

DTU The effect of antimicrobial use on tetracycline resistance genes in pig production

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Antimicrobial resistance is an emergent challenge to the world. Using data from the Danish pig industry, the relationship between antimicrobial consumption and antimicrobial resistance genes is investigated in order to get a better understanding of the selection of antimicrobial resistance.

Aim

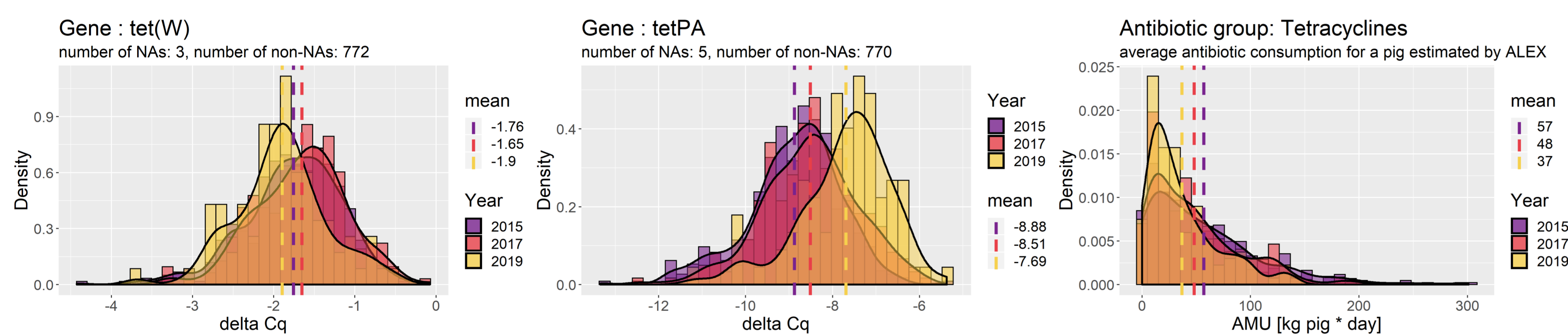
This work is carried out as part of the Veterinærforlig III project. The aim of the project is to develop a dynamic predictive model of the levels of antibiotic resistance in pig production.

Resistance genes from pig samples

To quantify levels of antimicrobial resistance, samples from slaughter pigs has been collected during three time periods in 2015, 2017 and 2019. The samples were analyzed by the qPCR method. The values are normalized by the house holding gene 16S (ΔCq -values).

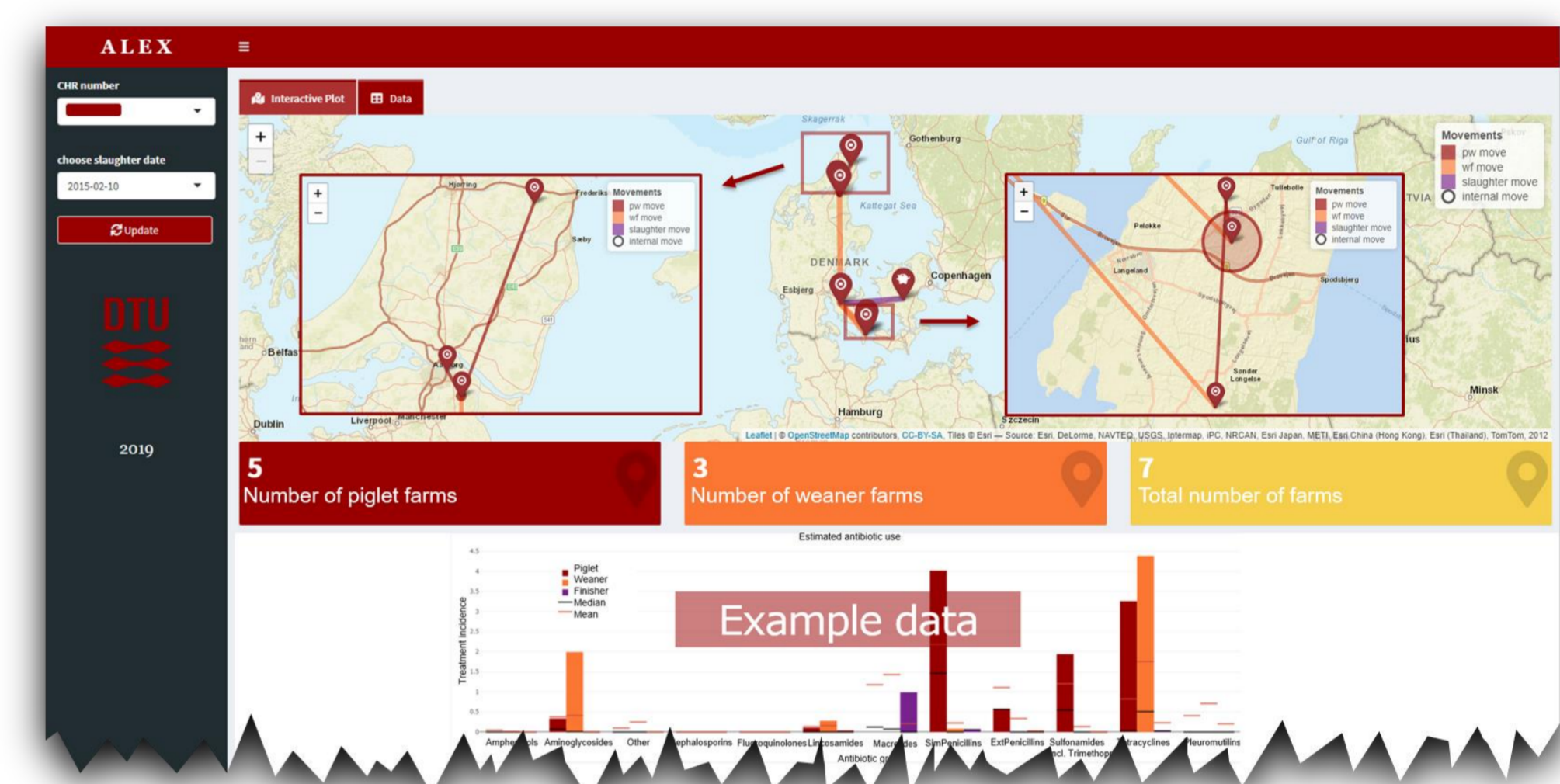
Register data

Data from the Danish registry concerning movements of pigs between farms and purchased antimicrobials for each farm was combined and through our pig tracing algorithm 'ALEX' (Average Lifetime EXposure) an average exposure was estimated per pig.



Distribution plots of two resistance genes (tetPA and tet(W)) over time, samples are collected in Danish slaughter pigs. Here 443, 236 and 88 samples from unique farms are plotted for 2015, 2017 and 2019, respectively. The two distributions are moving in opposite directions over time, the distribution of tetPA is moving toward higher ΔCq -values i.e. a higher occurrence. While the distribution of tet(W) is moving towards lower ΔCq -values and lower occurrence over time.

Distribution plot of purchase of the antimicrobial within the drug class of tetracyclines in Danish pig farms over time.



Screenshot of a shiny dashboard representing results from the ALEX algorithm. The algorithm combines data from Danish movement registers and purchased antimicrobial products in order to trace the pigs path and estimate the average exposure to antimicrobials during its lifetime.

Linear regression models of single tet-genes.

We have used linear regression models to show how the occurrence of individual tet-genes depends on the usages of the different antimicrobial classes within each age group during the pigs lifespan.

Results are shown in the table were black and white numbers represents negative and positive coefficients, respectively. It is important to notice, that the magnitude of the coefficients has not been corrected for the weight in the respective age groups and should therefore be interpreted with care.

	tet C-1	tet(32)	tet(W)	tetA	tetB-1	tetL	tetM	tetO-1	tetO-2	tetPA	tetQ	tetX
(Intercept)	-11.292***	-4.652***	-2.171***	-12.265***	-10.911***	-6.978***	-9.689	-4.726	-3.579***	-9.173	-3.519***	-9.921***
Aminoglycosides piglet								0.008*				
Aminoglycosides weaner		0.063***	0.024***			0.087**			0.043***			
Aminoglycosides finisher	-0.223**											0.015*
Amphenicols weaner												0.077**
ExtPenicillins piglet										0.016*		
ExtPenicillins weaner			0.006*	-0.043*		0.028*			0.012*			
ExtPenicillins finisher	-0.056**				-0.038*							
Lincosamides piglet		-0.025*				-0.038*			-0.018*			0.031**
Lincosamides weaner	-0.364**				-0.144*					0.045*	-0.036*	0.074*
Lincosamides finisher	0.463**											
Macrolides piglet			0.002**								0.003***	0.013***
Macrolides weaner												0.02**
Macrolides finisher												0.009***
Pleuromutilins piglet		0.006***	0.002**			0.007*			0.004***		0.003**	0.004*
Pleuromutilins weaner			0.003*		-0.039*						0.004*	
Pleuromutilins finisher							-0.005*				0.003*	
SimPenicillins piglet										0.006*		
SimPenicillins finisher		-0.011*										
Sulfa incl. TMP piglet	0.059*							0.007**				
Tetracyclines piglet		0.01***	0.008***			0.012***	0.005**	0.003***	0.008***	0.009***	0.005***	0.005*
Tetracyclines weaner			0.005*					0.006*			0.008*	
Tetracyclines finisher			0.002**					0.002**		0.003*	0.004**	

This table is showing results for independent linear regression models fitted for the individual tet-genes. The tet-genes are modelled as functions of the purchased amount of each antimicrobial class within the age groups of the pig. Black numbers represent negative relations while white numbers represent positive ones. Stars represent the level of significance of the estimates: 0**** 0.001*** 0.01** 0.05.

Discussion

The results of the linear regression models show that there are many different antimicrobial classes that affect the occurrence of resistant genes and it differentiates depending on when the exposure happens during the pigs lifecycle. Most noticeable is that the use of tetracyclines in the piglet stage seems to have an highly significant effect on most of the tet-genes

Future work

More complex modeling is needed to get a deeper understanding of the dynamics of antimicrobial resistance. Taking into account more resistance genes and the correlation between these, management factors such as size of farms and number of movements between farms as well as the dynamic behavior over time will help gaining even better understanding.