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Comparison of risk-based versus random sampling in the monitoring of antimicrobial residues in Danish finishing pigs

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ABSTRACT

In Denmark, a monitoring program for residues of antimicrobials in pork is in place involving annual testing of around 20,000 samples from finishing pigs corresponding to 0.1% of the animals slaughtered. Annually, zero to two samples are found above the maximum residue limit. Both authorities and industry have expressed interest in adjusting the monitoring to a risk-based system. The objective of this study was to assess the opportunities and consequences of the monitoring considering: 1) replacing the current bioassay with high-performance liquid chromatography–mass spectrometry (HPLC LC–MS/MS), 2) replacing kidney with muscles as sample matrix, and 3) using indicators to identify high-risk (HR) herds and increase sampling intensity in these herds, lowering sampling in the low-risk (LR) herds, while aiming at continued detection of similar numbers of test-positives at the lowest possible costs.

A state-of-the-art stochastic scenario tree modelling approach including economic evaluation of different model outcomes was used. A total of six scenarios were run for penicillin and tetracycline, respectively. Relevant information was obtained through the literature, statistical analysis of existing data as well as consultations with laboratory and slaughterhouse experts. Abattoir recordings of chronic pleuritis were used as an indicator for finishing pig herds (HR = within-herd prevalence > 40%). Such risk-based monitoring would have to use muscles and not kidneys, because of logistic challenges in identifying and storing of plucks until testing. However, the bioassay cannot be used on muscle tissue due to low sensitivity for tetracyclines. Different plausible combinations of sample sizes were also modelled.

The HPLC LC–MS/MS method detected the same number of cases compared to the bioassay when kidney was used as matrix. HPLC LC–MS/MS has a higher sensitivity when used on muscle but it is almost twice as costly as the bioassay. Risk-based sampling resulted in detection of more residue cases with higher cost-effectiveness than random monitoring. Sampling 7500 HR pigs and 5000 LR pigs resulted in the most cost-effective monitoring among the alternative scenarios. The associated costs would increase by 4%. A scenario involving testing of 5000 HR and 5000 LR animals would result in slightly fewer positives, but 17% savings in costs. The advantages of using HPLC LC–MS/MS compared to the bioassay are a fast response and a high sensitivity for all relevant substances used in pigs. The Danish abattoir companies have implemented a risk-based monitoring similar to the above per January 2016.

1. Introduction

Withdrawal periods for veterinary medical products are established to prevent treated animals and hereby products from treated animals from entering the food chain too soon after treatment. Such withdrawal periods are based on Maximum Residue Limits (MRL). However, if the withdrawal periods are not complied with, residues of pharmacologically active substances or their metabolites above MRL might be found in animal-derived food products, posing a potential risk to human health (Anon., 2010).

The European Union (EU) Member States are required to implement residue monitoring in live animals and animal products (Anon., 1996). The EU Directive 96/23 prescribes that a minimum of 0.01% of the pigs slaughtered annually in each country are tested for residues of antibacterial substances through official monitoring (Anon., 2009). Currently, the annual number of finishing pigs slaughtered in Denmark is around 20 million. Around 2000 samples – corresponding to 0.01% of the slaughter population – are tested for

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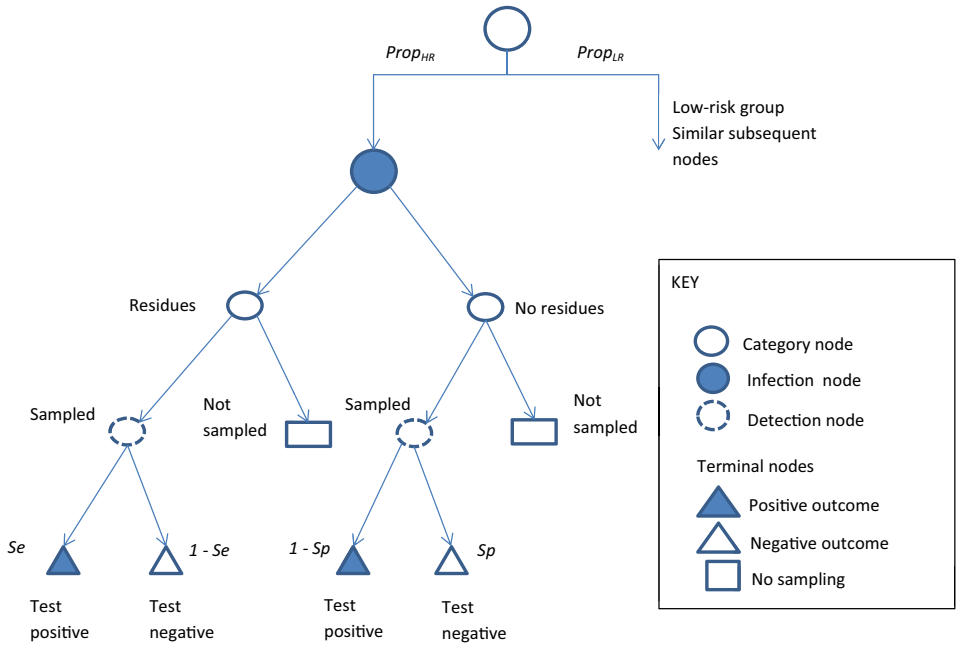

Fig. 1. Conceptual scenario tree developed to evaluate the performance of a monitoring system for detection of antimicrobial residues given true antimicrobial residue prevalence in Denmark. $Prop_{HR}$ and $Prop_{LR}$ are proportions of finishing pigs in the high-risk and low-risk groups, respectively. . $Prop_{HR}$ is the proportion of finishing pigs sampled in the high-risk subpopulation.

residues of antimicrobials through the official Danish national monitoring program. Another 17,000 samples (0.085%) are collected and tested for residues of antimicrobials through the Danish abattoirs' own-check program, which is described below. Hence, the entire monitoring for antimicrobial residues includes close to 0.1% of the finishing pigs slaughtered in Denmark.

The substances found in the residue surveillance are not reflecting the general use of antimicrobials in pigs, because injectables in general have a higher likelihood of resulting in presence of residues in the meat than per oral medicine, which is not necessarily absorbed but acting locally in the intestines (Alban et al., 2014). Furthermore, residues are more likely to be present in animals treated close to time of slaughter, and therefore are more likely to be found in slaughter pigs that have recently been ill.

In the Danish own-check, samples are analysed by use of a bioassay consisting of a microbiological four-plate test (NMKL 121, 2004) followed by a chemical verification. Since 2013, the chemical verification consists of using high-performance liquid chromatography–mass spectrometry (HPLC LC–MS/MS). Moreover, since January 2013 samples are analysed directly by HPLC LC–MS/MS in the national program (Olsen, 2015). Currently, the Danish abattoir companies are considering replacing the bioassay with HPLC LC–MS/MS. This would eliminate the potential problem related to using different analytical methods in the two parts of the programme.

Monitoring data collected over more than a decade indicate that the true prevalence of antimicrobial residues above the MRL is negligible in Danish finishing pigs (around 0.01%) (Baptista et al., 2012). In this situation, a risk-based approach targeting the monitoring activities to high-risk sub-populations might make it possible to reduce the number of samples taken without jeopardizing food safety, or even potentially improving food safety (Stärk et al., 2006; Hadorn and Stärk, 2008; Presi et al., 2008; Baptista et al., 2012).

According to the EU Directive, national residue monitoring should – in general – be targeted to high-risk animals using the following minimum criteria: sex, age, species, fattening system, all available background information, and all evidence of misuse or abuse of antimicrobials (Anon., 1996). In Denmark, this is interpreted as a higher sampling intensity in sows compared to finishing pigs as well as repeated testing in herds with previous findings of antimicrobial residues. In a future revision of the EU Directive, which is expected within in a few years, the goal is most likely to adopt a more risk-based monitoring.

The objective of this study was to investigate the opportunities and consequences of a risk-based approach to monitor antimicrobial residues in the Danish finishing pigs at slaughter. The specific objective was to compare the performance of two different diagnostic tests (HPLC LC–MS/MS versus a biological method) and sampling strategies (risk-based versus random). To enable such comparisons, a stochastic scenario tree model was built for estimation of costs and effects of changed sampling and testing strategies.

2. Materials and methods

The selected approach to address the study objectives is adapted from a state-of-the-art method developed over the last decade for use in quantitative veterinary epidemiology related to evaluation of the performance of surveillance programs. The approach is well-described and exemplified in international publications (Martin et al., 2007), and has been used in previous studies of related nature, e.g. Hadorn and Stärk (2008), Alban et al. (2008), Calvo-Artavia et al. (2012) and Foddai et al. (2015).

2.1. Scenario tree model structure

A stochastic scenario tree is a way to describe the detailed structure of the different components of a surveillance programme. The tree consists of mainly three different types of nodes: infection nodes, detection nodes and category nodes (Fig. 1). A stochastic scenario tree simulation model was developed as described by Martin et al. (2007), but modified to fit the circumstances being modeled here. The terminology and abbreviations are also slightly different from those used in the original publication by Martin et al. (2007) to describe the system being modeled.

The population of finishing pigs slaughtered in Denmark during a 1-year period (*Spop*) was divided into subpopulations. Within