Antimicrobial Resistance Monitoring in Swiss Pork Production

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Abstract An optimized national resistance monitoring program should deliver a precise estimate of the resistance situation for a given combination of bacteria and antimicrobial at a low cost. In order to achieve this, decisions need to be made on the number of samples to be collected at each of different possible sampling points along the food production line. Sampling decisions do not only depend on the prevalence of resistance and sensitivity and specificity of resistance testing, but also on the prevalence of the bacteria, and test characteristics of isolation of these bacteria. Our aim was to develop a stochastic simulation model that optimized a national resistance monitoring program in pig production, taking multi-stage sampling, imperfect sensitivity and specificity of diagnostic tests, and cost-effectiveness considerations into account.

Introduction The use of antimicrobial substances in animal production is one potential reason for the occurrence of resistant bacteria in humans. Thus monitoring the resistance status of various bacteria in the animal population is important for a timely intervention before resistant strains spread throughout the animal population. Currently, Switzerland is developing the scientific basis for the implementation of routine antimicrobial resistance monitoring in food producing animals. Through research projects and pilot monitoring programs in various animals species, data on the prevalence of selected bacteria and antimicrobial resistance are collected. Three major sources of information are available for a comprehensive assessment of the resistance situation (figure 1). The resistance situation in clinical isolates from diseased animals reflects resistance levels in problem animals, and provides information on the effectiveness of common veterinary drugs for the treatment of diseases on swine farms. Therefore, the focus of the resistance monitoring in this group of animals should be on bacteria pathogenic to animals, as well as on zoonotic bacteria such as Salmonella and Campylobacter. The resistance situation in bacteria isolates from healthy animals and food of animal origin, on the other hand, reflects the potential exposure of humans to resistant bacteria from animals. Finally, data on antimicrobial usage are crucial for establishing epidemiological links between treatment regimens in animals and changes in the resistance situation in animals and humans.

Along the food production chain, various sampling points are conceivable for resistance monitoring in healthy animals including sow, weaner pig or finishing pig farms, at slaughter, and at retail level. The optimal sampling point may differ depending on the targeted bacteria and antimicrobial resistance involved. When monitoring resistance of bacteria originating from live animals, decisions need to be made on the number of farms monitored, the number of animals tested per farm, the number of samples per animal, and the number of colonies that are submitted to susceptibility testing from each sample. Furthermore, decisions on the age of the tested animals need to be done. Market weight finishing pigs represent the end of the live animal production line. Besides the abattoir and fresh pork, this may be the best sampling point for estimating the risk for consumers deriving from resistant bacteria from food animal origin. On the other hand, testing sows is of interest as they remain on the farms for a longer time period than finishing pigs. Resistance testing of indicator bacteria such as E. coli or Enterococcus spp. from

Figure 1: Elements of a resistance monitoring program along the pork production chain.
sows may thus provide a more representative overview on the resistance situation. Finally, as the majority of pigs receiving antimicrobial treatment are piglets (Arnold et al, 2004) they can be regarded as a high risk subpopulation and should be included in a resistance monitoring as well.

While a lot of data on the resistance situation in Switzerland are available from different information sources, the methodology of data collection has not yet been standardized. Furthermore, at each of the different sampling points, samples were only collected selectively in one year, and no longitudinal data are available. In order to establish a continuous monitoring of antimicrobial resistance, decisions need to be made on the number of samples to collect at each sampling point, the sampling interval, the bacteria and antimicrobials to be monitored. As resources are limited, efforts should be made to obtain a maximum explanatory power of the monitoring with minimal cost for sample collection and analysis.

The objective of this project was the development of an optimized antimicrobial resistance monitoring program in pigs in Switzerland. To achieve this goal, existing information on antimicrobial resistance and antimicrobial use in pork production was collected, and data entered into a stochastic simulation model. Optimization was defined as allocating available resources to different sampling points to obtain the maximum precision of the prevalence estimate for resistant bacteria, given the financial constraints of the program.

### Pilot Monitoring of Antimicrobial Resistance

Data on the resistance situation of clinical isolates of pigs in Switzerland were collected by Wissing et al. (2001). Through a collaboration of Swiss laboratories, antimicrobial resistance data and isolates of important bacterial pathogens from animals were collected over a period of ten months. The resistance situation for various pathogens was assessed, and differences between animal species could be shown.

In healthy animals, testing for antimicrobial resistance is performed in sows, weaner pigs, finishing pigs, at the abattoir, and in pork. The prevalence of antimicrobial resistance in *E. coli*, *Enterococcus* spp., and *Campylobacter* spp. from sows and weaner pigs is currently assessed in a research project at the University of Zurich. On 60 pig farms, pooled fecal samples were taken from the floor of pens with sows and weaner pigs, respectively. Culture was performed using standard laboratory methods. For resistance testing, disc diffusion and microdilution was performed.

In a study on the prevalence of the most important bacterial zoonoses in Swiss finishing pigs and in pork (Ledergerber et al, 2003) fecal samples were collected on 88 farms from the floor of pens with market weight finishing pigs. Samples were pooled according to Stege et al. (2000) and cultured for *Salmonella* spp., *Campylobacter* spp., and *Yersinia enterocolitica*. Susceptibility of isolated *campylobacter* strains was tested with disc diffusion. *Campylobacter* spp. were isolated out of 91.5% of pooled fecal samples from finishing pigs. The percentage of resistant *campylobacter* strains isolated from finishing pigs is shown in figure 2. Thirty-six (13.4%) out of 263 strains were susceptible for all tested antimicrobials. One hundred sixty-eight (63.9%) strains were resistant against one or two antimicrobials, whereas 59 (22.4%) strains were resistant against three or more of the antimicrobials tested.

On retail level, 865 samples of fresh pork were taken from shops all over Switzerland. Samples included cutlet, meat cut into strips, and minced meat. Pork samples were cultured for *Salmonella* spp., *Campylobacter* spp., and *Yersinia enterocolitica*. On retail level, *Campylobacter* spp. prevalence was much lower than on the farm. In two (0.2%) out of 865 samples of fresh pork meat campylobacter was isolated. At the abattoir, fecal samples of 100 pigs will be collected in Summer 2005. Samples will be cultured for *E. coli*, *Enterococcus* spp., and *Campylobacter* spp., and resistance testing will be performed with the microdilution method.

Data on antimicrobial use in feed were collected by Arnold et al. (2004). Prescription patterns for medicated feedstuffs for pigs were analyzed over a period of four years and prescribed daily doses were derived. The consumption of antimicrobial treatments in feedstuffs was derived. The consumption of antimicrobials varies significantly between farms and animal species. The most frequently used antimicrobials are *erythromycin*, *tetracycline*, and *polymyxin*. The consumption of *erythromycin* and *tetracycline* is highest in sows, whereas *polymyxin* is mainly used in weaner pigs.
bacterial through medication by farmers and veterinarians will be assessed in a survey among veterinarians. In Switzerland, all antimicrobials except in-feed formulas are marketed by veterinary practitioners. Use of antimicrobial growth promoters has been illegal in Switzerland since 1999, and therefore does not need to be considered in the monitoring program.

**Development of an Optimized Resistance Monitoring Program**

The data described above are used to develop an optimized sampling plan for monitoring resistance. The influence of sampling more farms compared to sampling more animals per farm on the prevalence estimate for antimicrobial resistance is analyzed by simulation modeling. Accounting for the costs, the number of samples to be taken at the respective step in the production line is optimized. This will be the basis for implementing a continuous resistance monitoring program for pigs and the other major food animal species in Switzerland.

Data obtained from the preliminary resistance monitoring activity allowed for comparing the prevalence of *Campylobacter* spp. and antimicrobial resistance among sows, weaning pigs, finishing pigs, and pork. The resistance situation in commensal bacteria could be compared between sows and weaning pigs. The most effective points along the production line for monitoring antimicrobial resistance can be defined by evaluating the explanatory power of the information collected at each sampling point. To achieve this, a Monte Carlo simulation worksheet was developed, which models the effect of various sampling strategies on the precision of the estimate of the resistance prevalence in Swiss pigs. For the development of the model, Microsoft Excel, an Excel macro using Visual Basic programming language, and Palisade @RISK software were utilized. In the model, herds were randomly sampled from the pig population. The number of positive pooled samples in the animals sampled from one herd was simulated, taking the herd size and the within-herd prevalence for each sampled herd into account. The number of true and false positive samples detected by diagnostic testing was determined from a binomial distribution, with $p=\text{sensitivity}$ or $p=1-\text{specificity}$, respectively. Uncertain input parameters were also described using probability distributions available in @RISK. Prevalence estimates were described by a beta distribution. Expert opinion was modeled by a pert distribution. A partial budget approach was utilized to find the most cost-effective combination of samples to obtain a defined precision of the prevalence estimate.

Results of the model will allow the design of an optimized monitoring program for antimicrobial resistance in the Swiss pork production. As more data becomes available from continuous monitoring of the resistance situation, this information will help to further refine the monitoring program.

**References**


