

Evaluation of the potential use of risk-based sampling to surveillance of antibacterial residues in Danish pork

Alban, L.^{b*}

Baptista, F.M.^a, Toft, N.^a, Olsen, A.M.^b, Petersen, J.^b

^aDepartment of Large Animal Sciences, Faculty of Life Sciences, University of Copenhagen, Grønnegårdsvej 8, DK-1870 Frederiksberg C, Denmark

^bDanish Agriculture & Food Council, Axelborg, Axeltorv 3, DK-1609, Copenhagen, Denmark

*Danish Agriculture & Food Council, Axelborg, Axeltorv 3, DK-1609, Copenhagen, Denmark

Email: lia@lf.dk

Abstract

Consumers consider presence of chemical substances in food products as undesirable. In Denmark, more than 20,000 samples are analysed each year for presence of antibacterial residues in Danish slaughter pigs, and these surveillance data indicate that the true antibacterial residue prevalence in Danish slaughter pigs is negligible. The question has been raised whether it would be possible to improve the cost-effectiveness of the surveillance programme. This was addressed in this study.

A Bayesian model was developed and used to investigate the impact of a potential risk-based sampling approach to the residue surveillance programme in Danish slaughter pigs. Residue surveillance data covering the period from 2005 to 2009 were used. The probability of detecting at least one confirmed sample presenting residues above Maximum Residue Limits (MRLs) was modelled, for different sample sizes and prevalence scenarios.

For the current prevalence scenario and a sample size of 20,000 samples, the probability of detecting at least one pig presenting residues above MRLs was high (>70%) but below 95%, due to the very low antibacterial residue prevalence in Danish slaughter pigs. However, potential risk-based scenarios suggest that, if sampling is targeted to high-risk slaughter pigs, where the prevalence is at least 10 times higher than the average prevalence in slaughter pigs in 2009, a higher probability of detection can be achieved, even when the sample size is reduced to 10,000 samples (>95%).

Use of a risk-based approach is likely to increase the cost-effectiveness of the overall antibacterial residue surveillance programme in Danish slaughter pigs. Further research should focus on the identification of high-risk pigs/herds potentially presenting a higher likelihood of non-compliance with antibacterial use requirements. High-risk pigs might be identified based on clinical appearance, and high-risk herds might be identified based on data describing antibacterial use and/or post-mortem meat inspection data. A similar approach might be considered for surveillance for antibacterial residues in Danish sows.

In conclusion, the model results suggest that if high-risk slaughter pigs can be identified, the number of samples from slaughter pigs can be largely reduced while achieving the same or increased probability of detection.

Introduction

Residues of pharmacological active substances or their metabolites might be found in food products from food-producing animals, as a result of veterinary use. Accordingly, Maximum Residue Limits (MRLs) for pharmacological active substances in foodstuffs of animal origin are established to assure high food safety standards (Regulation (EC) No 470/2009; Commission Regulation (EU) No 37/2010). EU Member States are required to implement residue surveillance in live animals and animal products (Council Directive 96/23/EC). The EU requires that 0.03% of the livestock population is tested for residues. Additionally, according to EU requirements, national residue surveillance plans should be targeted to high-risk animals.

In Denmark, a residue surveillance programme has been in place since 1972. Each year, 0.1% of the number of slaughter pigs and more than 1% of the sows slaughtered in the previous year are tested for antibacterial residues. The majority of

the samples are taken as a part of the slaughterhouses' own check programmes. Annually, more than 20,000 samples are collected from finisher pigs. Data collected over the last 10 years indicate that antibacterial residues in Danish finisher pigs are found at a very low prevalence corresponding to around 0.01% (Table 1).

The question arose whether it would be possible to improve the cost-effectiveness of the surveillance programme. This was addressed in a project conducted at the Danish Agriculture & Food Council in 2010.

Material and Methods

A Bayesian model was used to investigate the impact of a potential risk-based sampling approach to the residue surveillance programme in Danish slaughter pigs. Bayesian modeling is a statistical method where information obtained a priori (i.e. through experiments or test evaluations), expressed as probability distributions, is combined with the observed data to form the posterior distribution. The posterior distribution thus reflects both the uncertainty of the prior knowledge as well as the information in the data, i.e., the higher the sample size, the higher the precision of the prior distribution. There are several examples of the use of Bayesian analyses in modern veterinary epidemiology. Among the commonly used examples are the estimation of true prevalence (Branscum et al., 2004) and evaluation of diagnostic tests in the absence of gold standard (Branscum et al., 2005).

Residue surveillance comprises the use of screening and confirmatory tests. Danish surveillance data from 2005-2009 (Table 1) and prior knowledge about true prevalence (uniform distribution: zero to 0.01); screening test sensitivity (beta distribution: mode 0.90 and 5th percentile 0.80) and specificity (beta distribution: mode 0.95 and 5th percentile 0.90) were included in the model. For the confirmation test, sensitivity and specificity were assumed to be perfect. The priors and the data were combined in a model to estimate the posterior true prevalence of samples with residues above the MRL value. Using the posterior true prevalence for 2009 as a basis, different hypothetical risk-based scenarios were used to estimate the probability of finding at least one sample presenting antibacterial residues above MRLs for selected sample sizes. To illustrate targeted sampling to high-risk slaughter pigs, the prevalence of antibacterial residues was increased five and ten times, respectively, compared to the antibacterial residue prevalence found in slaughter pigs in 2009.

Table 1. Antibacterial residue surveillance data in Danish slaughter pigs, 2005-2009.

Year	Total number of samples	Number of positive screening/confirmed* samples	Substances found either during screening or confirmation
2005	19,912	4/0	
2006	18,965	2/1	Amoxicillin, benzylpenicillin
2007	18,416	2/1	Tilmicosin, benzylpenicillin
2008	23,615	3/2	Benzylpenicillin, doxycycline
2009	22,498	3/1	Doxycycline

* the residues found were above the MRL value for confirmed samples

The model and the simulations based on the model were carried out using OpenBUGS (Lunn et al., 2009). The first 10,000 iterations were discarded as burn in and the following 10,000 iterations were used for inference. Convergence was assessed by checking plots of the sampled values as time series, as well as auto-correlation plots (Toft et al., 2007). The probability of detecting at least one truly positive sample was estimated as the proportion of iterations where at least one positive MRL was detected by the screening test, i.e., was present in the sampled pigs and subsequently identified by the screening test.

Results

Table 1 presents the total number of samples collected in the Danish residue surveillance programme and the number of positive samples (residues above MRLs) in slaughter pigs from 2005-2009. Table 2 presents the posterior estimates for the probability of detecting at least one sample presenting residues above MRLs, for different sample sizes and for different prevalence scenarios.

For the current prevalence scenario (median 0.008, 95% CPI[0.001-0.027]) and a sample size of 20,000 samples the probability of detecting a pig presenting residues above MRLs was high (>70%) but below 95%, due to the very low

antibacterial residue prevalence in slaughter pigs. However, when prevalence is increased, resembling a targeted sampling approach to high-risk slaughter pigs, a higher probability of detection can be achieved, even when the sample size is reduced to 10,000 samples (>95%).

Table 2. Posterior estimates of the probability of detecting at least one confirmed sample presenting residues above MRLs for the current situation as well as two different prevalence scenarios and different sample sizes in Danish slaughter pigs

Surveillance scenario	Median True Prevalence	Sample size	Probability of detecting at least one positive ^b sample (%)
Current	0.008 ^a	20,000	72
		10,000	52
		5,000	33
Risk-based (x5)	0.04	20,000	96
		10,000	90
		5,000	77
Risk-based (x10)	0.08	20,000	99
		10,000	97
		5,000	90

^a median true prevalence found in Danish slaughter pigs in 2009 [95% CrI [0.001-0.027]

^b residues confirmed above the MRL value

Discussion

In this study, we used a Bayesian model to combine the prior knowledge about the individual components of the Danish antimicrobial residue surveillance programme and the surveillance data, into an assessment of the true prevalence of residues above MRL. This enabled us to give an estimate of the probability of detecting at least one positive sample, while taking into account the uncertainty known about the individual components of the system.

The efficiency of the surveillance programme was modelled as the ability of detecting at least one sample presenting residues above MRLs. This was chosen because it reflects the current number of positive findings which is between one and two (Table 1). Hence, it will be feasible to explain to consumers and trade partners that the safety of the programme remains unchanged, because approximately the same number of positive samples will be identified in a hypothetical risk-based programme as in the current programme.

According to the current surveillance programme, the prevalence of residues of antibacterials in Danish finisher pigs is very low (~0.01%). A risk assessment by Baptista et al. (2011) - presented elsewhere in this proceeding - shows that the human health risk associated with antibacterial residues in Danish pork is low to negligible in sows and negligible in slaughter pigs. Hence, food safety is secured; however, the current surveillance does not seem to be very cost-effective. Our results strongly indicate that a risk-based approach to antibacterial residue surveillance in slaughter pigs should be further investigated, targeting sampling to high-risk pigs or high-risk herds. Hereby, the cost-effectiveness of the overall antibacterial residue surveillance programme would be increased. This is in agreement with previous studies evaluating a risk-based sampling strategy for residue surveillance in Swiss calves (Presi et al., 2008).

Further research should focus on the identification of high-risk pigs or herds potentially presenting a higher likelihood of non-compliance with antibacterial use requirements. High-risk pigs might be identified based on clinical appearance, and high-risk herds might be identified based on antibacterial use and post-mortem meat inspection data. In the Netherlands, a risk-based sampling for residues in pigs is in place. Here, data from meat inspection are used (A. Jelsma, personal communication 2010). A similar approach is expected to be investigated in Denmark. Moreover, a new policy in Denmark called the "Yellow Card Scheme" has recently been implemented. Pig producers using more than twice the average of the antimicrobial consumption will receive a yellow card which among others implies restrictions on future use of antimicrobials (Anon., 2011). It has been suggested to include animals from yellow card farms in a future risk-based surveillance for residues.

Conclusion

A potential risk-based sampling approach to antibacterial residue surveillance in slaughter pigs might allow reducing the sample size largely, while increasing or maintaining the probability of detection. Risk-based antibacterial residue surveillance might be a more cost-effective approach compared to the current surveillance in Danish slaughter pigs.

References

- ANONYMOUS (2011). Gult kort for højt antibiotikaforbrug (Yellow card for a high use of antimicrobials) – In Danish. The Danish Veterinary & Food Administration. http://www.foedevarestyrelsen.dk/Dyr/Dyresundhed_og_dyresygdomme/Laegemidler_til_dyr/Gult_kort_antibiotika/Forside.htm
- BAPTISTA, F.M., ALBAN, L., OLSEN, A.M., PETERSEN, J.V. (2010). Epidemiological evaluation of the residue surveillance programme in Danish pigs. Danish Agriculture & Food Council. 1-53. <http://www.lf.dk/Aktuelt/Publikationer/~media/lf/Aktuelt/Publikationer/Svinekod/UTF8Qreststoffer20overvUTF8QC3A5gning20RBRS20Filipa.ashx>
- BAPTISTA, F.M., ALBAN, L., OLSEN, A.M., PETERSEN, J. (2011). Human health risk of residues in Danish pork – in theory and practice. Proceeding from SafePork 2011.
- BRANSCUM, A.J., GARDNER, I.A., JOHNSON, W.O. (2004). Bayesian modeling of animal- and herd-level prevalences. *Prev. Vet. Med.* 66, 101-112.
- BRANSCUM, A.J., GARDNER, I.A., JOHNSON, W.O. (2005). Estimation of diagnostic-test sensitivity and specificity through Bayesian modeling. *Prev. Vet. Med.* 68, 145–163
- LUNN, D., SPIEGELHALTER, D., THOMAS, A., BEST, N. (2009). The BUGS project: Evolution, critique, and future directions. *Statistics in Medicine*, 28, 3049-3067.
- PRESI, P., STARK, K.D.C., KNOPF, L., BREIDENBACH, E., SANAA, M., FREY, J., REGULA, G. (2008) Efficiency of risk-based vs. random sampling for the monitoring of tetracycline residues in slaughtered calves in Switzerland. *Food Addit. Contam* 25, 566-573.
- TOFT, N., INNOCENT, G.T., GETTINBY, G., REID, S.W.J. (2007). Assessing the convergence of Markov Chain Monte Carlo methods: An example from evaluation of diagnostic tests in absence of a gold standard. *Prev. Vet. Med.* 79, 244-256.