

Antimicrobial stewardship in livestock and companion animals: the why and the how

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What is antimicrobial stewardship?

“Antimicrobial stewardship refers to coordinated interventions designed to improve and measure the appropriate use of antimicrobials by promoting the selection of the optimal antimicrobial drug regimen, dose, duration of therapy, and route of administration”.

Infectious Disease Society of America



Lecture outline

The why:

- Does antimicrobial use in animals contribute to AMR problems in human medicine?
- Is there any evidence antimicrobial use in animals can be reduced by antimicrobial stewardship programmes?

The how:

- How does implementation of such programmes differ compared to human medicine and between diverse types of animals?
- What are the main barriers to implementation of antimicrobial stewardship programmes in veterinary practice?





Major concerns in livestock

- Increasing evidence that certain AMR problems may at least in part be attributable to contaminated food (ESBL-producing *E. coli*) or direct exposure to animals (livestock-associated MRSA CC398)
- Increasing consumer demand and governmental pressure to reduce antimicrobial use in livestock
- Benchmarking has been shown a very effective tool to reduce antimicrobial use but how much can it be reduced without impacting animal welfare and AMR selection due to under-treatment and under-dosing?



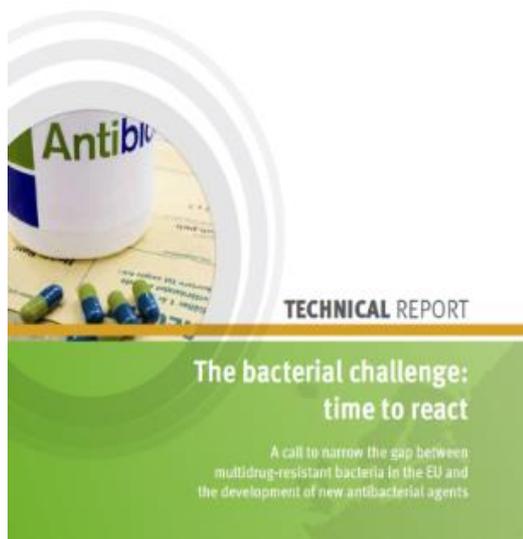
Major concerns in companion animals

- Infections caused by MRSA, methicillin-resistant *Staphylococcus pseudintermedius* (MRSP), ESBL-producing *E. coli* and carbapenemase-producing Enterobacteriaceae are increasingly reported in companion animals, especially dogs
- The current therapeutic options consist of older drugs (e.g. chloramphenicol and rifampicin) that are not always effective and have significant side effects and drawbacks
- Critically important antimicrobials such as third generation cephalosporins and fluoroquinolones are widely used but how much should the use of these drugs be restricted to manage infections in our 'best friends'?



Estimated burden of AMR on human health in the EU

ECDC (www.ecdc.europa.eu)



2009

AMR of major clinical relevance	No. deaths	No. Infections
Methicillin-resistant <i>Staphylococcus aureus</i> (MRSA)	5,400	171,200
Vancomycin-resistant enterococci (VRE)	1,500	18,100
ESBL-producing <i>Escherichia coli</i>	5,100	32,500
ESBL-producing <i>Klebsiella pneumoniae</i>	2,900	18,900
Carbapenem-resistant <i>Pseudomonas aeruginosa</i>	10,200	141,900
TOTAL	25,100	386,100



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%



Answers given in other conferences

Answer	ECCMID 2017	SAFEPORK 2017
Less than 5%	5%	80%
Between 5 and 30%	75%	20%
More than 30%	20%	0



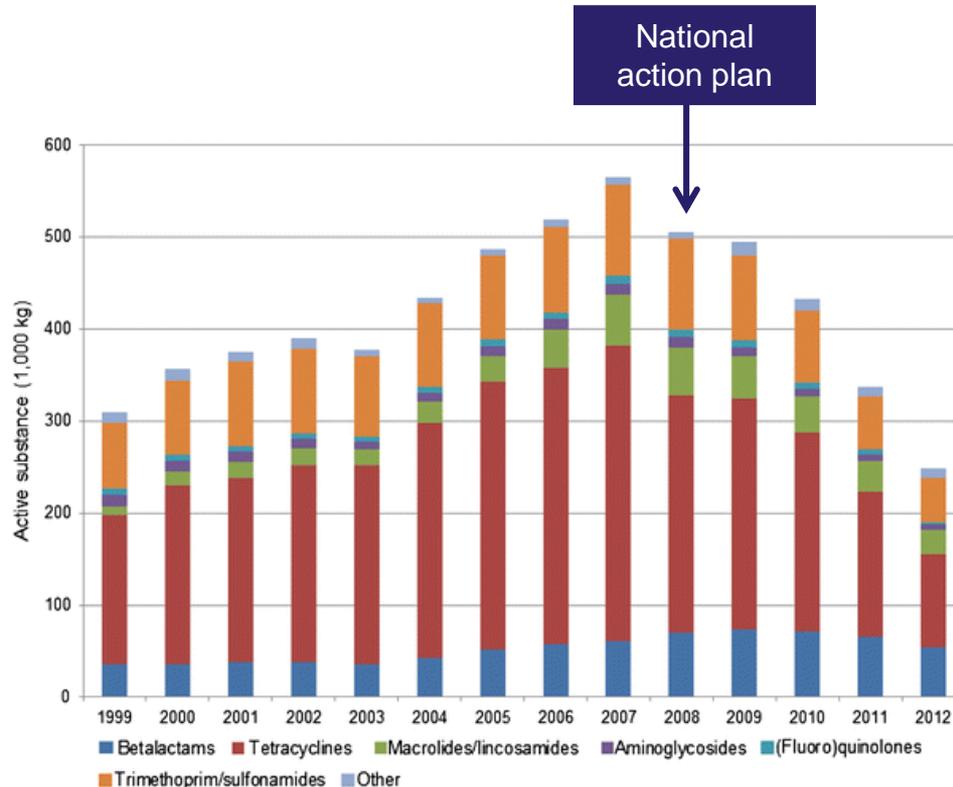
My answer(s)

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)



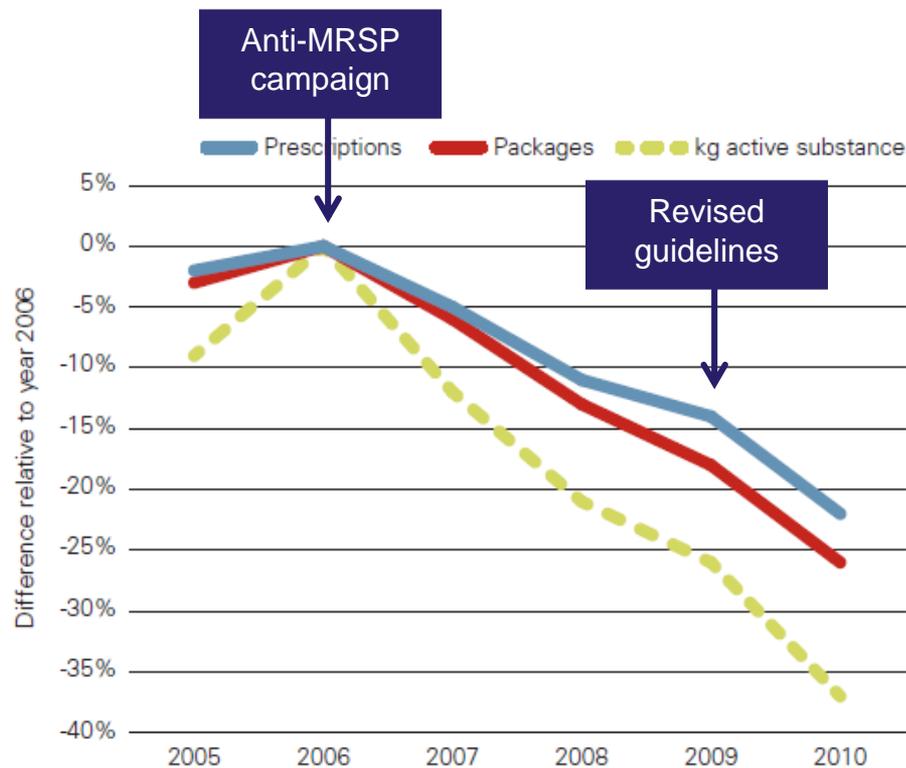
Sales of antimicrobials for animal use in the NL, 1999-2012

Nevius & Heederik 2014



Sales of antimicrobials in dogs in Sweden, 2005-2010

Data from Sweden (www.sva.se)





2015

Strategic objectives 8

Objective 1:

Improve awareness and understanding of antimicrobial resistance through effective communication, education and training 8

Objective 2:

Strengthen the knowledge and evidence base through surveillance and research 8

Objective 3:

Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures 9

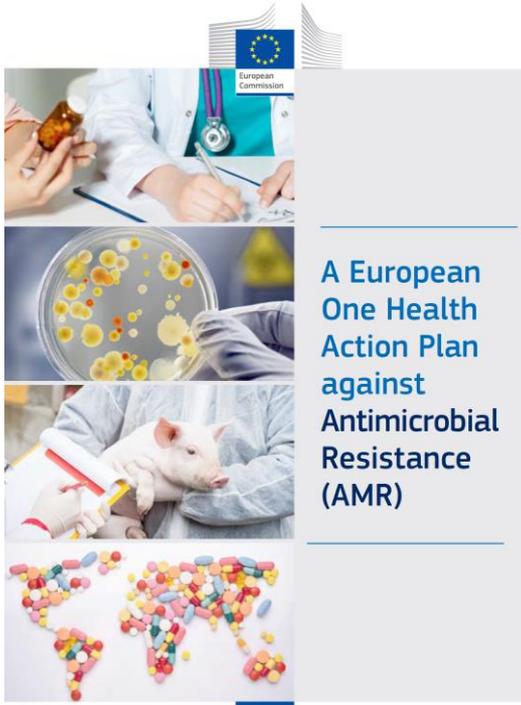
Objective 4:

Optimize the use of antimicrobial medicines in human and animal health 10

Objective 5:

Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions 11





2017

Promote the prudent use of antimicrobials

The appropriate and prudent use of antimicrobials is essential to limiting the emergence of AMR in human healthcare and in animal husbandry.

Cross-sectorial and coordinated actions to promote the prudent use of antimicrobials in humans and animals are necessary to slow down the development of AMR and preserve the effectiveness of antimicrobials. Such actions, often referred to as 'antimicrobial stewardship' actions, are in place in some sectors (e.g. EU guidelines for the prudent use of antimicrobials in veterinary medicine²⁹) but are not sufficiently developed for all situations in which antimicrobials are used.

Conclusions on the WHY

1. Does antimicrobial use in animals contribute to AMR problems in human medicine?

Although the actual contribution remains unclear in quantitative terms, there is evidence of zoonotic transmission of AMR and such evidence is sufficient to justify a reduction in antimicrobial use in animals on the basis of the precautionary principle.

2. Is there any evidence antimicrobial use in animals can be reduced by antimicrobial stewardship programmes?

Yes there is evidence indicating that antimicrobial stewardship programmes can drastically reduce antimicrobial use in the veterinary sector, which in turn suggests antimicrobial overuse.



The ↑ how

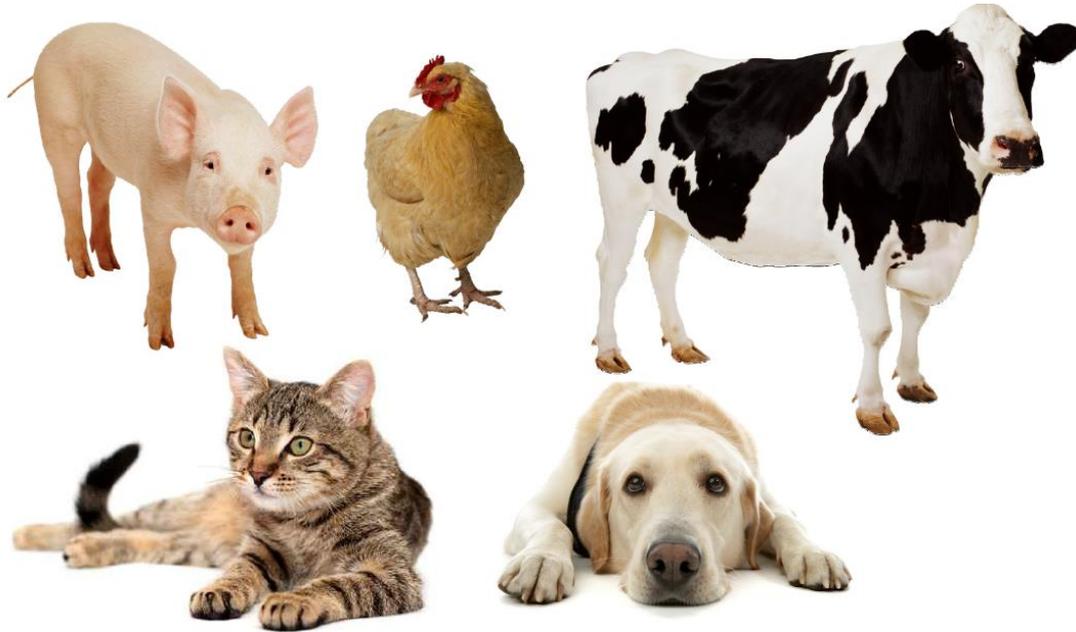
Differences to human medicine

- Veterinary practice is a highly competitive private business where economic interests easily prevail upon public health concerns.
- In most countries veterinarians make profit by dispensing antibiotics
- Animal patients do not talk and the anamnesis is provided by the client (farmer or owner), who may put pressure to dispense antibiotics
- Farm animals are often treated in groups (herd treatment) and the actual drug intake by individuals is unknown.
- Microbiology laboratories are situated outside the clinic/hospital, in some cases in another country, and do not always meet quality standards.
- Costs of microbiological tests are covered by the client and only in very few countries adequate insurance systems are established to reimburse diagnostic costs.
- The concept of antimicrobial stewardship is relatively new and there is a lack of access to education & training in this field



More diversity than in human medicine

Multiple animal species with different ethical implications & antimicrobial PK

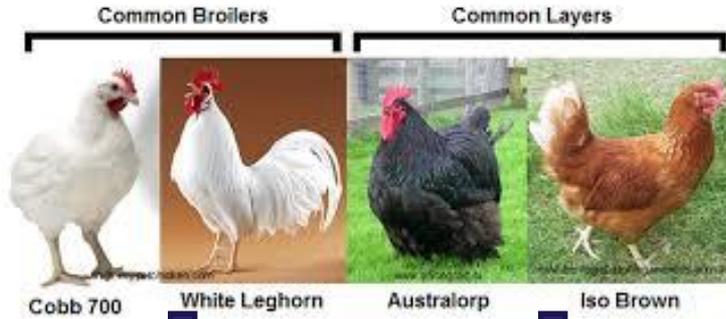


Oral bioavailability of amoxicillin varies from 28-33% in pigs to 64-77% in dogs

More diversity than in human medicine

Diverse breeds and production systems within species

Meat vs egg chickens

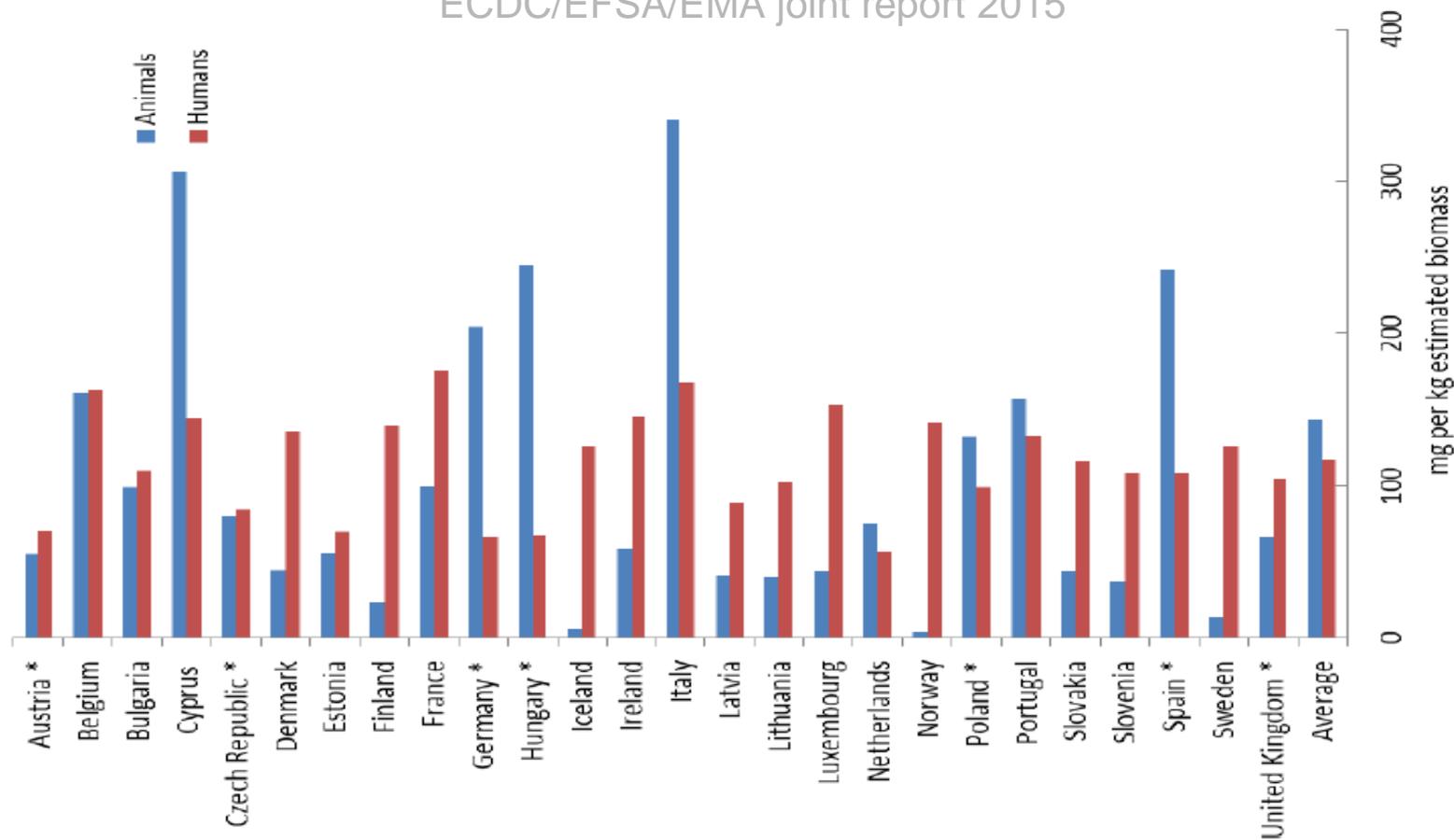


Dairy vs beef cattle



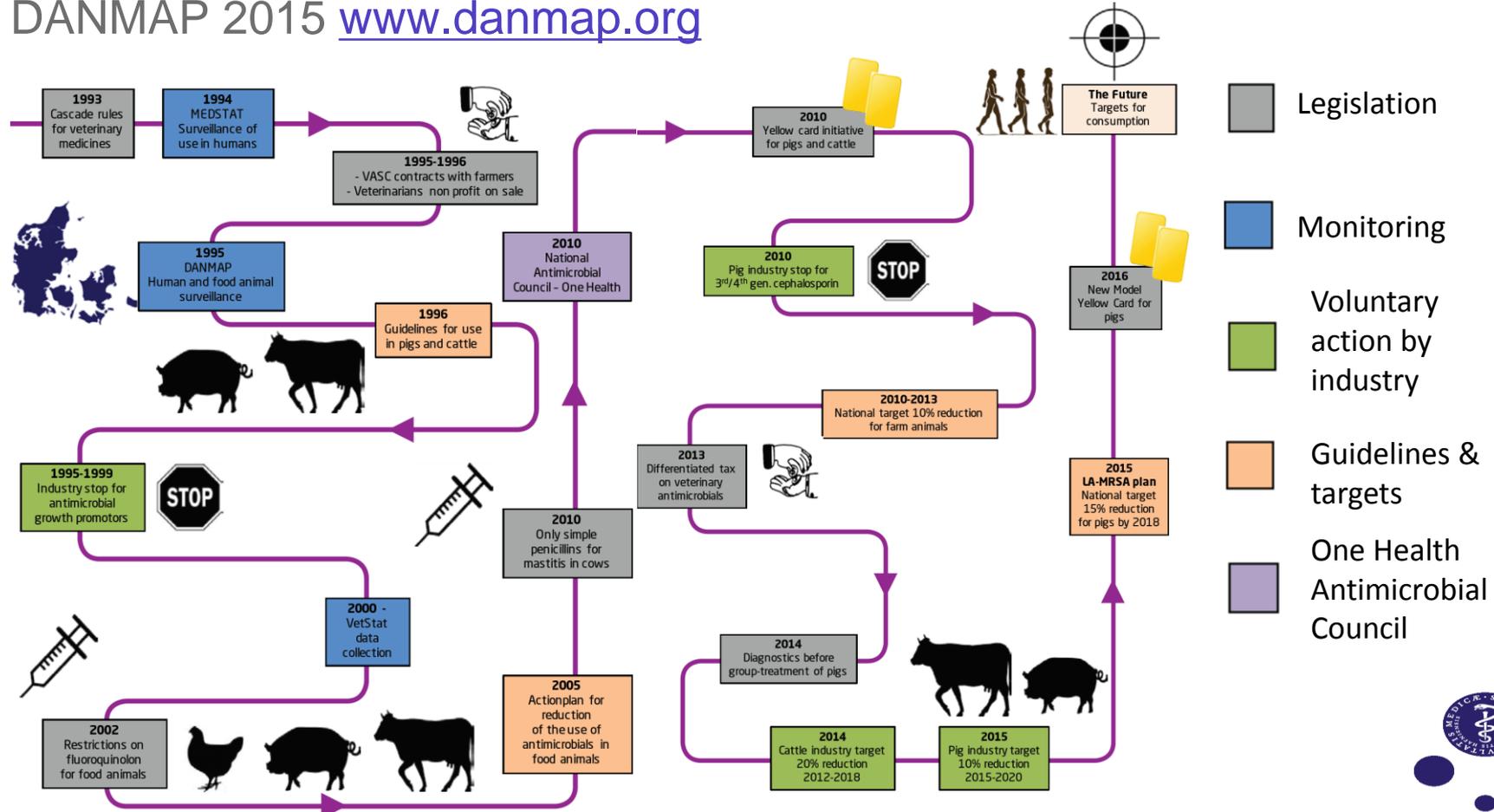
Antimicrobial consumption in the EU

ECDC/EFSA/EMA joint report 2015



Initiatives for control of antimicrobial use in Denmark

DANMAP 2015 www.danmap.org



Targets for implementation of antimicrobial stewardship

- Reducing overall antimicrobial consumption (quantitative restrictions)
 - Ban of growth promoters
 - Restricted prophylaxis and metaphylaxis (not ban)
- Prudent use of critically important antimicrobials (qualitative restrictions)
 - Restricted use of fluroquinolones & 3rd/4th generation cephalosporins
- **Improving diagnostic testing (guided antimicrobial choice)**
 - Increased use of cytology, culture and AST
 - Increased quality of veterinary microbiology laboratories employing state-of-the-art methods and offering fast and reliable service, including advice on pre- and post-analytical issues
- **Optimizing antimicrobial use (how much, how often and how long)**
 - Improved dose, administration interval and treatment duration
 - Established antibiotic policies and stewardship practices at clinic level



Barriers to implementing antimicrobial stewardship

1. Knowledge and technological barriers

- Lack of scientific evidence to make informed decision for development of evidence-based treatment guidelines
- Lack of rapid and cheap diagnostic tests at the point-of-care
- Lack of effective alternatives to antibiotics for management of key diseases contributing to overall antimicrobial consumption

2. Educational barriers

- Poor education of veterinary students on topics related to AMR and antimicrobial use
- Limited access to ongoing education activities on antimicrobial stewardship targeting veterinary practitioners and laboratory staff
- Lack of national experts in most countries



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 i) replace or minimize the use of antimicrobials that are being restricted or phased out in livestock (colistin and zinc oxide) because of public health concerns or ii) meet the demand for effective management of MDR infections in companion animals



Educational needs

- **Training of a new generation of antimicrobial stewards** that can provide veterinary students and practitioners with up-to-date education on AMR and antimicrobial use in all countries
- **Development of EU position papers/guidelines** that set the basis for the development and harmonization of national treatment guidelines
- **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



Conclusions on the HOW

1. How does implementation of such programmes differ compared to human medicine and between diverse types of animals?

Implementation of antimicrobial stewardship is more complex than in human medicine and requires species-specific interventions.

2. What are the main barriers to implementation of antimicrobial stewardship programmes in the veterinary sector?

Various knowledge, technological and educational gaps need to be filled to fully implement antimicrobial stewardship beyond reduction of total antimicrobial use and of critically important drugs – this is the next challenge.



ESGVM activities to promote antimicrobial stewardship

- ESGVM position paper on quality standards for veterinary clinical microbiology
- Course on antimicrobial stewardship in small animal veterinary medicine (next edition at the BSAVA Congress in Birmingham, 5-8 April 2018)
- Survey to evaluate veterinary education on AMR and antibiotic use in the EU (PREPARE-VET)
- ESGVM position papers on treatment of key diseases for which guidelines are lacking
 - SSI and gastroenteritis in small animals (2018)
 - Respiratory infections in cattle (2018)
 - Post-weaning enteritis in pigs (2019)



Course in Gothenburg in 2016

Let's do it One Health



Thanks for your attention