



# Why do we need antimicrobial stewardship in veterinary medicine?

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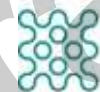
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27th  
**ECCMID** EUROPEAN CONGRESS OF  
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## Based on your perception, what is the contribution of antimicrobial use in animals to human mortality due to AMR?

1. Less than 5%
2. Between 5 and 30%
3. More than 30%





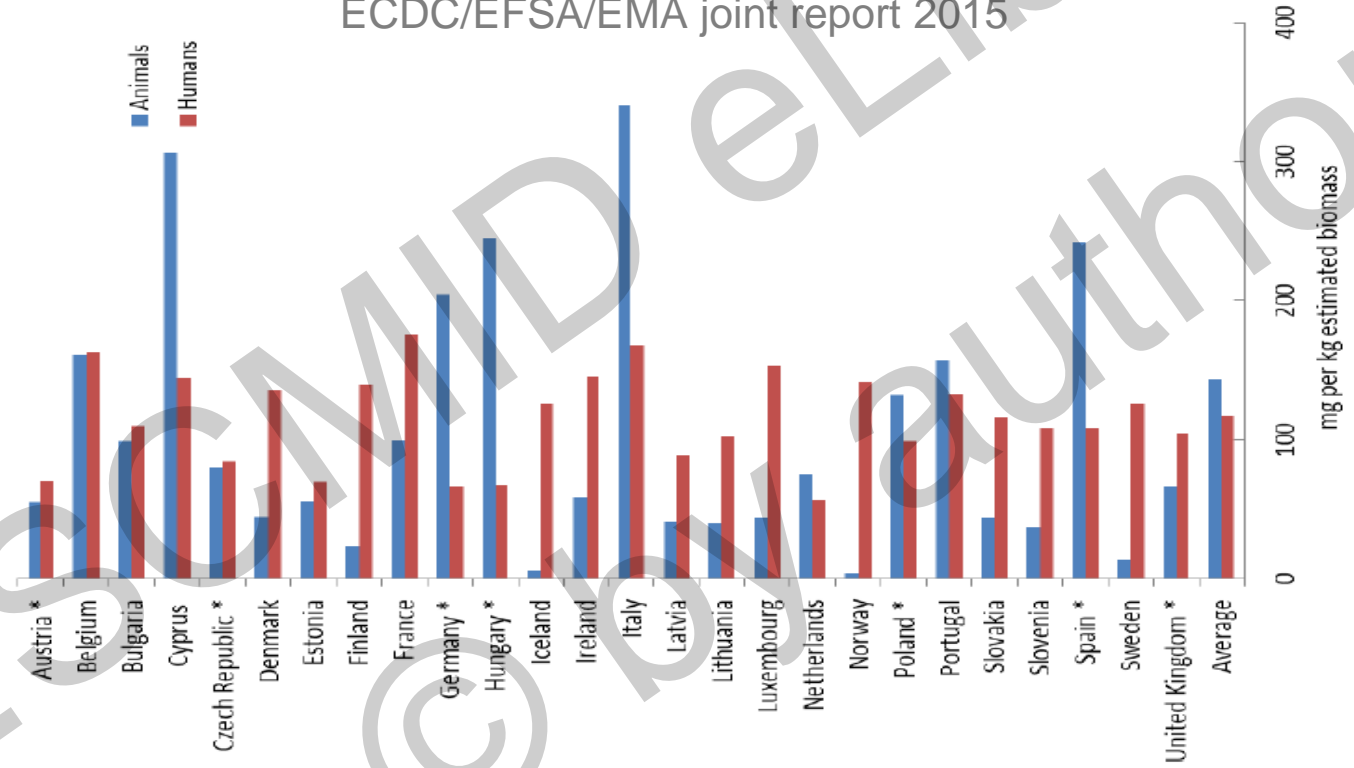
## My answer(s)

1. Most likely much less than 5%
2. I don't know, it is impossible to quantify it (I wasted 20 years of my life trying to answer this questions 😊)
3. Not negligible in any case. Antimicrobial use in animals is not worthy of a single human life (tolerance zero)



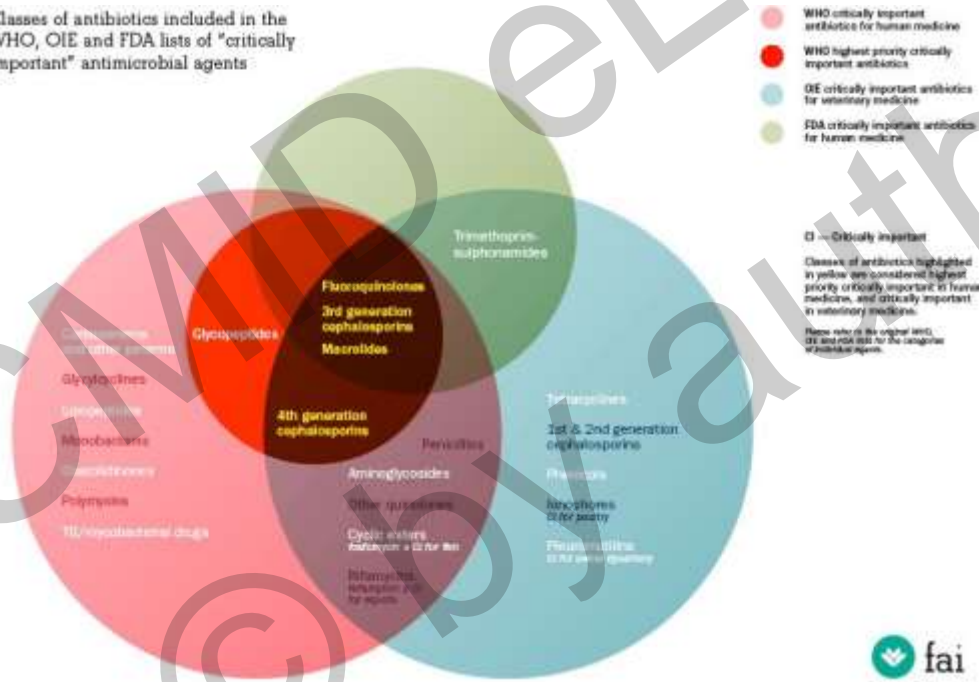
# Antimicrobial consumption in the EU

ECDC/EFSA/EMA joint report 2015



# Critically important antimicrobials in human and veterinary medicine

Classes of antibiotics included in the WHO, OIE and FDA lists of "critically important" antimicrobial agents



- WHO critically important antibiotics for human medicine
- WHO highest priority critically important antibiotics
- OIE critically important antibiotics for veterinary medicine
- FDA critically important antibiotics for human medicine

**□ — Critically important**  
Classes of antibiotics highlighted in yellow are considered highest priority critically important in human medicine, and critically important in veterinary medicine.  
Name refer to the original text, OIE and FDA lists for the complete list of antibiotics.



# Fluoroquinolone consumption in humans & livestock in the EU

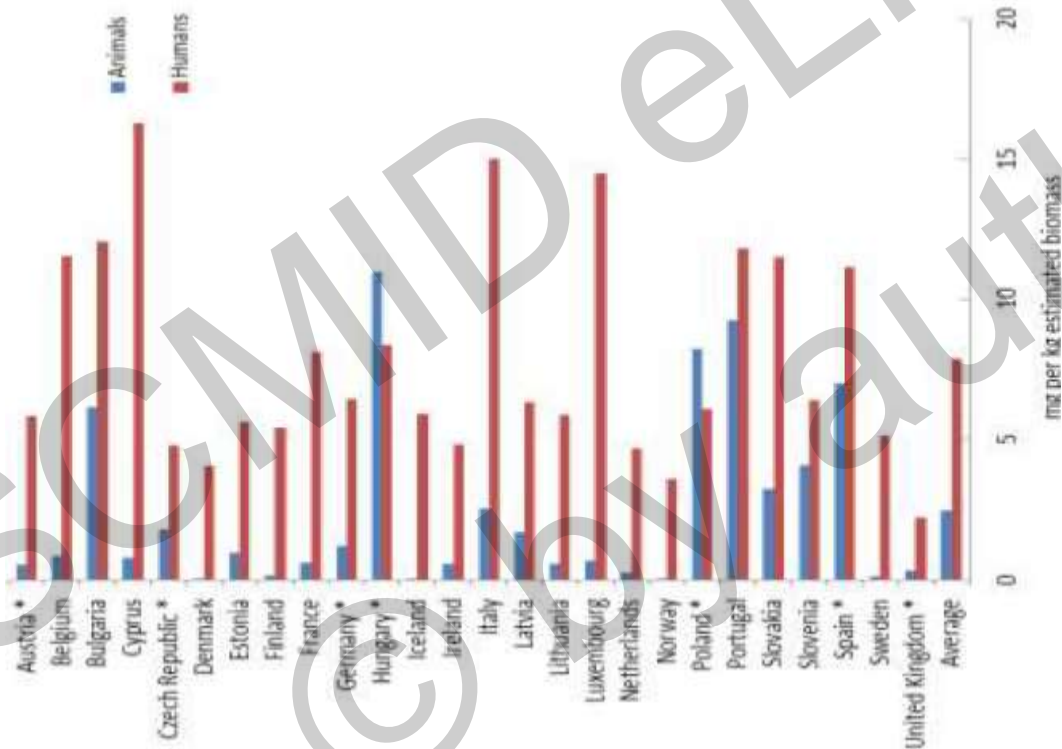


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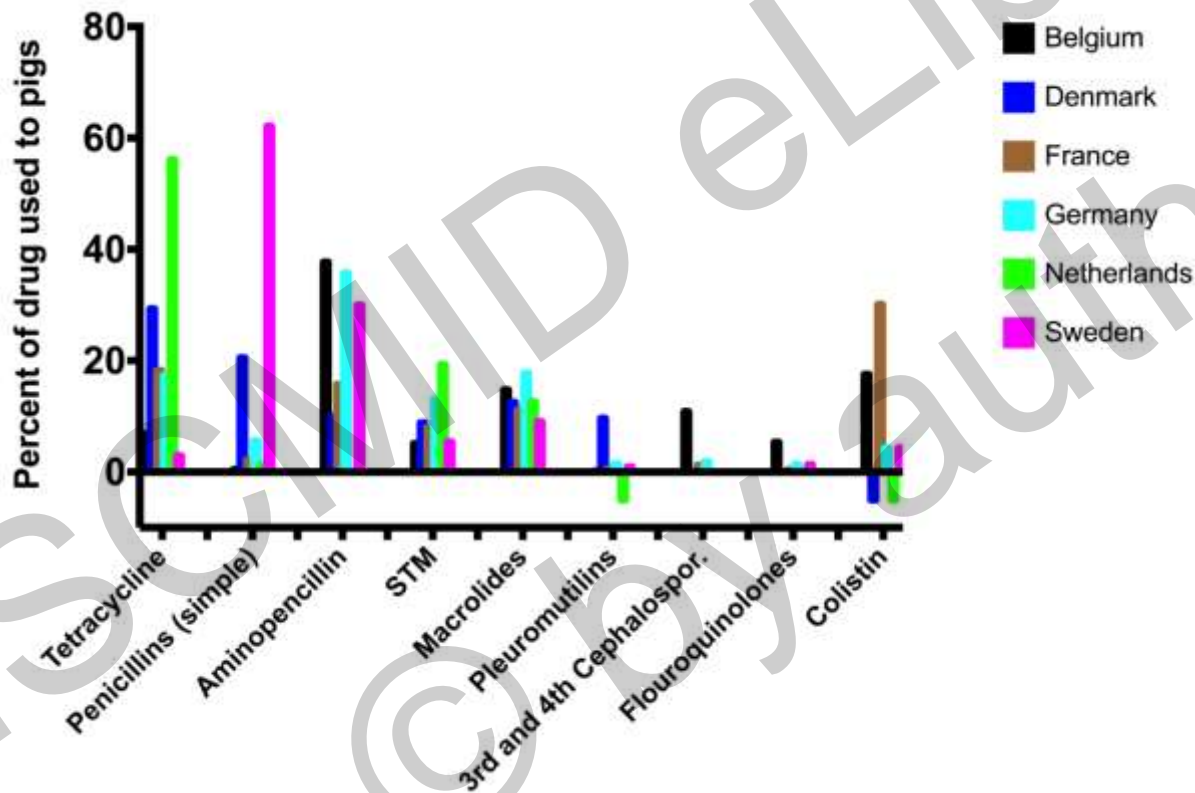
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# Antimicrobial use in pigs by class

Guardabassi et al. 2017 (ASM book chapter in press)







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# Factors that influence geographical patterns of antimicrobial consumption

- Differences in production systems
- Differences in pathogen distribution
- Differences in AMR prevalence
- Differences in drug market availability
- Differences between national regulations





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## More diversity than in human medicine

Multiple animal species with different ethical implications & antimicrobial PK



**Oral bioavailability of amoxicillin varies  
from 28-33% in pigs to 64-77% in dogs**

# More diversity than in human medicine

Diverse breeds and production systems within species

## Meat vs egg chickens

Common Broilers

Common Layers



Cobb 700

White Leghorn

Australorp

Iso Brown



## Dairy vs beef cattle





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# More diversity than in human medicine

High diversity within species



**Great Dane**  
Weight 45-90 Kg



**Chihuahua**  
Weight 1.5-3 Kg



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## Average lifespan in different animal species



**Chicken:** 6 weeks (natural life span: 1 to 8 years)



**Pig:** 6 months (natural life span: 6 to 10 years)



**Cattle:** 4-18 months (natural life span: 18 to 25+ years)



**Dog:** 7-17 years



**Horse:** 25-30 years

# Livestock vs companion animals

ANIMAL HEALTH CONSEQUENCES

LOW AMR IN  
PATHOGENS

FOOD ANIMALS



COMPANION ANIMALS

HIGH AMR IN  
PATHOGENS

PUBLIC HEALTH CONSEQUENCES

## Public health concerns in livestock

- Increasing evidence that certain human MDR infections may originate from food (CTX-M-1 *E. coli*) or direct exposure to animals (livestock MRSA)
- Increasing consumer demand and governmental pressure to reduce overall antimicrobial use in livestock production
- Benchmarking of antimicrobial use per herd and veterinarian has become a very trendy and effective tool to reduce antimicrobial consumption
- Risk of AMR selection by antimicrobial underdosing?





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## Animal health concerns in companion animals

- MDR MRSA, MRSP, ESBL *E. coli* and more recently even CPE in some countries have emerged in companion animals
- Limited therapeutic options are available against M bacteria compared to human medicine
- The current options consist of older drugs with significant side effects and drawbacks (e.g. chloramphenicol and rifampicin)
- Some veterinarians have started using reserve drugs for human use (e.g. carbapenems and vancomycin)...





# Measures for control of AMR in animals

## Control of antimicrobial use

### 1. Legal interventions

- Limiting profit of prescriber
- Penalties for high use
- Ban/restriction

### 2. Disease prevention

### 3. Antimicrobial stewardship

## Control of transmission

### 1. Hospital infection control

### 2. Farm biosecurity

### 3. Improved slaughter hygiene

### 4. Education of consumers and animal owners



# Effects of legal interventions on antimicrobial use in pigs in Denmark

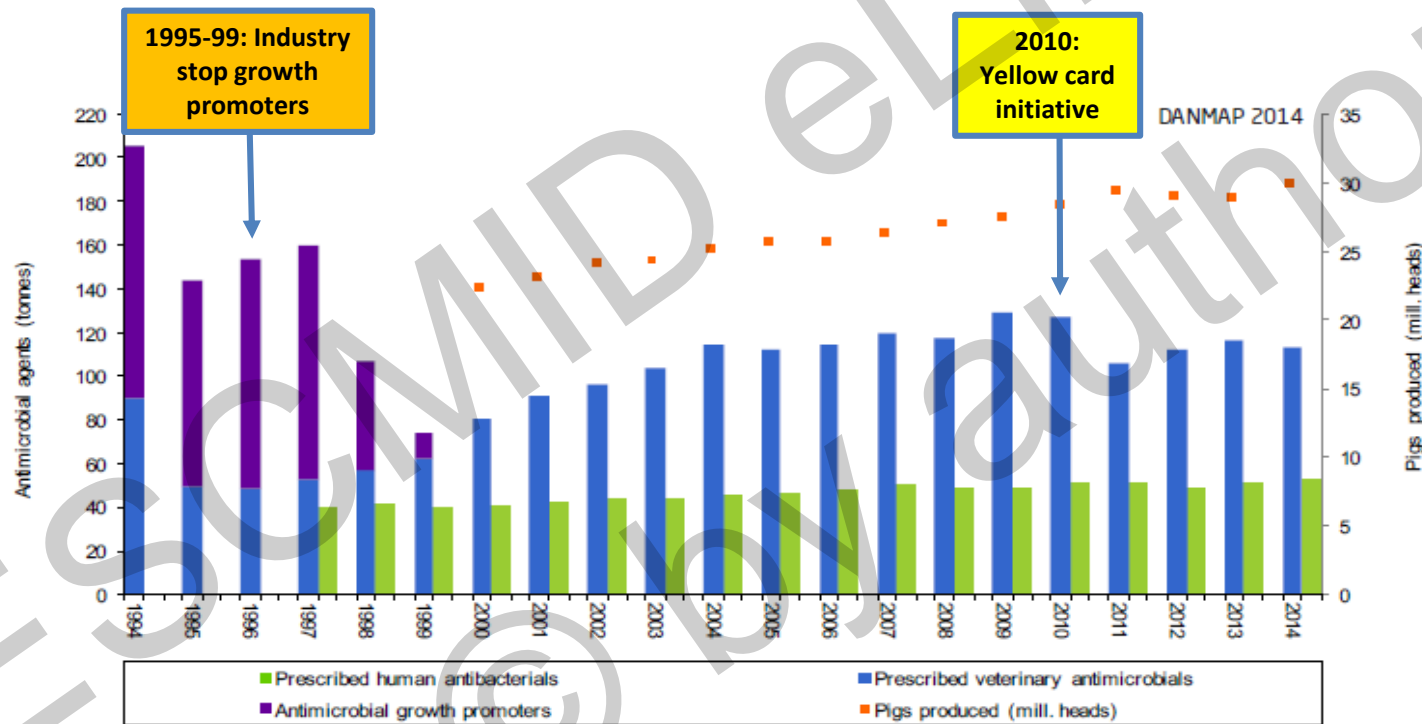


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DANMAP 2014 ([www.danmap.org](http://www.danmap.org))





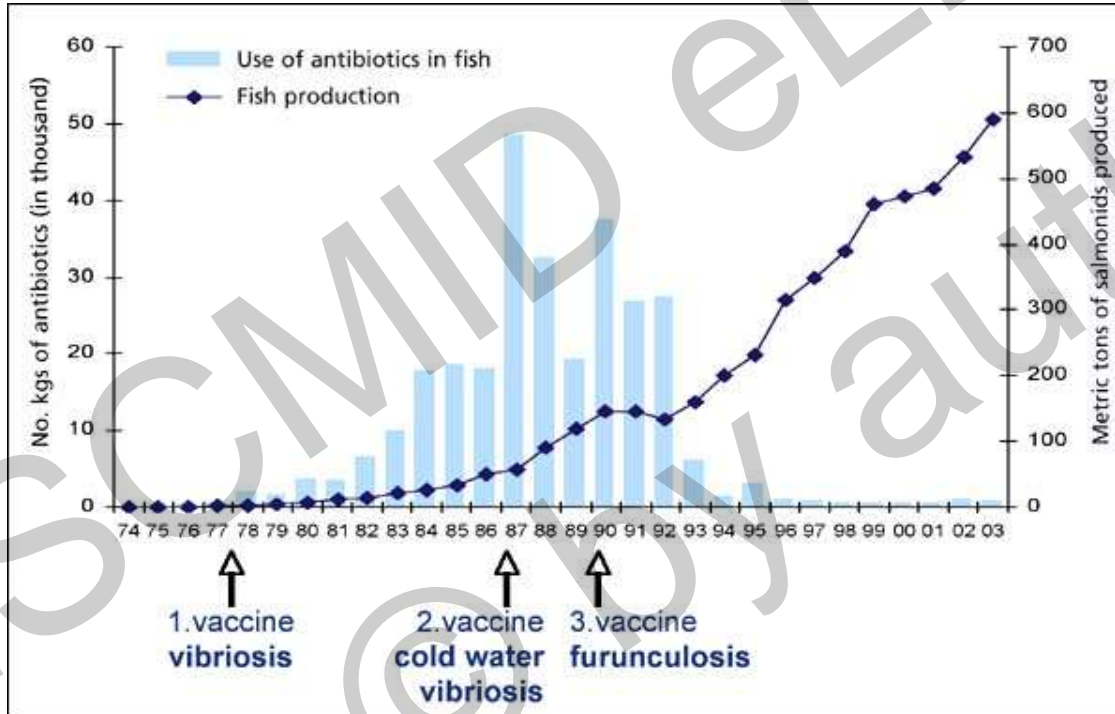
# Effects of vaccination on antimicrobial use in salmon farming in Norway



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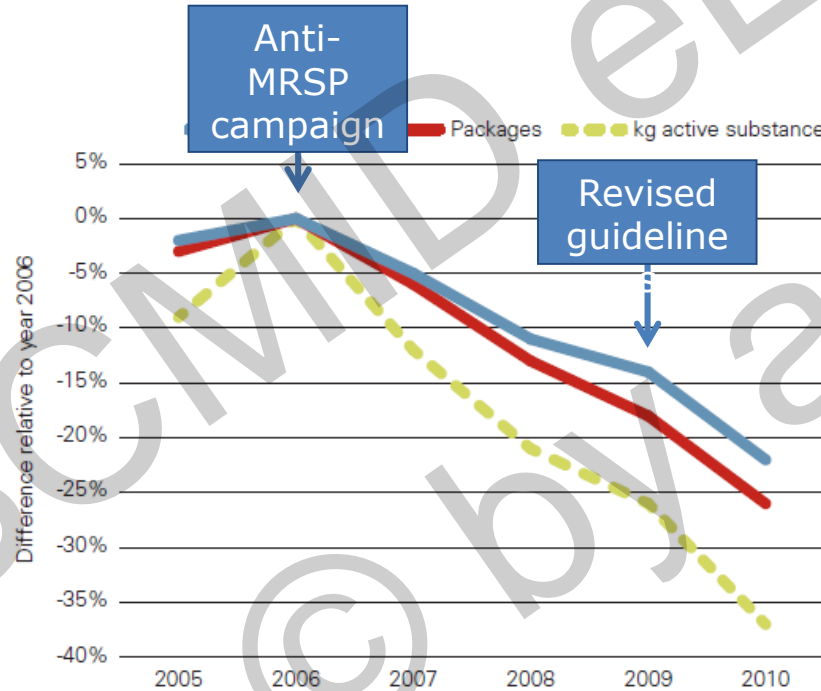
Håstein and Gudding 2005





# Effects of antimicrobial stewardship on antimicrobial use in dogs in Sweden

Data from Sweden ([www.sva.se](http://www.sva.se))





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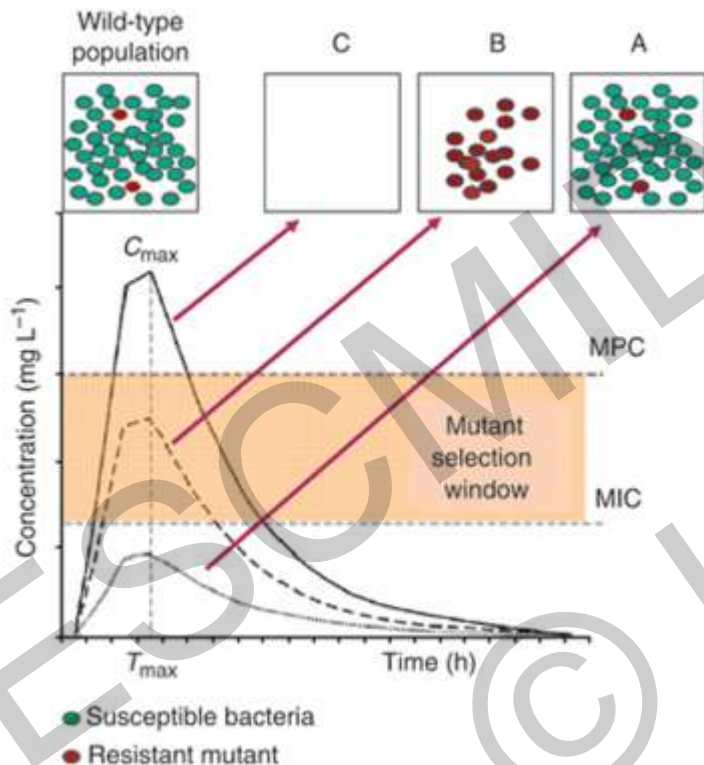
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# General principles of optimal antimicrobial use

- Reducing overall antimicrobial consumption
  - Ban of growth promoters
  - Restricted prophylaxis and metaphylaxis (not ban)
- Improving use of diagnostic testing
  - Increased use of cytology, culture and AST
  - Faster and cheaper testing
- Prudent use of second line, critically important antimicrobials (CIAs)
  - Restricted use of fluoroquinolones, extended generation cephalosporins (macrolides?)
- Optimizing dosage regimens
  - Improved dose, administration interval and treatment duration

# Are we using the right dose?

Awji et al. 2012



In conclusion, this is the first report on MPC of various fluoroquinolones against *S. pseudintermedius* isolates from dogs. Based on these results, the highest doses within the clinically recommended dose ranges of ciprofloxacin, enrofloxacin and marbofloxacin could minimize the selection of resistant mutants *in vitro*, whereas the possibility of selecting mutants with the currently used clinical doses of difloxacin and orbifloxacin, and the lowest doses within the clinically recommended dose ranges of all fluoroquinolones, seems high. Target mutations in *gyrA-84* and *gla-80* contribute

enrofloxacin	5–20 mg/kg once daily
marbofloxacin	2.75–5.5 mg/kg p.o. once daily
orbifloxacin	7.5 mg/kg p.o. once daily



## Are we using the right administration interval?

ANTIBIOTIC	Veterinary guidelines for superficial folliculitis <sup>1</sup>	Human guidelines for impetigo and other skin infections <sup>2</sup>
<b>Cephalexin</b>	15-30mg/kg BID	250 mg (25 mg/kg/day) QID
<b>Clindamycin</b>	5-10 mg/kg BID	3-400 mg (20 mg/kg/day) TID

<sup>1</sup> ISCAID guidelines. guidelines for diagnosis and antimicrobial therapy of superficial bacterial folliculitis. *Vet Dermatol* 2014, 25: 163-42

<sup>2</sup> IDSA guidelines. Practice guidelines for diagnosis and management of skin and soft tissue infections. *Clin Infect Dis* 2005, 41: 1373-406



## Are we using the right treatment duration?

### Veterinary guidelines for uncomplicated cystitis <sup>1</sup>

“Typically, uncomplicated UTIs are treated for 7–14 days. However, the ISCAID Working Group acknowledges the likelihood that a shorter treatment time (7 days) may be effective”

### Human guidelines for acute uncomplicated cystitis in women <sup>2</sup>

~ 3 to 5 days depending on the specific drug

<sup>1</sup> ISCAID guidelines. Weese et al. Antimicrobial use guidelines for treatment of urinary tract disease in dogs and cats. *Vet Med Intern* 2011 (open access)

<sup>2</sup> Gupta et al. IDSA-ESCMID guidelines for treatment of acute uncomplicated cystitis and pyelonephritis in women. *Clin Infect Dis* 2011, 52: 103-120





# Challenges in veterinary antimicrobial stewardship

- Lack of scientific evidence to make informed decision for development of evidence-based guidelines
- Lack of antimicrobial stewardship experts in the veterinary sector
- Poor education of veterinary students on topics related to AMR and antimicrobial students
- International species- and disease-specific practice guidelines are presently limited to selected conditions in small animals
- National clinical practice guidelines are missing in most countries
- Lack of rapid and cheap diagnostic tests
- Actual drug intake by individuals is unknown in herd treatment



## Education needs

- **Training of a new generation of antimicrobial stewards** that can provide veterinary students and practitioners with up-to-date training on AMR and antimicrobial use
- **Development of EU position papers** that set the basis for the development and harmonization of national guidelines since the necessary expertise and resources are not available in all countries
- **Development of national guidelines** that take into consideration local patterns of antimicrobial use and AMR, drug availability in the market, specificities of national livestock production systems as well as cultural and regulatory differences between countries



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## Research needs

- **Clinical trials** comparing the effects of different drugs, drug formulations, doses, administration forms and treatment durations on AMR selection and clinical efficacy
- **Cheap and fast Point-of-Care (PoC) tests** that facilitate discrimination between viral and bacterial disease, or detection of bacterial resistance to first line antimicrobial drugs
- **Innovative pharmaceuticals** (vaccines, new antimicrobials and alternative treatments) that may replace or minimize the use of antimicrobial drugs that are being restricted or phased out in livestock because of public health concerns and meet the demand for effective management of MDR infections in companion animals



## ESGVM activities to promote antimicrobial stewardship

- Course on antimicrobial stewardship in veterinary medicine (next edition in 2018)
- Evaluation of veterinary education in the EU (PREPARE-VET project)
- Mapping of national guidelines in the EU and development of species- and disease-specific position papers on prudent antimicrobial use (core group established)
- Setting quality standards for veterinary clinical microbiology (1<sup>st</sup> ESGVM position paper in 2017)



Course in Gothenburg in 2016



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# Let's do it One Health



## Thanks for your attention