Spatial and stochastic simulation to compare two emergency-vaccination strategies with a marker vaccine in the 1997/98 Dutch Classical Swine Fever epidemic

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Abstract

Two alternative emergency-vaccination strategies with a marker vaccine that could have been applied in the 1997/98 Dutch Classical Swine Fever (CSF) epidemic were evaluated in a modified spatial, temporal and stochastic simulation model, InterCSF. In strategy 1, vaccination would only be applied to overcome a shortage in destruction capacities. Destruction of all pigs on vaccinated farms distinguishes this strategy from strategy 2, which assumes intra-community trade of vaccinated pig meat.

InterCSF simulates the spread of CSF between farms through local spread and 3 contact types. Disease spread is affected by control measures implemented through different mechanisms. Economic results were generated by a separate model that calculated the direct costs (including the vaccination costs) and consequential losses for farmers and related industries subjected to control

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measures. The comparison (using epidemiological and economic results) between the different emergency-vaccination strategies with an earlier simulated preventive-slaughter scenario led to some general conclusions on the Dutch CSF-epidemic. Both emergency-vaccination strategies were hardly more efficient than the non-vaccination scenario. The intra-community trade strategy (vaccination strategy 2) was the least costly of all three scenarios.

Keywords: Classical Swine Fever; Pig-microbiological disease; Simulation model; Disease control; Emergency vaccination; Economics

1. Introduction

When all regular measures to eradicate an CSF-epidemic fail, paragraph 14 of the directive 80/217/EEC of the EU legislation foresees an emergency-vaccination (CEC, 1980). In the case of an emergency vaccination, the same directive forces the member state to exclude all meat originating from vaccinated pigs (except when heat treated) from the regular pork market. In the last decade, some severe CSF-epidemics occurred in the EU, but no emergency vaccination was applied. In 1994, the German proposal for an emergency vaccination was refused by the European Commission (Blaha, 1994). During the 1997/98 epidemic in the Netherlands, emergency vaccination was only proposed at the national level (Jorna, 1997) mainly on ethical grounds.

The use of a marker vaccine to help control a CSF outbreak seems to be technically feasible (Van Oirschot, 1994; Leopold, 1996; Vågsholm, 1996; Jorna, 1997), including serological test to distinguish infected pigs from vaccinated pigs. Changes in the swine herd structure combined with high-density pig populations incur logistic and organisational problems, as well as high costs, when adopting a regular stamping-out policy to eradicate an epidemic. Public objections against the destruction of healthy animals increase as well. Those factors are in favour of emergency vaccination. On the other hand, EU policy aims a high animal health status and therefore has adapted a non-vaccination policy for the control and eradication of animal diseases of major importance for international trade. In brief, the use of vaccine "means" the presence of disease (Westergaard, 1996).

Epidemiological, political and economic advantages and disadvantages have to be analysed and clarified before being able to decide if the use of marker vaccine is a realistic and attractive option. We improved the simulation model InterCSF, which was developed to simulate the 1997/98 Dutch CSF epidemic, (Jalvingh et al., 1999) by adding emergency-vaccination as a disease-control mechanism. InterCSF specifically was developed to answer "what-if" questions (Nielen et al., 1999). Vaccination costs were incorporated in EpiLoss (Meuwissen et al., 1999) for the present study, to be able to calculate the direct costs and consequential losses for farmers and related industries subjected to control measures.

The main goal of this paper was to analyse the epidemiological and economic consequences of two possible emergency-vaccination campaigns that could have been used in the Dutch CSF 1997-98 epidemic. They are compared with an earlier simulated preventive-slaughter strategy (Nielen et al. 1999), which we will call (in this paper) the "non-vaccination" (NV) scenario.

2. Material and methods

2.1 General outline

InterCSF is a spatial, temporal and stochastic simulation model (Jalvingh et al., 1999). InterCSF simulates disease spread from day to day from infected farms through 3 contact types (animals, vehicles, persons) and through local spread up to 1000 m. All Dutch pig farms are known by their geographical co-ordinates. The main disease-control mechanisms that influence the disease spread in InterCSF are: diagnosis of the infected farms, depopulation of infected farms, movement control areas, tracing and preventive slaughter (see Appendix I for more details).

Emergency vaccination was incorporated in the base scenario such that it reflected the start situation of the real epidemic as closely as possible. This involved incorporating historical data of 37 farms with an infection date before February 4 1997 (detection date of first farm) and fixed detection and herd-destruction dates later. New infections were simulated only after this date. In our simulations we assumed that after 5 detections in the first week, emergency vaccination would be ordered. In a densely populated area epidemiologists expect a large epidemic if there are at least 5 detections in the first week. In 1997/98, the first outbreak happened in a very densely populated area and 9 outbreaks were notified in the first week after the first detection (Elbers et al., 1999). In our simulation, the emergency-vaccination campaign was initiated 5 days after the decision on day 6 (assuming 5 days of preparation for a vaccination campaign). When the decision to start with the emergency-vaccination campaign was taken, all earlier-detected farms from the previous week were identified. In the base vaccination scenarios, a vaccination zone with a radius of 3 km was defined for each detected farm. To mimic restricted vaccination capacities, all defined vaccination zones were put on a vaccination list and all further-defined vaccination zones were listed also. If more than one new vaccination zone was defined on the same day, they were sorted depending on their pig-farm density, starting with the highest pig-farm density. We further assumed that emergency vaccination would be stopped based on certain criteria (defined later on in paper).

Vaccination zones are vaccinated one by one - not in parallel - by 150 vaccination teams. Each vaccination team (1 veterinarian and 4 helpers) was supposed to handle about 2000 pig places (fatteners[3] and gilts[4]) or 465[5] farrowing places per day (or various equivalent combinations).

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[3] A fattener is a finishing or fattening pig (from 45 kg until killed).

[4] A gilt is a female pig from 20-30 kg live weight until first insemination.

[5] Assuming 21.5 piglets/breeding sow/year, which is equal to 0.059 piglets born/breeding sow/day. We assume that a piglet will stay on a sow farm for 70 days. Because pigs need to be 14 days old for vaccination, we will have (0.059*56 days =) 3.30 piglets/farrowing place and 1 sow/farrowing place to vaccinate.

2.2 Vaccination effects

Vaccination has two effects: reduction in virus spread of an infected farm and protection against infection of a susceptible herd.

For virus reduction on an infected farm, two kinds of infected farms were distinguished. The first category consisted of infected farms that were never vaccinated and of farms that were first infected and later vaccinated. The second category was farms that were vaccinated and became later infected.

For the first category of infected farms, we assumed no reduction in virus spread. All parameters remained as described in Jalvingh et al. (1999). In short, the infectious period started between 5 and 10 days after infection. The infectivity of the farm remained the same for the total infectious period, which ended on the day that the farm was depopulated. The interval between infection and detection was modelled with a single probability distribution, based on observations of the real Dutch CSF epidemic. The selected interval could be influenced downward by certain events (see Table 1). The detection probabilities of non-vaccinated farms were used as a base to estimate the detection probabilities for all vaccinated farms (Table 1). Vaccination as such could also influence detection because infected farms could be detected earlier due to clinical inspection on the vaccination day. The detection probability depended on the time since infection and the source of infection (Table 2). For a direct animal contact we defined a higher probability of detection for the first weeks after infection than for all other contacts. If an infected farm was not detected during vaccination, we assumed that the virus was spread mechanically and massively over the farm during vaccination. After the incubation time of 1 week, the large number of sick animals could again lead to a possible earlier detection (Tielen; Personal communication). In both cases, we assumed that 2 days after suspicion, the diagnosis was established. For all other events, more time consuming tests are necessary; so, we defined 7 days after suspicion before diagnosis would be given (de Smit et al, 1999).

For vaccinated farms infected after vaccination (the second category), a reduction in virus spread was expressed by a reduction factor. This reduction factor depended on the time interval between vaccination and infection and was modelled with a probability distribution, based on EU experiments (Appendix II). The reduction factor was multiplied by the probabilities of transmission for a simulated contact and for local spread.

For the farms in the second category, we assumed no change in the latent period but the infectious period was reduced to at most 1 month. Only small outbreaks typically are expected on vaccinated farms. Assuming that vaccinated pigs show no or few clinical signs when infected, detection could only be by serological screening (Table 1).

Susceptible farms also were classified in two categories: non-vaccinated and vaccinated farms. We defined a non-vaccinated susceptible farm as one without protection against a possible infection, whereas a vaccinated susceptible farm was partly protected. The degree of protection depended on the time interval between vaccination and a possible infection and was expressed as a protection factor, modelled by a probability distribution (Appendix II). Similar to the reduction factor, the protection factor was multiplied by the probabilities of transmission for a simulated contact and for local spread. However, if an infectious pig was moved to a susceptible vaccinated farm, the protection factor was not considered. We assumed that this farm always became infected but could hardly ever become infectious.

In the EU field experiments, horizontal transmission was significantly reduced 3 weeks after vaccination for both marker vaccines (Anonymous, 1999). In our base emergency-vaccination scenarios, we assumed that maximum protection and reduction was reached after 21 days. For sensitivity analysis, this time interval was reduced by 5 days to 16, as well as increased by 5 days to 26 days (Appendix II). In an additional analysis, only 1 week was assumed to be needed to build up the maximum protection level (simulating a live-virus vaccine).

2.3 Delayed-destruction alternatives

The first emergency-vaccination strategy (called "delayed-destruction" (DD)), assumed no political acceptance of vaccinated pig meat as fresh meat (i.e. the current EU policy). Vaccination would only be applied to overcome a shortage in destruction capacity[6], created by regularly applied control measures. Because vaccination will reduce the risk of virus spread the destruction of the vaccinated farms can be postponed until destruction capacity is available. All pigs in the vaccination zone needed to be destroyed before the end-screening could be applied to declare the region free again of CSF. All pigs older than 14 days were vaccinated once. We assumed that vaccinated pigs had maximum protection for at least 6 months. If they were not slaughtered within 6 months, the pigs would be re-vaccinated to keep maximum protection.

As soon as a vaccination zone was defined, all farms inside this vaccination zone were put on the preventive-slaughter list. Priorities were set to deal with the insufficient destruction capacities. First, all farms located in the regular preventive-slaughter radius (1 km) and contact farms were destroyed. This group was further split up. Farms not predestined for vaccination had the highest priority, followed by farms where vaccination was not yet applied and finally vaccinated farms. In the category of the vaccinated farms, higher priority was given to farms without maximum protection. The second category consisted of farms lying in the vaccination zone (0-3 km), but outside the regular preventive-slaughter zone (0-1 km). Here again, the highest priority was given to non-vaccinated farms, followed by vaccinated, not maximum-protected farms and finally maximum-protected farms. Those priorities are handled over all the zones, whereby inside a subgroup, the farms of an older zone had priority to be destroyed. The decision criterion for stopping emergency vaccination depended on the delay caused by destruction capacities. The number of farms notified for preventive slaughter (including vaccinated farms) was divided by the daily destruction capacity to obtain the number of days needed for destruction of all those farms. When the delay was ≤ 3 days during a period of 14 days, no new vaccination zones were installed.

The installation of a breeding prohibition in a defined vaccination zone and the culling of newborn piglets on the vaccinated farms (not simulated as such) allowed the assumption that the pig population on vaccinated farms retained maximum protection. The implementation costs for both control measures were considered when calculating the costs and losses.

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[6] Under destruction capacities we include both the killing of the pigs and the rendering.

In the base scenario (DD-0), we assumed maximum vaccine protection in 21 days, 5 days of preparation, a 1 km preventive-slaughter zone and a vaccination radius of 3 km for each detected farm. In alternative scenarios (Table 3), we assumed that time to build maximum protection was reached in 1 week, 16 days or 26 days. In further sensitivity analysis, the time needed to prepare the emergency-vaccination campaign was changed from 5 days to 2 days (alternative I), to 8 days (alternative II) or to 25 days (alternative III). In alternative IV, the vaccination radius was reduced to 1 km instead of the 3 km, and alternative V assumed a 500 m regular preventive slaughter radius.

2.4 Intra-community trade alternatives

For the second emergency-vaccination strategy (the intra-community trade strategy (ICT)), we assumed that after removing the surveillance zone, pig meat originating from vaccinated pigs could be sold on the EU market. However, we assumed that for the vaccination zones, a so-called "post-vaccination zone" was installed for 4 months at the moment the surveillance zone was lifted. All movements were allowed, except that live pigs could leave this zone only directly to slaughter in specific slaughterhouses. This supplementary measure should convince all trading partners that no live carrier piglets could leave the vaccination zone to spread the disease, in case an infected sow was overlooked during the serological screening. In the ICT strategy, emergency vaccination was stopped when there were less than two new detections during the previous 4 weeks.

In the ICT strategy, all pigs older than 2 weeks in a vaccination zone (0-3 km) were vaccinated once similar to the DD strategy. In addition, we imposed (for the duration of the surveillance in a vaccination zone) that all newborn piglets and also all breeding sows would be re-vaccinated. These measures would assure a maximally protected pig population. The emergency-vaccination capacities were not influenced by the continued vaccination, because we assumed that the local veterinarians carried out the re-vaccinations. A further assumption was that maximum protection of vaccinated farms would last for the total duration of a post-vaccination zone. After the ending of the post-vaccination zone, all farms lost their protection.

With the ICT strategy, vaccination reduces the susceptible pig population so preventive slaughter is optional and not applied in the base scenario. If preventive slaughter is applied, only non-vaccinated farms would be destroyed (alternative VI, Table 3).

For the base scenario (ICT-0), maximum protection was reached in 21 days, no preventive slaughter was applied, a vaccination radius of 3 km was installed for each detected farm and 5 days of preparation were needed before the start of the emergency-vaccination campaign. Alternative scenarios were simulated for sensitivity analysis, similar to DD (Table 3).

2.5 Vaccination costs

Related to vaccination were various additional control costs, above the cost per dose vaccine per pig. They consisted of preparation, travel and bio-security costs for the vaccination teams, and costs for the application of the vaccine. In case of the ICT strategy, the continued vaccination caused some more costs. Table 4 summaries all vaccination related costs in detail.

All sows on vaccinated farms should be tested to reduce the probability that a carrier piglet goes undetected before an area can be declared CSF-free. Despite this, we used the same lump sum (for comparison reasons) for serological costs as Meuwissen et al. (1999). Further we assumed that the discriminatory test would cost the same as the conventional one.

2.6 Comparison of alternatives

To compare the alternatives, both epidemiological and economic parameters were used. InterCSF simulated the spread and the control of the epidemic, whereby different events (summarised in Appendix III) related to economic costs and losses could occur. Vaccination was added as a new event. Breeding prohibition and welfare slaughter of newborn piglets were applied only for the DD strategies. For each individual farm subjected to control measures, InterCSF wrote events per day to an event-output file. This event-file was used as input for EpiLoss, which calculated the total costs and losses for the epidemic (Meuwissen et al., 1999). Vaccination related costs (actually direct costs) were considered for comparison reasons as a separate cost factor.

Similar to Nielen et al. (1999), a two-tailed, two-sample Student's t-test with unequal variance was performed on mean final outcomes of the 100 replications per scenario, to test whether alternatives varied significantly from each other or from the non-vaccination scenario (NV). To correct for multiple comparisons, a Bonferroni correction was applied on a significance level of 0.05 (Jones and Rushton, 1982). Final outcomes that were compared were the mean total losses and the mean total number of infected farms, detected farms, preventively slaughtered farms and vaccinated farms. Testing was performed using SPSS software (version 8.02).

3. Simulation results

Nielen et al. (1999) compared the real 1997/98 CSF epidemic with various alternative eradication strategies, all simulated with the InterCSF model (Jalvingh et al., 1999). All simulated strategies were performed 100 times, in which the simulation time was set at maximum 1 year. The most-effective scenario according to Nielen et al. (1999) was to start preventive slaughter in a radius of 1 km from the day of the first detection (the so-called "preventive-slaughter scenario"; in this paper called the "non-vaccination scenario" (NV)). Complete results were shown in Nielen et al. (1999) and are partly shown in Tables 5 and 7. In the real epidemic, preventive slaughter of the neighbouring farms was only applied for the first 2 detected farms, stopped and re-started two months later for all newly detected farms (LNV, 1998). Table 5 recalls the most important key features of the real epidemic, the simulated epidemic and the NV. We chose the NV as the base scenario with which to compare all emergency-vaccination strategies. In the future, preventive slaughter would most likely be applied from the beginning making this scenario the best comparison for our simulated emergency-vaccination scenarios.

In Table 6, we compare the two base emergency-vaccination strategies with the NV scenario and with each other. Furthermore, all emergency-vaccination alternatives were compared to the corresponding base emergency-vaccination strategies. In total, 38 t-test comparisons were performed, which set the P-level for a significant difference between means to 0.001316 (0.05/38).

3.1 Delayed destruction alternatives

Compared to the NV scenario, DD strategies (Tables 6 and 7) reduced both the number of infected and detected farms, but not significantly. The duration of the epidemic was sharply reduced (for example, the median decreased from 164 days to 108 days for DD-21-0). The number of preventively slaughtered farms was significantly increased by a factor of almost four. The total costs and losses were comparable, except for the extreme replications. In the case of DD, the worst cases showed smaller epidemics. The composition of the cost factors varied between the NV scenario and the DD scenario. The direct costs for preventive slaughter in the case of the DD vaccination scenario were nearly three-times higher. The consequential losses for the farmers increased, but the direct cost for welfare slaughter was sharply reduced. Compensation paid to the farmers for the breeding prohibition, as well as vaccination costs, were extra costs compared to the NV scenario.

The results of the different DD alternatives, including the base version (DD-21-0) of this scenario, are shown in Tables 6-9. There was no significant difference in the size of the epidemic, when maximum protection was changed from 21 days to 7, 16 or 26 (Tables 6 and 8). The effect of preventive slaughter according to the vaccination-related priorities was apparently greater than the vaccine efficacy.

In the base DD vaccination scenario (DD-21-0), we assumed 5 days of preparation before the emergency vaccination actually started. In alternatives I, II and III, we assumed respectively 2, 8 and 25 days to prepare an emergency-vaccination campaign, following the decision on day 6. A longer preparation time only showed a larger epidemic for the worst iterations (Table 8). There was no significant difference in the number of detected farms, the number of infected farms, the number of preventively slaughtered farms or in the costs when comparing the simulated alternatives with the base DD scenario (Tables 6 and 8). Comparing alternatives I, II and III with the NV scenario, the number of preventively slaughtered farms were always significantly higher.

By changing the vaccination radius from 3 km to 1 km (alternative IV), the number of detected farms was slightly but not significantly higher compared to the base DD scenario (Tables 6, 8 and 9). Except for the worst iterations, the duration of the epidemic was the same (results not shown), but the number of preventively slaughtered and vaccinated farms was significantly lower leading to lower costs (compared to the base DD scenario). The 1-km vaccination alternative was significantly less costly than the NV scenario (1-km preventively slaughter) mainly due to the shorter duration of the epidemic.

3.2 Intra-community trade alternatives

The results of the different ICT alternatives, including the base version (ICT-21-0) of this scenario, are shown in Tables 6-9. In comparison to the NV scenario, the ICT base scenario was significantly cheaper (assuming no cost and losses for the post-vaccination zone). Preventive slaughter was not applied in the ICT scenario avoiding the large compensation costs. Furthermore, the consequential losses of the farmers were smaller compared to the NV scenario. No difference could be found for the number of detected and infected herds, except for the worst iterations. The same was true for the duration of the epidemic, when deducting the 120 days post-vaccination zone (Tables 6 and 7). Comparing the ICT base scenario with the DD base scenario, no farms were preventively slaughtered. Furthermore, the costs were significantly lower.

There was no significant difference in the size of the epidemic when the maximum protection level was varied from 21 days to 16 or 26 days (Tables 6 and 8). However, when maximum protection was reached in 7 days, the epidemic was shorter with a significantly lower number of infected and detected premises. This alternative was consequently less costly than the simulated base ICT. In comparison with the NV scenario, all three alternatives were significantly less costly.

There was no significant difference when comparing alternatives I and II of the intra-community trade with the base ICT (Tables 6 and 8). A slight (not significant) tendency of a decreased (increased) epidemic was found if the preparation time decreased (increased) by 3 days. However, alternative III (25 days preparation time) caused a significantly larger epidemic with significantly more detected, infected and vaccinated farms (as well as increased costs and losses). Alternatives I and II were significantly cheaper, when comparing with the NV scenario in contrast to scenario III.

A 1-km vaccination radius significantly reduced the number of vaccinated farms (for example the median decreased from 1135 vaccinated farms to 284 (result not shown)). The number of infected and detected farms was slightly higher (not significant) compared to the base (Tables 6, 8-9).

Applying preventive slaughter in ICT alternative VI showed no difference in the epidemiological parameters and did not increase the total costs significantly (Tables 6 and 8).

4. Discussion

Although the EU regulations currently prohibit routine vaccination against CSF, it is expected that the development of a marker vaccine will lead to a reassessment of the non-vaccination principle (Laddomada and Westergaard, 1999). Therefore, the main goal of our simulations was to analyse different possible emergency-vaccination campaigns, which could have been applied in the 1997/98 Dutch CSF epidemic. The vaccination alternatives were compared with the NV scenario discussed in Nielen et al. (1999). The NV scenario was considered to be the most effective that could have been reached with the regular control measures.

4.1 Comparison of vaccination strategies

The results of the significance testing should be used with caution as with more replications, even-smaller differences between alternatives would have become significant. The duration of the epidemic could not be tested in the current simulations because the epidemics were always stopped at 365 days. Other useful parameters not tested (such as the cost factors) could mostly be explained by changes in underlying parameters.

The main goal of any emergency-vaccination strategy (reduced number of infected herds) were reached in both emergency-vaccination scenarios compared to the NV strategy. The DD strategy seemed to be the most-effective strategy for reducing duration and size of an epidemic.

A shorter epidemic would lead to a reduction in direct costs paid for welfare slaughter and for organisation. For the DD strategy the reduction was countered by the higher preventive-depopulation costs (all vaccinated farms) as well as the higher consequential losses for farmers. Vaccination costs were only of minor importance. Except for the 95th percentile (DD was less costly), no overall difference could be found between a DD scenario and the NV strategy.

ICT entirely relies on a reliable and easy-to-handle serological test. Presuming no hindrance on the EU market for pig meat originating from vaccinated pigs and no extra cost and losses for the post-vaccination zone, ICT was significantly cheaper then NV or DD. The vaccination costs were more than compensated by the reduction in the direct costs paid for preventive slaughter and in the consequential losses. Furthermore, the numbers of infected and detected farms were on average smaller (but not significantly) for ICT then for NV. The worst-case iterations for ICT were never as severe as for the NV scenario. An ethical as well as an economic advantage of this strategy, compared to NV and also to DD, is that (except for welfare slaughter in the surveillance zone) no healthy pigs need to be destroyed.

The effectiveness of the DD strategy was mainly due to the applied preventive depopulation of the vaccination zones in which farms with the highest risk had the highest priority. When simulating a NV scenario with 3-km preventive-slaughter radius but without a classification into risk types the average epidemic increased from 120 to 209 detected farms (results not shown). So, the effectiveness of the DD scenario was partly the result of the classification into risk types and partly based on the reduced virus spread due to vaccination. The latter effect is mainly of importance in large epidemics and severely limited destruction capacity.

A small change in the effectiveness of the vaccine (16, 21, 26 days to maximum protection) had no extra influence on the epidemic for either emergency-vaccination strategy. Only a very-effective vaccine (maximum protection in 7 days) significantly reduced the epidemic for the ICT scenario. The 7 days refers more or less to the effectiveness of the conventional non-marker CSF vaccine, as has been used historically in Dutch epidemics (Brus, 1976; Tielen, 1977).

We presumed a fast implementation based on clear criteria about where and when to start an emergency-vaccination campaign (≥ 5 detections in the 1st week) combined with a short preparation time of 5 days. A longer delay (alternative III) had a negative effect especially in the case of the ICT alternative. This effect was much lower for the DD alternative because this scenario also depended on risk-based depopulation as a control measure from day 6 onwards.

Changing the preventive-slaughter radius from 1000 m to 500 m in the DD scenario had no negative effect, because the 500-m preventive slaughter was only applied during the first week of the epidemic, followed by a 3-km vaccination and preventive-slaughter zone.

Applying preventive slaughter as an additional measure in the ICT scenario showed no significant effect on the course of the epidemic. The main effect was to change the composition of total cost: higher consequential losses for farmers; extra depopulation costs; lower costs for welfare slaughter.

A reduction in the vaccination radius from 3 km to 1 km was significantly cheaper than the NV scenario; for DD due to a reduced number of preventively slaughtered farms, for both DD and ICT due to reduced vaccination costs. However, potentially the control of the post-vaccination zone would become more difficult (thus, costly) for ICT.

4.2 Model constraints

A discriminatory diagnostic test with a specificity of less than 1 could lead to the detection of false positive farms. As a consequence, new movement-control zones would be installed and healthy pig farms would be slaughtered out. High sensitivity is required, because we want to detect all infected farms. In the current simulations, we assumed a specificity of 1 (simplification reasons) whereas the sensitivity was based on the current conventional diagnostic test. So in our simulation, we detected nearly all infected farms but we would never "find" false positive farms.

The addition of vertical transmission (the sow conveys the infection to its unborn offspring) would have meant a complete overhaul of the transmission structure in the model (Jalvingh et al. 1999), and was excluded. In the case of ICT, vertical transmission could lead to an underestimation of the epidemic. We assumed for vaccinated and later-infected farms an infectious period of only 1 month (which does not take into consideration the birth of carrier piglets) whereas all other infected farms remained infectious until being slaughtered.

We assumed that only vaccinated and later-infected farms would show a reduction in virus spread (further research is needed). Infected and later vaccinated farms were supposed to stay infectious until detection without any reduction in infectivity. Because those farms had a high probability of being detected earlier due to vaccination, their effect on the outcomes is rather small. Vaccination activities also could lead to earlier detection of infected farms, but the effect on the simulation outputs was rather small (results not shown).

We assumed maximum protection of all vaccinated farms during the 120-day post-vaccination zone. This is an over-estimation because the number of not-vaccinated pigs will increase in that period. The duration of maternal immunity against transmission was not modelled, but would reduce the above over-estimation. At removal of a post-vaccination zone, the protection level of all vaccinated farms was set to zero, leading to an underestimation of the vaccination effect.

No reduction in the effectiveness of the vaccine in the case of maternal immunity of the piglets was assumed. For simulation at the animal level, the effect of maternal immunity against virus transmission needs to be quantified. InterCSF simulates at the herd level.

Vaccination has some disadvantages and possible hazards as it may engender a false sense of security (leading to relaxation of other control measures and/or less-strict sanitary behaviour of people involved) (Anonymous, 1997). In our simulations, we presumed no relaxation.

The high number of required diagnostic tests could lead to a delay in diagnosis. This effect was not considered as such in our simulation model. We assumed minimum 49 days instead of 42 days before removing the standstill, to mimic a waiting period for the laboratory results.

Simulating the actual 1997/98 Dutch CSF epidemic, we knew in advance that we would have a large epidemic in a very densely populated area. So, the decision to start an emergency-vaccination campaign was based in the current study only on a single criterion (i.e. 5 detections in the first week). In a more-generic model, further criteria may be compared (such as the pig density or the total number of outbreaks in relation to the length of the epidemic).

4.3 Economic model constraints

The breeding prohibition was not simulated, but the compensation paid to the farmers was calculated in EpiLoss. Because a decreasing pig population was only considered for fattening farms in a movement-control zone (Meuwissen et al., 1999), the total depopulation costs could have been overestimated (especially in large epidemics) in the case of DD. To be able to compare with NV, we accepted this slight overestimation by not adapting EpiLoss.

Serological costs were only incorporated as a lump sum per tested farm derived from the Dutch 1997/98 CSF epidemic. Serological cost calculations based on farm size and type would allow better and more-detailed comparisons of different simulated alternatives.

The direct costs for welfare slaughter were based on average pig prices over the year 1997 because no market reaction was simulated. In a real epidemic, compensation paid for welfare slaughter is based on weekly fluctuating slaughter prices. In the case of a large epidemic, the demand and the supply of growers[7] and fatteners will certainly be interrupted or distorted (which would lead to large price movements (see Asseldonk et al., 2000)). Large price changes would mainly influence the direct costs of welfare slaughter, but also the consequential losses of the farmers subjected to

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[7] A grower is a piglet of 20-45 kg.

control measures (such as higher repopulating costs). Consumer behaviour is not always rational, and a severe reaction against vaccinated meat could lead to a drastic price drop (not simulated).

EpiLoss is based on partial budgeting and calculates only the cost and losses of farms and related industries subjected to control measures. Benefits were not considered (such as higher profits of pig farmers outside the restricted areas or profits of the pharmaceutical industry).

To control a post-vaccination some organisational costs will be involved. Farmers situated in a post-vaccination zone may be restricted in their choice to sell their pigs resulting in lower weekly pig prices then paid outside the zone. The current zero cost assumption is therefore too optimistic.

5. Conclusion

Emergency vaccination (assuming a reliable diagnostic test and no relaxation of other control measures) seemed to be an effective strategy for reducing the size of an epidemic. Emergency-vaccination alternatives were at least as effective as the optimal NV scenario. The worst iterations were never so severe as in the case of the NV scenario. The large number of preventively slaughtered farms in the DD strategy is a negative aspect of the DD strategy compared to the NV strategy. This effect mainly reduces the positive effect of a shorter epidemic. If we compare the ICT strategy with the NV strategy, emergency vaccination is certainly the tool to choose. Vaccination costs (which are of minor importance compared to all other costs and losses) are mainly in competition with the cost of preventive slaughter, assuming no extra costs and losses for the post-vaccination zone. ICT avoids the destruction of a large number of healthy pigs, which can still be used for human consumption.

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Appendix I.

Chronological order of all control measures except vaccination in case of a newly detected CSF outbreak in InterCSF (Jalvingh et al., 1999)

Time	Measure
Day of detection	- Infected farm will be put on slaughter list and destroyed as soon as capacities are available (highest priority) - Movement standstill is imposed on the protection (3 km) and on the surveillance zone (10 km); fewer person contacts (50%) are allowed. Animal contacts and vehicles contacts are forbidden. - Farms within a certain radius could be subjected to pre-emptive slaughter, limited by destruction capacity. Preventive slaughter could lead to an earlier detection.
Start on 2nd day	- Surveillance (clinical inspection) of all farms in the protection zone (3 km), which may lead to earlier detection. - Tracing farms that had contact with the infected farm. Traced farms are put on surveillance (clinical inspection), which may lead to earlier detection, or may be subjected to preventive slaughter.
Start on day 28th	- Start welfare slaughter of fatteners and growers in the surveillance zone (3-10 km) until the movement-control zone is lifted. Welfare slaughter may lead to earlier detection.
Earliest on day 35th	- Start of serological end-screening of all farms situated in the restricted zone (10 km), if no additional farm was detected during those last 35 days.
Earliest on day 49th [a]	- If there is no new detection in a restricted zone, the movement standstill in the surveillance and the protection zone is lifted up

[a] We assumed 49 days instead of 42 days, to mimic a waiting period for the laboratory results

Appendix II

The calculated reduction and protection factors

In horizontal-transmission experiments co-ordinated by the EU, animals in groups of 10 were vaccinated with one of two alternative vaccines and 5 of each group were inoculated with CSF 7, 10, 14 or 21 days after vaccination. From the data generated by these experiments, parameters of the standard SIR model were estimated (Klinkenberg et al., 2000). These parameters were used to calculate the reduction in total infectivity of a herd depending on the time between vaccination and infection. Results showed that for both vaccines, 21 days was the time from vaccination until maximum protection of the individual animal. The relative decline of the estimated between-animal transmission parameter was used as protection factor. To see what a faster or slower working vaccine would do, time scales of protection and reduction curves were changed. Reference point of these changes was the maximum-protection date of the individual animals (21 days) which was changed to 7, 16 or 26 days. Because the vaccines do not differ in their ability to reduce horizontal transmission, we used the average of the estimated parameters from both vaccines. The applied reduction and protection factors are shown in Fig. 1 and 2.

Appendix III.

Control measures, related events in EpiLoss, and implications of the events

Control measures	Related events	Implications
Compulsory measures		
Stamping-out	- Depopulation	- Herd is destroyed, buildings empty till repopulation
	- Repopulation	- Restarting the farm
Movement standstill	- Start movement standstill	- No supply and delivery of animals allowed
	- End movement standstill	- Supply and delivery of animals allowed
Pre-emptive slaughter	- Depopulation	- Herd is destroyed, buildings empty till repopulation
	- Repopulation	- Restarting the farm
Additional measures		
Welfare slaughter	- Start welfare slaughter	- Animals for which measure applies are destroyed
	- End welfare slaughter	- End of destruction of animals under consideration
Breeding prohibition	- Start breeding prohibition	- Prohibition of insemination of sows
	- End breeding prohibition	- Insemination of sows allowed
Vaccination measures		
Vaccination	- Apply vaccination	- All pigs on the farm older than 14 days are vaccinated once, which may be repeated after 6 months - Continued vaccination may be included during the time of movement standstill for breeding sows and newborn piglets (only applied in the ICT strategy).
	- End movement standstill	- Vaccination stops

Table 1

Probability of detection based on a control event (such as traced contacts, surveillance, preventive slaughter, end-screening and welfare slaughter) depending on the time since infection and the farm specific vaccination status in a movement-restricted zone

Time since infection (days)	Probability of detection by control event (diagnosis date 7 days after event)														
	Traced contacts[a]			Surveillance (3 km radius)[a]			Preventive slaughter[a b]			End-screening[b]			Welfare slaughter[b]		
	NV[c]	IV[d]	VI[e]	NV[c]	IV[d]	VI[e]	NV[c]	IV[d]	VI[e]	NV[c]	IV[d]	VI[e]	NV[c]	IV[d]	VI[e]
0 – 14	0	0.9	0	0	0.9	0	0	0.9	0	0	0.9	0	0	0.9	0
15 – 28	1	1	0	0	1	0	1	1	0.5	0.25	1	0.5	0	1	0.5
29 – 42	1	1	0	0.25	1	0	1	1	1	0.5	1	1	0	1	1
> 42	1	1	0	1	1	0	1	1	1	1	1	1	1	1	1

[a] Based mainly on clinical inspection.

[b] Based mainly on serology.

[c] NV: No vaccination; farm already has an (undetected) infection (Jalvingh et al., 1999).

[d] IV: Vaccination of a farm already infected (but not yet detected).

[e] VI: Vaccination of a farm which later becomes infected.

Table 2
Probability of detection due to vaccination, relative to the time since infection on an (undetected) infected farm and depending on the source of infection

Time between infection entrance and vaccination (days)	Probability of detection related to vaccination (diagnosis date 2 days later)		
	Vaccination day [a]	Vaccination day [b]	1 week after vaccination
0 – 14	0.25	0.05	0.9
15 – 28	0.9	0.5	0.95
29 – 42	0.99	0.9	1
> 42	0.99	0.99	1

[a] Farm infected by direct animal contact.
[b] Farm infected by transport or person contact.

Table 3

An overview of the various alternatives for both emergency vaccination strategies: the Delayed Destruction strategy (DD) and the Intra-Community Trade strategy (ICT)

Assumption		DD - x[a]	ICT - x[a]
Preparation time	**5 days**	**0 (base)**	**0 (base)**
	2 days	I	I
	8 days	II	II
	25 days	III	III
Vaccination radius	**3 km**	**0 (base)**	**0 (base)**
	1 km	IV	IV
Preventive-slaughter radius	**1000 m**	**0 (base)**	-
	500 m	V	-
Applying preventive slaughter	**No**	-	**0 (base)**
	Yes	-	VI[b]

[a] x stands for 21 (base) respectively 7, 16 or 26 days needed to build up maximal protection.

[b] Preventive slaughter is only applied to non-vaccinated farms in a radius of 1 km.

Table 4

The vaccination-related costs

Description of the costs	€ /farm or pig
1. Bio-security cost and transport during the emergency vaccination:	
- Material needed for a farm visit (Overalls, sterile materials (no re-use))[a]	~ 45.4 € /farm
- Preparation needed for a farm visit (1/2 h * (25.0 € /h + 17.5 % B.T.W.)[a]	16.8 € /farm
- 1 hour for transport and hygiene measures (4 helpers (33.6 € /h[a]) and 1 veterinarian (74.4 € /h[b]))	213.3 € /farm
Total:	~ 272 € /farm
2. Vaccine and vaccination application during the emergency vaccination:	
- Vaccine	2.27 € /pig
- Application (2000 pigs/ vaccination group/ 8 hours) (4 helpers * 33.6 € /h[a] * 8 h + 1 vet. * 74.4 € /h[b] * 8)	0.83 € /pig
Total:	3.10 € /pig[c]
3. Costs for continued vaccination (only for ICT)[d]:	
- Vaccine	2.27 € /pig
- Vaccination application	0.45 € /pig
- Veterinary visit (20.42 € /farm[b])	0.07 € /pig
- Bio-security cost (no helpers) (45.4 € /farm[a])	0.16 € /pig
Total:	2.95 € /pig[e]

[a] Consulting specialist from Animal Health Service, Boxtel, The Netherlands (1999).

[b] Royal Netherlands Veterinary Association (1998).

[c] It will be 3.10 € /fattener or gilt place and 13.34 € /farrowing place (1 breeding sow + 3.30 piglets).

[d] Assuming an average sow herd of 150 breeding sows. Vaccination of new-born piglets and re-insemination of breeding sows will probably happen only once per month. In that case 292 pigs (piglets and breeding sows) will be re-vaccinated each month.

[e] 2.95 € /treated pig * 0.065 treated pigs/day = 0.19 € /farrowing place/day; 0.065 treated pigs = 0.006 breeding sow/ day + 0.059 newborn piglets/sow/day.

Table 5

Some key features of the real 1997/98 Dutch CSF epidemic, the median of the simulated epidemic and the median of the non-vaccination scenario[a] (Jalvingh et al., Nielen et al., 1999)

Real epidemic or simulated scenario	Key features (median for simulations)				
	# Detected farms	# Infected farms	# Preventively slaughtered farms	Duration of the epidemic (in days)	Costs (10^6 €)
Real epidemic	429	?	1247	>365	2124
97/98 simulated CSF epidemic	374[b]	464[b]	743[b]	306	1137[c]
Non-vaccination scenario	70	99	450	164	590[c]

[a] The preventive-slaughter scenario from Nielen et al. (1999) is in this paper called the "non-vaccination scenario" (NV).

[b] Numbers differ slightly from Jalvingh et al. (1999), due to some minor adaptations of InterCSF.

[c] Numbers are slightly higher than in Jalvingh et al. (1999) and Nielen et al. (1999), because movement standstill had been erroneously lifted 1 day too early for some farms in the original EpiLoss.

Table 6

Results of multiple comparisons (t-tests) between the results of the basic scenario, non-vaccination and the different emergency vaccination alternatives as calculated in InterCSF. The compared mean outcome parameters were: the number of infected farms(I), the number of detected farms (D) the number of preventive-slaughtered farms (P), the number of vaccinated farms (V) and the total losses (C), applying the Bonferroni corrected significance level[a]. Significantly different parameters are shown for comparison.

Scenario	**97/98 simulated CSF epidemic**	**NV**	**DD-21-0**	**ICT-21-0**[b]
Non-vaccination scenario				
NV[c]	I,D,P,C	-[d]	-	-
Delayed destruction alternatives				
DD-21-0	I,D,P,V,C	I[e],P,V	-	-
DD-7-0	-	I[e],P,V	n.s.[f]	-
DD-16-0	-	I[e],P,V	n.s.	-
DD-26-0	-	I[e],P,V	n.s.	-
DD-21-I	-	I[e],P,V	n.s.	-
DD-21-II	-	I[e],P,V,C[e]	n.s.	-
DD-21-III	-	I[e],P,V	*I*[e]	-
DD-21-IV	-	V,C	P,V, C[e]	-
DD-21-V	-	I[e],P,V	n.s.	-
Intra-community trade alternatives				
ICT-21-0	I,D,P,V,C	I[e],P,V,C	P,C	-
ICT-7-0	-	I[e],P,V,C	-	I,D,C
ICT-16-0	-	I[e],P,V,C	-	n.s.
ICT-26-0	-	I[e],P,V,C	-	n.s.
ICT-21-I	-	I[e],P,V,C	-	n.s.
ICT-21-II	-	I[e],P,V,C	-	n.s.
ICT-21-III	-	P,V,C[e]	-	I,D,V,C
ICT-21-IV	-	I[e],P,V,C	-	I[e],D[e],V
ICT-21-VI	-	I[e],P,V,C	-	P

[a] Bonferroni corrected significance level for the two-tailed test was 0.001316, based on 38 comparisons for $P < 0.05$.

[b] In case of ICT, preventive slaughter is with one exception (alternative VI) never applied.

[c] Vaccination was not applied in the simulated 1997/98 Dutch epidemic and in the NV scenario.

[d] Not tested.

[e] If the Bonferroni corrected significance level was not applied, this parameter would have been significant at $\alpha = 0.05$.

[f] None of the compared parameters were significant for $\alpha = 0.05$ (n.s. = not significant) or for the Bonferroni-corrected significance level $\alpha = 0.001316$.

Table 7

Comparison of the non-vaccination NV strategy with the two base emergency-vaccination strategies, delayed destruction (DD-0) and intra-community trade (ICT-0) (maximum protection is reached on day 21)

	Scenario											
Epidemiological and economic	NV				DD-21-0				ICT-21-0			
characteristics	Mean	5%	50%	95%	Mean	5%	50%	95%	Mean	5%	50%	95%
Number of farms :												
Detected	120	47	**70**	232	68	48	**58**	92	74	57	**68**	133
Infected	166	69	**99**	349	76	54	**64**	113	75	57	**68**	133
Preventive slaughtered[a]	566	342	**450**	1210	1335	1084	**1177**	1930	-	-	-	-
Duration of epidemic (days)	-	114	**164**	344	-	99	**108**	177	-	236[b]	**258[b]**	322[b]
Route of infection:												
Local	107	29	**54**	222	32	15	**25**	52	32	18	**29**	63
Animal contact	2	0	**0**	9	1	0	**0**	4	0	0	**0**	4
Transport contact	12	0	**4**	41	4	0	**1**	18	3	0	**1**	14
Personal contact	8	0	**4**	19	2	0	**2**	6	2	0	**2**	6
# Vaccinated Farms	-	-	-	-	1240	958	**1038**	1602	1243	1043	**1135**	1961
# Infected farms vaccinated	-	-	-	-	32	20	**28**	38	32	21	**30**	56
# Vaccinated farms infected	-	-	-	-	7	3	**6**	12	10	5	**9**	19
Start of vaccination[c]	-	-	-	-	-	11	**11**	11	-	11	**11**	11
Decision to stop with vaccination[c]	-	-	-	-	-	96	**102**	154	-	78	**101**	164
Direct costs in 10^6 € :												
Stamping out infected herds	10	5	**7**	14	7	5	**7**	10	11	8	**10**	15
Preventive slaughter[a]	69	45	**59**	116	153	130	**141**	184	-	-	-	-
Welfare slaughter	347	226	**290**	677	201	157	**169**	250	305	253	**290**	423
Breeding prohibition	-	-	-	-	6	4	**5**	7	-	-	-	-
Costs of organisation	59	39	**49**	112	44	36	**39**	54	46	39	**44**	66
Consequential losses in 10^6 € for :												
Farmers	73	43	**61**	157	88	70	**78**	106	31	24	**29**	51
Related industries	154	103	**127**	277	141	115	**123**	170	114	99	**107**	155
Vaccination costs in 10^6 €	-	-	-	-	3	3	**3**	4	5	5	**5**	8
Total losses in 10^6 €	**712**	**465**	**590**	**1349**	**644**	**522**	**567**	**769**	**514**	**429**	**484**	**708**

[a] In case of DD, preventive slaughter includes all vaccinated farms.

[b] Includes 120-day post-vaccination zone.

[c] The criteria to start or to stop respectively, installing new vaccination areas was fulfilled (days after 1st detection).

Table 8
Number of farms detected and preventive slaughtered for different simulated emergency-vaccination scenarios

Scenario	# Detection		Preventive slaughter[a]		Costs 10^6 €	
	50 %	5% - 95%	50 %	5% - 95%	50 %	5% - 95%
			Delayed destruction scenarios[b]			
DD-21-0	**58**	**48- 92**	**1177**	**1084-1930**	**567**	**522- 769**
DD-7-0	57	49-111	1174	1086-2051	560	522- 988
DD-16-0	58	48-135	1176	1084-2860	568	522-1155
DD-26-0	58	48- 93	1176	1084-1925	567	522- 806
DD-21-I	54	45- 79	1161	1076-1845	561	519- 831
DD-21-II	60	50- 80	1189	1088-1518	566	522- 751
DD-21-III	58	47-141	1267	1107-3049	595	530-1617
DD-21-IV	63	51-193	422	374-1082	451	405- 812
DD-21-V	59	49-110	1175	1083-2279	573	526- 962
			Intra-community trade			
ICT-21-0	**68**	**57-133**	-[c]	-	**484**	**429-708**
ICT-7-0	59	50-95	-	-	370	330-538
ICT-16-0	66	56-102	-	-	477	420-687
ICT-26-0	69	58-133	-	-	486	434-710
ICT-21-I	64	53-117	-	-	481	415-720
ICT-21-II	73	61-125	-	-	489	432-702
ICT-21-III	113	92-169	-	-	554	487-909
ICT-21-IV	77	61-146	-	-	500	428-747
ICT-21-VI[c]	66	55-100	258[c]	237-307[c]	491	443-669

[a] In case of DD, preventive slaughter includes all vaccinated farms.

[b] All farms in a defined vaccination zone (0-3 km) will be slaughtered from day 6 onwards, if destruction capacities are available, independent of the vaccination preparation time. Except for alternative I until III this will be always 5 days extra. It will be 2 days for alternative I, 8 days for alternative II and 25 days for alternative III.

[c] In case of ICT, preventive slaughter is only applied in strategy VI, wherein only non-vaccinated farms can be preventively slaughtered.

Table 9
Comparing direct costs and losses of the base scenario with alternative IV for the intra-community trade strategy (ICT) and for the delayed destruction strategy (DD).

	DD-21-0		DD-21-IV		ICT-21-0		ICT-21-IV	
	50%	5- 95%	50%	5 - 95%	50%	5 - 95%	50%	5 - 95%
Direct costs in 10^6 € :								
Stamping out inf herds	**7**	5-10	**8**	6-12	**10**	8-15	**12**	9-18
Preventive slaughter[a]	**141**	130-184	**56**	48-89	-	-	-	-
Welfare slaughter	**169**	157-250	**202**	181-391	**290**	253-423	**301**	255-443
Breeding prohibition	**5**	4-7	**0.5**	0.5-0.5	-	-	-	-
Costs of organisation	**39**	36-54	**36**	33-68	**44**	39-66	**45**	39-69
Consequential losses in 10^6 € for :								
Farmers	**78**	70-106	**44**	38-97	**29**	24-51	**31**	24-59
Related industries	**123**	115-170	**103**	95-178	**107**	99-155	**111**	99-160
Vaccination costs in 10^6 €	**3**	3-4	**0.5**	0.5-0.9	**5**	5-8	**1.4**	0.9-2.3
Total losses in 10^6 €	**567**	522-769	**451**	405-812	**484**	429-708	**500**	428-747

[a] In case of DD, preventive slaughter includes all vaccinated farms.

Figure 1

Reduction factor for the probability of transmission from a vaccinated farm, related to the time interval between vaccination and subsequent infection. Vaccine efficacy was maximum at 7 (A), 16 (B), 21 (C) or 26 (D) days after vaccination.

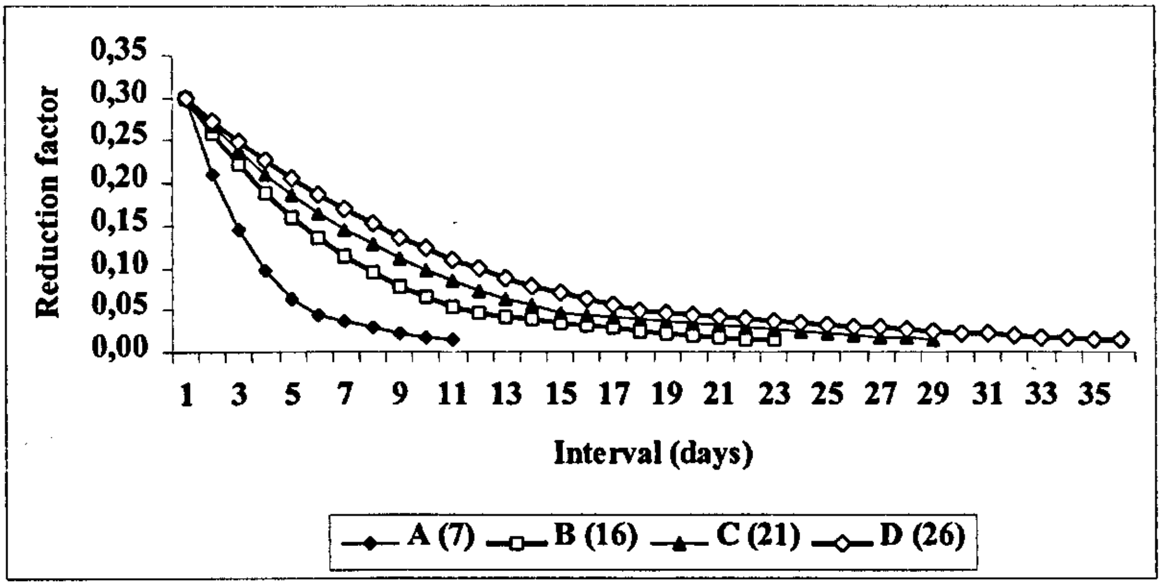

Figure 2
Reduction factor (called "protection factor") for the probability that a vaccinated farm became infected, related to the time interval between vaccination and a possible infection. Vaccine efficacy was maximum at 7 (A), 16 B), 21 (C) or 26 (D) days after vaccination.