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Modeling the cost of eradicating livestock-associated methicillin-resistant *staphylococcus aureus* in countries with a high proportion of positive herds

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ABSTRACT

Due to an increased incidence of human infections, livestock-associated methicillin-resistant *Staphylococcus Aureus* (LA-MRSA) in pigs and its spread into the human population has been a major public and political issue in Denmark. Similar concerns are also being raised about LA-MRSA in other Western European countries. At a time when the proportion of LA-MRSA-positive pig farms was low, Norway adopted a 'trace and destroy' strategy aimed at keeping LA-MRSA out of the pig population. However, to date, no country with a high proportion of LA-MRSA-positive pig herds has chosen to use an eradication strategy. This study analyses the cost and complexities of conducting an LA-MRSA eradication program in a situation where a large proportion of herds are positive. The total cost of the eradication program was estimated based on the following components: 1) planning, 2) monitoring and testing, 3) cleaning and disinfection, 4) production gains and losses, 5) net reduction in breeding exports, and 6) loss of genetic progress, including the costs of a mitigating caesarean section strategy in breeding herds. Costs were related to the depopulation of 1 million sows, to gilt supply (as this was an important limiting factor during an eradication program in Denmark), and to aggregated losses linked to a temporary halt on breeding progress. Using conservative assumptions, the total eradication costs were estimated at €1.8 billion, broken down into: planning costs (3%), monitoring and testing (6%), cleaning and disinfection (19%), production gains and losses (33%), net loss from breeding exports (19%) and loss of genetic progress (20%). The long-term effects of an LA-MRSA eradication program for Danish pig production were uncertain and were therefore not taken into account in the analysis.

1. Introduction

The livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) clonal complex (CC) 398 has been reported in pig populations and humans in contact with pigs, especially farm workers (Voss et al., 2005; Armand-Lefevre et al., 2005), since 2004. The occurrence of LA-MRSA in Danish pig herds increased rapidly from 3% positive farms in 2008 to 88% positive farms in 2016 (Danish Veterinary and Food Administration, 2017). The pig population in Denmark therefore constitutes a major reservoir of LA-MRSA CC-398. In addition, there was an annual increase in the incidence of LA-MRSA CC398 infections within the Danish human population of 66% per year between 2004 and 2011 (Larsen et al., 2015). This, together with a fierce public debate among experts and stakeholders, amplified by media exposure, has prompted Danish politicians to consider control measures for LA-MRSA in Danish pig herds, as well as initiatives to prevent further spread to humans.

In Norway, a country with an initially very low proportion of positive farms, a "trace and destroy" strategy has been implemented, through which farms delivering or receiving pigs from positive farms are tested. LA-MRSA-positive farms are depopulated without bringing pigs to slaughter, followed by re-stocking with uninfected animals after cleaning and disinfection of the premises. This strategy has a reported 90% probability of successfully eradicating LA-MRSA on a positive Norwegian farm (Grøntvedt et al., 2016). It has been suggested by several influential stakeholders that the best option to control LA-MRSA in Danish pig herds would be to follow the Norwegian example and depopulate LA-MRSA-positive pig herds. Indeed, part of the political mandate of an expert group reconvened by the Danish Minister for the Environment, Food and Agriculture in 2016 was to consider this option. However, when the proportion of positive herds is as high as in Denmark, bottleneck issues and production constraints (e.g. the availability of replacement animals) adds to the complexity of the problem.

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When considering the costs and benefits of eradicating LA-MRSA from the Danish pig herd, it is important to realise that *direct* benefits are almost exclusively achieved outside the pig sector, i.e. in the public health sector. While it is important to consider these benefits when deciding whether or not to initiate an eradication program within a country, they are not relevant when trying to calculate the associated costs. Furthermore, societal costs associated with losses in slaughterhouses, feed mills and various other services for the primary pig industry are most likely to be directly related to a reduction in the number of pigs produced during eradication, and will depend on the structure of the pig industry in the country. Hence, societal costs are not considered further in this study. The costs incurred in the primary production sector, however, can probably be extrapolated from the Danish situation to any industrialised pig production sector with a high proportion of LA-MRSA-positive farms.

There may also be some *indirect* benefits of an LA-MRSA eradication program. For example, it may be possible to include the benefits of eradicating one or more further diseases such as Porcine Reproductive and Respiratory Syndrome (PRRS), Actinobacillus pleuropneumoniae and Enzootic Pneumonia into the cost analysis.

The purpose of this study was to analyse the cost and complexities of conducting an eradication program for LA-MRSA-positive herds in Denmark – a country with a high proportion of positive herds to assess the production losses using similar methods as in previous studies (Houe, 2003; Rushton, 2009; Asheim et al., 2017; Thomann et al., 2017). The main challenge for our analysis is the uncertainty about the underlying assumptions, for example regarding reintroduction rate. To address this uncertainty, we use a conservative approach by which assumptions are chosen so that the combined costs reflect an optimistic estimate of the total cost, and by subsequently performing a sensitivity analysis comparing this estimate to the worst-case scenarios.

2. Material and methods

2.1. Analytical approach

The proposed eradication strategy consisted of: an initial one-year planning phase, a five-year eradication phase and a nine-year monitoring and control phase, during which LA-MRSA-positive farms were depopulated and restocked. In total, a timescale of 15 years was considered.

The cost of an LA-MRSA eradication program for the primary pig sector in Denmark was calculated as the net present value (NPV) of the costs and losses of the program (Eq. (1)). The cost analysis was divided into costs during the planning period, direct net costs during the eradication period, and derived net costs after the eradication period. The calculation was similar to that of Asheim et al. (2017):

$$NPV = \sum_{i=1}^{n} \frac{-CostProg_i - LossProg_i}{(1+r)^i} \quad (1)$$

Where i is the year (with 2018 considered as the start of the eradication program); n is the timescale of the program (15 years); r is the real interest rate (4%). The $CostProg_i$ is the cost of the planning, testing and monitoring, cleaning, disinfection and caesarean section in year i (Fig. 1). $LossProg_i$ includes production losses, the losses from a reduced export of genetics, and losses from reduced breeding progress in year i. The expected benefits related to an improvement in the health status of the pigs were subtracted from the losses. A static approach was adopted without assuming long-term effects on the farm or production structure.

The sensitivity was calculated using a static *ceteris paribus* analysis based on an assessment of relevant assumptions. The costs and losses were recalculated with one of the assumptions changed, and the difference compared to the baseline was calculated. If several assumptions were mutually dependent, the cumulative effect was calculated by changing these assumptions simultaneously and subtracting the baseline costs.

2.1.1. Planning and initial screening

It was assumed that 200 h of planning were required per LA-MRSA-positive farm throughout the eradication and restocking phases based on previous Danish experience from the unsuccessful eradication attempts concerning *Salmonella Typhimurium DT 104*. The initial planning phase was set to one year, including an initial screening of all herds in Denmark to establish the LA-MRSA status of the farms. The planning phase would involve public authorities, veterinarians, consultants and farmers.

2.1.2. Testing and monitoring

We assumed that all herds were tested during the planning phase (year one) to establish the true LA-MRSA status of all farms. During years two and three, one-third of the farms would each be tested four times per year. During years three and four, two-thirds of the farms would each be tested four times per year, and in the fifth year, all farms would be tested once to ensure that the eradication program had been successful. During years six to 15, all herds would be tested annually to confirm their continued negative status. Simulation studies have been conducted showing that frequent testing is necessary to keep the transmission rate between herds low. Each herd was tested with 5 pooled tests per herd at an expected cost of €934 per herd.

2.1.3. Production gains and losses

Production loss was calculated according to the following equation (Eq. (2)):

$$\text{Production loss} = \sum_{j=1}^{2} \sum_{k=1}^{3} production_{jk} \bullet fraction\ of\ year_{jk} \bullet annual\ gross\ margin_k \quad (2)$$

Where *production* was the total number of pigs from farms with LA-MRSA; *fraction of year* was the period with no pigs delivered from the farm; *annual gross margin* was the national average (see Appendix A for detailed description); j was the type of production (integrated = 1, specialised farms = 2), and k was the age group of the pigs (piglets = 1, weaners = 2, finishers = 3).

In farm accounts, not all variable costs are deducted from the revenue to obtain the gross margin (Huirne and Dijkhuizen, 1997). Nonetheless, gross margins are often used to approximate the losses during ceased production (Thomann et al., 2017). However, energy and labour costs are usually also affected by the eradication program because the number of pigs is lower during the eradication and restocking phase. The expected losses from the eradication program were therefore calculated as the gross margin adjusted with 50% of the energy and 10% of labour costs during the depopulation and restocking period. Labour costs were not expected to decrease further due to additional cleaning tasks and logistic constraints on the workforce to avoid reintroduction of LA-MRSA through human contact.

The eradication program evaluated in this study allowed for slaughter pigs to be reared to commercial weight and for piglets to be sold at a commercial price. However, a loss was expected due to productive sows being slaughtered prematurely. This loss was calculated using the costs associated with rearing gilts to about 35 weeks and buying 10% extra gilts, since they would not all be expected to be useful for production.

2.1.4. Cleaning and disinfection

Cleaning and disinfection in relation to LA-MRSA was expected to be costly since the bacteria can survive in the environment. The scope of eradication was considered to be comparable to a *Salmonella typhimurium* DT104 eradication program, conducted (unsuccessfully) in Denmark in the late 1990s. The unpublished costs from this eradication program were divided into: destruction of feedstuffs (22%), cleaning and disinfection of pens (40%), cleaning of machinery and outdoor premises (14%) and reduction in slurry value (24%; Danish Pig Research Centre, unpublished).