Effects of control measures on the spread of LA-MRSA among Danish pig herds between 2006 and 2015 – a simulation study

There has been a rapid increase in Danish pig herds testing positive for livestock-associated Methicillin-resistant Staphylococcus aureus (LA-MRSA) since the first screening in 2008. Despite a national action plan to control LA-MRSA in the Danish pig population, 88% of pig herds tested positive in a 2016 cross-sectional study of 57 herds. The national action plan was initiated in April 2015 and aimed to reduce the spread of LA-MRSA among pig herds. However, its success is uncertain. We used a simulation model mimicking the spread of LA-MRSA among pig herds between 2006 and 2015 to evaluate the impact of control strategies if these had been implemented in 2007 or 2010. The strategies were combinations of the following control measures: (1) a reduced number of herds using high-risk antibiotics, (2) a reduced probability of indirect transmission among herds via humans, (3) movement restrictions, and (4) voluntary eradication in 5–7.5% of the herds. Almost all tested control strategies simulated a reduction in the spread of LA-MRSA. The combination of two, three or four intervention strategies showed additive effects and led to larger reductions in the predicted herd prevalence. In addition, the prevalence of LA-MRSA-positive herds at the time when control measures were initiated influenced the effects of the control strategies. Combining the simulated control measures can be considered in future action plans to control LA-MRSA.
Continuing occurrence of vancomycin resistance determinants in Danish pig farms 20 years after removing exposure to avoparcin

Vancomycin-resistant Enterococcus spp. is a major health problem worldwide and livestock have been implicated in constituting a reservoir for the transmission of vancomycin resistance to zoonotic pathogens. Vancomycin resistance determinants can be situated on mobile genetic elements and transferred between bacterial species. The livestock reservoir must therefore be included in a risk assessment of the vancomycin resistance burden. Avoparcin, a vancomycin analogue, has not been used in Danish pig production for over 20 years and vancomycin has never been used. The objective of this study was to screen faecal samples from Danish pig farms for nine selected vancomycin resistance determinants. We found at least four different vancomycin resistance determinants in all screened Danish pig farms (665 finisher farms and 78 sow farms). The vancomycin resistance determinants present in vanB or vanG clusters were found at significantly different levels in sow and finisher farms. However, vanA was not detected in any of the farms. In conclusion, vancomycin resistance determinants are still present in Danish pig production 20 years after the ban on avoparcin use.

Economic and epidemiological impact of different intervention strategies for clinical contagious mastitis

The overall aim of this study was to compare different intervention strategies for clinical intramammary infections (IMI). We conducted a simulation study to represent a Danish dairy cattle herd with IMI caused mostly by Staphylococcus aureus and 9 different intervention strategies for clinical IMI. A standard intervention of 3 d of treatment consisting of intramammary injections for all clinical cases was used. Two of the strategies reflected the use of more antibiotics and 6 strategies reflected cow-specific treatment or culling decisions. For these strategies, we assessed the cost and effectiveness of culling as an IMI intervention. Our results showed that nearly all strategies could reduce the number of IMI cases [e.g., a median of 37 clinical cases with the extended intramammary treatment over 5 d strategy (Basic5) and 30 clinical cases with the cow culled with recovery probability below 50% (Before50)] compared with the standard intervention (median of 42 clinical cases). This happened alongside either increased antibiotic usage (e.g., from a median of 123 treatment days up to 179 treatment days with strategy Basic5) or an increased number of cows culled in relation to IMI (e.g., from a median of 16 up to 24 cows with strategy Before50). Strategies with more antibiotics or reactive culling had a slightly higher net income (e.g., €190,014 median net income with strategy Basic5 or €196,995 with strategy Before50 compared with €187,666 with the standard strategy). This shows that a cow-specific clinical intervention approach can be cost-effective in reducing IMI incidence.
The objective of this study was to evaluate and compare different combinations of intervention strategies for contagious or opportunistic subclinical and clinical intramammary infections (IMI). We simulated two different Danish dairy cattle herds with ten different intervention strategies focusing on cow-specific treatment or culling, including three baseline strategies without subclinical interventions. In one herd, the main causative pathogen of IMI was Staphylococcus (S.) aureus. In the other herd, Streptococcus (St.) agalactiae was the main causative agent. For both herds, we investigated costs and effectiveness of all ten intervention strategies. Intervention strategies consisted of measures against clinical and subclinical IMI, with baselines given by purely clinical intervention strategies. Our results showed that strategies including subclinical interventions were more cost-effective than the respective baseline strategies. Increase in income and reduction of IMI cases came at the cost of increased antibiotic usage and an increased culling rate in relation to IMI. However, there were differences between the herds. In the St. agalactiae herd, the clinical intervention strategy did not seem to have a big impact on income and number of cases. However, intervention strategies which included cow-specific clinical interventions led to a higher income and lower number of cases in the S. aureus herd. The results show that intervention strategies including interventions against contagious or opportunistic clinical and subclinical IMI can be highly cost-effective, but should be herd-specific.
Simulation of transmission and persistence of African swine fever in wild boar in Denmark

African swine fever (ASF) is caused by ASF virus (ASFV) and is currently circulating in the eastern part of Europe posing a serious risk regarding transmission to western European countries. Wild boar is a main driver of the transmission and persistence of ASFV in the endemic infected countries in Europe. Some European countries free from ASF, such as Denmark and the Netherlands, have limited population sizes of wild boar, but have large swine productions. In these countries, the patterns of transmission and persistence of ASFV in the existing wild boar population, in case of introduction of ASFV, are unknown. It is important to get a better understanding of ASFV in these wild boar populations, in order to better manage the existing wild boar population and thereby minimize the risk of virus introduction and transmission to domestic pigs, in case of an ASFV incursion. We created an agent-based spatio-temporal model and simulated the transmission of ASFV within Danish wild boar populations, using actual landscape data. The model was run with 50 and 100 wild boar groups used as initial population sizes, respectively, either distributed across the southern part of the mainland (Jutland) or across both the southern and middle parts of Jutland, where wild boar groups are believed to exist. At first, the model was run without ASFV for 25 years to assess wild boar population dynamics in both regions. Thereafter, ASFV was added to the model 1 year after initiation and run for up to another 4 years. The model predicted that wild boar populations may increase drastically over the next 25 years, if wild boar groups were distributed across both southern and middle Jutland and no mitigation actions were taken, while the population sizes will be restricted, if groups were distributed only across the southern part of Jutland. The density of the population is an important factor affecting the transmission and persistency of the disease. Model results indicated that ASF epidemics in the simulated populations would generally persist for few months. However, due to the high stochasticity of the process, in certain situations the epidemics may last for more than one year, posing a serious risk of ASFV introduction to domestic pigs.

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Transmission dynamics of Staphylococcus aureus within two Danish dairy cattle herds

Staphylococcus aureus is a major pathogen causing intramammary infections (IMI) in dairy cattle herds worldwide. Simulation models can be used to investigate the epidemiologic and economic outcomes of different control strategies against IMI. The transmission rate parameter is one of the most influential parameters on the outcomes of these simulation models. Very few studies have estimated the transmission rate parameter and investigated the transmission dynamics of Staph. aureus IMI in dairy cattle herds. The objective of our study was therefore to analyze the transmission dynamics of Staph. aureus in 2 Danish dairy herds participating in a longitudinal study. The 2 herds had 180 and 360 milking cows, and animals were tested at quarter level once per month over a period of 1 yr. We estimated the quarter-level prevalence to be 34% for herd 1 and 2.57% for herd 2. The daily quarter-level transmission rate was estimated to be 0.0132 and 0.0077 cases/quarter-day for herds 1 and 2, respectively, and the median duration of infection was estimated to be 91 and 64 d for herds 1 and 2, respectively. We also estimated the reproductive ratio at 1.21 for herd 1 and 0.52 for herd 2. The results can provide valuable information for simulation models to aid decision-making in terms of the prevention and control of Staph. aureus IMI in dairy cattle herds.

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**Vildsvinehegn virker som en del af løsningen**

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**Afrikansk svinepest - en alvorlig trussel for hele svinebranchen**
A strain-, cow-, and herd-specific bio-economic simulation model of intramammary infections in dairy cattle herds

Intramammary infections (IMI) in dairy cattle lead to economic losses for farmers, both through reduced milk production and disease control measures. We present the first strain-, cow- and herd-specific bio-economic simulation model of intramammary infections in a dairy cattle herd. The model can be used to investigate the cost-effectiveness of different prevention and control strategies against IMI. The objective of this study was to describe a transmission framework, which simulates spread of IMI causing pathogens through different transmission modes. These include the traditional contagious and environmental spread and a new opportunistic transmission mode. In addition, the within-herd transmission dynamics of IMI causing pathogens were studied. Sensitivity analysis was conducted to investigate the influence of input parameters on model predictions. The results show that the model is able to represent various within-herd levels of IMI prevalence, depending on the simulated pathogens and their parameter settings. The parameters can be adjusted to include different combinations of IMI causing pathogens at different prevalence levels, representing herd-specific situations. The model is most sensitive to varying the transmission rate parameters and the strain-specific recovery rates from IMI. It can be used...
for investigating both short term operational and long term strategic decisions for the prevention and control of IMI in dairy cattle herds.

Drivers for Livestock-Associated Methicillin-Resistant Staphylococcus Aureus Spread Among Danish Pig Herds - A Simulation Study
To gain insight into the rapid increase in the number of livestock-associated Methicillin-resistant Staphylococcus aureus (LA-MRSA)-positive herds in Denmark, we developed an individual-based Monte Carlo simulation model. We aimed to assess whether transmission of LA-MRSA via pig movements could explain the observed increase in the number of positive herds in Denmark, and to evaluate the effect of other between-herd transmission mechanisms. Pig movements alone were not sufficient to mimic the observed increase in LA-MRSA-positive herds in Denmark in any of the modelled scenarios. The model identified three factors that played important roles in the between-herd spread of LA-MRSA: (1) the within- herd dynamics, (2) the frequency and effectiveness of indirect transmissions, and (3) unexplainable introduction of LA-MRSA to swine herds. These factors can act as starting points for the development of LA-MRSA control programs in pig herds in order to limit the risk of its transmission to humans.
Evaluating the impact of transmission mode, calibration level and farmer compliance in simulation models of paratuberculosis in dairy herds

Simulation models can predict the outcome of different strategies for the control and eradication of paratuberculosis (PTB) in dairy herds. Two main transmission modes have previously been used to simulate the spread of PTB: direct (contact between animals) and indirect (through the environment). In addition, previous models were calibrated to either low or high within-herd prevalence levels, which we refer to as normal and low hygiene levels, respectively. We simulated both direct and indirect transmission with the same model in both normal and low hygiene level scenarios. The effectiveness of a test-and-cull strategy was dependent on the calibration level of the simulation model, and eradication occurred less frequently with the more biologically plausible indirect transmission mode. The results were compared to within-herd prevalence records from 314 dairy herds. The prevalence in 50% of the herds varied less than 0.9% per year on average, and less than 4% in 90% of the herds. We therefore conclude that the normal-hygiene scenario best describes most dairy herds in Denmark. Finally, we simulated different levels of farmer compliance with a test-and-cull strategy and found that a 60% compliance level was not sufficient to reach eradication within 10 years.

Infection of pigs with African swine fever virus via ingestion of stable flies (Stomoxys calcitrans)

Within Eastern Europe, African swine fever virus (ASFV) has unexpectedly spread to farms with high biosecurity. In an attempt to explain this process, pigs were allowed to ingest flies that had fed on ASFV-spiked blood, which had a realistic titre for an infected pig. Some of the pigs became infected with the virus. Thus, ingestion of blood-sucking flies, having fed on ASFV-infected wild boar before entering stables, represents a potential route for disease transmission.
Mechanistic modelling of interventions against spread of livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) within a Danish farrow-to-finish pig herd

Knowledge on successful interventions against livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) within pig herds is sparse. In situations like this, a mechanistic simulation model can be a valuable tool for assessing the effect of potential intervention strategies, and prioritising which should be tested in the field. We have simulated on-farm interventions in a farrow-to-finish pig herd, with a previously published LA-MRSA spread model, within four different areas: 1) Reduced antimicrobial consumption, 2) Reduced number of pigs within each section, 3) Reduced mixing of pigs, and 4) Improved internal biosecurity. To model a decrease in the selective pressure, the transmission rates were reduced after LA-MRSA had become fully established within a herd, which resulted in a marked decrease in the prevalence within all stable units. However, LA-MRSA rarely disappeared completely from the herd; this was only observed in scenarios where the transmission rates were reduced to ≤ 30% of the original level. While changes in antimicrobial consumption patterns might be a very important step towards reducing the spread of LA-MRSA, the simulation results indicate that it may need to be paired with other preventive or intervention measures. Reducing the number of pigs within each section, reducing mixing of pigs, or improving internal biosecurity after LA-MRSA had become established within the herd only resulted in marginal changes in the median prevalence within the herd. However, these factors might be important in relation to being able to achieve or maintain a low level of antimicrobial consumption, and thus still indirectly influence the LA-MRSA prevalence within the herd. The results of a sensitivity analysis indicated the assumptions regarding the existence of pigs persistently shedding MRSA have a noticeable influence on the model results. The assumptions regarding transmission from sow to offspring at the day of birth also had a considerable influence on the MRSA prevalence within the farrowing unit but did not cause any marked changes in the simulated effect of interventions. Effects might differ between different farm types contaminated in different levels and this simulation study highlights a strong need for more knowledge from on-farm trials.

Modeling the Effects of Duration and Size of the Control Zones on the Consequences of a Hypothetical African Swine Fever Epidemic in Denmark

African swine fever (ASF) is a notifiable infectious disease. The disease is endemic in certain regions in Eastern Europe constituting a risk of ASF spread toward Western Europe. Therefore, as part of contingency planning, it is important to continuously explore strategies that can effectively control an epidemic of ASF. A previously published and well documented simulation model for ASF virus spread between herds was used to examine the epidemiologic and economic impacts of the duration and size of the control zones around affected herds. In the current study, scenarios were run, where the duration of the protection and surveillance zones were reduced from 50 and 45 days to 35 and 25 days or to 35 and 25 days, respectively. These scenarios were run with or without enlargement of the surveillance zone around detected herds from 10 to 15 km. The scenarios were also run with only clinical or clinical and serological surveillance of herds within the zones. Sensitivity analysis was conducted on influential input parameters in the model. The model predicts that reducing the duration of the protection and surveillance zones has no impact on the epidemiologic consequences of the epidemics, while it may result in a substantial reduction in the total economic losses. In addition, the model predicts that increasing the size of the surveillance zone from 10 to 15 km may reduce both the epidemic duration and the total economic losses, in case of large epidemics. The ranking of the control strategies by the total costs of the epidemics was not influenced by changes of input parameters in the sensitivity analyses.
Persistence of antimicrobial resistance genes from sows to finisher pigs
Antimicrobial resistance in pigs has been under scrutiny for many years. However, many questions remain unanswered, including whether the initial antimicrobial resistance level of a pig will influence the antimicrobial resistance found at slaughter. Faecal samples from finishers pigs from 681 farms and from sows from 82 farms were collected, and levels of seven antimicrobial resistance genes, ermB, ermF, sulI, sulII, tet(M), tet(O), and tet(W), were quantified by high-capacity qPCR. There were 40 pairs of observations where the finishers were born in the farms of the sows. The objective of this study was to evaluate whether the levels of AMR genes found in finisher pigs at slaughter were associated with the levels in the farm where the finishers were born, and whether the levels of the AMR genes were equal in the sow and finisher pig populations. We found a significant positive correlation between the levels of AMR genes in finishers and the sows in the farms where the pigs were born for some of the genes (ermB (\(\rho = 0.47, p\)-value = 0.002), ermF (\(\rho = 0.41, p\)-value = 0.03), and tet(O) (\(\rho = 0.33, p\)-value = 0.04)). Furthermore, there were significant differences between AMR gene levels for the sow and finisher populations for ermB, ermF, sulI, sulII, tet(O), and tet(W), though not for tet(M).

Risk factors for the occurrence of livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) in Danish pig herds
Livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) is widespread in many European countries including Denmark, where 88% of randomly selected production herds tested positive in 2016. In the present study, we investigated herd-level risk factors for farms being classified as LA-MRSA positive (study 1), in addition to herd-level risk factors for farms changing status from LA-MRSA negative to LA-MRSA positive during a 2-year period (study 2). Risk factors previously identified in other studies were confirmed in study 1: large herd size, herd type (lower risk in herds with sows) and number of pig suppliers. Due to the effect of herd type, data from sow herds (N=41) and herds without sows (N
were analysed separately. A univariable analysis found that the variables significantly associated with LA-MRSA status for sow herds were: use of wet feed in the sow units; higher weights of piglets at weaning; availability of a delivery room on the farm; cleaning of aisles after pigs were moved; number of pigs per weaner section; number of pigs purchased in the past year, and factors related to rodent control and human traffic in the herd. In herds without sows, the univariable analysis showed that the presence of other species of animal on the farm; negative pressure ventilation; full sectioning; frequent visits from the veterinarian; peroral use of tetracyclines for weaners; number of pigs purchased in the past year, and factors related to rodent control and human traffic in the herd were significantly associated with LA-MRSA status. For herds that changed from LA-MRSA negative to positive (study 2), having a company contract for mouse control, having more than one pig supplier and using group medication in the drinking water were the variables associated with LA-MRSA status. We did not succeed in building a biologically meaningful multivariable model based on any of the datasets and, as observed in similar studies, many of the risk factors identified in the univariable analysis were related to herd size. It was therefore not possible to determine whether it was the size of the herd or related factors that were the causal risk factors for being LA-MRSA positive.

Send more data: a systematic review of mathematical models of antimicrobial resistance

Antimicrobial resistance is a global health problem that demands all possible means to control it. Mathematical modelling is a valuable tool for understanding the mechanisms of AMR development and spread, and can help us to investigate and propose novel control strategies. However, it is of vital importance that mathematical models have a broad utility, which can be assured if good modelling practice is followed. The objective of this study was to provide a comprehensive systematic review of published models of AMR development and spread. Furthermore, the study aimed to identify gaps in the knowledge required to develop useful models. The review comprised a comprehensive literature search with 38 selected studies. Information was extracted from the selected papers using an adaptation of previously published frameworks, and was evaluated using the TRACE good modelling practice guidelines. None of the selected papers fulfilled the TRACE guidelines. We recommend that future mathematical models should: a) model the biological processes mechanistically, b) incorporate uncertainty and variability in the system using stochastic modelling, c) include a sensitivity analysis and model external and internal validation. Many mathematical models of AMR development and spread exist. There is still a lack of knowledge about antimicrobial resistance, which restricts the development of useful mathematical models.
Short time window for transmissibility of African swine fever virus from a contaminated environment

Since the introduction of African swine fever virus (ASFV) into the Baltic states and Poland in 2014, the disease has continued to spread within these regions. In 2017, the virus spread further west and the first cases of disease were reported in the Czech Republic and Romania, in wild boar and domestic pigs, respectively. To control further spread, knowledge of different modes of transmission, including indirect transmission via a contaminated environment, is crucial. Up until now, such an indirect mode of transmission has not been demonstrated. In this study, transmission via an environment contaminated with excretions from ASFV-infected pigs was investigated. Following euthanasia of pigs that were infected with an isolate of ASFV from Poland (POL/2015/Podlaskie/Lindholm), healthy pigs were introduced into the pens, in which the ASFV-infected pigs had been housed. Introduction was performed at 1, 3, 5 or 7 days, following euthanasia of the infected pig groups. Pigs, that were introduced into the contaminated environment after 1 day, developed clinical disease within 1 week, and both ASFV DNA and infectious virus were isolated from their blood. However, pigs introduced into the contaminated pens after 3, 5 or 7 days did not develop any signs of ASFV infection and no viral DNA was detected in blood samples obtained from these pigs within the following 3 weeks. Thus, it was shown that exposure of pigs to an environment contaminated with ASFV can result in infection. However, the time window for transmissibility of ASFV seems very limited, and, within our experimental system, there appears to be a rapid decrease in the infectivity of ASFV in the environment.

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A Cow- and Herd-specific Bio-Economic Model of Intramammary Infections in Dairy Cows

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A mechanistic model for spread of livestock-associated methicillin-resistant Staphylococcus aureus (LA-MRSA) within a pig herd

Before an efficient control strategy for livestock-associated methicillin resistant Staphylococcus aureus (LA-MRSA) in pigs can be decided upon, it is necessary to obtain a better understanding of how LA-MRSA spreads and persists within a pig herd. Once it is introduced, we here present a mechanistic stochastic discrete-event simulation model for spread of LA-MRSA within a farrow-to-finish sow herd to aid in this. The model was individual-based and included three different disease compartments: susceptible, intermittent or persistent shedder of MRSA. The model was used for studying transmission dynamics and within-farm prevalence after different introductions of LA-MRSA into a farm. The spread of LA-MRSA throughout the farm mainly followed the movement of pigs. After spread of LA-MRSA had reached equilibrium, the prevalence of LA-MRSA shedders was predicted to be highest in the farrowing unit, independent of how LA-MRSA was introduced. LA-MRSA took longer to spread to the whole herd if introduced in the finisher stable, rather than by gilts in the mating stable. The more LA-MRSA positive animals introduced, the shorter time before the prevalence in the herd stabilised. Introduction of a low number of intermittently shedding pigs was predicted to frequently result in LA-MRSA fading out. The model is a potential decision support tool for assessments of short and long term consequences of proposed intervention strategies or surveillance options for LA-MRSA within pig herds.

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A Cow- and Herd-specific Bio-Economic Model of Intramammary Infections in Dairy Cows

Introduction. Mastitis, or intramammary infection (IMI), is one of the most significant diseases in dairy herds worldwide. It is caused by environmental and contagious bacteria. Simulation models have proven useful for evaluating the effect of different control strategies. However, previous published models are not cow-specific and therefore not so detailed in the simulation of host-pathogen interactions. If a simulation model is to be used by dairy farmers as a decision-making tool, it needs to be cow-specific because daily management decisions are made on cow level. Furthermore, as IMI is often caused by more than one pathogen in the same herd, such a simulation model should also be pathogen-specific to account for different transmission characteristics and treatment effects. Moreover, as different strains of pathogens can have different transmission routes (i.e. environmental, contagious or mixed), the model should be able to reflect this diversity. Our objective was thus to create a pathogen-, cow- and herd-specific bio-economic simulation model that could simulate multiple pathogens and strains at the same time within a dairy herd. This model should be able to simulate realistic scenarios for specific herds, thus being a tool for decision-making for individual farmers. Methods We used an existing mechanistic, stochastic simulation model framework to create an IMI simulation model. This mechanistic model simulates a dairy herd in great detail; i.e. with individual lactation curves for all cows, continuous movement of cows between farm sections and continuous culling decisions made by the farmer. We expanded the model to simulate the individual quarters of cows. This procedure made it possible for cows to have up to four different infections at a time, one per quarter. We implemented two different transmission modes, namely environmental transmission based on a continuous reservoir of pathogens in the farm, and contagious IMI originating from other infected animals in the herd. Currently, the environmental pathogen included is Escherichia coli, and the contagious pathogens are Staphylococcus aureus, Streptococcus agalactiae and Streptococcus uberis. The contagious transmission is simulating transmission, e.g. via milk liners, and depends on the number of quarters with contagious pathogens in the herd. We chose to focus on these four pathogens because they are common in Danish dairy farms. We modelled the increase in somatic cell count (SCC) due to subclinical infection. The reduction in milk yield for individual cows is then based on their SCC. Thus we are able to estimate the economic consequences of each IMI pathogen in the herd, simulate different control scenarios and estimate their epidemiological and economic effects.

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A Robust Statistical Model to Predict the Future Value of the Milk Production of Dairy Cows Using Herd Recording Data

The future value of an individual dairy cow depends greatly on its projected milk yield. In developed countries with developed dairy industry infrastructures, facilities exist to record individual cow production and reproduction outcomes consistently and accurately. Accurate prediction of the future value of a dairy cow requires further detailed knowledge of the costs associated with feed, management practices, production systems, and disease. Here, we present a method to predict the future value of the milk production of a dairy cow based on herd recording data only. The method consists of several steps to evaluate lifetime milk production and individual cow somatic cell counts and to finally predict the average production for each day that the cow is alive. Herd recording data from 610 Danish Holstein herds were used to train and test a model predicting milk production (including factors associated with milk yield, somatic cell count, and the survival of individual cows). All estimated parameters were either herd- or cow-specific. The model prediction deviated, on average, less than 0.5 kg from the future average milk production of dairy cows in multiple herds after adjusting for the effect of somatic cell count. We conclude that estimates of future average production can be used on a day-to-day basis to rank cows for culling, or can be implemented in simulation models of within-herd disease spread to make operational decisions, such as culling versus treatment. An advantage of the approach presented in this paper is that it requires no specific knowledge of disease status or any other information beyond herd recorded milk yields, somatic cell counts, and reproductive status.
A simulation study to evaluate the performance of five statistical monitoring methods when applied to different time-series components in the context of control programs for endemic diseases

Disease monitoring and surveillance play a crucial role in control and eradication programs, as it is important to track implemented strategies in order to reduce and/or eliminate a specific disease. The objectives of this study were to assess the performance of different statistical monitoring methods for endemic disease control program scenarios, and to explore what impact of variation (noise) in the data had on the performance of these monitoring methods. We simulated 16 different scenarios of changes in weekly sero-prevalence. The changes included different combinations of increases, decreases and constant sero-prevalence levels (referred as events). Two space-state models were used to model the time series, and different statistical monitoring methods (such as univariate process control algorithms–Shewart Control Chart, Tabular Cumulative Sums, and the V-mask- and monitoring of the trend component–based on 99% confidence intervals and the trend sign) were tested. Performance was evaluated based on the number of iterations in which an alarm was raised for a given week after the changes were introduced. Results revealed that the Shewhart Control Chart was better at detecting increases over decreases in sero-prevalence, whereas the opposite was observed for the Tabular Cumulative Sums. The trend-based methods detected the first event well, but performance was poorer when adapting to several consecutive events. The V-Mask method seemed to perform most consistently, and the impact of noise in the baseline was greater for the Shewhart Control Chart and Tabular Cumulative Sums than for the V-Mask and trend-based methods. The performance of the different statistical monitoring methods varied when monitoring increases and decreases in disease sero-prevalence. Combining two of more methods might improve the potential scope of surveillance systems, allowing them to fulfill different objectives due to their complementary advantages.

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Association between selected antimicrobial resistance genes and antimicrobial exposure in Danish pig farms
Bacterial antimicrobial resistance (AMR) in pigs is an important public health concern due to its possible transfer to humans. We aimed at quantifying the relationship between the lifetime exposure of antimicrobials and seven antimicrobial resistance genes in Danish slaughter pig farms. AMR gene levels were quantified by qPCR of total-community DNA in faecal samples obtained from 681 batches of slaughter pigs. The lifetime exposure to antimicrobials was estimated at batch level for the piglet, weaner, and finisher periods individually for the sampled batches. We showed that the effect of antimicrobial exposure on the levels of AMR genes was complex and unique for each individual gene. Several antimicrobial classes had both negative and positive correlations with the AMR genes. From 10-42% of the variation in AMR gene levels could be explained in the final regression models, indicating that antimicrobial exposure is not the only important determinant of the AMR gene levels.
Computational algorithm for lifetime exposure to antimicrobials in pigs using register data – the LEA algorithm

Accurate and detailed data on antimicrobial exposure in pig production are essential when studying the association between antimicrobial exposure and antimicrobial resistance. Due to difficulties in obtaining primary data on antimicrobial exposure in a large number of farms, there is a need for a robust and valid method to estimate the exposure using register data. An approach that estimates the antimicrobial exposure in every rearing period during the lifetime of a pig using register data was developed into a computational algorithm. In this approach, data from national registers on antimicrobial purchases, movements of pigs, and farm demographics registered at farm level are used. The algorithm traces batches of pigs retrospectively from slaughter to the farm(s) that housed the pigs during their finisher, weaner, and piglet period. Subsequently, the algorithm estimates the antimicrobial exposure as the number of Animal Defined Daily Doses for treatment of one kg pig in each of the rearing periods. Thus, the antimicrobial purchase data at farm level are translated into antimicrobial exposure estimates at batch level. A batch of pigs is defined here as pigs sent to slaughter at the same day from the same farm. In this study we present, validate, and optimise a computational algorithm that calculates the lifetime exposure of antimicrobials for slaughter pigs. The algorithm was evaluated by comparing the computed estimates to data on antimicrobial usage from farm records in 15 farm units. We found a good positive correlation between the two estimates. The algorithm was run for Danish slaughter pigs sent to slaughter in January to March 2015 from farms with more than 200 finishers to estimate the proportion of farms that it was applicable for. In the final process, the algorithm was successfully run for batches of pigs originating from 3,026 farms with finisher units (77% of the initial population). This number can be increased if more accurate register data can be obtained. The algorithm provides a systematic and repeatable approach to estimating the antimicrobial exposure throughout the rearing period, independent of rearing site for finisher batches, as a lifetime exposure measurement.
Determinants for Treatments in Relation to Udder Health in Danish Dairy Cattle Farms

Regular cow level registrations in the Danish Cattle Database include registrations about e.g. milk yield, SCC and calvings, but also about diseases and antibiotic treatments of cows. These data could potentially be a useful source of information for the development of herd-specific udder health management programs tailored to the farmer’s preference. With tailored programs farmers may be more motivated to adopt effective management programs that can also enhance a prudent use of antibiotics.

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Determinants of antimicrobial treatment for udder health in Danish dairy cattle herds

Societal pressure to limit the use of antibiotics in livestock production systems, including dairy cattle systems, is consistently increasing. To motivate farmers to reduce antibiotic usage, it is important to understand the factors that determine whether a cow will be treated with antibiotics or not. If farmers’ usual practices regarding antibiotic treatments are taken into account, they may be motivated to adopt control measures that can facilitate prudent use of antibiotics and are at the same time cost-effective. In this study, we analyzed database recordings of milk yield and somatic cell count from the routine milk recording scheme, clinical registrations of mastitis and PCR results, and cow factors such as days in milk and parity in relation to antibiotic treatments for 518 dairy herds in Denmark. Farm-wise logistic regressions were used to predict antimicrobial treatment based on these factors. The resulting regression coefficients of 422 herds were further analyzed by principal component analysis and clustering to determine the driving predictors for treatment in different groups of farms. The results showed that determinants that were most important for predicting antibiotic treatments vary from one farm to another. Health indicators such as PCR or somatic cell count were most indicative for treatment on some farms, whereas other groups seemed to depend more on production factors (milk yield) or later culling of the cows. This shows that farmers behave differently and differences can be identified in register data. This information can be considered when developing cost-effective herd-specific control measures of mastitis to promote prudent use of antibiotics in Danish dairy cattle farms.

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Estimation of the transmission dynamics of African swine fever virus within a swine house

The spread of African swine fever virus (ASFV) threatens to reach further parts of Europe. In countries with a large swine production, an outbreak of ASF may result in devastating economic consequences for the swine industry. Simulation models can assist decision makers setting up contingency plans. This creates a need for estimation of parameters. This study presents a new analysis of a previously published study. A full likelihood framework is presented including the impact of model assumptions on the estimated transmission parameters. As animals were only tested every other day, an interpretation was introduced to cover the weighted infectiousness on unobserved days for the individual animals (WIU).

Based on our model and the set of assumptions, the within- and between-pen transmission parameters were estimated to $\beta_w = 1.05$ (95% CI 0.62-1.72), $\beta_b = 0.46$ (95% CI 0.17-1.00), respectively, and the WIU = 1.00 (95% CI 0-1). Furthermore, we simulated the spread of ASFV within a pig house using a modified SEIR-model to establish the time from infection of one animal until ASFV is detected in the herd. Based on a chosen detection limit of 2.55% equivalent to 10 dead pigs out
of 360, the disease would be detected 13-19 days after introduction.

**Evaluation of Strategies to Control a Potential Outbreak of Foot-and-Mouth Disease in Sweden**

To minimize the potential consequences of an introduction of foot-and-mouth disease (FMD) in Europe, European Union (EU) member states are required to present a contingency plan. This study used a simulation model to study potential outbreak scenarios in Sweden and evaluate the best control strategies. The model was informed by the Swedish livestock structure using herd information from cattle, pig, and small ruminant holdings in the country. The contact structure was based on animal movement data and studies investigating the movements between farms of veterinarians, service trucks, and other farm visitors. All scenarios of outbreak control included depopulation of detected herds, 3km protection and 10 km surveillance zones, movement tracing, and 3days national standstill. The effect of availability of surveillance resources, i.e., number of field veterinarians per day, and timeliness of enforcement of interventions, was assessed. With the estimated currently available resources, an FMD outbreak in Sweden is expected to be controlled (i.e., last infected herd detected) within 3 weeks of detection in any evaluated scenario. The density of farms in the area where the epidemic started would have little impact on the time to control the outbreak, but spread in high density areas would require more surveillance resources, compared to areas of lower farm density. The use of vaccination did not result in a reduction in the expected number of infected herds. Preemptive depopulation was able to reduce the number of infected herds in extreme scenarios designed to test a combination of worst-case conditions of virus introduction and spread, but at the cost of doubling the number of herds culled. This likely resulted from a combination of the small outbreaks predicted by the spread model, and the high efficacy of the basic control measures evaluated, under the conditions of the Swedish livestock industry, and considering the assumed control resources available. The results indicate that the duration and extent of FMD outbreaks could be kept limited in Sweden using the EU standard control strategy and a 3days national standstill.
Farm-level risk factors for Fasciola hepatica infection in Danish dairy cattle as evaluated by two diagnostic methods

The prevalence of bovine fasciolosis in Denmark is increasing but appropriate guidelines for control are currently lacking. In order to help develop a control strategy for liver fluke, a risk factor study of farm management factors was conducted and the utility of bulk tank milk (BTM ELISA) as a tool for diagnosis in Danish dairy cattle farms was assessed. This case-control study aimed to identify farm-level risk factors for fasciolosis in Danish dairy farms (>50 animals slaughtered in 2013) using two diagnostic methods: recordings of liver condemnation at slaughter, and farm-level Fasciola hepatica antibody levels in BTM. A case farm was defined as having a minimum of 3 incidents of liver condemnation due to liver fluke at slaughter (in any age group) during 2013, and control farms were located within 10 km of at least one case farm and had no history of liver condemnation due to liver fluke during 2011-2013. The selected farmers were interviewed over telephone about grazing and control practices, and BTM from these farms was collected and analysed by ELISA in 2014. The final complete dataset consisting of 131 case and 63 control farms was analysed using logistic regression. Heifers grazing on wet pastures, dry cows grazing on wet pastures, herd size, breed and concurrent beef cattle production were identified as risk factors associated with being classified as a case farm. With the categorised BTM ELISA result as the response variable, heifers grazing on wet pastures, dry cows grazing on wet pastures, and purchase of cows were identified as risk factors. Within the case and control groups, 74.8 and 12.7% of farms were positive for fasciolosis on BTM ELISA, respectively. The differences are likely to be related to the detection limit of the farm-level prevalence by the BTM ELISA test, time span between slaughter data and BTM, and the relatively low sensitivity of liver inspection at slaughter. Control of bovine fasciolosis in Denmark should target heifers and dry cows through grazing management and appropriate anthelmintic treatment, and BTM ELISA can be a useful diagnostic tool for fasciolosis in Danish dairy farms.

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Methods for estimating disease transmission rates: Evaluating the precision of Poisson regression and two novel methods

Precise estimates of disease transmission rates are critical for epidemiological simulation models. Most often these rates must be estimated from longitudinal field data, which are costly and time-consuming to conduct. Consequently, measures to reduce cost like increased sampling intervals or subsampling of the population are implemented. To assess the impact of such measures we implement two different SIS models to simulate disease transmission: A simple closed population model and a realistic dairy herd including population dynamics. We analyze the accuracy of different methods for estimating the transmission rate. We use data from the two simulation models and vary the sampling intervals and the size of the population sampled. We devise two new methods to determine transmission rate, and compare these to the frequently used Poisson regression method in both epidemic and endemic situations. For most tested scenarios these new methods perform similar or better than Poisson regression, especially in the case of long sampling intervals. We conclude that transmission rate estimates are easily biased, which is important to take into account when using these rates in simulation models.

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Modelling spread of MRSA within a pig herd

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Mulighederne for en bedre udnyttelse af de økonomiske ressourcer til det veterinære beredskab for mund- og klovsyge

General information
Network analysis of pig movements: Loyalty patterns and contact chains of different holding types in Denmark
Understanding animal movements is an important factor for the development of meaningful surveillance and control programs, but also for the development of disease spread models. We analysed the Danish pig movement network using static and temporal network analysis tools to provide deeper insight in the connection between holdings dealing with pigs, such as breeding and multiplier herds, production herds, slaughterhouses or traders. Pig movements, which occurred between 1st January 2006 and 31st December 2015 in Denmark, were summarized to investigate temporal trends such as the number of active holdings, the number of registered movements and the number of pigs moved. To identify holdings and holding types with potentially higher risk for introduction or spread of diseases via pig movements, we determined loyalty patterns, annual network components and contact chains for the 24 registered holding types. The total number of active holdings as well as the number of pig movements decreased during the study period while the holding sizes increased. Around 60-90% of connections between two pig holdings were present in two consecutive years and around one third of the connections persisted within the considered time period. Weaner herds showed the highest level of in-loyalty, whereas we observed an intermediate level of in-loyalty for all breeding sites and for production herds. Boar stations, production herds and trade herds showed a high level of out-loyalty. Production herds constituted the highest proportion of holdings in the largest strongly connected component. All production sites showed low levels of in-going contact chains and we observed a high level of out-going contact chain for breeding and multiplier herds. Except for livestock auctions, all transit sites also showed low levels of out-going contact chains. Our results reflect the pyramidal structure of the underlying network. Based on the considered disease, the time frame for the calculation of network measurements needs to be adapted. Using these adapted values for loyalty and contact chains might help to identify holdings with high potential of spreading diseases and thus limit the outbreak size or support control or eradication of the considered pathogen.
Opportunities and challenges when pooling milk samples using ELISA

Testing large quantities of samples in order to detect one or more test-positive sample(s) is expensive and time-consuming. It is possible to optimize this process by pooling samples. Two frameworks to produce different hierarchical and non-hierarchical pooling schemes were tested and compared to standard pooling. Their efficiency and the potential savings were determined as a function of prevalence and the number of pooled samples.

The potential benefit of pooling samples is dependent upon the changes in the analytical sensitivity and specificity of the test used when diluting test-positive samples by pooling. To illustrate this, the sensitivity of antibody ELISA on pooled samples of bovine milk for Salmonella Dublin, Mycobacterium avium spp. paratuberculosis, and bovine virus diarrhea was tested. For these milk assays, the analytical sensitivity decreased rapidly with increasing pool sizes.

The efficiency of pooling is usually only measured by the number of tests performed, yet real savings depend on all the costs involved in the pooling process. These may differ between laboratories depending on the available equipment and the salaries of the technicians, among other factors. Therefore, several cost parameters were introduced to describe the total cost and thereby calculate the total savings. In terms of overall savings, both tested schemes were potentially optimal depending on the prevalence, possible pool size, and the cost of retesting. For the pool sizes of interest in this study, the three-stage hierarchical pooling scheme was often marginally more efficient in terms of the total number of tests. However, if the price of re-pooling was high, the two-stage scheme performed better in terms of total savings. In addition, for low prevalences and the possibility of pooling a large number of samples, the two-stage non-hierarchical test may be more efficient, both in terms of number of tests and overall cost. In order to apply these results in different laboratory settings, a free Shiny WebApp was developed, to compare several pooling schemes with different cost parameters.

Resource Estimations in Contingency Planning for Foot-and-Mouth Disease

Preparedness planning for a veterinary crisis is important to be fast and effective in the eradication of disease. For countries with a large export of animals and animal products, each extra day in an epidemic will cost millions of Euros due to the closure of export markets. This is important for the Danish husbandry industry, especially the swine industry, which had an export of (sic)4.4 billion in 2012. The purposes of this project were to (1) develop an iterative tool with the aim of estimating the resources needed during an outbreak of foot-and-mouth disease (FMD) in Denmark, (2) identify areas, which can delay the control of the disease. The tool developed should easily be updated, when knowledge is gained from other veterinary crises or during an outbreak of FMD. The stochastic simulation model DTU-DADS was used to simulate spread of FMD in Denmark. For each task occurring during an epidemic of FMD, the time and personnel needed per herd
was estimated by a working group with expertise in contingency and crisis management. By combining this information, an iterative model was created to calculate the needed personnel on a daily basis during the epidemic. The needed personnel was predicted to peak within the first week with a requirement of approximately 123 (65-175) veterinarians, 33 (23-64) technicians, and 36 (26-49) administrative staff on day 2, while the personnel needed in the Danish Emergency Management Agency (responsible for the hygiene barrier and initial cleaning and disinfection of the farm) was predicted to be 174 (58-464), mostly recruits. The time needed for surveillance visits was predicted to be the most influential factor in the calculations. Based on results from a stochastic simulation model, it was possible to create an iterative model to estimate the requirements for personnel during an FMD outbreak in Denmark. The model can easily be adjusted, when new information on resources appears from management of other crisis or from new model runs.

Sampling pig farms at the abattoir in a cross-sectional study – Evaluation of a sampling method
A cross-sectional study design is relatively inexpensive, fast and easy to conduct when compared to other study designs. Careful planning is essential to obtaining a representative sample of the population, and the recommended approach is to use simple random sampling from an exhaustive list of units in the target population. This approach is rarely feasible in practice, and other sampling procedures must often be adopted. For example, when slaughter pigs are the target population, sampling the pigs on the slaughter line may be an alternative to on-site sampling at a list of farms. However, it is difficult to sample a large number of farms from an exact predefined list, due to the logistics and workflow of an abattoir. Therefore, it is necessary to have a systematic sampling procedure and to evaluate the obtained sample with respect to the study objective. We propose a method for 1) planning, 2) conducting, and 3) evaluating the representativeness and reproducibility of a cross-sectional study when simple random sampling is not possible. We used an example of a cross-sectional study with the aim of quantifying the association of antimicrobial resistance and antimicrobial consumption in Danish slaughter pigs. It was not possible to visit farms within the designated timeframe. Therefore, it was decided to use convenience sampling at the abattoir. Our approach was carried out in three steps: 1) planning: using data from meat inspection to plan at which abattoirs and how many farms to sample; 2) conducting: sampling was carried out at five abattoirs; 3) evaluation: representativeness was evaluated by comparing sampled and non-sampled farms, and the reproducibility of the study was assessed through simulated sampling based on meat inspection data from the period where the actual data collection was carried out. In the cross-sectional study samples were taken from 681 Danish pig farms, during five weeks from February to March 2015. The evaluation showed that the sampling procedure was reproducible with results comparable to the collected sample. However, the sampling procedure favoured sampling of large farms. Furthermore, both under-sampled and over-sampled areas were found using scan statistics. In conclusion, sampling conducted at abattoirs can provide a spatially representative sample. Hence it is a possible cost-effective alternative to simple random sampling. However, it is important to assess the properties of the resulting sample so that any potential selection bias can be addressed when reporting the findings.
Semiquantitative Decision Tools for FMD Emergency Vaccination Informed by Field Observations and Simulated Outbreak Data

We present two simple, semiquantitative model-based decision tools, based on the principle of first 14 days incidence (FFI). The aim is to estimate the likelihood and the consequences, respectively, of the ultimate size of an ongoing FMD epidemic. The tools allow risk assessors to communicate timely, objectively, and efficiently to risk managers and less technically inclined stakeholders about the potential of introducing FMD suppressive emergency vaccination. To explore the FFI principle with complementary field data, we analyzed the FMD outbreaks in Argentina in 2001, with the 17 affected provinces as the units of observation. Two different vaccination strategies were applied during this extended epidemic. In a series of 5,000 Danish simulated FMD epidemics, the numbers of outbreak herds at day 14 and at the end of the epidemics were estimated under different control strategies. To simplify and optimize the presentation of the resulting data for urgent decisions to be made by the risk managers, we estimated the sensitivity, specificity, as well as the negative and positive predictive values, using a chosen day-14 outbreak number as predictor of the magnitude of the number of remaining post-day-14 outbreaks under a continued basic control strategy. Furthermore, during an ongoing outbreak, the actual cumulative number of detected infected herds at day 14 will be known exactly. Among the number of epidemics lasting >14 days out of the 5,000 simulations under the basic control scenario, we selected those with an assumed accumulated number of detected outbreaks at day 14. The distribution of the estimated number of detected outbreaks at the end of the simulated epidemics minus the number at day 14 was estimated for the epidemics lasting more than 14 days. For comparison, the same was done for identical epidemics (i.e., seeded with the same primary outbreak herds) under a suppressive vaccination scenario. The results indicate that, during the course of an FMD epidemic, simulated likelihood predictions of the remaining epidemic size and of potential benefits of alternative control strategies can be presented to risk managers and other stakeholders in objective and easily communicable ways.
Spatial patterns of antimicrobial resistance genes in a cross-sectional sample of pig farms with indoor non-organic production of finishers

Antimicrobial resistance (AMR) in pig populations is a public health concern. There is a lack of information of spatial distributions of AMR genes in pig populations at large scales. The objective of the study was to describe the spatial pattern of AMR genes in faecal samples from pig farms and to test if the AMR genes were spatially randomly distributed with respect to the geographic distribution of the pig farm population at risk. Faecal samples from 687 Danish pig farms were collected in February and March 2015. DNA was extracted and the levels of seven AMR genes (ermB, ermF, sulI, sulII, tet(M), tet(O) and tet(W)) were quantified on a high-throughput real-time PCR array. Spatial differences for the levels of the AMR genes measured as relative quantities were evaluated by spatial cluster analysis and creating of risk maps using kriging analysis and kernel density estimation. Significant spatial clusters were identified for ermB, ermF, sulII and tet(W). The broad spatial trends in AMR resistance evident in the risk maps were in agreement with the results of the cluster analysis. However, they also showed that there were only small scale spatial differences in the gene levels. We conclude that the geographical location of a pig farm is not a major determinant of the presence or high levels of AMR genes assessed in this study.

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Transmission of African swine fever virus from infected pigs by direct contact and aerosol routes

In 2014, African swine fever virus (ASFV) was introduced into the Baltic states and Poland. Since then, the disease has continued to spread within these regions, and recently, cases were reported in the Czech Republic and Romania. Currently, there is an increasing risk of ASFV introduction into Western Europe. Hence, there is an urgent need to assess current contingency plans. For this purpose, knowledge of modes-of-transmission and clinical outcome in pigs infected with new European ASFV strains is needed. In the present study, two experiments were conducted in pigs using an isolate of ASFV from Poland (designated here POL/2015/Podlaskie/Lindholm). In both studies, pigs were inoculated intranasally with the virus and contact pigs were exposed to the experimentally infected pigs, either directly (contact within and between pens) or by air. Pigs exposed to the virus by intranasal inoculation, by direct contact to infected animals and by aerosol developed acute disease characterized by viremia, fever and depression. Infectious virus was first detected in blood obtained from the inoculated pigs and then sequentially among the within-pen, between-pen and air-contact pigs. ASFV DNA and occasionally infectious virus was found in nasal-, oral-, and rectal swabs obtained from the pigs, and ASFV DNA was detected in air samples. No anti-ASFV antibodies were detected in sera. In conclusion, the study shows that the currently circulating strain of ASFV can be efficiently transmitted via direct contact and by aerosols. Also, the results provide quantitative transmission parameters and knowledge of infection stages in pigs infected with this ASFV.

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Treatment Patterns for Mastitis in Danish Dairy Cattle Farms

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**What tools are useful for monitoring endemic diseases? A simulation study based on different time-series components.**

Control and eradication programs play an important role in disease monitoring and surveillance. It is important to follow up on implemented strategies to reduce and/or eliminate a specific disease. The objectives of this study were to investigate the performance of different detection methods, including methods commonly used in biosurveillance as well as state space models, for monitoring the effect of endemic disease control and eradication programs. We simulated 16 different scenarios of changes in disease sero-prevalence, inspired by real-world data from the Danish PRRS (Porcine Reproductive and Respiratory Syndrome) monitoring program. The changes included increases, decreases and/or constant sero-prevalence levels in different combinations. Two state space models were used to model the simulated data and different monitoring methods, such as univariate process control algorithms (UPCA) and monitoring of the trend component were tested. The performance was evaluated as the proportion of iterations with an alarm for a given week. Results revealed that the different UPCA performed differently with respect to detecting increasing and decreasing changes in sero-prevalence. The trend-based methods performed well for detecting the first event but its performance was poorer in adapting to several consecutive events. The different monitoring methods had different performances in monitoring increasing and decreasing changes in disease sero-prevalence, showing that the objectives of the monitoring program should be taken into account when choosing which methods to use. The principles used in this study can also be applied in disease surveillance of (re-)emerging diseases.

**Adaptive Test Schemes for Control of Paratuberculosis in Dairy Cows**

Paratuberculosis is a chronic infection that in dairy cattle causes reduced milk yield, weight loss, and ultimately fatal diarrhea. Subclinical animals can excrete bacteria (Mycobacterium avium ssp. paratuberculosis, MAP) in feces and infect other animals. Farmers identify the infectious animals through a variety of test-strategies, but are challenged by the lack of perfect tests. Frequent testing increases the sensitivity but the costs of testing are a cause of concern for farmers. Here, we used a herd simulation model using milk ELISA tests to evaluate the epidemiological and economic consequences of continuously adapting the sampling interval in response to the estimated true prevalence in the herd. The key results were that the true prevalence was greatly affected by the hygiene level and to some extent by the test-frequency. Furthermore, the choice of prevalence that will be tolerated in a control scenario had a major impact on the true prevalence in the normal hygiene setting, but less so when the hygiene was poor. The net revenue is not greatly affected by the test-strategy, because of the general variation in net revenues between farms. An exception to this is the low hygiene herd, where frequent testing results in lower revenue. When we look at the probability of eradication, then it is correlated with the testing frequency and the target prevalence during the control phase. The probability of eradication is low in the low hygiene herd, and a test-and-cull strategy should probably not be the primary strategy in this herd. Based on this study we suggest that, in order to control MAP, the standard Danish dairy farm should use an adaptive strategy where a short sampling interval of three months is used when the estimated true prevalence is above 1%, and otherwise use a long sampling interval of one year.
A herd- and cow-specific decision support tool for control of mastitis

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A simulation model for the spread of LA-MRSA within a pig herd

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A space-time analysis of Mycoplasma bovis: bulk tank milk antibody screening results from all Danish dairy herds in 2013-2014

Mycoplasma bovis is an important pathogen causing severe disease outbreaks in cattle farms. Since 2011, there has been an apparent increase in M. bovis outbreaks among Danish dairy cattle herds. The dairy cattle industry performed cross-sectional antibody screening for M. bovis on four occasions, using the indirect BIO K 302 M. bovis enzyme-linked immunosorbent assay (ELISA) (Bio-X, Belgium) in bulk tank milk from all dairy herds between June 2013 and July 2014. The objective of this study was to investigate the evolution of the spatial distribution of M. bovis in the Danish dairy herd population throughout the study period. Repeated bulk tank milk samples were used as a proxy for the herd-level diagnosis. Descriptive and spatial analyses were performed for the four screening rounds. Based on a previous diagnostic
test evaluation study, the M. bovis status for each herd was determined as test-positive or test-negative using a cut-off of 50 optical density coefficient %. The spatial global clustering was evaluated through a modified K-function method, and local clusters were identified by scan statistics. The results showed that M. bovis test-positive herds had a dynamic pattern in space. The global clustering analysis showed that M. bovis test-positive herds were spatially correlated in rounds one, three and four. These findings were supported to some extent by the local clustering analysis, which found significant high- and low-risk spatial clusters in rounds one and three in the north and south of the mainland. The clusters with a high risk of observing test-positive herds did not remain between sampling rounds, indicating that M. bovis did not tend to persist upon emergence in dairy herds. In contrast, the clusters with a low risk of observing test-positive herds persisted in the same area throughout the study period.

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Comparing algorithms performance for monitoring endemic disease: a simulation study based on the Danish PRRSV monitoring program

General information
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Organisations: National Veterinary Institute, Section for Epidemiology, National Veterinary Institute
Contributors: Lopes Antunes, A. C., Dorea, F., Hisham Beshara Halasa, T., Toft, N.
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Comparing algorithms performance for monitoring endemic disease: a simulation study based on the Danish PRRSV monitoring program

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Organisations: National Veterinary Institute, Section for Epidemiology, National Veterinary Institute
Contributors: Lopes Antunes, A. C., Dorea, F., Hisham Beshara Halasa, T., Toft, N.
Number of pages: 1
Publication date: 2016
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Event: Poster session presented at 24th International Pig Veterinary Society (IPVS) Congress, Dublin, Ireland.
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Research output: Contribution to conference → Poster – Annual report year: 2016 → Research → peer-review

Control of African swine fever epidemics in industrialized swine populations
African swine fever (ASF) is a notifiable infectious disease with a high impact on swine health. The disease is endemic in certain regions in the Baltic countries and has spread to Poland constituting a risk of ASF spread toward Western Europe. Therefore, as part of contingency planning, it is important to explore strategies that can effectively control an epidemic of ASF. In this study, the epidemiological and economic effects of strategies to control the spread of ASF between domestic swine herds were examined using a published model (DTU-DADS-ASF). The control strategies were the basic EU and national strategy (Basic), the basic strategy plus pre-emptive depopulation of neighboring swine herds, and intensive surveillance of herds in the control zones, including testing live or dead animals. Virus spread via wild boar was not modelled.

Under the basic control strategy, the median epidemic duration was predicted to be 21 days (5th and 95th percentiles; 1-55 days), the median number of infected herds was predicted to be 3 herds (1–6), and the total costs were predicted to be €326 million (€256–€442 million). Adding pre-emptive depopulation or intensive surveillance by testing live animals resulted in marginal improvements to the control of the epidemics. However, adding testing of dead animals in the protection and surveillance zones was predicted to be the optimal control scenario for an ASF epidemic in industrialized swine populations without contact to wild boar. This optimal scenario reduced the epidemic duration to 9 days (1–38) and the total costs to €294 million (€257–€392 million). Export losses were the driving force of the total costs of the epidemics.

General information
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Organisations: National Veterinary Institute, Section for Epidemiology, Ministry of Environment and Food of Denmark
Contributors: Hisham Beshara Halasa, T., Bøtner, A., Mortensen, S., Christensen, H., Toft, N., Boklund, A.
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Determining the optimal number of individual samples to pool for quantification of average herd levels of antimicrobial resistance genes in Danish pig herds using high-throughput qPCR
The primary objective of this study was to determine the minimum number of individual fecal samples to pool together in order to obtain a representative sample for herd level quantification of antimicrobial resistance (AMR) genes in a Danish pig herd, using a novel high-throughput qPCR assay. The secondary objective was to assess the agreement between different methods of sample pooling. Quantification of AMR was achieved using a high-throughput qPCR method to quantify the levels of seven AMR genes (ermB, ermF, sulI, sulII, tet(M), tet(O) and tet(W)). A large variation in the levels of AMR genes was found between individual samples. As the number of samples in a pool increased, a decrease in sample variation was observed. It was concluded that the optimal pooling size is five samples, as an almost steady state in the variation was observed when pooling this number of samples. Good agreement between different pooling methods was found and the least time-consuming method of pooling, by transferring feces from each individual sample to a tube using a 10 μl inoculation loop and adding 3.5 ml of PBS, approximating a 10% solution, can therefore be used in future studies.

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Dynamic generalized linear models for monitoring endemic diseases: moving beyond univariate process monitoring control algorithms

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Contributors: Lopes Antunes, A. C., Jensen, D., Hisham Beshara Halasa, T., Toft, N.
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Economic analysis of activities to prevent foot and mouth disease in Denmark
The latest foot and mouth disease (FMD) epidemic in Denmark dates back to 1982-1983. Hence, Denmark has not experienced an FMD outbreak in more than 30 years. Still this disease poses a serious threat either as a risk of introduction and spread in Denmark or as a risk of a ban on Danish export of pigs, pork, cattle, beef and milk products due to an outbreak in another country within the EU. It is estimated that a middle sized outbreak of FMD would cost around € 1 billion. It is evident that even though the probability of introducing FMD is very low the consequences are devastating for
the agricultural sector and society because the expected costs are so enormous. Therefore, the industry and the public authority have implemented a number of mitigating and preventive activities. The costs of FMD and swine fever related activities in Denmark in 2013 were estimated to be approximately € 32 million. The purpose of the present study is to estimate how changes in resources allocated to the FMD related activities may affect the costs of an FMD outbreak. Nine alternative scenarios describing changes in the contingency plan were formulated by a group of experts from the livestock industry, universities and public authorities. A modified version of Davis Animal Disease Simulation model (DADS version 0.05) was used to estimate costs of FMD outbreaks in each of these alternative scenarios. The modified and updated version by the technical university of Denmark (DTU) is called DTU-DADS. The model simulations indicate that some changes in risk-reducing activities may significantly affect expected costs of an outbreak while other changes have no effect. Our results suggest that increased efforts in terms of efficiently restricting low-risk contacts between farms, such as non-professional visitors and trucks, might reduce the size and costs of an FMD outbreak. In addition, simulations indicate that current resources allocated to depopulation and surveillance could – but only to some extent – be reduced without affecting the size and costs of an outbreak.

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Experimental pig-to-pig transmission study with a recent European African Swine Fever virus isolate

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Organisations: National Veterinary Institute, Section for Epidemiology, Section for Virology
Contributors: Olesen, A. S., Lohse, L., Boklund, A., Hisham Beshara Halasa, T., Rasmussen, T. B., Bøtner, A.
Pages: 80-80
Publication date: 2016

Models to Estimate Lactation Curves of Milk Yield and Somatic Cell Count in Dairy Cows at the Herd Level for the Use in Simulations and Predictive Models

Typically, central milk recording data from dairy herds are recorded less than monthly. Over-fitting early in lactation periods is a challenge, which we explored in different ways by reducing the number of parameters needed to describe the milk yield and somatic cell count of individual cows. Furthermore, we investigated how the parameters of lactation models correlate between parities and from dam to offspring. The aim of the study was to provide simple and robust models for cow level milk yield and somatic cell count for fitting to sparse data to parameterize herd- and cow-specific simulation of dairy herds. Data from 610 Danish Holstein herds were used to determine parity traits in milk production regarding milk yield and somatic cell count of individual cows. Parity was stratified in first, second, and third and higher for milk, and first to sixth and higher for somatic cell count. Fitting of herd level parameters allowed for cow level lactation curves with three,
two, or one parameters per lactation. Correlations of milk yield and somatic cell count were estimated between lactations and between dam and offspring. The shape of the lactation curves varied markedly between farms. The correlation between lactations for milk yield and somatic cell count was 0.2–0.6 and significant on more than 95% of farms. The variation in the daily milk yield was observed to be a source of variation to the somatic cell count, and the total somatic cell count was less correlated with the milk production than somatic cells per milliliter. A positive correlation was found between relative levels of the total somatic cell count and the milk yield. The variation of lactation and somatic cell count curves between farms highlights the importance of a herd level approach. The one-parameter per cow model using a herd level curve allows for estimating the cow production level from first the recording in the parity, while a two-parameter model requires more recordings for a credible estimate, but may more precisely predict persistence, and given the independence of parameters, these can be easily drawn for use in simulation models. We also conclude that using total somatic cell count may stabilize models, and therefore, the dilution factor is of importance in Danish Holstein.

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Organisations: Department of Applied Mathematics and Computer Science, National Veterinary Institute, Section for Epidemiology, Dynamical Systems, University of Copenhagen
Contributors: Græsbøll, K., Kirkeby, C. T., Nielsen, S. S., Hisham Beshara Halasa, T., Toft, N., Christiansen, L. E.
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Monitoring endemic livestock diseases using laboratory diagnostic data: A simulation study to evaluate the performance of univariate process monitoring control algorithms

Surveillance systems are critical for accurate, timely monitoring and effective disease control. In this study, we investigated the performance of univariate process monitoring control algorithms in detecting changes in seroprevalence for endemic diseases. We also assessed the effect of sample size (number of sentinel herds tested in the surveillance system) on the performance of the algorithms.

Three univariate process monitoring control algorithms were compared: Shewart p Chart 1 (PSHEW), Cumulative Sum2 (CUSUM) and Exponentially Weighted Moving Average3 (EWMA). Increases in seroprevalence were simulated from 0.10 to 0.15 and 0.20 over 4, 8, 24, 52 and 104 weeks. Each epidemic scenario was run with 2000 iterations. The cumulative sensitivity4 (CumSe) and timeliness were used to evaluate the algorithms’ performance with a 1% false alarm rate. Using these performance evaluation criteria, it was possible to assess the accuracy and timeliness of the surveillance system working in real-time.

The results showed that EWMA and PSHEW had higher CumSe (when compared with the CUSUM) from week 1 until the end of the period for all simulated scenarios. Changes in seroprevalence from 0.10 to 0.20 were more easily detected (higher CumSe) than changes from 0.10 to 0.15 for all three algorithms. Similar results were found with EWMA and PSHEW, based on the median time to detection. Changes in the seroprevalence were detected later with CUSUM, compared to EWMA and PSHEW for the different scenarios. Increasing the sample size 10 fold halved the time to detection (CumSe = 1), whereas increasing the sample size 100 fold reduced the time to detection by a factor of 6.

This study investigated the performance of three univariate process monitoring control algorithms in monitoring endemic diseases. It was shown that automated systems based on these detection methods identified changes in seroprevalence at different times. Increasing the number of tested herds would lead to faster detection. However, the practical implications of increasing the sample size (such as the costs associated with the disease) should also be taken into account.

General information
Publication status: Published
Simulating the epidemiological and economic effects of an African swine fever epidemic in industrialized swine populations

African swine fever (ASF) is a notifiable infectious disease with a considerable impact on animal health and is currently one of the most important emerging diseases of domestic pigs. ASF was introduced into Georgia in 2007 and subsequently spread to the Russian Federation and several Eastern European countries. Consequently, there is a non-negligible risk of ASF spread towards Western Europe. Therefore it is important to develop tools to improve our understanding of the spread and control of ASF for contingency planning. A stochastic and dynamic spatial spread model (DTU-DADS) was adjusted to simulate the spread of ASF virus between domestic swine herds exemplified by the Danish swine population. ASF was simulated to spread via animal movement, low- or medium-risk contacts and local spread. Each epidemic was initiated in a randomly selected herd – either in a nucleus herd, a sow herd, a randomly selected herd or in multiple herds simultaneously. A sensitivity analysis was conducted on input parameters. Given the inputs and assumptions of the model, epidemics of ASF in Denmark are predicted to be small, affecting about 14 herds in the worst-case scenario. The duration of an epidemic is predicted to vary from 1 to 76 days. Substantial economic damages are predicted, with median direct costs and export losses of €12 and €349 million, respectively, when epidemics were initiated in multiple herds. Each infectious herd resulted in 0 to 2 new infected herds varying from 0 to 5 new infected herds, depending on the index herd type.

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Organisations: National Veterinary Institute, Section for Epidemiology, Ministry of Environment and Food of Denmark
Contributors: Hisham Beshara Halasa, T., Bøtner, A., Mortensen, S., Christensen, H., Toft, N., Boklund, A.
Simulating the Epidemiological and Economic Impact of Paratuberculosis Control Actions in Dairy Cattle

We describe a new mechanistic bioeconomic model for simulating the spread of Mycobacterium avium subsp. paratuberculosis (MAP) within a dairy cattle herd. The model includes age-dependent susceptibility for infection; age-dependent sensitivity for detection; environmental MAP build up in five separate areas of the farm; in utero infection; infection via colostrum and waste milk, and it allows for realistic culling (i.e., due to other diseases) by including a ranking system. We calibrated the model using a unique dataset from Denmark, including 102 random farms with no control actions against spread of MAP. Likewise, four control actions recommended in the Danish MAP control program were implemented in the model based on reported management strategies in Danish dairy herds in a MAP control scheme. We tested the model parameterization in a sensitivity analysis. We show that a test-and-cull strategy is on average the most cost-effective solution to decrease the prevalence and increase the total net revenue on a farm with low hygiene, but not more profitable than no control strategy on a farm with average hygiene. Although it is possible to eradicate MAP from the farm by implementing all four control actions from the Danish MAP control program, it was not economically attractive since the expenses for the control actions outweigh the benefits. Furthermore, the three most popular control actions against the spread of MAP on the farm were found to be costly and inefficient in lowering the prevalence when used independently.
Simulation of Spread of African Swine Fever, Including the Effects of Residues from Dead Animals

To study the spread of African swine fever (ASF) within a pig unit and the impact of unit size on ASF spread, a simulation model was created. In the model, an animal can be in one of the following stages: susceptible, latent, subclinical, clinical, or recovered. Animals can be infectious during the subclinical stage and are fully infectious during the clinical stage. ASF virus (ASFV) infection through residues of dead animals in the slurries was also modeled in an exponentially fading-out pattern. Low and high transmission rates for ASFV were tested in the model. Robustness analysis was carried out in order to study the impact of uncertain parameters on model predictions. The results showed that the disease may fade out within the pig unit without a major outbreak. Furthermore, they showed that spread of ASFV is dependent on the infectiousness of subclinical animals and the residues of dead animals, the transmission rate of the virus, and importantly the unit size. Moreover, increasing the duration of the latent or the subclinical stages resulted in longer time to disease fade out. The proposed model is a simple and robust tool simulating the spread of ASFV within a pig house taking into account dynamics of ASFV spread and the unit size. The tool can be implemented in simulation models of ASFV spread between herds.

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Organisations: National Veterinary Institute, Section for Epidemiology, Helmholtz Center for Environmental Research (UFZ)
Contributors: Hisham Beshara Halasa, T., Boklund, A., Bøtner, A., Toft, N., Thulke, H.
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Spatial patterns of Antimicrobial Resistance Genes in Danish Pig Farms

Samples from 687 Danish pig farms were collected at five finisher slaughterhouses in February and March 2015. Faecal samples from five pigs per farm were collected randomly at the slaughter line and pooled into one sample per farm. DNA was extracted from the pooled samples and the level of seven antimicrobial resistance genes, ermB, ermF, sulII, sulf, tet(M), tet(O) and tet(W), was quantified by a high-throughput qPCR. It was evaluated whether the sample method resulted in a study population representative of Danish pig farms with finishers where it was found that the study population was biased towards farms having more finisher and a higher productivity. Spatial cluster analyses were performed in SaTScan®. The results showed significant spatial clusters for ermF, ermB, sulII and tet(W) whereas no significant clusters were found for sulf, tet(M) and tet(O).

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Organisations: National Veterinary Institute, Epidemiology, Bacteriology & Parasitology, National Food Institute, Research group for Genomic Epidemiology, University of Copenhagen
Contributors: Birkegård, A. C., Ersbøll, A. K., Hisham Beshara Halasa, T., Clasen, J., Folkesson, A., Vigre, H., Toft, N.
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Towards control of LA-MRSA - Simulation modeling of LA-MRSA spread between pig farms

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What to look for when monitoring animal diseases?

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Contributors: Lopes Antunes, A. C., Jensen, D., Hisham Beshara Halasa, T., Toft, N.
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A Bayesian herd-level diagnostic test evaluation - Mycoplasma bovis

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Organisations: National Veterinary Institute, Section for Epidemiology, University of Copenhagen
Contributors: Nielsen, P. K., Petersen, M. B., Nielsen, L. R., Hisham Beshara Halasa, T., Toft, N.
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A space-time analysis of Mycoplasma bovis in Denmark

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Comparison of individual and pooled samples for quantification of antimicrobial resistance genes in swine feces by high-throughput qPCR

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iCull – A bioeconomic model for herd management and disease control

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Publication status: Published
Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
Contributors: Kirkby, C., Græsbøll, K., Nielsen, S. S., Christiansen, L. E., Toft, N., Hisham Beshara Halasa, T.
Number of pages: 1
Publication date: 2015
Peer-reviewed: No
Research output: Contribution to conference › Poster – Annual report year: 2015 › Research

Improving the Effect and Efficiency of FMD Control by Enlarging Protection or Surveillance Zones
An epidemic of foot-and-mouth disease (FMD) in a FMD-free country with large exports of livestock and livestock products would result in profound economic damage. This could be reduced by rapid and efficient control of the disease spread. The objectives of this study were to estimate the economic impact of a hypothetical FMD outbreak in Denmark based on changes to the economic assumptions of the model, and to investigate whether the control of an FMD epidemic can be improved by combining the enlargement of protection or surveillance zones with pre-emptive depopulation or emergency vaccination. The stochastic spatial simulation model DTU-DADS was used to simulate the spread of FMD in Denmark. The control strategies were the basic EU and Danish strategy, pre-emptive depopulation, suppressive or protective vaccination, enlarging protection or surveillance zones, and a combination of pre-emptive depopulation or emergency vaccination with enlarged protection or surveillance zones. Herds are detected either based on basic detection through the appearance of clinical signs, or as a result of surveillance in the control zones. The economic analyses consisted of direct costs and export losses. Sensitivity analysis was performed on uncertain and potentially influential input parameters. Enlarging the surveillance zones from 10 to 15 km, combined with pre-emptive depopulation over a 1-km radius around detected herds resulted in the lowest total costs. This was still the case even when the different input parameters were changed in the sensitivity analysis. Changing the resources for clinical surveillance did not affect the epidemic consequences. In conclusion, an FMD epidemic in Denmark would have a larger economic impact on the agricultural sector than previously anticipated. Furthermore, the control of a potential FMD outbreak in Denmark may be improved by combining pre-emptive depopulation with an enlarged protection or surveillance zone.

General information
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Organisations: National Veterinary Institute, Section for Epidemiology
Contributors: Hisham Beshara Halasa, T., Toft, N., Boklund, A.
Number of pages: 10
Publication date: 2015
Latent class analysis of bulk tank milk PCR and ELISA testing for herd level diagnosis of Mycoplasma bovis

The bacterium Mycoplasma bovis causes disease in cattle of all ages. An apparent increase in the occurrence of M. bovis associated outbreaks among Danish dairy cattle herds since 2011 has prompted a need for knowledge regarding herd-level diagnostic performance. Therefore, the objective of this study was to evaluate the herd-level diagnostic performance of an indirect ELISA test by comparison to a real-time PCR test when diagnosing M. bovis in cattle herds of bulk tank milk. Bulk tank milk samples from Danish dairy herds (N=3437) were analysed with both the antibody detecting BIO K 302 M. bovis ELISA kit and the antigen detecting PathoProof Mastitis Major-3 kit. As none of these are considered a gold standard test for herd-level diagnostics we applied a series of Bayesian latent class analyses for a range of ELISA cut-off values. The negative and positive predictive values were calculated for hypothetical true national prevalences (1, 5, 10, 15 and 20%) of infected herds. We estimated that the ELISA test had a median sensitivity and specificity of 60.4 [37.5-96.2 95% Posterior Credibility Interval] and 97.3 [94.0-99.8 95% PCI] at the currently recommended cut-off (37% Optical density Coefficient). These changed to 43.5 [21.1-92.5 95% PCI] and 99.6 [98.8-100 95% PCI] if the cut-off was increased to 50 ODC%. In addition, herd-level diagnosis by ELISA would result in fewer false positives at a cut-off value of 50 ODC% compared to 37 ODC% without compromising the negative predictive value.

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Contributors: Nielsen, P. K., Petersen, M. B., Nielsen, L. R., Hisham Beshara Halasa, T., Toft, N.
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Mean effective sensitivity for *Mycobacterium avium* subsp paratuberculosis infection in cattle herds

Background: *Mycobacterium avium* subsp. paratuberculosis (MAP) infections in cattle are generally challenging to detect and cost-effective test strategies are consequently difficult to identify. MAP-specific antibody ELISAs for milk and serum are relatively inexpensive, but their utility is influenced by a number of factors such as herd size, herd composition and diagnostic sensitivity. The sensitivity of the test increases with the age of the tested animal, and therefore the general, or "mean effective sensitivity" (defined as the mean of the sensitivities for all animals within a population, MES), for detecting MAP within a herd is dependent upon the age distribution of the herd. For this study we used a dataset of cattle from 4,259 dairy herds and 4,078 non-dairy herds. The aim was to investigate the MES for groups of cattle considered to be reasonable entities for MAP surveillance and control, in order to assist the decision-makers in planning and optimizing these programs economically. We compared six different groups of cattle (three dairy and three non-dairy) in Denmark by calculating the MES for each herd in each group.

Results: The distribution of MES showed a large variation within and between groups, and in some groups we found a bimodal distribution of MES. Dairy herds generally showed higher MES than non-dairy herds. Dairy herds in a control programme for paratuberculosis showed a MES similar to all other dairy herds from which animals >2.0 years were tested (both groups had a median MES = 0.60). For the non-dairy groups, the sensitivity became much higher when animals <2.0 years and herds with less than 25 cattle were excluded, resulting in a median MES of 0.65. Conclusion: The results showed that MES could indicate the effectivity of testing different cattle groups for MAP, given that the data used are unbiased.

**General information**

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Organisations: National Veterinary Institute, Section for Epidemiology, Department of Applied Mathematics and Computer Science, Dynamical Systems, University of Copenhagen
Contributors: Kirkeby, C., Græsbøll, K., Hisham Beshara Halasa, T., Toft, N., Nielsen, S. S.
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Monitoring PRRS based on laboratory submissions: a simulation study to evaluate detection algorithms performance

**General information**

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Organisations: National Veterinary Institute, Section for Epidemiology
Contributors: Lopes Antunes, A. C., Dorea, F., Hisham Beshara Halasa, T., Toft, N.
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Monitoring PRRS sero-prevalence in Danish breeding herds: Evaluation of algorithms performance

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Planning a cross-sectional study of antimicrobial resistance genes in Danish pig farms

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Contributors: Birkegård, A. C., Hisham Beshara Halasa, T., Toft, N.
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Planning a cross-sectional study of antimicrobial resistance genes in Danish pig farms

Prevalence, risk factors and spatial analysis of infections with liver flukes in Danish cattle herds

Prevalence, risk factors and spatial analysis of liver fluke infections in Danish cattle herds
local factors that clustered geographically.

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Simulator bruges i kampen mod plasmacytose

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Organisations: National Veterinary Institute, Section for Epidemiology, Copenhagen Fur
Contributors: Boklund, A., Hisham Beshara Halasa, T., Chriél, M., Struve, T., Østergaard, J., Clausen, J.
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Simulering af kontroforanstaltninger til bekæmpelse af plasmacytose i minkfarme

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Contributors: Boklund, A., Hisham Beshara Halasa, T., Struve, T., Østergaard, J., Clausen, J., Chriél, M.
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Spatial analysis and temporal trends of porcine reproductive and respiratory syndrome in Denmark from 2007 to 2010 based on laboratory submission data

Porcine reproductive and respiratory syndrome (PRRS) has been a cause for great concern to the Danish pig industry since it was first diagnosed in 1992. The causative agent of PRRS is an RNA virus which is divided into different genotypes. The clinical signs, as well as its morbidity and mortality, is highly variable between herds and regions. Two different genotypes of PRRS virus (PRRSV) are found in Denmark: type 1 and type 2. Approximately 40 % of Danish swine herds are seropositive for one or both PRRSV types. The objective of this study was to describe the temporal trend and spatial distribution of PRRSV in Danish swine herds from 2007 to 2010, based on type-specific serological tests from the PRRS surveillance and control program in Denmark using the results stored in the information management system at the National Veterinary Institute, Technical University of Denmark (DTU Vet). The average monthly seroprevalence of PRRSV type 1 was 9 % (minimum of 5 %; maximum of 13 %) in breeding herds, and 20 % (minimum of 14 %; maximum of 26 %) in production herds; PRRSV type 2 had an average seroprevalence of 3 % (minimum of 1 %; maximum of 9 %) in breeding herds and of 9 % (minimum of 5 %; maximum of 13 %) within production herds. The seroconversion rate followed a similar and consistent pattern, being higher for type 1 than for type 2 for both PRRSV types. Regarding the spatiotemporal results, the relative risk distribution maps changed over time as a consequence of the changes in PRRSV seroprevalence, suggesting a general decline in the extent of areas with higher relative risk for both type 1 and 2. Local spatial analysis results demonstrated the existence of statistically significant clusters in areas where the relative risk was higher for both herds. PRRSV type 1 seroprevalence was constantly higher than for PRRSV type 2 in both herd types. Significant spatial clusters were consistently found in Denmark, suggesting that PRRSV is endemic in these areas. Furthermore, relative risk distribution maps revealed different patterns over time as a consequence of the changes in seroprevalence.
A Comparison between Two Simulation Models for Spread of Foot-and-Mouth Disease

Two widely used simulation models of foot-and-mouth disease (FMD) were used in order to compare the models' predictions in term of disease spread, consequence, and the ranking of the applied control strategies, and to discuss the effect of the way disease spread is modeled on the predicted outcomes of each model. The DTU-DADS (version 0.100), and ISP (version 2.001.11) were used to simulate a hypothetical spread of FMD in Denmark. Actual herd type, movements, and location data in the period 1st October 2006 and 30th September 2007 was used. The models simulated the spread of FMD using 3 different control scenarios: 1) A basic scenario representing EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds within a 500 meters radius around the detected herds, and 3) suppressive vaccination of susceptible herds within a 1,000 meters radius around the detected herds. Depopulation and vaccination started 14 days following the detection of the first infected herd. Five thousand index herds were selected randomly, of which there were 1,000 cattle herds located in high density cattle areas and 1,000 in low density cattle areas, 1,000 swine herds located in high density swine areas and 1,000 in low density swine areas, and 1,000 sheep herds. Generally, DTU-DADS predicted larger, longer duration and costlier epidemics than ISP, except when epidemics started in cattle herds located in high density cattle areas. ISP supported suppressive vaccination rather than pre-emptive depopulation, while DTU-DADS was indifferent to the alternative control strategies. Nonetheless, the absolute differences between control strategies were small making the choice of control strategy during an outbreak to be most likely based on practical reasons.

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Copyright: 2014 Halasa et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
Association of MAP specific ELISA-responses and productive parameters in 314 Danish dairy farms

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Organisations: Department of Applied Mathematics and Computer Science, Dynamical Systems, National Veterinary Institute, Section for Epidemiology, University of Copenhagen
Contributors: Græsbøll, K., Nielsen, S. S., Hisham Beshara Halasa, T., Kirkeby, C., Toft, N., Christiansen, L. E.
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Association of map specific ELISA-responses and productive parameters in 367 danish dairy farms

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iCull - a herd-specific tool for financial evaluation of the impact of paratuberculosis

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Impact of clinical surveillance during a foot-and-mouth disease epidemic
The objectives of this study were to assess, whether the current surveillance capacity is sufficient to fulfill EU and Danish regulations to control a hypothetical foot-and-mouth disease (FMD) epidemic in Denmark, and whether enlarging the protection and/or surveillance zones could reduce epidemic duration, number of infected herds and the economic losses from an epidemic.

The stochastic spatial simulation model DTU-DADS was enhanced to include simulation of surveillance of herds within the protection and surveillance zones and the model was used to model spread of FMD between herds. A queuing system was included in the model, and based on a daily surveillance capacity of 450 herds per day, it was decided whether herds appointed for surveillance would be surveyed on the current day or added to the queue. The model was run with a basic scenario representing the EU and Danish regulations, which includes a 3 km protection and 10 km surveillance zone around detected herds. In alternative scenarios, the protection zone was enlarged to 5 km, the surveillance zone was enlarged to 15 or 20 km, or a combined enlargement of the protection and surveillance zones was modelled. Sensitivity analysis included changing 1) surveillance capacity to 200, 350 or 600 herds per day, 2) frequency of repeated visits for herds in overlapping surveillance zones from every 14 days to every 7, 21 and 30 days, and 3) the size of the zones combined with a surveillance capacity increased to 600 herds per day.

The results showed that the default surveillance capacity is sufficient to survey herds within one week of the zones establishment, as the regulations demand. Extra resources for surveillance did not reduce the costs of the epidemics, but fewer resources could result in larger epidemics and costs. Furthermore, enlarging the surveillance zone may result in shorter epidemic duration, and lower number of affected herds, while enlargements of the protection zone resulted in lower economic losses when epidemics were large. Given the assumptions, enlarging the surveillance zone did not reduce the economic losses.

Infections with cardiopulmonary and intestinal helminths and sarcoptic mange in red foxes from two different localities in Denmark
Monitoring parasitic infections in the red fox is essential for obtaining baseline knowledge on the spread of diseases of veterinary and medical importance. In this study, screening for cardiopulmonary and intestinal helminths and sarcoptic mange (Sarcoptes scabiei) was done on 118 foxes originating from two distinct localities in Denmark, (Copenhagen) greater area and southern Jutland. Fifteen parasite species were recorded in 116 foxes (98.3%), nine parasitic species are of zoonotic potential. Parasite diversity was greater in foxes of Copenhagen in terms of overall parasite species richness and species richness of all helminth groups individually: trematodes; cestodes; and nematodes. Six parasite species were recovered from foxes of Copenhagen, but not from foxes of Southern Jutland: Echinococcum perfoliatus; Echinostoma sp.; Pseudophistomum truncatum; Dipylidium caninum; Angiostrongylus vasorum; and Sarcoptes scabiei, but Toxascaris leonina was only recorded in foxes of southern Jutland. A high prevalence and abundance of A. vasorum in foxes of Copenhagen was observed. The prevalence of four nematode species; Eucoleus (Capillaria) aerophilus, Uncinaria stenocephala, Toxocara canis, and Crenosoma vulpis, in foxes of both localities were comparable and ranging from 22.9% to 89%. The prevalence of Mesocestoides sp. was significantly higher in foxes of Copenhagen. Taenia spp. were detected using morphological and molecular analysis, which revealed the dominance of T. polycanthan in foxes of both localities. Infections with sarcoptic mange were evident only among foxes of Copenhagen (44.9%), which significantly affected the average weight of the infected animals. Further remarks on the zoonotic and veterinary implications of the parasites recovered are given.
Opportunities and challenges of using diagnostic databases for monitoring livestock diseases in Denmark

Several databases are being used in Denmark to record information at different stages and levels of modern livestock production. These databases are all developed for different purposes and gather large volumes of routinely collected data. Examples of existing databases for livestock are the Central Husbandry Register (CHR), Meat inspection database for cattle and swine, mortality database and movement database. These databases are owned by the Ministry of Food, Agriculture and Fisheries. Other databases, such as the Danish Cattle Database, are owned by the agricultural sector. In addition to the technical and political bottlenecks of gathering and combining data from the different databases, the questions remain on the sensitivity and timeliness of data for detecting unexpected animal health events. Thus, it is important to explore changes in data records over time from different databases in order to detect potential patterns. This includes describing trends, seasonality and the potential impact of covariates on the baseline patterns. The potential of these data as monitoring tools can be evaluated using performance indicators such as residuals, predictive positive values, sensitivity and specificity, and by comparing the predictions of models with previous diseases events in Denmark.

A further challenge is to identify the most adequate surveillance timescale (i.e. daily, weekly or monthly basis) as well as suitable spatial distances, in order to identify outlier events when the features of the alarm (e.g. shape and amplitude) are unknown. Using rule-based anomaly detection will allow developing a spatio-temporal monitoring framework based on time-series analysis and statistical process control in order to optimize methods for detection of anomalies in data patterns and methods for early warning. It is expected that the use of such information in space and time, might provide information which can be used either directly as a syndromic surveillance tool or to aid in a more targeted or directed disease surveillance program. This will enable a timely and appropriate response to a disease outbreak, minimizing economic impacts through timely implementation of disease prevention and control measures.

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Opportunities and challenges of using diagnostic databases for monitoring livestock diseases in Denmark
Several databases are being used in Denmark to record information at different stages and levels of modern livestock production gathering large volumes of routinely collected data. This poster describes an ongoing PhD project at the National Veterinary Institute of the Technical University of Denmark with the objective of developing a monitoring framework based on spatiotemporal analysis to optimize methods for detection of anomalies in submission patterns and methods for early warning.

General information
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Resource estimations in contingency planning for FMD

Based on results from a stochastic simulation model, it was possible to create a simple model in excel to estimate the requirements for personnel and materiel during an FMD outbreak in Denmark. The model can easily be adjusted, when new information on resources appears from management of other crisis or from new model runs.

Introduction
Preparedness planning for a veterinary crisis is important to be fast and effective in the eradication of disease. For countries with a large export of animals and animal products, each day in an epidemic will cost millions of euros due to the closure of export markets. This is important for the Danish swine industry, which had an export of €4.4 billion in 2012.

Materials and methods
The purposes of this project were to: 1) estimate the resources needed during an outbreak of FMD in Denmark, 2) identify areas, which can delay the control of the disease, and 3) develop an iterative tool, which can easily be updated, when knowledge is gained from other veterinary crises or during an outbreak of FMD.

A stochastic simulation model was developed in InterSpread Plus to simulate spread of FMD in Denmark. The personnel and resource needs was estimated using results from this model.

Results
We estimated that the need for personnel would peak on day 7 with a requirement of approximately 170 veterinarians, 70 technicians and 45 administrative staff. However, the need for personnel in the Danish Emergency Management Agency (responsible for the hygiene barrier and initial cleaning and disinfection of the farm) would peak already on day 4 with a requirement for almost 500 persons, mostly recruits.

On average, 53000 animals were culled during the simulated epidemics, leading to a daily need for rendering capacity of up to 210 tons for swine and 379 tons for ruminants.

Discussion
Based on results from a stochastic simulation model, it was possible to create a simple model in excel to estimate the requirements for personnel and materiel during an FMD outbreak in Denmark. The model can easily be adjusted, when new information on resources appears from management of other crisis or from new model runs.
Resource Estimations in Contingency Planning for Foot-And-Mouth Disease

Preparedness planning for a veterinary crisis is important to be fast and effective in the eradication of disease. For countries with a large export of animals and animal products, each extra day in an epidemic will cost millions of euros due to the closure of export markets. This is important for the Danish swine industry, which had an export of €4.4 billion in 2012.

The purposes of this project were to: 1) estimate the resources needed during an outbreak of foot and mouth disease (FMD) in Denmark, 2) identify areas, which can delay the control of the disease, and 3) develop an iterative tool, which can easily be updated, when knowledge is gained from other veterinary crises or during an outbreak of FMD.

A stochastic simulation model was developed in InterSpread Plus to simulate spread of FMD in Denmark. The personnel and resource needs was estimated using results from this model.

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On average, 53000 animals were culled during the simulated epidemics, leading to a daily need for rendering capacity of up to 210 tons for swine and 379 tons for ruminants.

Based on results from a stochastic simulation model, it was possible to create a simple model in excel to estimate the requirements for personnel and materiel during an FMD outbreak in Denmark. The model can easily be adjusted, when new information on resources appears from management of other crisis or from new model runs.

Spatiotemporal analysis of the Porcine Reproductive and Respiratory Syndrome epidemic in Denmark using laboratory submission data

Porcine reproductive and respiratory syndrome (PRRS) virus infects domestic swine populations causing production losses in many European countries. The virus has two different strains designated as European (EU) and American (US) strain. It has been assumed that 30% of Danish swine herds are sero-positive with one or both PRRS strains. The PRRS surveillance program is based on serology tests performed in a monthly or annual basis for the breeding and intensive production herds respectively. The objective of this study was to characterize the PRRS epidemic in Denmark from 2007 to 2010 using retrospective spatiotemporal analysis of serological tests. Records of PRRS serology submissions made from January 2007 to December 2010 stored in the DIANOVA Information Management System at the National Veterinary Institute (DTU Vet) were used in the analysis. Each submission consists in individual blood samples collected for surveillance purposes and its frequency depends on the herd type. The herds were classified as PRRS positive or negative based on the individual serology test results for both virus strains. The prevalence of both PRRS strains was calculated on a monthly basis for the breeding and intensive production herds. The herd numbers registered in the laboratory submissions were merged with the Danish Herd Identification System database, in order to obtain the geo-
coordinates of the herds. Spatiotemporal analysis was performed, in order to characterize PRRS-EU and PRRS-US distributions for both control levels.

The analyses indicated a seasonal pattern in the between-herd prevalences of PRRS-EU and PRRS-US for both herd types. The prevalence of both PRRS strains was higher in the intensive production herds (mean=37%) when compared with the breeding herds (mean=17%). The spatiotemporal analysis detected a number of clusters of PRRS-EU and PRRS-US in both herd types. This suggests that PRRS still disperse between herds and that additional control efforts should be considered.

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Spatiotemporal patterns, annual baseline and movement-related incidence of Streptococcus agalactiae infection in Danish dairy herds: 2000–2009
Several decades after the inception of the five-point plan for the control of contagious mastitis pathogens, Streptococcus agalactiae (S. agalactiae) persists as a fundamental threat to the dairy industry in many countries. A better understanding of the relative importance of within- and between-herd sources of new herd infections coupled with the spatiotemporal distribution of the infection, may aid in effective targeting of control efforts. Thus, the objectives of this study were: (1) to describe the spatiotemporal patterns of infection with S. agalactiae in the population of Danish dairy herds from 2000 to 2009 and (2) to estimate the annual herd-level baseline and movement-related incidence risks of S. agalactiae infection over the 10-year period. The analysis involved registry data on bacteriological culture of all bulk tank milk samples collected as part of the mandatory Danish S. agalactiae surveillance scheme as well as live cattle movements into dairy herds during the specified 10-year period. The results indicated that the predicted risk of a herd becoming infected with S. agalactiae varied spatiotemporally; the risk being more homogeneous and higher in the period after 2005. Additionally, the annual baseline risks yielded significant yet distinctive patterns before and after 2005 – the risk of infection being higher in the latter phase. On the contrary, the annual movement-related risks revealed a non-significant pattern over the 10-year period. There was neither evidence for spatial clustering of cases relative to the population of herds at risk nor spatial dependency between herds. Nevertheless, the results signal a need to beef up within-herd biosecurity in order to reduce the risk of new herd infections.

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Stochastic simulation modeling to determine time to detect Bovine Viral Diarrhea antibodies in bulk tank milk

A stochastic simulation model was developed to estimate the time from introduction of Bovine Viral Diarrhea Virus (BVDV) in a herd to detection of antibodies in bulk tank milk (BTM) samples using three ELISAs. We assumed that antibodies could be detected, after a fixed threshold prevalence of seroconverted milking cows was reached in the herd. Different thresholds were set for each ELISA, according to previous studies. For each test, antibody detection was simulated in small (70 cows), medium (150 cows) and large (320 cows) herds. The assays included were: (1) the Danish blocking ELISA, (2) the SVANOVIR®-BVDV-Ab ELISA, and (3) the ELISA BVD/MD p80 Institute Pourquier. The validation of the model was mainly carried out by comparing the predicted incidence of persistently infected (PI) calves and the predicted detection time, with records from a BVD infected herd. Results showed that the SVANOVIR, which was the most efficient ELISA, could detect antibodies in the BTM of a large herd 280 days (95% prediction interval: 218; 568) after a transiently infected (TI) milking cow has been introduced into the herd. The estimated time to detection after introduction of one PI calf was 111 days (44; 605). With SVANOVIR ELISA the incidence of PIs and dead born calves could be limited and the impact of the disease on the animal welfare and income of farmers (before detection) could be minimized. The results from the simulation modeling can be used to improve the current Danish BVD surveillance program in detecting early infected herds.

The Impact of Resources for Clinical Surveillance on the Control of a Hypothetical Foot-and-Mouth Disease Epidemic in Denmark.

The objectives of this study were to assess whether current surveillance capacity is sufficient to fulfill EU and Danish regulations to control a hypothetical foot-and-mouth disease (FMD) epidemic in Denmark, and whether enlarging the protection and/or surveillance zones could minimize economic losses. The stochastic spatial simulation model DTU-DADS was further developed to simulate clinical surveillance of herds within the protection and surveillance zones and used to model spread of FMD between herds. A queuing system was included in the model, and based on daily surveillance capacity, which was 450 herds per day, it was decided whether herds appointed for surveillance would be surveyed on the current day or added to the queue. The model was run with a basic scenario representing the EU and Danish regulations, which includes a 3 km protection and 10 km surveillance zone around detected herds. In alternative scenarios, the protection zone was enlarged to 5 km, the surveillance zone was enlarged to 15 or 20 km, or a combined enlargement of the protection and surveillance zones was modelled. Sensitivity analysis included changing surveillance capacity to 200, 350 or 600 herds per day, frequency of repeated visits for herds in overlapping surveillance zones from every 14 days to every 7, 21 and 30 days, and the size of the zones combined with a surveillance capacity increased to 600 herds per day. The results showed that the default surveillance capacity is sufficient to survey herds on time. Extra resources for surveillance did not improve the situation, but fewer resources could result in larger epidemics and costs. Enlarging the protection zone was a better strategy than the basic scenario. Despite that enlarging the surveillance zone might result in
shorter epidemic duration, and lower number of affected herds, it resulted frequently in larger economic losses.

Comparing control strategies against foot-and-mouth disease: Will vaccination be cost-effective in Denmark?
Recent outbreaks of foot-and-mouth disease (FMD) in Europe have highlighted the need for assessment of control strategies to optimise control of the spread of FMD. Our objectives were to assess the epidemiological and financial impact of simulated FMD outbreaks in Denmark and the effect of using ring depopulation or emergency vaccination to control these outbreaks. Two stochastic simulation models (InterSpreadPlus (ISP) and the modified Davis Animal Disease Simulation model (DTU-DADS)) were used to simulate the spread of FMD in Denmark using different control strategies. Each epidemic was initiated in one herd (index herd), and a total of 5000 index herds were used. Four types of control measures were investigated: (1) a basic scenario including depopulation of detected herds, 3km protection and 10km surveillance zones, movement tracing and a three-day national standstill, (2) the basic scenario plus depopulation in ring zones around detected herds (Depop), (3) the basic scenario plus protective vaccination within ring zones around detected herds, and (4) the basic scenario plus protective vaccination within ring zones around detected herds. Disease spread was simulated through direct animal movements, medium-risk contacts (veterinarians, artificial inseminators or milk controllers), low-risk contacts (animal feed and rendering trucks, technicians or visitors), market contacts, abattoir trucks, milk tanks, or local spread. The two simulation models showed different results in terms of the estimated numbers. However, the tendencies in terms of recommendations of strategies were similar for both models. Comparison of the different control strategies showed that, from an epidemiological point of view, protective vaccination would be preferable if the epidemic started in a cattle herd in an area with a high density of cattle, whereas if the epidemic started in an area with a low density of cattle or in other species, protective vaccination or depopulation would have almost the same preventive effect. Implementing additional control measures either 14 days after detection of the first infected herd or when 10 herds have been diagnosed would be more efficient than implementing additional control measures when more herds have been diagnosed. Protective vaccination scenarios would never be cost-effective, whereas depopulation or suppressive vaccination scenarios would most often be recommended. Looking at the median estimates of the cost-benefit analysis, depopulation in zones would most often be recommended, although, in extreme epidemics, suppressive vaccination scenarios could be less expensive. The vast majority of the costs and losses associated with a Danish epidemic could be attributed to export losses.
Decisions on control of foot-and-mouth disease informed using model predictions

The decision on whether or not to change the control strategy, such as introducing emergency vaccination, is perhaps one of the most difficult decisions faced by the veterinary authorities during a foot-and-mouth disease (FMD) epidemic. A simple tool that may predict the epidemic outcome and consequences would be useful to assist the veterinary authorities in the decision-making process. A previously proposed simple quantitative tool based on the first 14 days outbreaks (FFO) of FMD was used with results from an FMD simulation exercise. Epidemic outcomes included the number of affected herds, epidemic duration, geographical size and costs. The first 14 days spatial spread (FFS) was also included to further support the prediction. The epidemic data was obtained from a Danish version (DTU-DADS) of a pre-existing FMD simulation model (Davis Animal Disease Spread – DADS) adapted to model the spread of FMD in Denmark. The European Union (EU) and Danish regulations for FMD control were used in the simulation. The correlations between FFO and FFS and the additional number of affected herds after day 14 following detection of the first infected herd were 0.66 and 0.82, respectively. The variation explained by the FFO at day 14 following detection was high (P-value < 0.001). This indicates that the FFO may take a part in the decision of whether or not to intensify FMD control, for instance by introducing emergency vaccination and/or pre-emptive depopulation, which might prevent a "catastrophic situation". A significant part of the variation was explained by supplementing the model with the FFS (P-value < 0.001). Furthermore, the type of the index-herd was also a significant predictor of the epidemic outcomes (P-value < 0.05). The results of the current study suggest that national veterinary authorities should consider to model their national situation and to use FFO and FFS to help planning and updating their contingency plans and FMD emergency control strategies.

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Decisions on foot-and-mouth disease control informed by model prediction

The predictive capability of the first fortnight incidence (FFI), which is the number of detected herds within the first 14 days following detection of the disease, of the course of a foot-and-mouth disease (FMD) epidemic and its outcomes were investigated. Epidemic outcomes included the number of affected herds, epidemic duration, geographical size, and costs. The first fourteen days spatial spread (FFS) was also included to support the prediction. The epidemic data were obtained from a Danish version (DTU-DADS) of the Davis Animal Disease Spread simulation model.

The FFI and FFS showed good correlations with the epidemic outcomes. The predictive capability of the FFI was high. This indicates that the FFI may take a part in the decision of whether or not to boost FMD control, which might prevent occurrence of a large epidemic in the face of an FMD incursion. The prediction power was improved by supplementing the models with information on FFS and characteristics of the index-herd. Results presented here will contribute to improve preparedness of Denmark to early control of a hypothetical FMD epidemic.

Simulated effects of changes in herd sizes and densities with regard to FMD outbreaks in Denmark

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Social network analysis provides a valuable framework for understanding the dynamics of diseases on networks as well as a means for defining effective control measures. An understanding of the underlying contact pattern for a susceptible population is advisable before embarking on any strategy for disease control. The objective of this study was to characterise the network of Danish cattle movements over a 10-year period from 2000 to 2009 with a view to understanding: (1) cohesiveness of the network, (2) influential holdings and (3) structural vulnerability of the network. Network analyses of data involving all cattle movements in Denmark registered during the period of interest were performed. A total of 50,494 premises participated in 4,204,895 individual movements during the 10-year period. The results pointed to a predominantly scale-free structure of the network; though marked by small-world properties in March–April 2001 as well as in 24 other months during the period October 2006 to December 2009. The network was sparsely connected with markets being the key influential holdings. Its vulnerability to removal of markets suggests that targeting highly connected holdings during epidemics should be the focus of control efforts.

Annual incidence, prevalence and transmission characteristics of Streptococcus agalactiae in Danish dairy herds

Contagious mastitis pathogens continue to pose an economic threat to the dairy industry. An understanding of their frequency and transmission dynamics is central to evaluating the effectiveness of control programmes. The objectives of this study were twofold: (1) to estimate the annual herd-level incidence rates and apparent prevalences of Streptococcus agalactiae (S. agalactiae) in the population of Danish dairy cattle herds over a 10-year period from 2000 to 2009 inclusive and (2) to estimate the herd-level entry and exit rates (demographic parameters), the transmission parameter, $\beta$, and recovery rate for S. agalactiae infection.

Data covering the specified period, on bacteriological culture of all bulk tank milk samples collected annually as part of the mandatory Danish S. agalactiae surveillance scheme, were extracted from the Danish Cattle Database and subsequently analysed. There was an increasing trend in both the incidence and prevalence of S. agalactiae over the study period. Per 100 herd-years the value of $\beta$ was 54.1 (95% confidence interval [CI] 46.0–63.7); entry rate 0.3 (95% CI 0.2–0.4); infection-related exit rate 7.1 (95% CI 5.6–8.9); non-infection related exit rate 9.2 (95% CI 7.4–11.5) and recovery rate 40.0 (95% CI 36.8–43.5). This study demonstrates a need to tighten the current controls against S. agalactiae in order to lower...
Bioeconomic modeling of intervention against clinical mastitis caused by contagious pathogens

The objective of this study was to assess the epidemiologic and economic consequences of intervention against contagious clinical mastitis during lactation. A bioeconomic model of intramammary infections (IMI) was used to simulate contagious spread of Staphylococcus aureus, Streptococcus uberis, and Streptococcus dysgalactiae, and an environmental spread of Escherichia coli IMI in a 100-cow dairy herd during 1 quota year. The costs of clinical IMI, subclinical IMI, and intervention were calculated into the total annual net costs of IMI during lactation per scenario and compared with a default scenario. Input parameter values were based on the scientific literature. The scenarios were 3-d intramammary lactational treatment (default), 5-d intramammary treatment, 5-d intramammary treatment and 3-d systemic treatment, 3-d intramammary treatment and culling bacteriologically unrecovered clinical IMI cows, and 5-d intramammary treatment and culling bacteriologically unrecovered clinical IMI cows. Sensitivity analysis was conducted on parameter input values. The results showed that interventions including antibiotic treatment combined with culling unrecovered clinical IMI cows resulted in the lowest transmission, number of IMI cases, and persistent subclinical IMI cases. Nonetheless, the high associated costs of culling bacteriologically unrecovered clinical IMI cows made the other scenarios with a long and intensive antibiotic treatment, but without culling, the most cost effective. The model was sensitive to changes to the cure rate of clinical IMI following treatment, but the ranking of the intervention scenarios did not change. The model was most sensitive to the changes to the transmission rate of Staph. aureus. The ranking of the intervention scenarios changed at low transmission rate of this pathogen, in which the default scenario became the most cost-effective scenario. In case of high transmission of contagious IMI pathogens, long and intensive treatment of clinical IMI should be preceded by strategies that lower the transmission.
Comparison of different control strategies on FMD in Denmark

The purpose of this study was to compare different control strategies that could be used in Denmark during an outbreak of FMD, based on epidemiological, ethical and economic parameters. Nearly a hundred different control strategies and more than 30 sensitivity analyses were run, changing between depopulation (Depop), suppressive (VacToKill) and protective (VacToLive) vaccination with different times for implementation and different zone sizes. It is therefore obvious that not all results can be included here; neither will all results be presented at the seminar. However, we have done our best to extract the essence of the results. All results will be presented in the final project report, which will be available on request to the authors.

Comparing epidemiological outputs showed that extra control measures will always reduce the average duration and size of an epidemic. However, the variations in duration and size of epidemics are large, and if epidemics are small, extra control measures may not always be necessary. Comparing depopulation to suppressive and protective vaccination shows that from an epidemiologic point of view, vaccination will be beneficial. However, comparing the economy of the epidemics, it is shown that vaccination is more expensive compared to depopulation.

Results from 1000 epidemics starting in cattle herds in cattle dense areas. Epidemiological results from ISP presented as medians and 5-95 percentiles (brackets), economical as means.

The size, duration and costs of epidemics vary much with the type of index herd (starting points). Furthermore, not only economy, but also ethical and political issues will also play an important role in decision making. Therefore, it is important to keep in mind that this work will not give the answer as to which strategy to use during an epidemic, but can be used as a decision support tool. Sometimes, even though one strategy will be predicted to be cheaper, the second cheapest strategy might reduce the number of killed animals so much that it will become a better option.

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Consequence of changes in herd size and densities for the contingency planning

The objective of the current work was to evaluate whether the effects and control of foot-and-mouth disease (FMD) spread would differ following the structural changes to the Danish agricultural sector from now until 2030.

Following the predicted structural changes, a new farm file was created, representing active farms in 2030. Index herds were randomly selected from the created farm file. The farm file contains information about the herd ID, coordinates, number of animals and movement rates. DTU-DADS and ISP were used to simulate the spread of FMD in Denmark in 2030. Following discussions with the industry, low risk contacts are assumed to increase with increasing herd size, and thus the number of low risk contacts was increased by 50%. All other input values were assumed to stay the same.

Four different control scenarios were run: 1) A basic scenario representing current EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds in a radius of 0.5, 1, 1.5 and 3 km around the detected herds, 3) suppressive vaccination in a radius of 1, 2, 3, and 5 km around the detected herds 4) protective vaccination in similar radiuses to suppressive vaccination. Depopulation and vaccination started after detecting 10 infected herds.
Compared to the current situation, future FMD outbreaks are, based on median values, predicted to be shorter and cheaper. Nonetheless, we also predicted that extreme epidemics would be larger and more expensive. Epidemiologic results predict that pre-emptive depopulation and protective vaccination are good choices to control the disease in future populations. However, economically, protective vaccination is predicted to be too expensive in Denmark, and thus pre-emptive depopulation and suppressive vaccination are better options to control FMD in the future. It is also important to mention that enlarging the depopulation and vaccination zones might not be a good option, because direct costs would increase and resources problems might arise leading to larger economic damage.

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**General introduction to simulation models**

Monte Carlo simulation can be defined as a representation of real life systems to gain insight into their functions and to investigate the effects of alternative conditions or actions on the modeled system. Models are a simplification of a system. Most often, it is best to use experiments and field trials to investigate the effect of alternative conditions or actions on a specific system. Nonetheless, field trials are expensive and sometimes not possible to conduct, as in case of foot-and-mouth disease (FMD). Instead, simulation models can be a good and cheap substitute for experiments and field trials. However, if simulation models would be used, good quality input data must be available.

To model FMD, several disease spread models are available. For this project, we chose three simulation model; Davis Animal Disease Spread (DADS), that has been upgraded to DTU-DADS, InterSpread Plus (ISP) and the North American Animal Disease Spread Model (NAADSM). The models are rather data intensive, but in varying degrees. They generally demand data on the farm level, including farm location, type, number of animals, and movement and contact frequency to other farms.

To be able to generate a useful model of FMD spread that can provide useful and trustworthy advises, there are four important issues, which the model should represent: 1) The herd structure of the country in question, 2) the dynamics of animal movements and contacts between herds, 3) the biology of the disease, and 4) the regulations attached to the occurrence of the disease. Model inputs are usually given in distributions to represent biological variability as well as uncertainty. Subsequently, model outputs are usually given as distributions, sometimes with wide ranges.

Use of modeling will help us to gain insight to a system as well as support decision making. However, several other factors affect decision making such as, ethics, politics and economics. Furthermore, the insight gained when models are build leads to point out areas where knowledge is lacking.
Influence of livestock markets on the spread of FMD

The purpose of this study was to investigate whether cattle markets would influence the duration, size and economic consequences of a potential FMD epidemic in Denmark.

The spread of FMD was simulated using the InterSpread Plus. For movements of cattle to and from markets, we modeled the frequency of movements to markets for the individual herd and categorized herds that could receive contacts from markets. The epidemics were initiated in herds with market contacts. In a basic market scenario, we used the individual herds’ probability of moving animals to markets, while in a control scenario we reduced all probabilities of movements to markets to zero, to reflect a situation with no markets. Each scenario was initiated in 366 different herds (index), and for each index herd, the model was run 100 times. The number of extra contacts generated through a market was set to 3.5 and the probability of transmission from markets was modeled as a normal distribution with a mean of 0.415 and a standard deviation of 0.06. This probability was a combination of the risk from purchase of animals from markets and the indirect contact from visitors on markets. Danish markets would be closed as soon as FMD is detected. Therefore, markets were only active during the first three weeks of the epidemic, as time from infection to first detection was assumed to be 21 days.

The results show an effect of markets on the size, duration and costs of a FMD epidemic (Table 1); the median duration of epidemics is 1 week longer, and 28 more herds are detected with FMD. In the scenarios with markets, the epidemics included a larger area compared to scenarios without markets. It is also shown that epidemics with markets are more expensive compared to epidemics without markets.

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Input parameters and scenarios, including economic inputs

Geographical locations of the farms are the core in these models. We used geographical data, number of animals and specification of herd types for the 50,853 herds in the Danish Husbandry Register (CHR) in 2007. For each herd, the daily probability of moving animals, to another herd or to the abattoir, was calculated as the sum of all registered movements off the herd in the period from October 1, 2006 to September 30, 2007 divided by 365. Swine movements originated from the Movement database for swine and cattle and sheep movements from the Danish Cattle database.

From an infected herd, disease was simulated to spread via direct contacts (movements of animals), indirect contacts (trucks and persons) and local spread (mice, birds, airborne spread in limited distances). Furthermore, in some scenarios airborne spread was included.

For all contact types, when a contact was simulated to take place, a receiving herd needed to be found. The distance, in which the receiving herd should be found, was calculated from movement data for animals and from data from trucks and abattoirs for movements to slaughter and milk tankers. For persons visiting herds, we used a combination of expert opinions, data from other countries and survey data. Local spread was simulated within a distance of three kilometers around infected herds, with a decreasing probability of spread with increasing distance.

All epidemics were simulated to be detected on day 21. When an epidemic was detected, a three day national stand still was initiated. Furthermore, infected herds were depopulated and a 3 km detection zone and a 10 km surveillance zone were implemented around all infected herds. Within the protections zones, all herds were simulated to be clinically surveyed twice, first within 7 days after implementing the zone, and second 21 days later.

Sheep within the zone were simulated to be tested. Within the surveillance zone, all herds were simulated to be clinically surveyed within 7 days, and sheep within the zone were simulated to be tested within 7 days and again before lifting the zone. Herds, which had received animals from an infected herd, were simulated to be traced and depopulated. Herds delivering animals to an infected herd were simulated to be traced and surveyed.

In the alternative scenarios, extra control measures were added to the basic measures. Extra measures were depopulation or vaccination in ringzones of varying radii around infected herds.

In alternative scenarios, we tested the effect of depopulating in zones of 500, 1000 and 1500 meters from infected herds.
Depopulation was started on day 14 after detection of the first herd, or after detecting 10, 20, 30 or 50 infected herds. In some scenarios, we excluded hobby-type farms.

In the vaccination scenarios, herds within the vaccination zone were simulated to be vaccinated 14 days after detection of the first herd or when 10, 20, 30 or 50 herds were infected. All herds within the zones were simulated to be vaccinated. We used vaccination zones of either a 1, 2, 3 or 5 km. In some scenarios, hobby herds were not vaccinated. In one scenario, no sheep were vaccinated, and in another scenario no swine were vaccinated. From depopulation in zones. The resources for depopulation were estimated to 4,800 swine and 2,000 ruminants a day. Resources for depopulation in zones was shared with depopulation of infected and depopulation of traced herds, however zone depopulation would be number three on the resource list. All herds depopulated in zones would be tested before slaughter. The probability of detection was assumed to be 50% from day 0 to day 8 after the herd was infected, and increased to 1 after day 8.

The outputs from the epidemiological models were used as inputs in an economic model to calculate costs and losses for each epidemic.

The costs of an epidemic were divided into direct and indirect costs. The direct costs consisted of surveillance, depopulation, cleaning and disinfection, empty stable, compensation, national standstill, and vaccination costs. The indirect costs included losses incurred from restrictions on exports to EU and non-EU countries. The total costs were calculated as the sum of the direct and indirect costs. Costs were calculated per iteration, and summaries were thereafter calculated.

Meta-analysis on the efficacy of foot-and-mouth disease emergency vaccination

The objectives of this study were to provide a summary quantification of the efficacy of FMD emergency vaccination based on a systematic review and a meta-analysis of available literature, and to further discuss the suitability of this review and meta-analysis to summarize and further interpret the results. Peer-reviewed, symposium, and unpublished studies were considered in the analysis.

Clinical protection and virological protection against foot and mouth disease were used as parameters to assess the efficacy of emergency vaccination. The clinical protection was estimated based on the appearance of clinical signs including FMD lesions and fever, while the virological protection parameter was estimated based on the outcome of laboratory tests that were used to diagnose FMD infection. A meta-analysis relative risk was calculated per protection parameter. Results of the meta-analyses were examined using publication bias tests.

In total, 31 studies were included in the analyses, of which 26 were peer-reviewed studies, 1 was a symposium study and 4 were unpublished studies. Cattle, swine and sheep were well protected against clinical disease and foot-and-mouth
disease infection following the use of emergency vaccine. Fortunately, no significant bias that would alter the conclusions was encountered in the analysis. Meta-analysis showed to be a useful tool to summarize literature results from a systematic review of the efficacy of foot and mouth disease emergency vaccination.

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Model's comparison
Three popular disease spread simulation models were used to simulate the spread of foot-and-mouth disease (FMD) in Denmark. The models' predictions in term of disease spread, consequence, and the ranking of the applied control strategies were compared. The original Davis Animal Disease Spread (DADS version 0.05) was adapted to DTU-DADS, and this model as well as InterSpread Plus (ISP version 2.001.11) and the North American Animal Disease Spread Model (NAADSM version 3.0.81) were all used to simulate hypothetical spread of FMD in Denmark. Data on Danish herds were used including herd type, movements, and location in the period 1st October 2006 to 30th September 2007. The three models to the highest possible extend set up to simulate the same epidemics in 3 different control scenarios: 1) A basic scenario representing EU and Danish control strategies, 2) pre-emptive depopulation of susceptible herds in a 500 meters radius around the detected herds, and 3) suppressive vaccination of susceptible herds in a 1,000 meters radius around the detected herds. Depopulation and vaccination started either 14 days following the detection of the first infected herd or following detection of 5 infected herds. Five thousand index herds were selected randomly in which there were 1,000 cattle herds located in high density cattle area and 1,000 in low density cattle area, 1,000 swine herds located in high density swine area and 1,000 in low density swine area, and 1,000 sheep herds. Generally, NAADSM predicted the largest, longest duration and costliest epidemics. DTU-DADS predicted larger, longer duration and costlier epidemics than ISP, except when epidemics started in cattle herds located in high density cattle area. ISP predicted suppressive vaccination to be less costly than depopulation, while the least costly control strategy predicted by DTU-DADS differed depending on the species and density area of the index herd. It was not possible to run the depopulation scenarios in the NAADSM due to limitations in the model. Running several models in parallel gives better insight in disease spread, limits typing and coding errors and improves understanding of modeled processes. The chosen control strategy might depend on the chosen model.

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Optimizing the control of foot-and-mouth disease in Denmark by simulation: Foot-and-mouth disease simulation modeling

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Optimizing the control of foot-and-mouth disease in Denmark by simulation: Comparison of different control strategies on FMD in Denmark

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Predicting the structural development in Danish livestock and how it affects control strategies against FMD

The purpose of this study was to assess if the optimal control strategy against foot-and-mouth disease (FMD) spread is invariant to structural development in Danish livestock until 2030. The DTU-DADS model as presented by Halasa et al. uses demographic information of all farms including their location, size, and production type. The main challenge was to predict the demographic data.

Based on data for all herds with animals susceptible to FMD in the Central Husbandry Registry from 1999 to 2010 and supplementary data for swine herds from Danish Agriculture & Food Council (2002 to 2009), all farms were classified by production type and size each year. A total of 88 classes were used. For each species group (cattle, swine, and sheep and goat) a transition probability matrix (TPM) was estimated based on the ten year to year transitions.

It was hypothesized that there might be regional differences. This was assessed by dividing Denmark into 7 regions, counting all transitions per region, and comparing these counts to the country wide counts using a ChiSq test. Due to the regionalization, some of the less populated size categories were merged to reduce noise. All regions were found to have significantly different TPMs. These TPMs were used in a Markov chain to predict the distribution of farms in year 2030. However, the predictions were unrealistic as far too many farms opened – since all closed farms were allowed to reopen. It was decided to make the closed state a terminal state and make an independent prediction of how many farms should open each year. The best model was a log-linear model for each region. The combined result is a reduction from 51,031 herds in 2007 to 14,126 farms in 2030 with larger average size.

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Simple decision tools to help optimize the control strategy 2 weeks into a Danish FMD epidemic

The choice of whether or not to apply emergency vaccination is one of the most difficult decisions facing the authorities when foot-and-mouth disease (FMD) breaks out in a free country (Barnett et al. 2002). A simple quantitative tool has been proposed using the first 14-days incidence (FFI) of outbreaks by 12 regional foci in the 2001 UK epidemic to predict the duration and the cumulative number of outbreaks at the end of the epidemic (Hutber et al. 2006). Contingency planning should include provision for emergency vaccination and must address the complex decisions of not only when, where, and how to apply vaccine, but also its economic consequences. Computer modelling may be a useful aid to cost benefit and decision support systems in this context (Barnett et al. 2002). We used a modified FFI procedure to analyze data from a series of 5,000 FMD simulations with current Danish population data at the national level and the basic EU control strategy using a modified DADS model (DTU-DADS).

The primary independent variable in regressions and correlations was the number of outbreaks detected during the first 14 days of the epidemic. The dependent variables were the number of outbreaks detected after day 14, the epidemic duration after day 14 and the size of the affected region at the end of the epidemic.

Statistically significant positive correlations were found in all regression analyses of the data. There was, however, a high degree of variation (Fig. 1), which is to be expected, since we simulated 5000 different epidemics, while the original publication analyzed regional variations in field data from one and the same epidemic (Hutber et al. 2006).

We also simplified the presentation of the results for operational use during a potential outbreak, using a 2-by-2 table format to estimate predictive values by applying selected cut-off- values for both the dependent and the independent variables (Table 1).

Emergency vaccination should be considered during an outbreak if the predicted cumulative size, duration or cost of the epidemic appears alarming (EU 2003, Kitching et al. 2005, Hagerman et al. 2010). The overall results from our project support this conclusion when comparing the expected outcomes from applying the basic control measures, emergency vaccination after day 14 and zonal culling after day 14, respectively (Boklund et al., in prep.).

Conclusion: Our results indicate that predicting the final outcome of an epidemic from the number of outbreaks by day 14 and modifications hereof might be useful in informing decisions two weeks into the epidemic about the potential introduction of control strategies based on emergency vaccination or zonal culling.

Simulated Effects of Introducing Emergency Vaccination or Depopulation During FMD Outbreaks in Denmark

The purpose of this study was to explore the effects of modifying FMD control 14 days following detection of the first infected herd in a simulated FMD epidemic in Denmark. The spread of FMD was simulated using an adapted version of the well described DADS simulation model, called DTU-DADS, using Danish herd locations and movements data. The epidemics were initiated in 1000 randomly chosen cattle herds located in cattle-dense areas.
The basic scenario consisted of: the minimum EU control measures, culling of forward-traced herds and a 3-day national stand-still on animal movements. Alternative scenarios included depopulation, suppressive or preventive vaccination within 1 km.

The results show that there may be positive effects of applying additional control measures on the size, duration and costs of the epidemics. The median duration decreased from 56 days in the basic scenario to 45-47 days in the vaccination scenarios, and to 40 days in the depopulation scenarios. Furthermore, the number of infected herds decreased, but with fewer infected herds in the protective vaccination scenario. The total costs of an epidemic, including export losses, changed from €562 million in the basic scenario to €515, €535 and €610 million in the depopulation, suppressive and protective vaccination scenarios, respectively.

These results suggest that vaccination will often be a more expensive strategy in a country with a large export, like Denmark. Furthermore, the simulated results show that from an economic point of view depopulation in zones is often preferable.

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Simulation of the influence of Danish cattle markets on a Foot-and-Mouth epidemic

During the epidemic of Foot-and-Mouth disease (FMD) in the United Kingdom in 2001, live animal markets had large influence on the spread of the disease. The culture of and behavior around markets are expected to be different between countries. During the last decade, the number of animals traded through markets in Denmark has decreased and only few cattle markets are left.

The purpose of this study was to investigate, whether cattle markets would influence the duration, size and economic consequences of a potential FMD epidemic in Denmark.

The spread of FMD was simulated using the stochastic and spatial disease-spread InterSpread Plus, version 2.001.11. From Danish databases, we collected data movements of animals. These were used to model movements of animals for each individual herd. For movements of cattle to and from markets, we modeled the frequency of movements to markets for the individual herd and categorized herds that could receive contacts from markets. The epidemics were initiated in herds with market contacts. In a basic market scenario, we used the individual herds' probability of moving animals to markets, while in a control scenario we reduced all probabilities of movements to markets to zero, to reflect a situation with no markets. Each scenario was initiated in 100 different herds (index), and for each index herd, the model was run 100 times. The number of extra contacts generated through a market was set to 3.5 and the probability of transmission from markets was modeled as a normal distribution with a mean of 0.415 and a standard deviation of 0.06. This probability was a combination of the risk from purchase of animals from markets and the indirect contact from visitors on markets.

Danish markets would be closed as soon as FMD is detected. Therefore, markets were only active during the first three weeks of the epidemic, as time from infection to first detection was modeled as 21 days.

The results was described as epidemic duration (from first detection day to last detection day), number of detected herds and infected area, direct costs (costs of surveillance visits, tests, slaughter etc.) and indirect losses due to the epidemic (export losses).

The results show an effect of markets on the size and duration of a FMD epidemic (Table 1); the median duration of epidemics is 1 week longer, and 28 more herds are detected with FMD. In the scenarios with markets, the epidemics included a larger area compared to scenarios without markets. Economic results will be described in the final paper. Markets can influence spread of other diseases as well. Little is known about the influence of markets on spread of other diseases. Even though FMD is more contagious than many other diseases, the markets effect on spread of other diseases might be more prominent, as the activity of markets is not influenced by the presence of endemic diseases.
Simuleringsstudier af konsekvenser af mund- og klovesyge i Danmark

General information
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Organisations: National Veterinary Institute, Division of Veterinary Diagnostics and Research, Section for Veterinary Epidemiology and public sector consultancy, Section for Epidemiology
Contributors: Boklund, A., Hisham Beshara Halasa, T., Enøe, C.
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Source attribution of human campylobacteriosis using a meta-analysis of case-control studies of sporadic infections
Campylobacter spp. is a widespread and important cause of human illness worldwide. Disease is frequently associated with foodborne transmission, but other routes of exposure, such as direct contact with live animals and person-to-person transmission, are also recognized. Identifying the most important sources of human disease is essential for prioritizing food safety interventions and setting public health goals. Numerous case-control studies of sporadic infections of campylobacteriosis have been published. These studies investigated a variety of potential risk factors for disease, often using different methodologies and settings. Systematic reviews (SRs) consist of a formal process for literature review focused on a specific research question, and include the identification of relevant literature, quality assessment of relevant studies, summarization or statistical analysis of data, and conclusions. With the objective of identifying the most important risk factors for human sporadic campylobacteriosis, we performed a SR of case-control studies of human sporadic cases and a meta-analysis of the obtained results. A combined SR focusing on Salmonella and Campylobacter studies was performed and the results analysed separately. From 1295 identified references, 131 passed the relevance screening, 73 passed the quality assessment stage, and data was extracted from 72 studies. Of these, 38 focused on campylobacteriosis. Information on exposures of cases and controls, and estimated odds ratios for investigated risk factors were collected and analysed. In the meta-analysis, heterogeneity between the studies and possible sources of bias were investigated, and pooled odds ratios for identified risk factors were estimated. Results suggest that travelling abroad, eating undercooked chicken, environmental sources, and direct contact with farm animals were significant risk factors for campylobacteriosis. Sub-analyses by geographical region, age group, and study period were performed, and differences were discussed.

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Contributors: Coutinho Calado Domingues, A. R., Pires, S. M., Hisham Beshara Halasa, T., Hald, T.
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Web of Science (2012): Impact factor 2.867
ISI indexed (2012): ISI indexed yes
Web of Science (2012): Indexed yes
Original language: English
Source attribution of human salmonellosis using a meta-analysis of case-control studies of sporadic infections
Salmonella is an important cause of human illness. Disease is frequently associated with foodborne transmission, but other routes of exposure are recognized. Identifying sources of disease is essential for prioritizing public health interventions. Numerous case-control studies of sporadic salmonellosis have been published, often using different methodologies and settings. Systematic reviews consist of a formal process for literature review focused on a research question. With the objective of identifying the most important risk factors for salmonellosis, we performed a systematic review of case-control studies and a meta-analysis of obtained results. Thirty-five Salmonella case-control studies were identified. In the meta-analysis, heterogeneity between studies and possible sources of bias were investigated, and pooled odds ratios estimated. Results suggested that travel, predisposing factors, eating raw eggs, and eating in restaurants were the most important risk factors for salmonellosis. Sub-analyses by serotype were performed when enough studies were available.

Meta-analysis on the efficacy of foot-and-mouth disease emergency vaccination
The objectives of this study were to provide a summary quantification of the efficacy of FMD emergency vaccination based on a systematic review and a meta-analysis of available literature, and to further discuss the suitability of this review and meta-analysis to summarize and further interpret the results. Peer-reviewed, symposium, and unpublished studies were considered in the analysis. Clinical protection and virological protection against foot and mouth disease were used as parameters to assess the efficacy of emergency vaccination. The clinical protection was estimated based on the appearance of clinical signs including FMD lesions and fever, while the virological protection parameter was estimated based on the outcome of laboratory tests that were used to diagnose FMD infection. A meta-analysis relative risk was calculated per protection parameter. Results of the meta-analyses were examined using publication bias tests. In total, 31 studies were included in the analyses, of which 26 were peer-reviewed studies, 1 was a symposium study and 4 were unpublished studies. Cattle, swine and sheep were well protected against clinical disease and foot and mouth disease infection following the use of emergency vaccine. Fortunately, no significant bias that would alter the conclusions was encountered in the analysis. Meta-analysis can be a useful tool to summarize literature results from a systematic review of the efficacy of foot and mouth disease emergency vaccination.
Modelling food safety and economic consequences of surveillance and control strategies for Salmonella in pigs and pork

Targets for maximum acceptable levels of Salmonella in pigs and pork are to be decided. A stochastic simulation model accounting for herd and abattoir information was used to evaluate food safety and economic consequences of different surveillance and control strategies, based among others on Danish surveillance data. An epidemiological module simulated the Salmonella carcass prevalence for different scenarios. Cost-effectiveness analysis was used to compare the costs of the different scenarios with their expected effectiveness. Herd interventions were not found sufficient to attain Salmonella carcass prevalence.
A simulation model to calculate costs and benefits of dry period interventions in dairy cattle

General information
Publication status: Published
Organisations: Utrecht University
Contributors: Hisham Beshara Halasa, T., Nielen, M., van Werven, T., Hogeveen, H.
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Peer-reviewed: Yes

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Web of Science (2010): Indexed yes
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DOIs: 10.1016/j.livsci.2010.01.009
Source: orbit
Source-ID: 269034

Bioeconomic modeling of lactational antimicrobial treatment of new bovine subclinical intramammary infections caused by contagious pathogens

This study determined the direct and indirect epidemiologic and economic effects of lactational treatment of new bovine subclinical intramammary infections (IMI) caused by contagious pathogens using an existing bioeconomic model. The dynamic and stochastic model simulated the dynamics of Staphylococcus aureus, Streptococcus uberis, Streptococcus dysgalactiae, and Escherichia coli during lactation and the dry period in a 100-cow dairy herd during 1 quota year. Input parameters on cure were obtained from recent Dutch field data. The costs of clinical IMI, subclinical IMI, and intervention were calculated into the combined total annual net costs of IMI per herd. The cost effectiveness of 4 scenarios with lactational intervention was determined; scenarios included no intervention, treatment after 1 mo of infection, treatment after 2 mo of infection, and treatment after 1 mo of infection and culling of uncured cows after 2 mo of infection. Model behavior was observed for variation in parameter input values. Compared with no lactational intervention, lactational intervention of new subclinical IMI resulted in fewer clinical flare ups, less transmission within the herd, and much lower combined total annual net costs of IMI in dairy herds. Antimicrobial treatment of IMI after 1 mo of infection and culling of uncured cows after 2 mo of infection resulted in the lowest costs, whereas treatment after 2 mo of infection was associated with the highest costs between the scenarios with intervention. Changing the probability of cure resulted in a nonlinear change in the cumulative incidence of IMI cases and associated costs. Lactational treatment was able to prevent IMI epidemics in dairy herds at high transmission rates of Strep. uberis, Strep. dysgalactiae, and E. coli. Lactational treatment did not limit the spread of Staph. aureus at high transmission rates, although the associated costs were lower compared with no intervention. To improve udder health in a dairy herd, lactational treatment of contagious subclinical IMI must therefore be preceded by management measures that lower the transmission rate. Lactational treatment of environmental subclinical IMI seemed less cost effective. Detection of subclinical IMI needs improvement to be able to most effectively treat subclinical IMI caused by contagious pathogens during lactation.

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Meta-analysis of dry cow management for dairy cattle. Part 1. Protection against new intramammary infections

General information
Publication status: Published
Organisations: Norwegian School of Veterinary Medicine, Utrecht University
Contributors: Hisham Beshara Halasa, T., Østerås, O., Hogeveen, H., van Werven, T., Nielen, M.
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Scopus rating (2009): SJR 1.276 SNIP 1.706
Web of Science (2009): Indexed yes
Original language: English
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10.3168/jds.2008-1740
Source: orbit
Source-ID: 269027
Research output: Contribution to journal › Journal article – Annual report year: 2009 › Research › peer-review

Meta-analysis of dry cow management for dairy cattle. Part 2. Cure of existing intramammary infections

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Organisations: Utrecht University, Norwegian School of Veterinary Science, TINE SA
Contributors: Hisham Beshara Halasa, T., Nielen, M., Østerås, O., Whist, A. C.
Pages: 3150
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Journal: Journal of Dairy Science
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Ratings:
BFI (2009): BFI-level 2
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Original language: English
DOIs:
10.3168/jds.2008-1741
Source: orbit
Source-ID: 269033
Research output: Contribution to journal › Journal article – Annual report year: 2009 › Research › peer-review
Production loss due to new subclinical mastitis in Dutch dairy cows estimated with a test-day model

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Volume: 92
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Scopus rating (2009): SJR 1.276 SNIP 1.706
Web of Science (2009): Indexed yes
Original language: English
DOIs:
10.3168/jds.2008-1564
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Source-ID: 269022
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Stochastic bio-economic model of bovine intramammary infection

General information
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Organisations: Utrecht University, Wageningen IMARES
Contributors: Hisham Beshara Halasa, T., Nielen, M., Huirne, R., Hogeveen, H.
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Source-ID: 269024
Research output: Contribution to journal › Journal article – Annual report year: 2009 › Research › peer-review

Economic effects of bovine mastitis and mastitis management: A review

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Publication status: Published
Organisations: Utrecht University, Norwegian School of Veterinary Science
Contributors: Hisham Beshara Halasa, T., Huijps, K., Østerås, O., Hogeveen, H.
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Peer-reviewed: Yes
Projects:

Veterinary epidemiology with emphasis on the association between spatial proximity, contact structures, antibiotic consumption and antibiotic resistance
Birkegård, A. C., PhD Student, National Veterinary Institute
Toft, N., Main Supervisor
Hisham Beshara Halasa, T., Supervisor
Boklund, A., Examiner
Dewulf, J., Examiner
Nielsen, S. S., Examiner
Samfinansieret - Andet
01/12/2013 → 20/12/2017
Award relations: Veterinary epidemiology with emphasis on the association between spatial proximity, contact structures, antibiotic consumption and antibiotic resistance
Project: PhD

Development of a herd- and cow-specific decision support tool for control of mastitis
Gussmann, M. K., PhD Student, National Veterinary Institute
Hisham Beshara Halasa, T., Main Supervisor
Toft, N., Supervisor
Boklund, A., Examiner
Denwood, M., Examiner
Rajala-Schultz, P. J., Examiner
Nielsen, S. S., Supervisor
Samfinansieret - Andet
01/07/2015 → 30/09/2018
Award relations: Development of a herd- and cow-specific decision support tool for control of mastitis
Project: PhD

Simulation modeling of LA-MRSA dispersal and control between swine herds
Schulz, J., PhD Student, National Veterinary Institute
Hisham Beshara Halasa, T., Main Supervisor
Boklund, A., Supervisor
Toft, N., Supervisor
Jensen, V. F., Examiner
Baekbo, P., Examiner
Selhorst, T., Examiner
Offentlig finansiering
01/05/2015 → 21/02/2019
Award relations: Simulation modeling of LA-MRSA dispersal and control between swine herds
Project: PhD

The spread and control of LA-MRSA within Danish pig herds
Serensen, A. I. V., PhD Student, National Veterinary Institute
Hisham Beshara Halasa, T., Main Supervisor
Boklund, A., Supervisor
Toft, N., Supervisor
Kirkeby, C. T., Examiner
Wagenaar, J. A., Examiner
Veterinary Epidemiology with focus on monitoring livestock disease using diagnostic databases
Lopes Antunes, A. C., PhD Student, National Veterinary Institute
Toft, N., Main Supervisor
Hisham Beshara Halasa, T., Supervisor
Jensen, V. F., Examiner
Revie, C. W., Examiner
Mortensen, S., Examiner
01/07/2010 → 09/03/2015
Award relations: Veterinary Epidemiology with focus on monitoring livestock disease using diagnostic databases
Project: PhD

Optimizing the bulk milk tank surveillance in Danish dairy cattle
Foddai, A., PhD Student, National Veterinary Institute
Lind, P., Main Supervisor
Hisham Beshara Halasa, T., Supervisor
Utenthal, Å., Supervisor
Larsen, L. E., Examiner
Houe, H., Examiner
01/07/2010 → 09/03/2015
Award relations: Optimizing the bulk milk tank surveillance in Danish dairy cattle
Project: PhD

iCull: iCull
Herd-specific economic decision tool for farmers.
Kirkeby, C. T., Project Participant, National Veterinary Institute, Section for Epidemiology
Hisham Beshara Halasa, T., Project Manager, National Veterinary Institute, Section for Epidemiology
Græsbøll, K., Project Participant, Section for Veterinary Epidemiology and public sector consultancy, Department of Applied Mathematics and Computer Science, Dynamical Systems
Christiansen, L. E., Project Manager, Department of Applied Mathematics and Computer Science, Dynamical Systems
Toft, N., Project Manager, National Veterinary Institute, Section for Epidemiology
Saxmose, S., Project Manager
Project ID: 23176
01/11/2013 → 31/10/2015
Project: Research

Activities:

Maul- und Klauenseuche – verschiedene Bekämpfungsmethoden und ihre Auswirkungen
Period: 6 Sep 2017 → 8 Sep 2017
Carola Sauter-Louis (Other)
Christoph Staubach (Other)
Thomas Selhorst (Other)
Tariq Hisham Beshara Halasa (Guest lecturer)
Christine Pottgiese (Other)
Jorn Gethmann (Other)
Carolina Probst (Other)
Brend Haas (Other)
Franz J. Conraths (Other)
National Veterinary Institute
Epidemiology

Description
Poster presentation in the DVG-Epidemiologie Conference, DACH-Epi 2017, 6th -8th September 2017, Hall in Tirol, Austria
Degree of recognition: International

Related event
the DVG-Epidemiologie Conference,
06/09/2017 → 08/09/2017
Activity: Talks and presentations › Conference presentations