Simulation modelling of LA-MRSA dispersal and control between swine herds

Staphylococcus aureus (SA) is a ubiquitous bacterium in humans and animals. It can cause minor skin infections that do not usually require treatment. SA, as well as Methicillin-resistant SA (MRSA), which is resistant to a wide range of antimicrobials, can lead to severe infections in humans, especially in individuals with a suppressed immune status. MRSA can originate from livestock and is referred to as livestock-associated MRSA (LA-MRSA) with pigs as the main reservoir.

In Denmark, the number of pig herds tested positive for LA-MRSA has increased rapidly since 2008, when a Europe-wide study found only 3.5% of production herds positive for LA-MRSA. However, in 2016, the prevalence found in a national LA-MRSA screening had reached 88%. At the same time, the number of human cases increased in people working at pig farms but also in people with no livestock contact.

In 2014, Denmark initialised a national action plan to limit the spread of LA-MRSA. However, the effects were not sufficient to reduce the number of LA-MRSA-positive herds, nor to limit the number of newly infected humans. To be able to increase the efficacy of control programmes in the pig industry, it is necessary to understand the transmission routes of LA-MRSA among pig herds. This includes the trade of pigs as a potential mechanism for spread, as well as other contact among herds that might lead to the transmission of LA-MRSA. Such knowledge would help to evaluate control options that might reduce the number of LA-MRSA-positive herds in the future.

A network analysis using information on Danish pig holdings and their trade connections between 2006 and 2015 was performed to gain a general knowledge of temporal trends in the number of registered pig herds and pig movements. In addition, we investigated loyalty patterns and contact chains for the 24 registered holding types to identify holding types with a potentially higher risk of disease spread via pig movements (Manuscript I).

The total number of active holdings and the number of pig movements both decreased during the study period, while the holding size increased. We observed a large out-going contact chain for breeding and multiplier herds, which reflects the pyramidal structure of the underlying network and highlights the risk of spreading a disease via pig movements to a wide range of other herds if a pathogen were to affect breeding and multiplier herds. However, horizontal connections among pig herds also exist, which could lead to additional spread among herds of the same holding type.

An agent-based Monte Carlo simulation model mimicking the spread of LA-MRSA among pig herds was developed to study the epidemic behaviour and to identify the driving factors for LA-MRSA spread among pig herds (Manuscript II). As well as transmission based on pig movements registered in the study period from 2006 to 2015, indirect transmissions between holdings were modelled based on distance-dependent probability distributions. Three types of indirect contact were modelled: (1) abattoir trucks collecting pigs from several holdings, (2) humans such as veterinarians, farm workers or guests visiting several holdings on the same day and (3) contact between herds with the same owner. Within-herd dynamics were modelled as a three-compartment SIS model with different transmission rates within the three compartments of sows, weaners and finishers, and with high- and low-risk transmission routes between these compartments. Several scenarios were evaluated to simulate the spread after introduction of LA-MRSA in varying proportions of breeding and multiplier and production herds in 2006 and/or 2009. We compared the model outcomes to the results of LA-MRSA surveys conducted in Denmark during the study period. An extensive sensitivity analysis was performed to study the effect of uncertainty of model parameters (Manuscript II).

Pig movements alone were not sufficient to mimic the observed increase in LA-MRSA-positive herds in Denmark in any of the modelled scenarios. However, 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 transmission via humans and (3) unexplained introduction of LA-MRSA to swine herds.

We enhanced this simulation model to retrospectively evaluate how different control strategies would have influenced the spread of LA-MRSA (Manuscript III). These strategies were combinations of the following control measures: (1) reduced numbers of herds using high-risk antibiotics, (2) reduced probability for indirect transmission between herds via humans, (3) movement restrictions and (4) voluntary eradication in 5-7.5% of the herds. The effects of implementing control in 2007 were compared to implementation in 2010.

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. An extreme scenario (impeding the use of high-risk antibiotics, reducing risk of spread via indirect contact by 75%, implementing movement restriction and culling a percentage of positive herds) was able to reduce the predicted prevalence by 86% compared to the predicted prevalence without control. Control measures initialised in 2007 had a greater effect compared to initialisation in 2010 due to the lower initial prevalence in 2007.

In conclusion, pig movements alone were not sufficient to mimic the development of LA-MRSA herd prevalence observed in Denmark in 2008 and 2014. However, they were responsible for around 75% of transmissions. Within-herd dynamics and the frequency and effectiveness of indirect contact between pig herds via humans showed the highest impact on the predicted herd prevalence. Control measures showed the highest relative reduction when implemented in 2007 and when
all four potential control measures were combined. Categorising herds according to the size of their out-going contact chain increased the effect of eradication as a control measure, as herds with higher risk of spreading LA-MRSA via pig movements were prioritised in the eradication process. However, eradication should be combined with movement restrictions to minimise the risk of re-introduction.