# ADVISORY COMMITTEE ON ANIMAL FEEDINGSTUFFS

## 68th Meeting of ACAF on 28 October 2015

## Antimicrobial Resistance - Presentation on the work of JIACRA

**John Threlfall - JIACRA**
**October 2015**

# *JIACRA*

## Joint Interagency Antimicrobial Consumption and Resistance Analysis

## Final Report

Advisory Committee on Animal Feedingstuffs

28th October 2015

## WHAT IS JIACRA?

- First joint report by ECDC/EFSA/EMA on the integrated analysis of consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from the human and food-producing animal sectors

- Published by EMA, 30th January 2015

## WHO PROVIDED DATA?

The EU Agencies and other members of various networks providing data from their surveillance networks were:

- ECDC: EARS-Net, ESAC-Net and FWD-Net;
- EFSA: Scientific Network for Zoonosis Monitoring Data;
- EMA: ESVAC.

**Chair of JIACRA: Gérard Moulin (ANSES)**

# REPORT CONTENT (1)

- Description of existing monitoring and / or surveillance systems
- Methodological considerations and included data
- Consumption of antimicrobials by humans and food-producing animals in the EU from 2011-2012
- Antimicrobial resistance in bacteria from food-producing animals and from humans over this period
- Possible correlations between the occurrence of resistance in isolates made from humans and in bacteria originating from food-producing animals

# REPORT CONTENT (2)

- Report utilises data from 2011 and 2012 from 5 different surveillance networks, collecting data from the EU countries, Iceland, Norway and Switzerland.

- Datasets used collected for purposes that were not *a priori* an integrated analysis.

- Analyses limited to certain combinations of antimicrobials and bacterial species.

# ESTIMATED BIOMASS AND CONSUMPTION DATA

- Estimated biomass, expressed as 1000-tonnes: 28 884 for humans, 55 421 for animals.

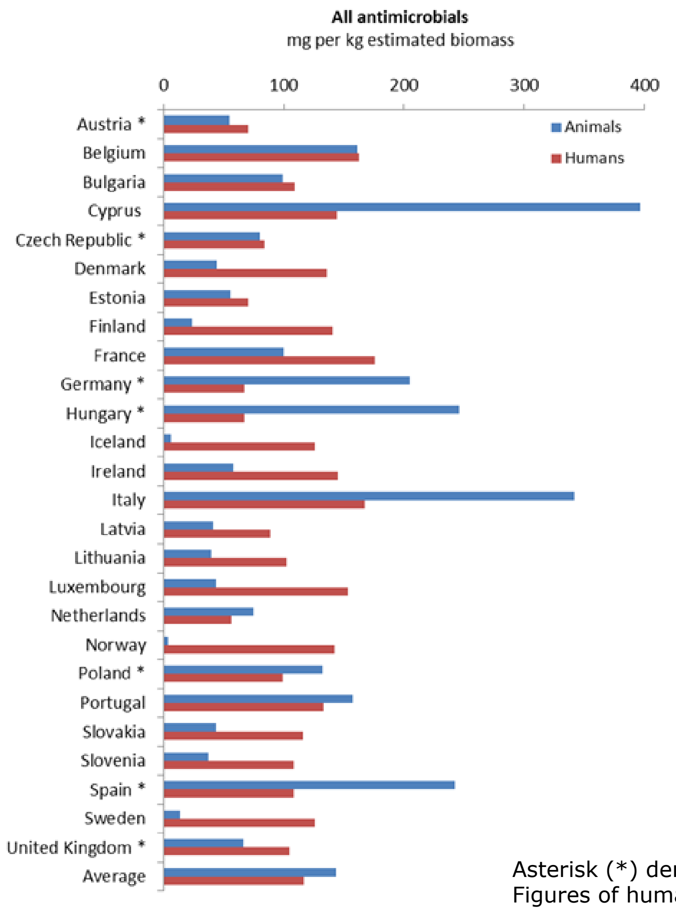
- Human: Total consumption: 116.4 mg/kg of estimated biomass (range: 56.7 – 175.8 mg/kg)

- Animal:144.0 mg/kg. (range: 3.8 – 396.5 mg/kg)

- In 11/26 (42 %) countries, consumption for animals lower than for people; in five countries (19 %) consumption was similar. in 10 (38 %) countries sales for animals clearly higher than for  people and in five of these consumption in animals much higher than in humans.

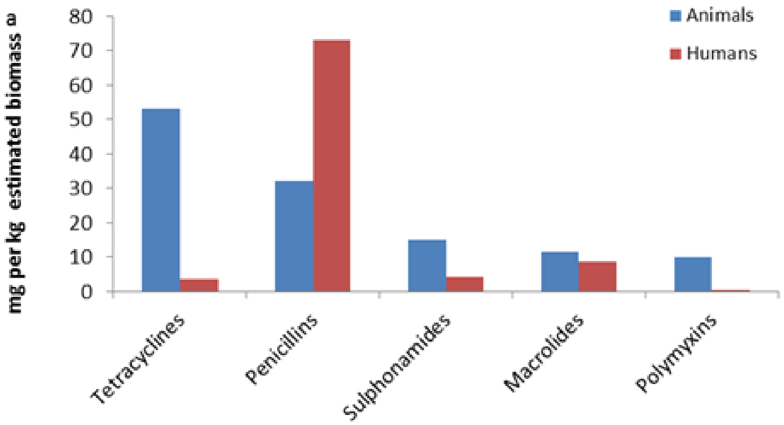
- Overall consumption of antimicrobials (population weighted mean) higher for animals than for humans.

# Comparison of biomass-corrected consumption of antimicrobials (milligrams per kilogram estimated biomass) in humans and animals by country in 26 EU/EEA countries in 2012




Asterisk (*) denotes that only community consumption data were available for human medicine. Figures of human sales from these countries probably represent a considerable underestimate.

# Comparison of consumption of selected antimicrobial classes for humans and food-producing animals in 26 EU/EEA countries in 2012



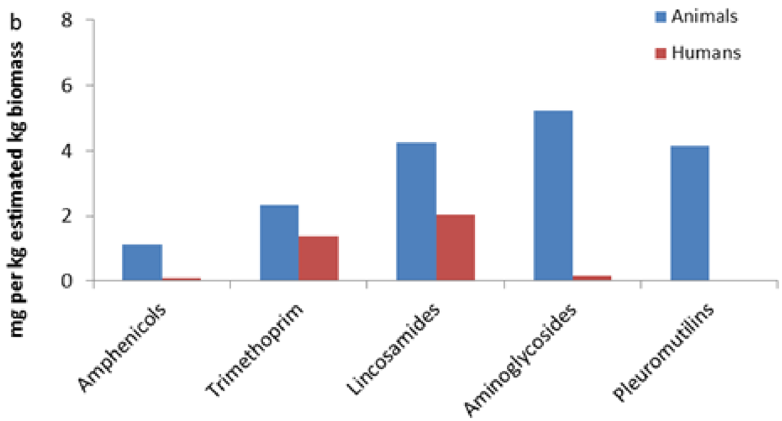

Highest selling AM classes:

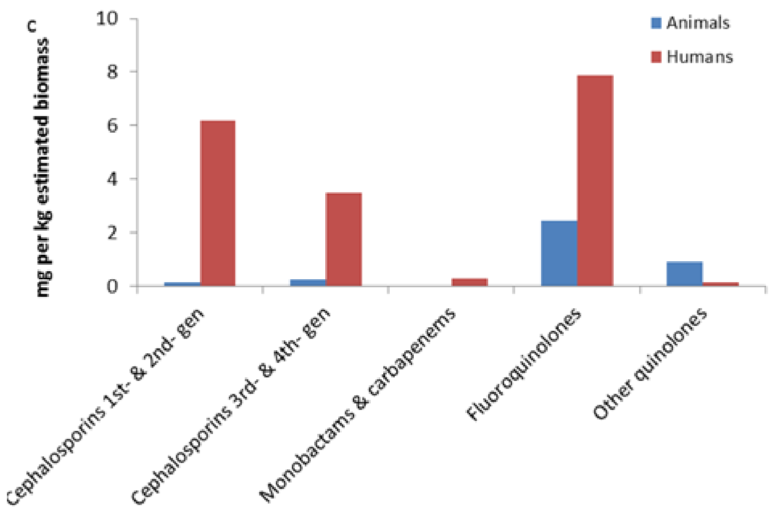
- Human medicine:

penicillins, macrolides, fluoroquinolones

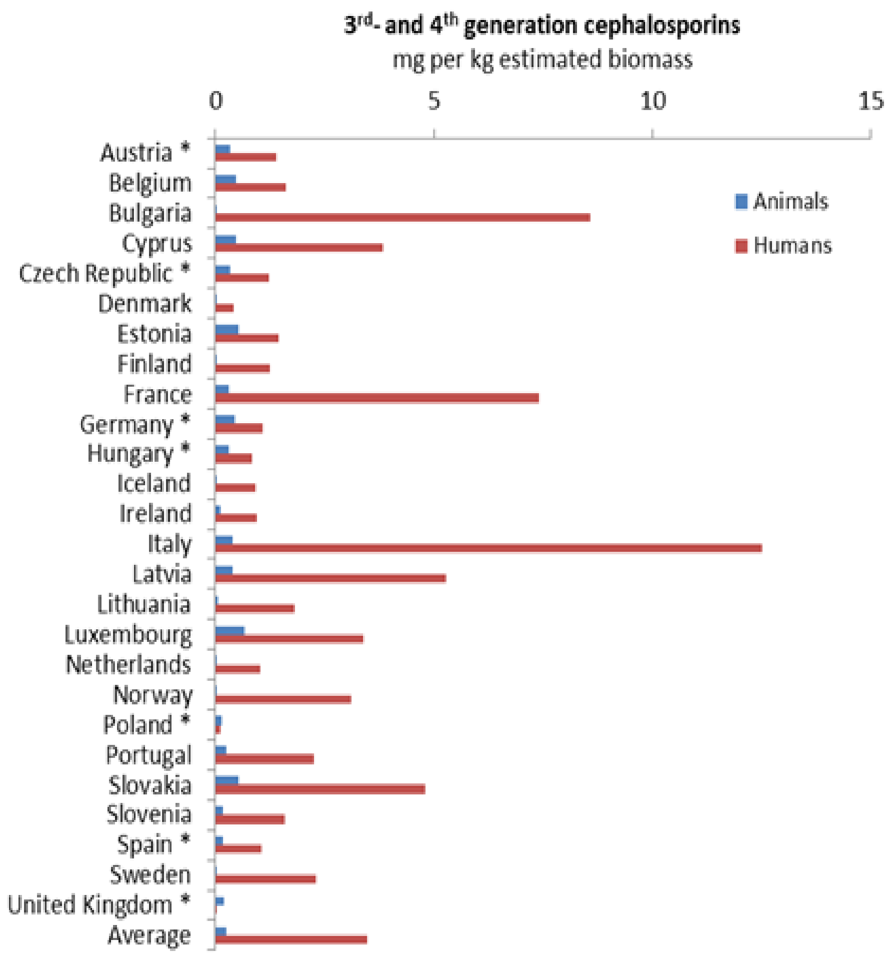
- Food-producing animals:

tetracyclines, penicillins, sulphonamides



# *Biomass-corrected consumption of 3rd- and 4th-generation cephalosporins by humans and food-producing animals by country in 26 EU/EEA countries in 2012*




Consumption of 3rd- and 4th-generation cephalosporins much lower for animals than for humans.

These antimicrobial classes ares predominantly used in hospitals, and therefore the comparison may be misleading for countries not reporting (*) such hospital consumption.

Asterisk (*) denotes that only community consumption data were available for human medicine. Figures of human sales from these countries probably represent a considerable underestimate.

COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

# Overview of data available in animals

Cattle

Pigs

Poultry

Others

All animal species addressed together

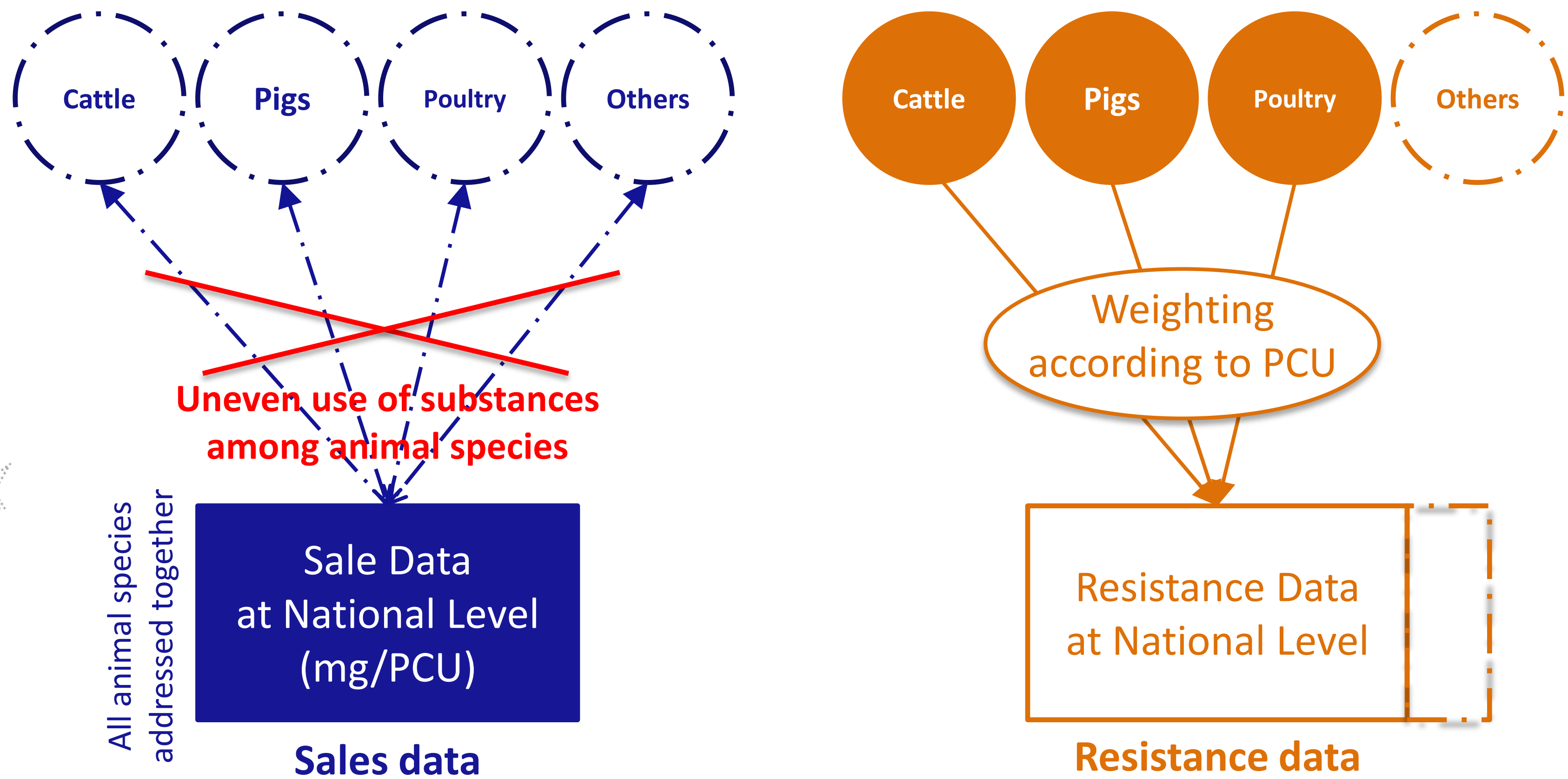
Sales Data
at National Level
(in mg/PCU)

**Sales data**

**Resistance data**

COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

# Summary indicator of resistance in animals



# COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

## Sales (mg/PCU) vs. 'summary indicator' of Resistance

- 'Summary indicators' of resistance:
- Combining two or three animal species: Broilers / Pigs / Cattle
    - Weighted mean of 'Resistance per species'
    - PCU: weight to allow comparability between sales data
    - Implicit assumption: Excretion proportional to the PCU

$$Ind_{Res} = \frac{1}{\mathrm{PCU}_{cattle} + \mathrm{PCU}_{fowl} + \mathrm{PCU}_{pigs}} . (\mathrm{PCU}_{cattle} . \mathrm{Res}_{cattle} + \mathrm{PCU}_{fowl} . \mathrm{Res}_{fowl} + \mathrm{PCU}_{pigs} . \mathrm{Res}_{pigs})$$

## COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

# Graphical comparisons – WG approach

- Logistic regression accounting for the true nature of data
- *Proc logistic* using SAS software
- Grouped data: group=country
  - ‘Overdispersion’
    - Isolates are grouped into naturally occurring clusters. Isolates originating from the same country (the same domestic production sectors) are not independent, as they are exposed to many common factors that may produce the same outcome (antimicrobial susceptibility status).
  - Small sample sizes: Profile Likelihood CLs
  - Sensitivity analysis to ‘influential points’

# KEY ANTIMICROBIALS

**Antimicrobials surveilled in terms of sales / resistance in indicator organisms were:**

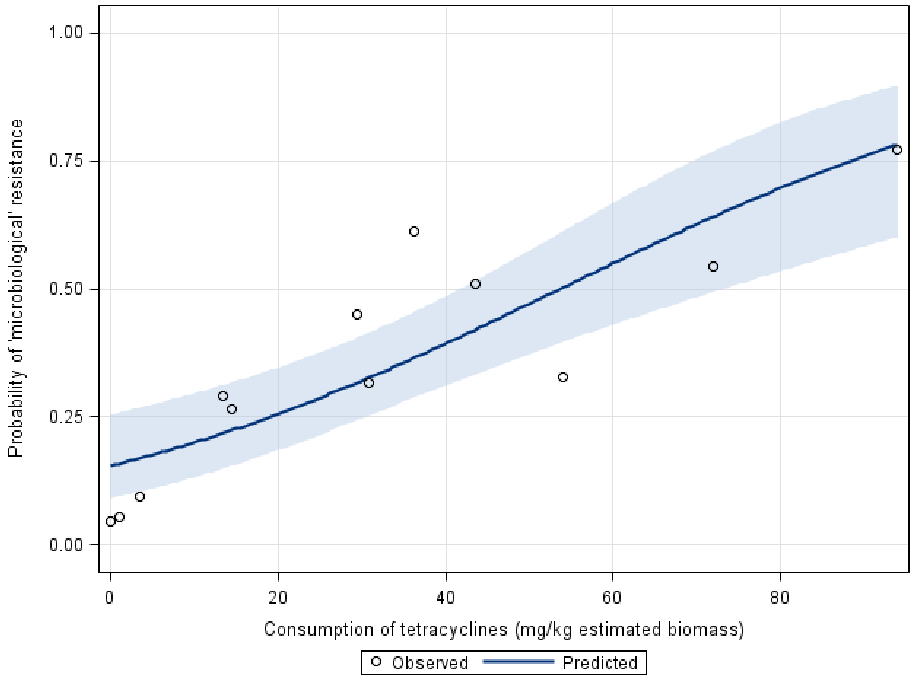
| | |
|---|---|
| Tetracyclines* | (TET) |
| Cephalosporins (CEPH) † | Cefotaxime |
| Fluoroquinolones / Quinolones (FQ, Q)** | Ciprofloxacin (CIP) |
| Macrolides † † | Erythromycin (ERY) |

**Indicator organisms**

* *E. coli* and *Campylobacter jej*uni
† *E. coli*
** *E. coli*
† † *C. jejuni*

# COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

## Indicator *E. coli:* Sales of TET / Resistance to TET



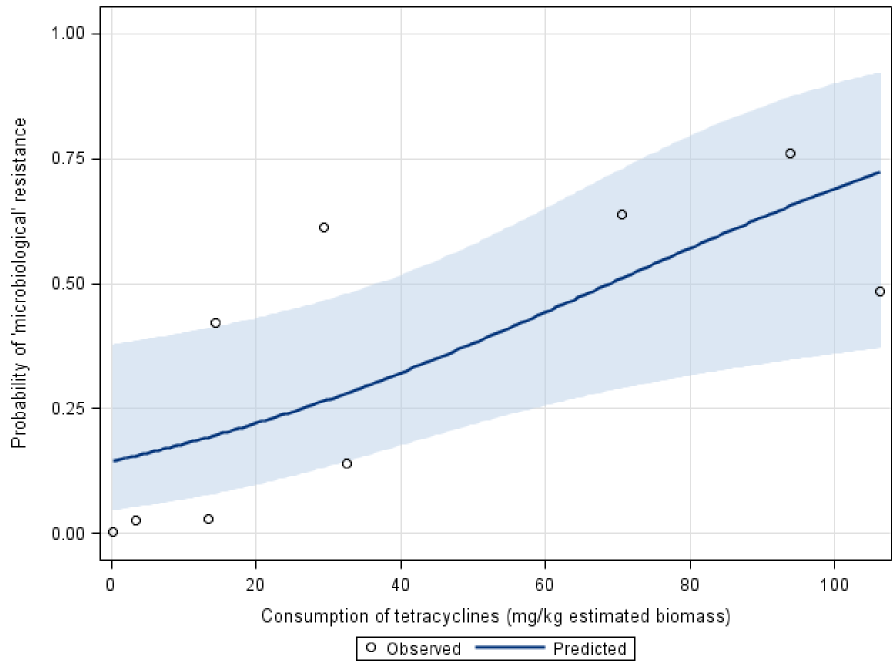

<u>Countries included</u>:
AT, BE, DE, DK, ES, FI, FR, NL, PL, SE + CH, NO

P<.05; OR=1.032; 95% PL CI: [1.019, 1.047]

<u>Note:</u> the association remains significantly positive after ignoring the point displayed on the upper right corner of the graph: p-value<0.05; OR=1.033; 95% PL CI: [1.014, 1.052]

COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

# Indicator *C. jejuni* – Sales of TET – Resistance to TET

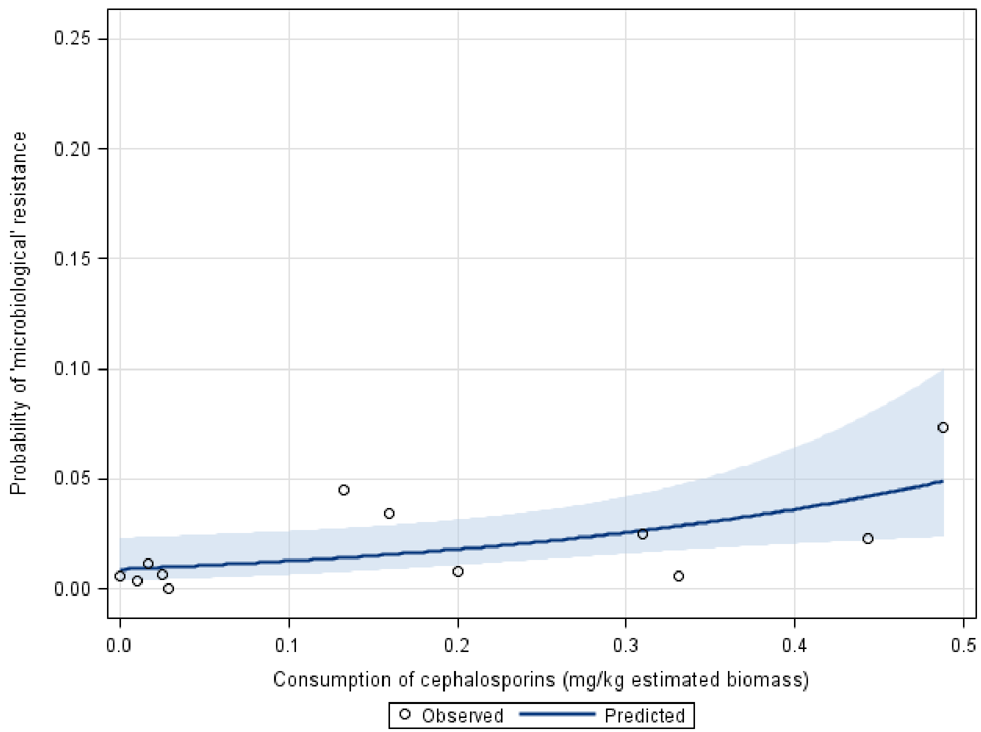



Countries included: AT, DE, DK, ES, FI, IT, NL + CH, NO

P<.05; OR=1.026; 95% PL CI: [1.006, 1.050]

Note: the association remains significantly positive after ignoring the point displayed on the middle right side of the graph: P<.05; OR=1.038; 95% PL CI: [1.012, 1.073]

# Indicator *E. coli:* Sales of CEPH / Resistance to CTX




Countries included:

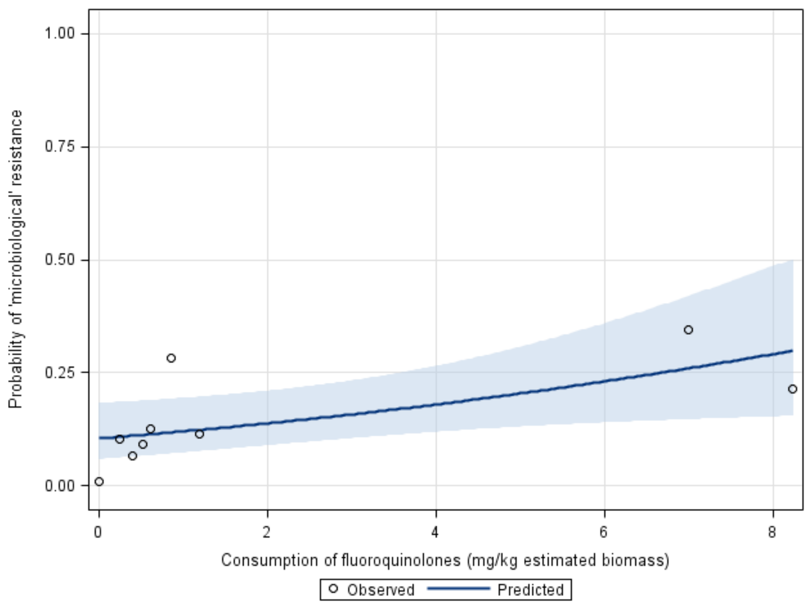
AT, BE, DE, DK, ES, FI, NL, PL, SE + CH, NO

P<.05; $OR_{0.1\text{-unit increment}}$=1.429; 95% PL CI: [1.079, 1.930]

# COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

## Indicator *E. coli:* Sales of FQ and Q /Resistance to CIP

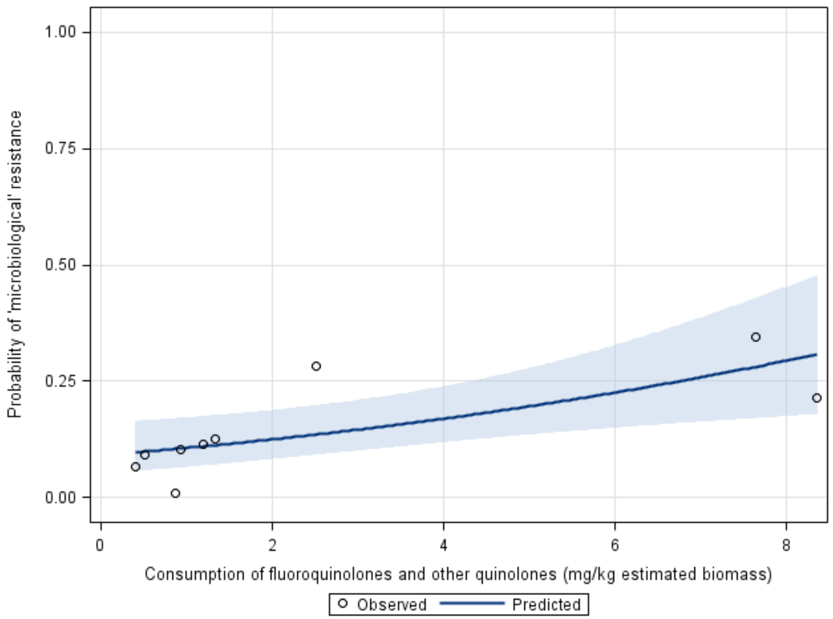
**A.**




Countries included: AT, BE, DE, DK, ES, FR, NL, PL + CH

P<.05; OR=1.170; 95% PL CI: [1.015, 1.344]

**B.**



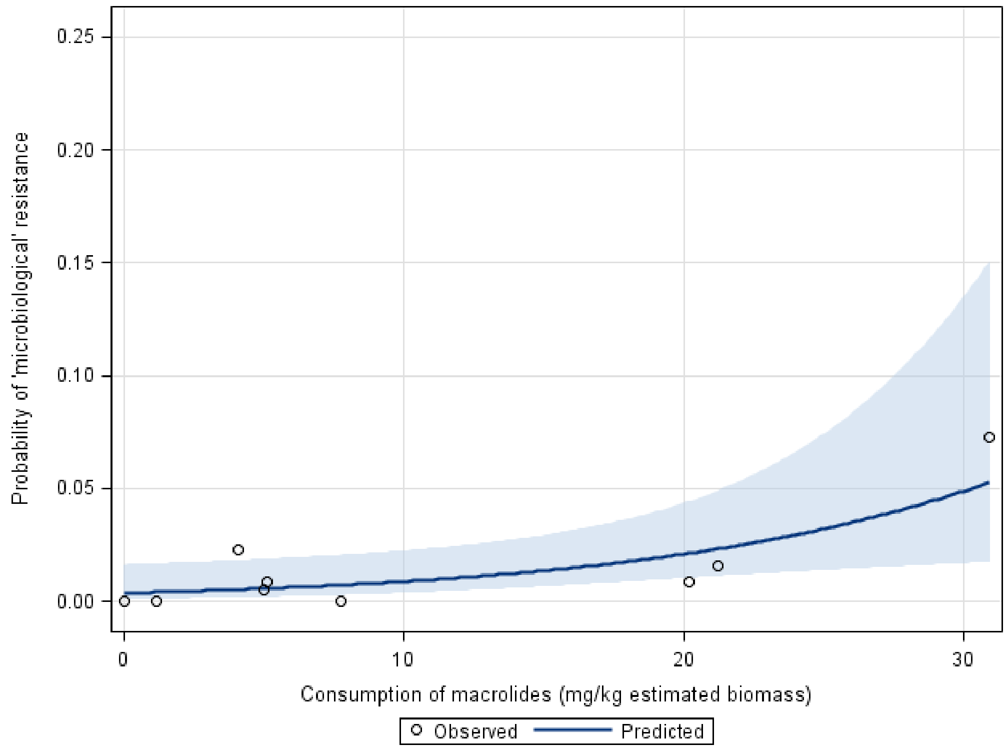

Countries included: AT, BE, DE, DK, ES, FR, NL, PL + CH

P<.05; OR=1.195; 95% PL CI: [1.052, 1.356]

Note: the association does remain significantly positive after ignoring the two points displayed on the right side of the graph: P<.05; OR= 2.415; 95% PL CI: [1.596, 3.652]

COMPARISON OF ANTIMICROBIAL SALES AND RESISTANCE IN ANIMALS

# Indicator *C. jejuni:* Sales of MACROLIDES / Resistance to ERY




Countries included: AT, DK, FI, DE, IT, NL, NO, ES, CH

P<.05; OR=1.091; 95% PL CI: [1.018, 1.176]

## CONSUMPTION AND RESISTANCE - ANIMALS

- Positive association between antimicrobial consumption in food-producing animals and occurrence of resistance in bacteria from such animals.
- Strongest associations for antimicrobials studied were in relation to indicator *Escherichia coli*.
- Positive associations also noted for *Salmonella* spp. and *Campylobacter* spp.
- Positive association between total consumption of $3^{rd}$- and $4^{th}$-generation cephalosporins and occurrence of resistance to $3^{rd}$-generation cephalosporins in *E. coli*.

# CONSUMPTION AND RESISTANCE - HUMANS

- Positive association between total consumption of $3^{rd}$- and $4^{th}$-generation cephalosporins and occurrence of resistance to $3^{rd}$-generation cephalosporins in *E. coli*.
- Positive association between total consumption of fluoroquinolones and occurrence of fluoroquinolone resistance in *E. coli*.
- No association between consumption of fluoroquinolones and occurrence of fluoroquinolone resistance in *Salmonella* spp., *S.* Enteritidis and *S.* Typhimurium from cases of human infection.

## CONSUMPTION AND RESISTANCE : ANIMALS – HUMANS (1)

- Resistance in *E. coli* causing bloodstream infections could be correlated with usage of antimicrobials in animals and in the human population.
- For both cephalosporins and fluoroquinolones, positive associations between occurrence of resistance in indicator *E. coli* from animals and occurrence of resistance in *E. coli* from humans.
- No associations between the consumption of $3^{rd}$- and $4^{th}$-generation cephalosporins in food-producing animals and occurrence of resistance to this sub-class in selected bacteria from humans.

## CONSUMPTION AND RESISTANCE : ANIMALS – HUMANS (2)

- Positive associations for consumption of fluoroquinolones in food-producing animals and occurrence of resistance in *E. coli* from humans, but not for *Salmonella* spp. and *Campylobacter* spp.

- Positive associations for consumption of macrolides in food-producing animals and occurrence of resistance in *Campylobacter* spp. from cases of human infection.

- Positive associations for consumption of tetracyclines in food-producing animals and occurrence of resistance in *Salmonella* spp. and *Campylobacter* spp. from cases of human infection.

# CONCLUSIONS

- Associations between consumption of selected combinations of antimicrobials and the occurrence of resistance in bacteria mostly, but not always, observed.

- Epidemiology of resistance is complex. Several factors aside from antimicrobial consumption influence occurrence of resistance.

- Wide variations between countries, both in the overall consumption figures and for consumption of the $3^{rd}$- and $4^{th}$-generation cephalosporins and fluoroquinolones.

# CAVEATS

- Data on antimicrobial consumption in food-producing animals not available by species.

- Differences in systems for collection and reporting of data on antimicrobial consumption and resistance in bacteria from humans and food-producing animals have limited the potential for direct comparison.

- Due to characteristics of data, interpretation criteria, and units of measurement, results should be interpreted with caution.

# DISCUSSION POINTS FOR FUTURE ANALYSES

- To improve integrated analyses, more detailed and comprehensive data required.

- Factors such as antimicrobial consumption per animal species, resistance data from all countries, from relevant animal species and food, at a detailed level, would be required.

- Other factors to be considered include: resistance to other antimicrobials (co-resistance), resistance in non food-producing animals (e.g., reptiles), travel, imports of meat from countries outwith the EU.

Thank you for your attention!

Questions ??