The acceptance will depend on the quality of the diagnostic tests in vaccinated and unvaccinated pigs, but should also depend on the possible consequences of importing a false-negatively tested pig and the expected number of infected, yet undetected pigs. A risk analysis might be used to weigh these factors. Regarding the public opinion, we have seen that preventive slaughter has raised a major discussion on the ethics of killing and destroying healthy animals (Terpstra et al., 2000), which can influence the eventual decision on which control scenario to use. However, it will be helpful if the epidemiological aspects of the decision making are already quantified and available before a new CSFV entry occurs. We think the model results can prove useful for optimally preparing for CSFV epidemics.

Acknowledgements

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Appendix 5A

5A.1 Parameters

Input parameters

- $\lambda$ within-herd transmission parameter
- $\mu$ animal recovery rate
- $R (:= \lambda/\mu)$ within-herd basic reproduction ratio
- $r (:= \lambda - \mu)$ within-herd exponential growth rate
- $\beta_f$ between-herd transmission parameter for infection of finishing herds through indirect contacts
- $\beta_m$ between-herd transmission parameter for infection of multiplier herds through indirect contacts
- $\beta_{ind} := \beta_f + \beta_m$ total between-herd transmission parameter for indirect contacts
- $\beta_{tr}$ between-herd transmission parameter for infection of finishing herds by multiplier herds through transport contacts
- $\alpha$ herd detection parameter

Derived parameters

- $\beta_f' := \beta_f \varphi_f(\cdot)$ adjusted finishing herd transmission parameter for indirect contacts
- $\beta_m' := \beta_m \varphi_m(\cdot)$ adjusted multiplier herd transmission parameter for indirect contacts
- $\beta_{tr}' := \beta_{tr} \varphi_{tr}(\cdot)$ adjusted transmission parameter for transport contacts
- $R_h$ between-herd basic reproduction ratio
- $z_f$ probability of extinction if only one finishing herd is infected
- $z_m$ probability of extinction if only one multiplier herd is infected

5A.2. Variables

General model

- $t$ time since start of the control scenario
- $H$ height of the within-herd exponential infectious curve
Chapter 5

Likelihood function \( L_1(r, R) \)

- \( t_{det} \) time between infection and detection
- \( n_{tot} \) total number of animals in the herd
- \( n_{test} \) number of animals serologically tested
- \( N_{ser} \) total number of serologically positive animals in the herd
- \( N_{pos} \) number of serologically positive animals in the group of tested animals

Likelihood function \( L_2(r, R, \alpha) \)

- \( T_{det} \) time between infection and detection

Likelihood function \( L_3(r, R, \alpha, \beta_{ind}) \)

- \( j \) average number of infected herds within the week
- \( C \) number of newly infected herds (cases) within the week

5A.3 Functions

General model

- \( I(t) \) number of infectious animals within the herd as a function of time since infection of the herd
- \( \phi_f(t) \) reduction factor of the transmission to finishing herds through indirect contacts as a function of time since start of the control scenario
- \( \phi_m(t) \) reduction factor of the transmission to multiplier herds through indirect contacts as a function of time since start of the control scenario
- \( \phi_{tr}(t) \) reduction factor of the transmission from multiplier herds to finishing herds through transport contacts as a function of time since start of the control scenario

Likelihood function \( L_3(r, R, \alpha, \beta_{ind}) \)

- \( \nu(r, R, \alpha) \) conversion factor for converting the number of infectious herds within a week to the number of infectious ‘animal days’ within a week

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Appendix 5B

Here we derive the distribution of the continuous variable $I'(t)$, which has been used as an approximation to the distribution of the discrete variable $I(t)$, defined as

$$P(I(t) = i) = (1 - Rp_0(t))(Rp_0(t))^{-1} = \frac{1 - Rp_0(t)}{Rp_0(t)}(Rp_0(t))'. \quad (5.3)$$

By using Eq. (5.2.1), $P(I(t) = i)$ can be rewritten as

$$P(I(t) = i) = \left(\frac{R - 1}{R} \frac{1}{\exp(rt) - 1}\right) \left(1 - \frac{R - 1}{R} \frac{1}{\exp(rt) - 1/R}\right)$$

$$= \left(\frac{R - 1}{R} \frac{\exp(-rt)}{1 - \exp(-rt)}\right) \left(1 - \frac{R - 1}{R} \frac{\exp(-rt)}{1 - \exp(-rt)/R}\right).$$

For large $t$, the following approximations can be made:

$$\frac{\exp(-rt)}{1 - \exp(-rt)} \approx \exp(-rt)$$

$$\frac{\exp(-rt)}{1 - \exp(-rt)/R} \approx \exp(-rt).$$

Hence, $P(I(t) = i)$ can be approximated by

$$P(I(t) = i) \approx \frac{R - 1}{R} \exp(-rt) \exp\left(-\frac{R - 1}{R} \exp(-rt)\right),$$

which has the form of the pdf of an exponential distribution. Therefore, the continuous variable $I'(t)$ is distributed as

$$I'(t) \sim \text{ExponentialDistribution}\left[\frac{R - 1}{R} \exp(-rt)\right].$$
By defining $H = \Gamma(t)\exp(-rt)$ and by dropping the accent for notational convenience, $l(t)$ becomes

$$I(t) = H\exp(rt), \text{ with } (5.4.1)$$

$H \approx \text{ExponentialDistribution}\left[\frac{R-1}{R}\right]$ (5.4.2)

Appendix 5C

Here we derive equations (5.19) for determining the probabilities of extinction $z_f$ and $z_m$ starting with one finishing herd or multiplier herd, respectively. Diekmann and Heesterbeek (Diekmann and Heesterbeek, 2000) derive a similar equation from a model with one type of infectious individual. Since both equations (5.19) are derived in a similar way, only the derivation for the first of the two equations is shown.

The probability $z_f$, that a chain of infected herd $s$ starting with one finishing herd will eventually go extinct, is

$$z_f = \sum_{k=0}^{\infty} \sum_{l=0}^{\infty} q_{k,l} z_f^k z_m^l,$$ (5C.1)

in which $q_{k,l}$ is the probability that a finishing herd infects $k$ finishing herds and $l$ multiplier herds:

$$q_{k,l} = \frac{\left(\frac{\mu}{r}h\left(\exp(rt) - 1\right)\right)^k}{k!} \exp\left(-\frac{\mu}{r}h\left(\exp(rt) - 1\right)\right) \ldots \frac{\left(\frac{\mu}{r}h\left(\exp(rt) - 1\right)\right)^l}{l!} \exp\left(-\frac{\mu}{r}h\left(\exp(rt) - 1\right)\right) \ldots \cdot dh \exp\left(rt - \frac{\mu}{r}h\left(\exp(rt) - 1\right)\right) \frac{R-1}{R} \exp\left(-\frac{R}{R}h\right) dt dh$$ (5C.2)

The first two lines of Eq. (5C.2) are the probabilities of infecting $k$ finishing herds and $l$ multiplier herds according to a Poisson distribution with a mean depending on
the height $h$ of the infectious curve and detection time $t$ of the infectious finishing herd. The third line consists of the distributions for $h$ and $t$ over which the Poisson probabilities are integrated.

If $q_{k,l}$ is put into the formula for $z_f$, the generating function for the Poisson distribution can be used to obtain

$$ z_f = \int_0^\infty \int_0^\infty q_{k,l} \exp \left[ rt - \frac{h}{r} \left( \exp(rt) - 1 \right) (\alpha - \beta_f (z_f - 1) - \beta_m (z_m - 1)) \right] \ldots $$

$$ \left. \left. \left. \left. \left. \exp \left( - \frac{R-1}{R} t \right) \right) \right) \right) \right) \right) \right) \right) dt \, dh $$

(5C.3)

Evaluation of Eq. (5C.3) leads to the final result:

$$ z_f = \frac{1}{1 - \frac{\beta_f}{\alpha} (z_f - 1) - \frac{\beta_m}{\alpha} (z_m - 1)} $$

(5.19.1)

**Appendix 5D**

Continuous time stochastic simulations were performed in Mathematica® (Wolfram, 1999). Epidemics were simulated in generations of infected herds. The initially infected herds were the $0^{th}$ generation and were by definition infected at $t = 0$, the moment the control strategy was implemented. For each herd of the $0^{th}$ generation, the following values were drawn from the appropriate distributions in the designated order:

1. The height of the infectious curve
2. The detection time
3. The numbers of finishing herds and multiplier herds in the $1^{st}$ generation, infected by this herd
4. The infection times of these herds of the $1^{st}$ generation

When for each herd of the $0^{th}$ generation all the values had been drawn, the same 4 values were drawn for each herd of the $1^{st}$ generation, etc.

The distributions for the 4 steps in the simulation for each herd in generation $i$ were:
1. The height $H$ of the infectious curve of the herd in generation $i$ was exponentially distributed with parameter $(R-1)/R$

2. The detection time $t_{det}$ of the herd in generation $i$ was equal to its infection time (determined in step 4 of its source herd in generation $i-1$, or equal to 0 if $i = 0$) plus a random number from the distribution of the length of the infectious period $\delta_i$ with probability density function:

$$pdf(\delta) = ah \exp \left( r\delta - \frac{ah}{r} (\exp(r\delta) - 1) \right), \quad (5D.1)$$

in which $h$ was the height of the infectious curve, drawn in step 1.

3. The numbers of finishing and multiplier herds infected in generation $i+1$ by the considered herd in generation $i$ were Poisson distributed with parameters depending on the herd type of the herd in generation $i$. If the herd is a finishing herd, the parameters of the Poisson distributions for the numbers of finishing herds $\sigma_{ff}$ and multiplier herds $\sigma_{mf}$ in generation $i+1$ were:

$$\sigma_{ff} = \beta_f \int_{t_{det}}^{t_{inf}} \varphi_f(\tau) \exp(\tau + t_{inf}) d\tau \quad (5D.2.1)$$

$$\sigma_{mf} = \beta_m \int_{t_{det}}^{t_{inf}} \varphi_m(\tau) \exp(\tau + t_{inf}) d\tau \quad (5D.2.2)$$

If the herd is a multiplier herd, the parameters of the Poisson distributions for the numbers of finishing herds $\sigma_{fm}$ and multiplier herds $\sigma_{mm}$ in generation $i+1$ were:

$$\sigma_{fm} = \beta_f \int_{t_{det}}^{t_{inf}} \varphi_f(\tau) \exp(\tau + t_{inf}) d\tau + \beta_m \int_{t_{det}}^{t_{inf}} \varphi_m(\tau) \exp(\tau + t_{inf}) d\tau \quad (5D.2.3)$$

$$\sigma_{mm} = \beta_m \int_{t_{det}}^{t_{inf}} \varphi_m(\tau) \exp(\tau + t_{inf}) d\tau \quad (5D.2.4)$$

4. The infection times of the infected herds of generation $i+1$ were distributed according to the normalised infectious curve of the source herd in generation $i$. For example, the probability density function for infection times of finishing herds in generation $i+1$, $t_{inf(j)}$, infected by a finishing herd in generation $i$ with infection time $t_{inf(i)}$ and detection time $t_{det(i)}$, is
The $pdf$s for infection times of other herd types were derived analogously.