Quantitative AMR-trend analysis in Dutch livestock

Ayla Hesp[1,2], Kees Veldman[1], Jeanet van der Goot[1], Joop Testerink[1], Marga Japing[1], Arie Kant[1], Ben Wit[3], Gerdien van Schaik[2,4], Dik Mevius[1,2]

[1] Department of Bacteriology and Epidemiology, Wageningen Bioveterinary Research, Lelystad, Netherlands; [2] Faculty of Veterinary Medicine, Utrecht University; [3] Netherlands Food and Consumer Product Safety Authority (NVWA); [4] GD Animal Health, Deventer, Netherlands

Introduction & objective

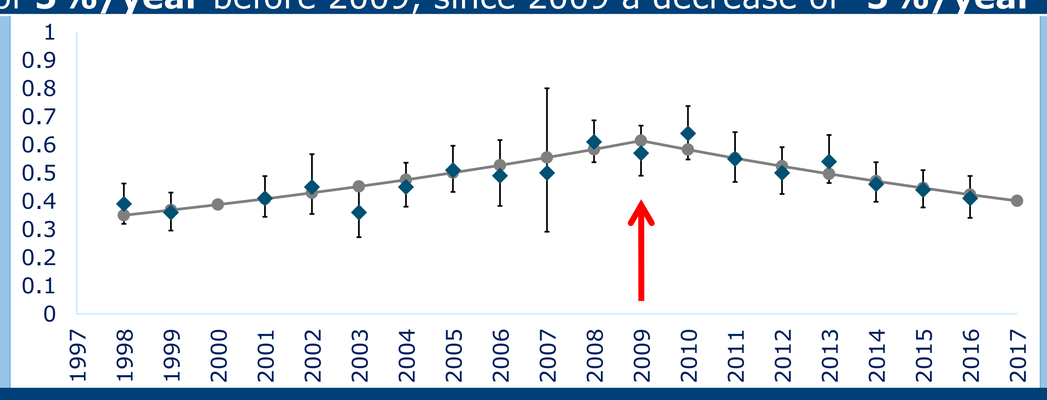
Since 1998 continuous monitoring of antimicrobial resistance (AMR) is performed in commensal *E. coli* from Dutch livestock.

Objectives of the monitoring program are:
1) to monitor trends in AMR in Dutch livestock, including effects of antibiotic use and
2) to detect emergence of AMR of public health concern(1).

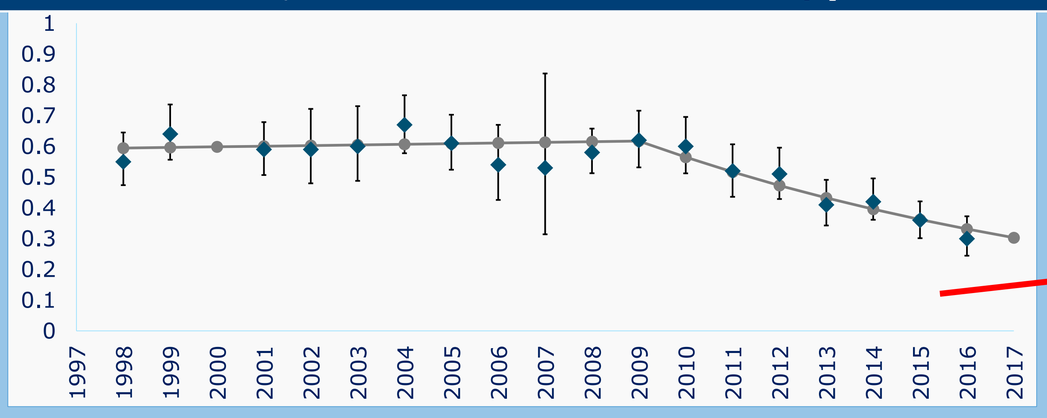
The aim of this study was to evaluate the AMR-monitoring program from 1998–2016 by quantitative data analysis, investigating the effects of antibiotic use interventions since 2009 in AMR monitoring data.

Results

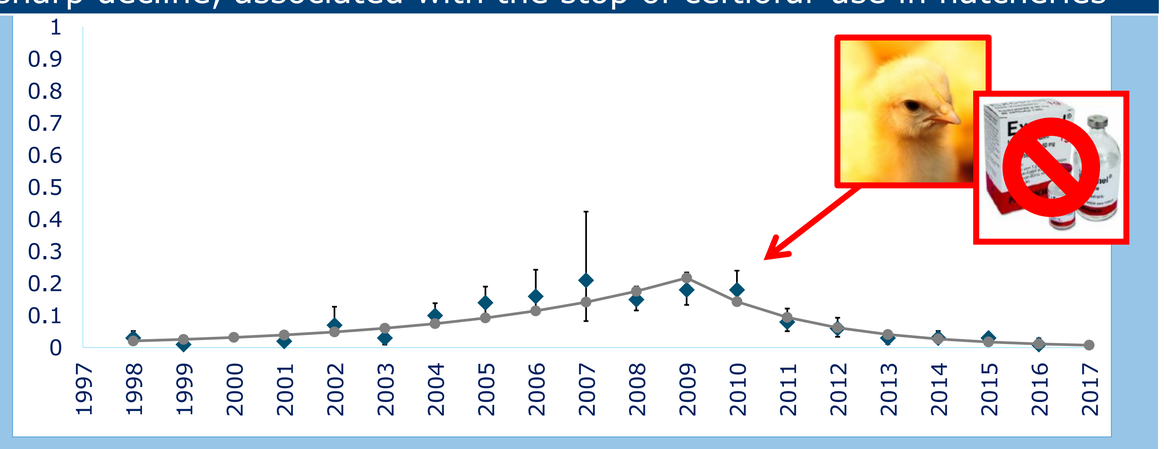
1) Ciprofloxacin - broilers: Observed resistant proportions with 95%CI (checked) versus fitted values (trendline with dots). Increase of **5%/year** before 2009, since 2009 a decrease of **-5%/year**



2) Doxycycline/tetracycline - broilers: Although resistant proportions seemed stabilized, since 2009 a decrease of **-9%/year**

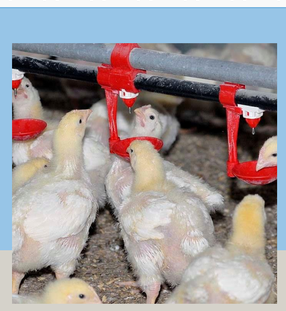


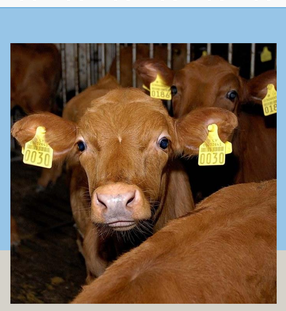
3) Cefotaxime - broilers: Observed resistant proportions with 95%CI (checked) versus fitted values (trendline with dots). After 2010 a sharp decline, associated with the stop of ceftiofur use in hatcheries

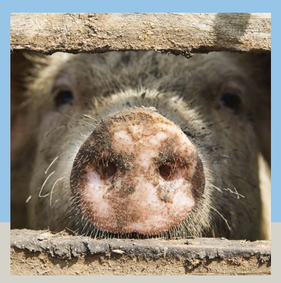


Antibiotic	Variable	Estimate	Pr(>|z|)	e^(estimate)	AIC	Scaled deviance
Amoxicillin/ampicillin	(Intercept)	-0.27	0.00	0.76		
	x1	0.06	0.00	1.06	146.56	1.21
	x2	-0.06	0.00	0.94		
Cefotaxime	(Intercept)	-1.53	0.00	0.22		
	x1	0.21	0.00	1.24	126.24	2.68
	x2	-0.42	0.00	0.66		
Gentamicin	(Intercept)	-2.20	0.00	0.11		
	x1	0.12	0.00	1.13	115.51	1.93
	x2	-0.13	0.00	0.88		
Doxycycline/ tetracycline	(Intercept)	-0.48	0.00	0.62		
	x1	0.00	0.56	1.00	136.34	0.63
	x2	-0.09	0.00	0.91		
Chloramphenicol	(Intercept)	-1.24	0.00	0.29		
	x1	0.12	0.00	1.13	126.68	1.52
	x2	-0.17	0.00	0.84		
Ciprofloxacin	(Intercept)	-0.49	0.00	0.61		
	x1	0.05	0.00	1.05	135.46	0.69
	x2	-0.05	0.00	0.95		

Table 1. Results of modelling AMR-trends 1998-2016 in indicator *E. coli* from broilers







Methods

Yearly, animal faecal samples were collected by the Netherlands Food and Consumer Product Safety Authority (NVWA) in slaughterhouses.
Approx. 300 samples were randomly collected from broilers, pigs and calves. Cows were sampled by taking faecal floor samples on dairy farms.
From samples, *E. coli* were isolated on MacConkey agar and randomly selected colonies were identified (MALDI-TOF). Susceptibility was tested for fixed panels of antimicrobials with Sensititre® broth microdilution.

In this study, MICs of >15.000 *E. coli* isolates were analysed to determine trends. Resistant proportions were modelled, using a log-linear model with Poisson distribution, to determine trends and trend changes.

Conclusion

This model quantified trends in resistant proportions over time from phenotypic data (MICs). Significant decrease of AMR in *E. coli* from Dutch livestock was observed for all antibiotic classes since 2009, corresponding to both specific and general interventions leading to AMU reduction (64%) from 2009-2016 (2).
These findings demonstrate potential of AMR-monitoring programs to identify trends, related to interventions.
This analytical evaluation resulted in recommendations for phenotypic AMR-data analysis:

1) **A log-linear model with time as independent variable enables reliable detection of trend changes over time, even with changes in monitoring aspects, such as sample size.**

2) **Use of Poisson distribution enables detailed interpretation of aberrations in very low proportions. However, for each outcome, the fit of the model (AIC and scaled deviance) determines relevance of aberrations.**

Wageningen Bioveterinary Research (WBVR)
Contact: ayla.hesp@wur.nl
M +31 **(0) 6 14 750 460**
www.wur.nl/bioveterinary-research

References
1. MARAN 2017, *Monitoring of antimicrobial resistance and antibiotic usage in animals in the Netherlands in 2016*, C.M.D. D.J. Mevius, K.T. Veldman, W. van Pelt, D. Heederik, Editor. 2017.
2. Dorado-Garcia, A., et al., *Quantitative assessment of antimicrobial resistance in livestock during the course of a nationwide antimicrobial use reduction in the Netherlands.* J Antimicrob Chemother, 2016. 71(12): p. 3607-3619.