# Assessing the possible association between veterinary antimicrobial consumption and resistance in indicator *E. coli* isolated from farm animals in Belgium

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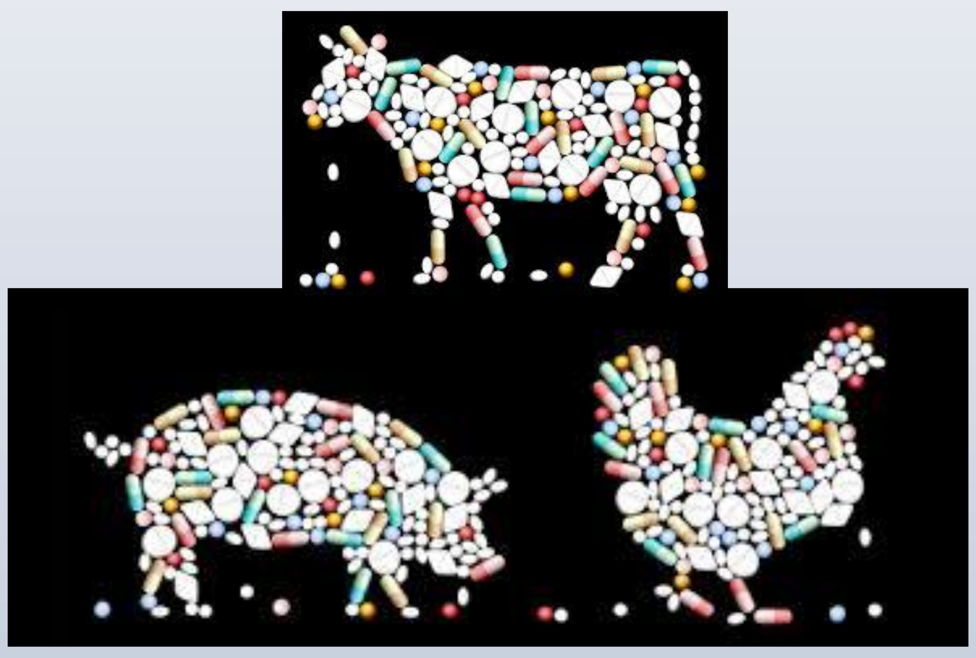
## Introduction

Antimicrobial use is significant factor accounting for the selection and spread of antimicrobial resistance in commensal and pathogenic bacteria (Burow *et al*., 2014; Horigan *et al*., 2016). Bacteria are frequently found resistant to many antimicrobials to the point that both animal and public health are now seriously challenged (Megha *et al*.,2014). Exploring the trend possibly associating antimicrobial consumption and resistance is a highly desirable exercise, that was tentatively completed in the present study focused on indicator *Escherichia coli* from farm animals in Belgium.

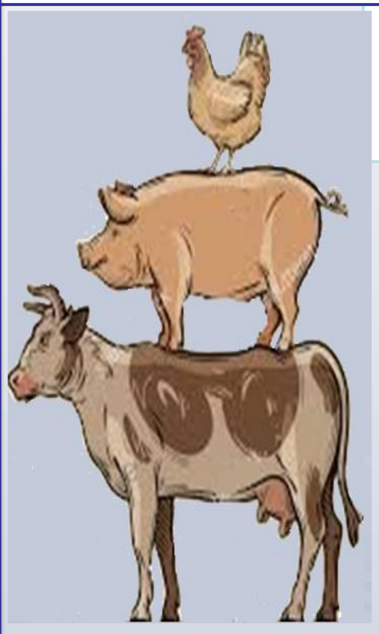
## Materials and methods

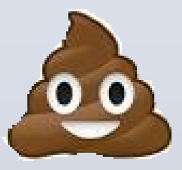
### Antimicrobial consumption evaluation

Total of all veterinary antimicrobials sold in Belgium (2011 to 2015) adjusted with the biomass



### Antimicrobial resistance evaluation



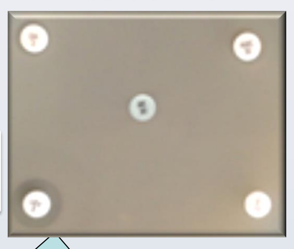


Isolate *E. coli* and determine Minimal Inhibitory Concentration (MIC) for

- Ampicillin (AMP)
- Chloramphenicol (CHL)
- Ciprofloxacin (CIP)
- Colistin (COL)
- Cefotaxime (FOT)
- Gentamicin(GEN)
- Nalidixic acid (NAL)
- Sulphamethoxazole (SMX)
- Ceftazidime (TAZ)
- Tetracycline (TET)
- Trimethoprim (TMP)

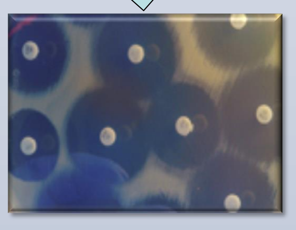
≥170 faecal isolates per year (2011-2015) for veal calves, beef cattle, broiler chickens, pigs

If MIC>cut-off → Resistant

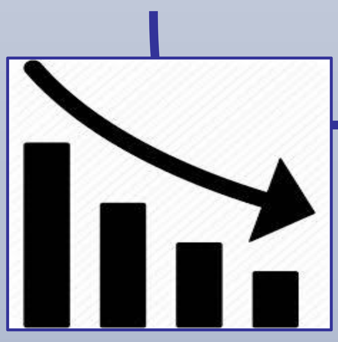


Epidemiological Cut-offs defined by the European Committee on Antimicrobial Susceptibility Testing

If MIC≤cut-off → Susceptible

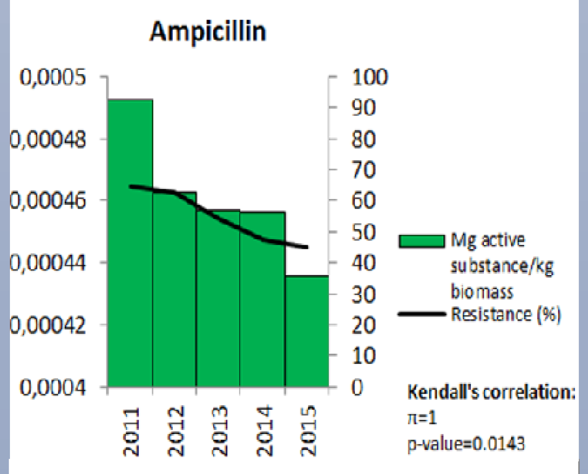


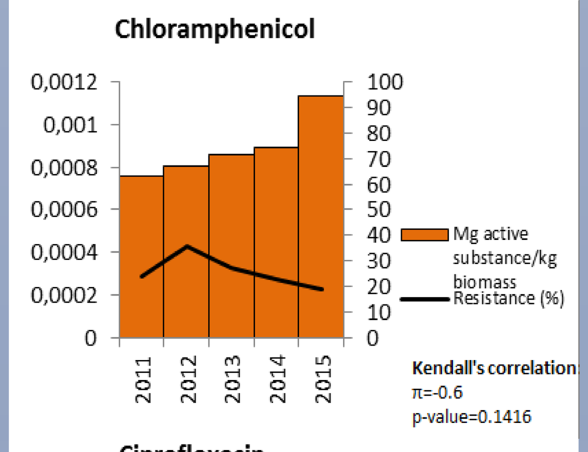
### Correlation?

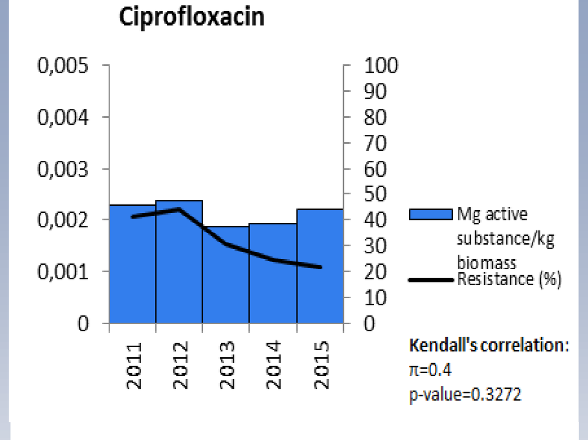


Pearson
Spearman's rho
Kendall's tau
Logistic regression

## Results and perspectives



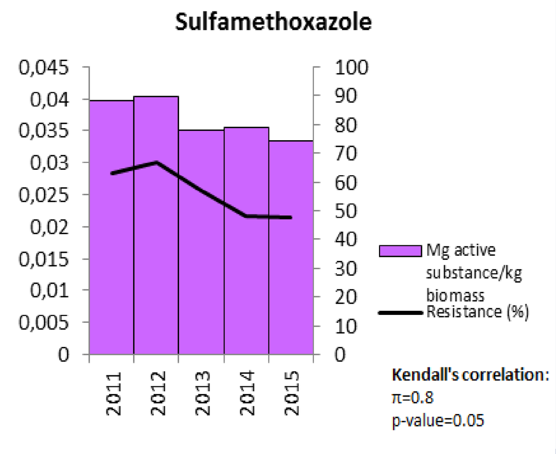



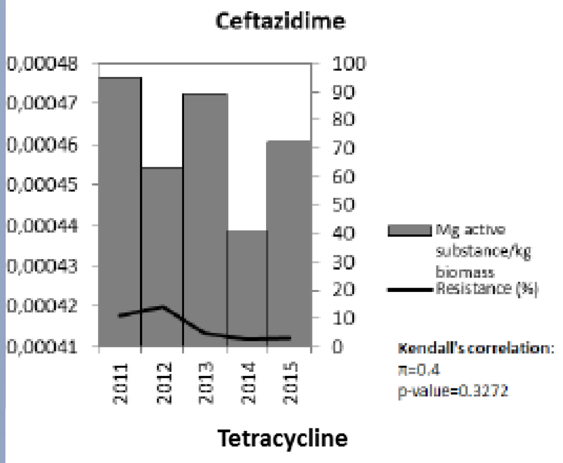



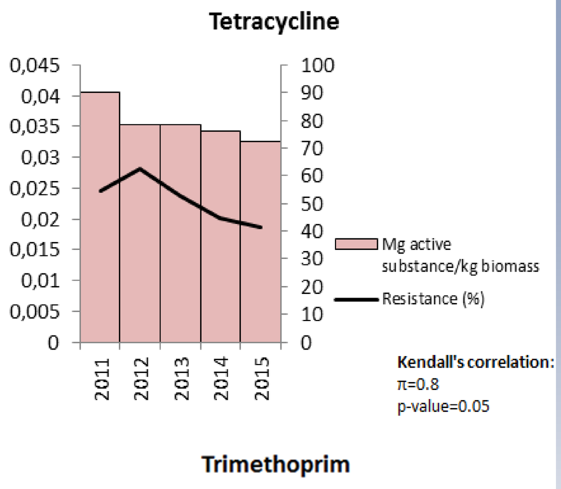

Results were obtained by Kendall's model that best suited our aggregated, non-parametric, non-linear data. It is also better resistant to outliers than the Spearmans' model (Croux and Dehon,2010). The effect was subsequently quantified via logistic regression.

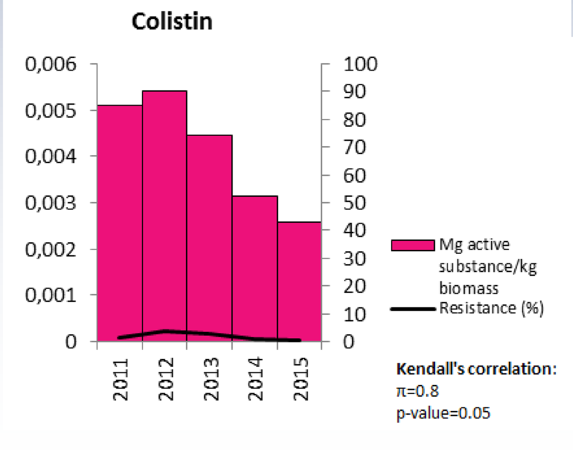
Interestingly, in spite of **continuous decrease in consumption** of most antimicrobials and complete prohibition for chloramphenicol in food animals, marked resistance is still observed.
Except for ampicillin ($p$=0.01), the **Kendall's model could not assess a significant correlation** ($p$<0.05) between antimicrobial consumption and resistance during the study period. It should be noticed that **positive correlations** were found for most antimicrobials, yet borderline significant for colistin, sulfamethoxazole, trimethoprim and tetracycline ($p$=0.05).
Logistic regression models showed **significant positive associations** between specific antimicrobial use and resistance, except for gentamicin and chloramphenicol. When considering total use, there is a **significant positive association** between resistance and total use, except for colistin and gentamicin.

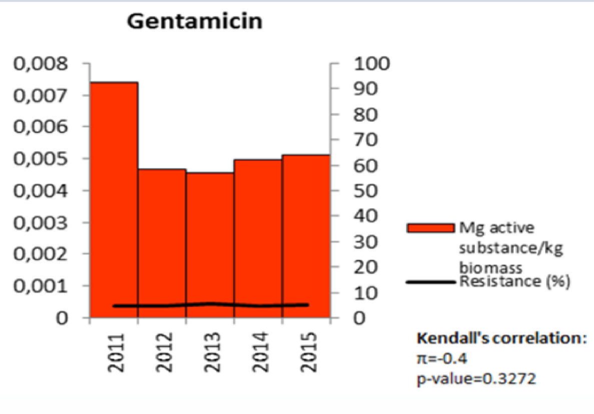
Results should only be considered valid for indicator *E.coli,* and should not be readily extrapolated to other antimicrobial–bacteria combinations. Consumption can induce direct resistance but resistance can also occur through indirect selection (co-resistance) (Bell *et* al., 2014; Harada and Asai, 2010), through exposure to disinfectants, antiseptics, preservatives and heavy metals (European Food Safety Authority, 2016; Wales and Davis, 2015).
These analyses were performed on small datasets, though, and care must be taken while making inference.
From 2017 onwards, data concerning resistance and consumption will be collected each year in Belgium following the launching of a mandatory notification and documentation system (SANITEL-MED) allowing the analysis on non-aggregated data.

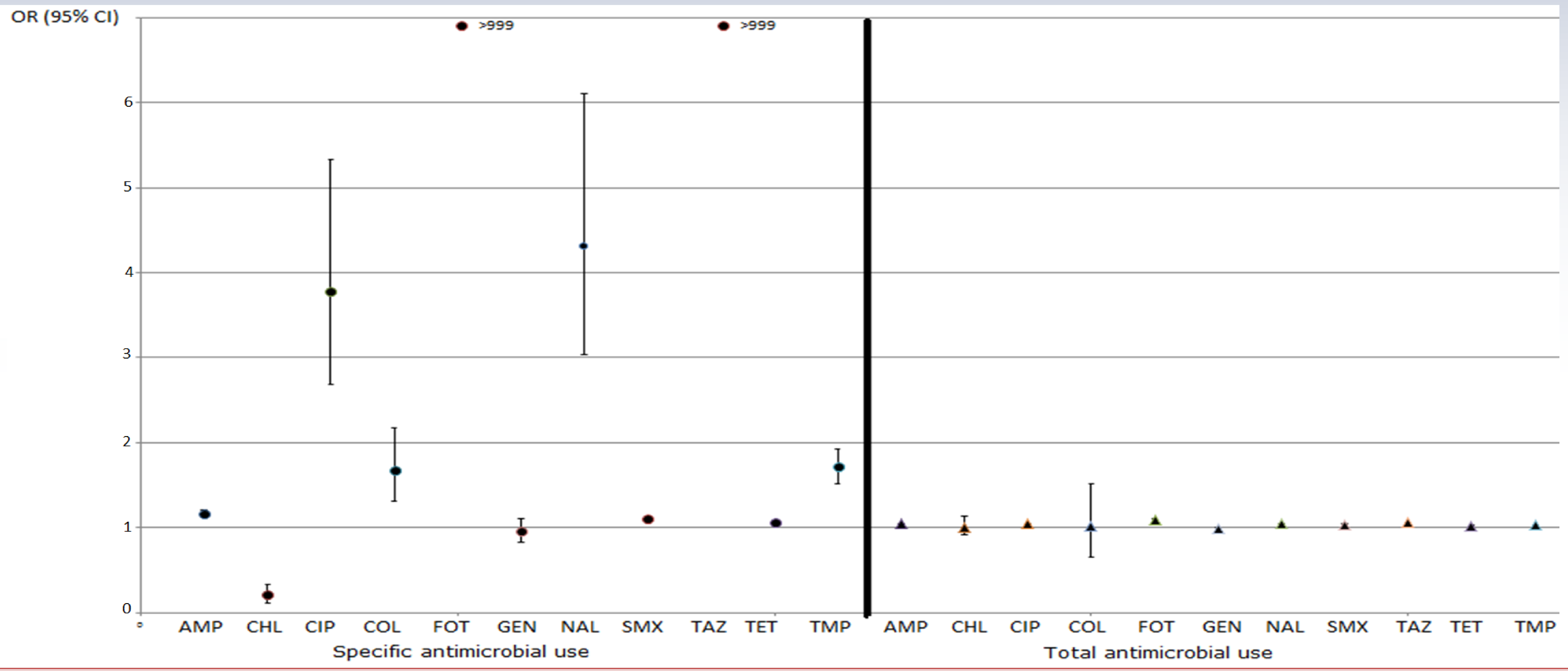


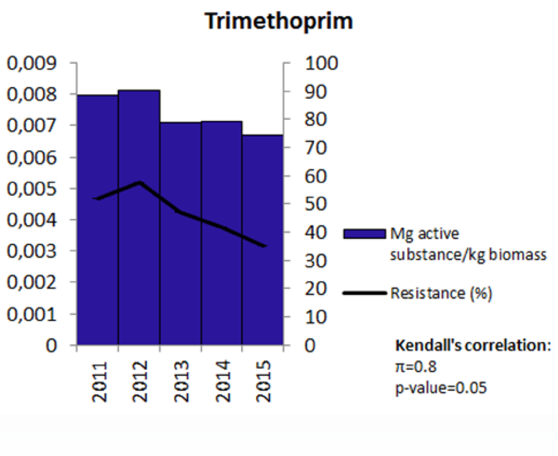



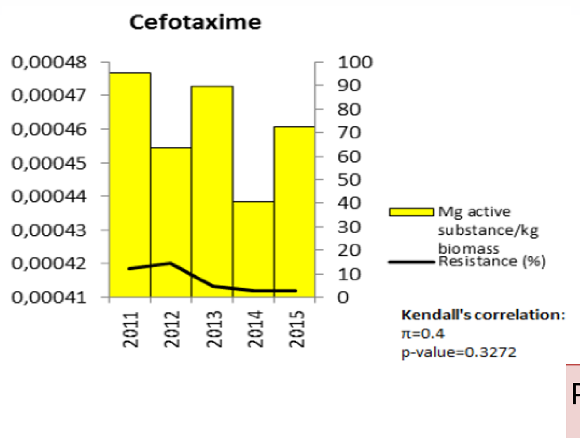



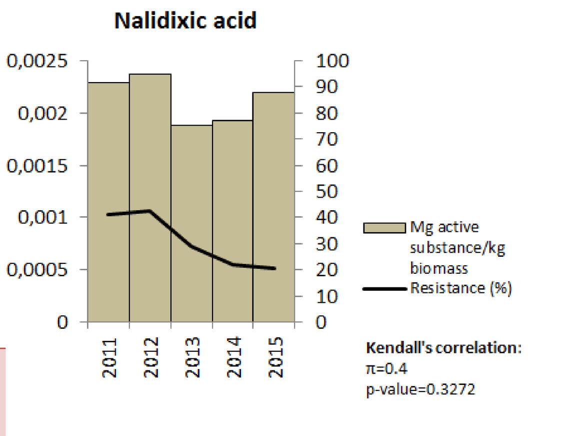




Probabilities (Odds ratios and 95% Confidence Interval (CI)) for an *E. coli* isolate to be resistant to an antimicrobial tested per increase in use of 1 kg of the corresponding antimicrobial class/kg biomass or the total antimicrobial use/kg biomass for all animals in Belgium between 2011 and 2015.

BELL B., SCHELLEVIS E., STOBBERINGH E., GOOSSENS H., PRINGLE M., A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance, *BMC Infect. Dis*., 2014,**14**,13,
BUROW E., SIMONEIT C., TENHAGEN B.-A., KASBOHRER A. Oral antimicrobials increase antimicrobial resistance in porcine *E. coli* – A systematic review. *Prev. Vet. Med.,* 2014, **113**, 364-375.
CROUX C., DEHON C., Influence functions of the Spearman and Kendall correlation measures, *Stat, Methods Appt,*2010,**19**,497-515.
EUROPEAN FOOD SAFETY AUTHORITY, Revision of the currently authorised maximum copper content in complete feed, 2016, *EFSA J.*, **14,**
HARADA K., ASAI T., Role of antimicrobial selective pressure and secondary factors on antimicrobial resistance prevalence in *Escherichia coli* from food-producing animals in Japan. *J. Biomed. Biotechnol.*,2010,**12**
HORIGAN V., KOSMIDER R., HORTON R., RANDALL L., SIMONS R., An assessment of evidence data daps in the investigation of possible transmission routes of extended spectrum B-lactamase producins Escherichia coli from livestock to humans in the UK. *Prev. Med. Vet.*,2016,**124**,1-8.
MEGHA M. Current scenario of antibiotic resistance and latest strategies to overcome it, *Indian J. Community Health*,2014,**26**,3.
WALES A., DAVIS R., Co-selection of resistance to antibiotics, biocides and heavy metals, and its relevance to foodborne pathogens. *Antibiotics*,2015,**4**,567-604