Prudent use of antimicrobials - Workshop 2

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Concern about use of antimicrobials (AM)

Use of antimicrobials

Development of resistance

Treatment failure

Risk mitigation needed

- In livestock, pets and humans

In this presentation, focus will be on livestock

Actions are taken in most countries

Movement in the same direction - prudent use

- Not allowing use of AM as growth promoter
- Limiting/prohibiting preventive use
- Restricting access to highly critical AM
 - Such as 3rd and 4th generation cephalosporins and fluoroquinolones
- Lowering use for treatment with other AM

Some began earlier than others

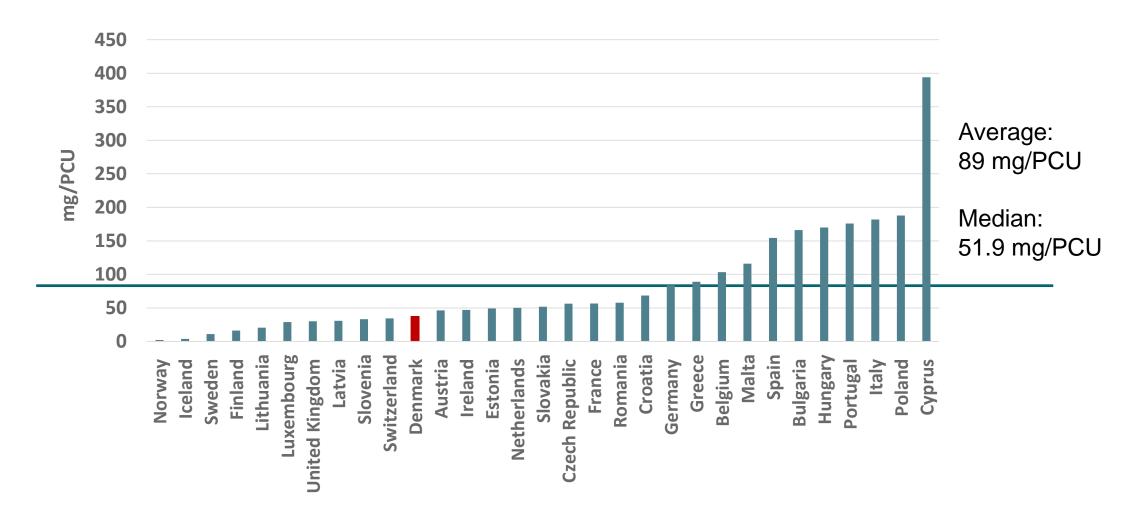
- Reflected in large variation in use of AM between countries
- See next slide, showing the ESVAC report results for 2019-2020
 - AM consumption relative to animal production in each country
 - Measured as mg per population correction units (mg/PCU)



Sales of veterinary antimicrobial agents in 31 European countries in 2019 and 2020

Trends from 2010 to 2020 Eleventh ESVAC report

AM consumption relative to animal production in European countries, 2019-2020 (mg/PCU)



Source: https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2019-2020-trends-2010-2020-eleventh_en.pdf

Responsibility?

Unrealistic to expect that farmers or vets will change habits, unless regulation of AM area takes place

- Because of difficulty in "feeling" responsibility for society
- Moreover, legislative conditions should be equal for all producers
 - If not, problems with competetiveness may arise
 - Important to inform the animal sector about usefulness of legislation

Necessary to ensure productivity, if we want livestock producers and their vets to comply with legislation

- Identify cost-effective measures to apply to ensure responsible use at different levels
 - Herd level
 - Sector level
 - National level

Be inspired by what works in other countries, while adapting to own country



Systems Thinking – to understand which measures will work at which level and how

Event (what happened)



Patterns and trends (what happened before)

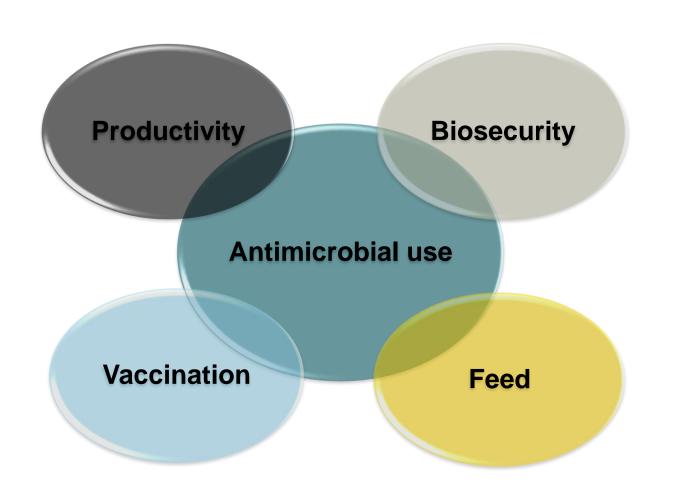


Underlying structures (what led to the patterns)



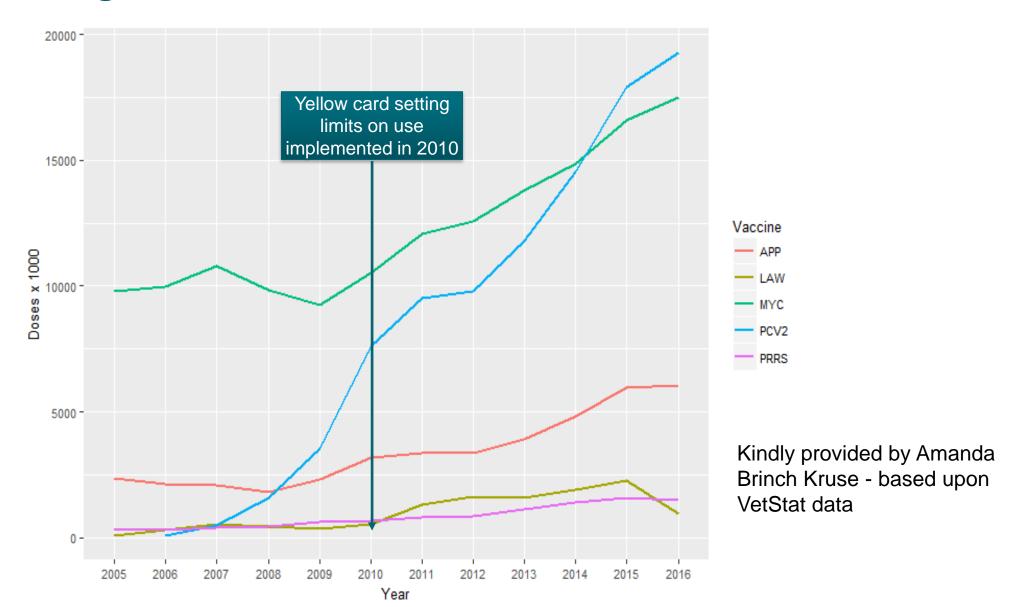
Mental models (assumptions, beliefs and values)

HERD LEVEL - What can the livestock producers do to lower their consumption of antimicrobials?



Get assistance from the vet!

Prevention through use of vaccines - on the increase in Denmark



DK experience

Vaccines work

- But mandatory vaccination for production diseases will not necessarily lower use of AM
 - Because vaccines are used in herds with infections
 - = Reverse causality

Use vaccines where needed

- Vaccines against E. coli, PRRS, mycoplasma, and Lawsonia may in many cases help to improve health in the herd
- However, if infection is not present effect of a vaccine cannot be expected

Temtem et al. Pordne Health Management (2016) 2:23 DOI 10.1186/s40813-016-0042-1

Porcine Health Management

RESEARCH

Open Access



Comparison of the antimicrobial consumption in weaning pigs in Danish sow herds with different vaccine purchase patterns during 2013

Carolina Temtem¹, Amanda Brinch Kruse², Liza Rosenbaum Nielsen², Ken Steen Pedersen³ and Lis Alban^{3*}

Abstract

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Background: There is growing concern about development of antimicrobial resistance due to use of antimicrobials (AMs) in livestock production. Identifying efficient alternatives, including vaccination, is a priority. The objective of this study was to compare the herd-level amount of AMs prescribed for weaner pigs, between Danish sow herds using varying combinations of vaccines against Porcine Circovirus Type 2 (PCV2), *Mycoplasma hyopneumoniae* (MYC) and *Lawsonia intracellularis* (LAW). It was hypothesised that herds purchasing vaccines, use these to prevent disease, and hence reduce their AM consumption, compared to herds purchasing fewer or no vaccines against

Data
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ORIGINAL RESEARCH published: 16 January 2017 doi: 10.3389/fvets.2016.00120



No Clear Effect of Initiating
Vaccination against Common
Endemic Infections on the Amounts
of Prescribed Antimicrobials for
Danish Weaner and Finishing Pigs
during 2007–2013

Amanda Brinch Kruse^{1*}, Leonardo Victor de Knegt¹, Liza Rosenbaum Nielsen¹ and Lis Alban²

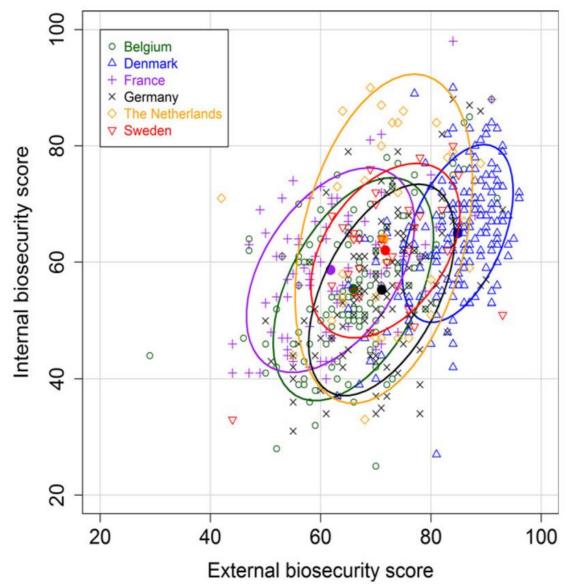
Biosecurity in pig herds

Necessary to keep infections at bay

Assessment of external vs. internal biosecurity scores from Biocheck

- Obtained by interviewing pig farmers from Belgium, Denmark, France, Germany, The Netherlands and Sweden (Fillippitzi et al., 2017)
- Not just of importance to keep AM use low, but also to keep out African Swine Fever!





Source: Filippitzi et al. (2017)

Detailed evaluation of biosecurity in a herd => enables vet to undertake herd health advisory service

Fictive score for a Danish sow herd	Score	Mean score in
External biosecurity		160 DK herds
Overall external score	89	86
Purchase of animals and semen	99	96
Transport, manure and dead animals	84	81
Feed, water and materials	87	84
Employees and visitors	95	92
Rodent and bird control	83	80
Location and environment	78	75
Internal biosecurity		
Overall internal score	58	67
Disease control	90	95
Farrowing unit	60	65
Nursery unit	35	62
Finishing unit	47	47
Measures between compartments	54	59

Low score for nursery unit may reflect extensive use of foster sows and multiple movements of piglets between litters – not healthy for the piglets!

Solution: Get advice from the vet on how to improve crossfostering

The role of feed

AM are put into feed

Sometimes too much a result of an automatic decision

Today Spanish legislation allows only one kind of AM put into feed at a time

AM use in Spain lowered by 68% from 2015-2017

Proper diagnostics needed regularly to ensure prudent use

Do not solely look at the piglets – but also the sows

We have not looked sufficiently into the positive role of feed

- Effective measure to ensure high milk production in sows
- ffective against post-weaning diarrhea in weaners
 - Important, when zinc oxide will be phased out in the EU



SECTOR LEVEL – Knowledge about on-farm infection status

Knowledge of infection status will enable farmer to buy in replacement animals with similar status

- Preferably through a contract with a single supplier only
- Targeted vaccination can then be applied economic approach

Quarantene needed, when buying in new animals

- Else infections may enter the herd unexpectedly
- Take care of the livestock trucks assume they are all infected with dysenteria!

Confidence in herd status requires blood testing at least annually

- And open access to results
- In place in the Danish SPF system

Eradication of the most important infections can be the next step

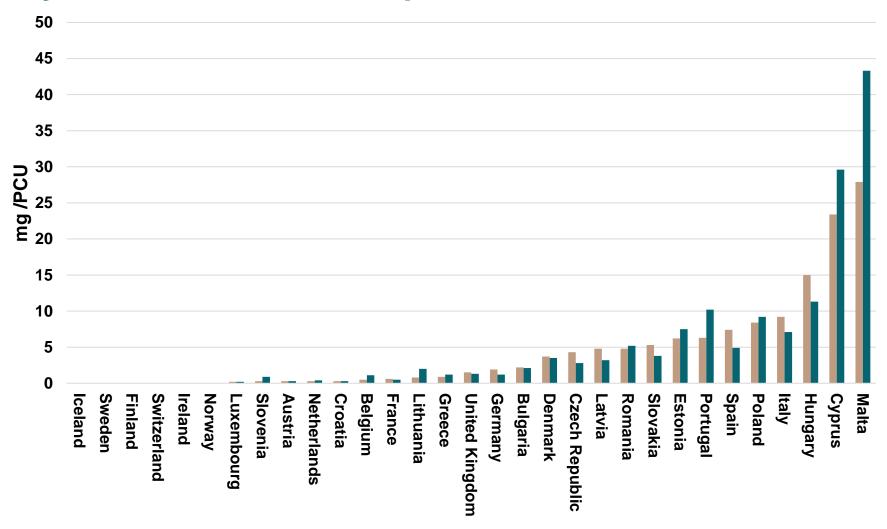
All these initiatives need to be made at the sector level





Impact of eradication of infection on use of AM

- dysenteria as the example



Sales of pleuromutilins in 2018, expressed as mg/PCU Source: EMA, 2020

Huge difference in use of pleuromutilins between countries

 May be related to presence of dysenteria

- Pleuromutilin is the only way of treating dysenteria

■ Year

■ Year

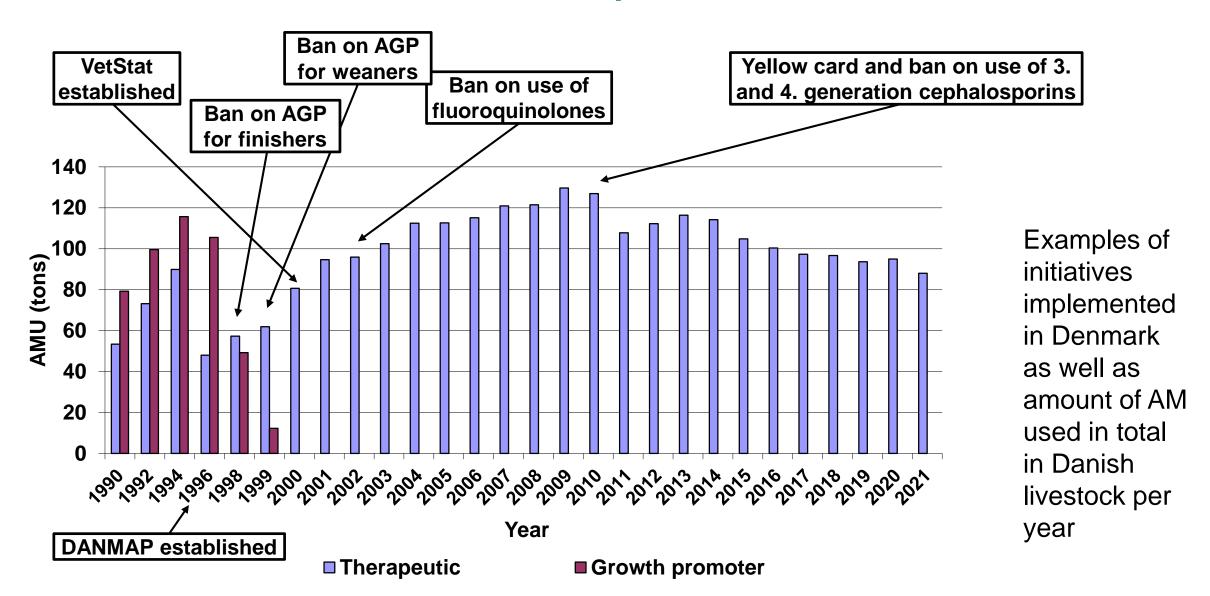
2017

2018

Eradication
 feasible through
 public-private
 partnership

Focus on livestock trucks!

ACTIONS ON NATIONAL LEVEL – Equal conditions for all farmers



The Yellow Card Scheme



Adopted in July 2010 by Danish Veterinary and Food Administration

Makes use of data recordings

- AM consumption in the individual farm (VETSTAT)
- No. of animals in herd (Central Husbandry Register)
 - Divided into age groups

Restrictions imposed on pig farmers who used more than twice the average

Divided into age groups

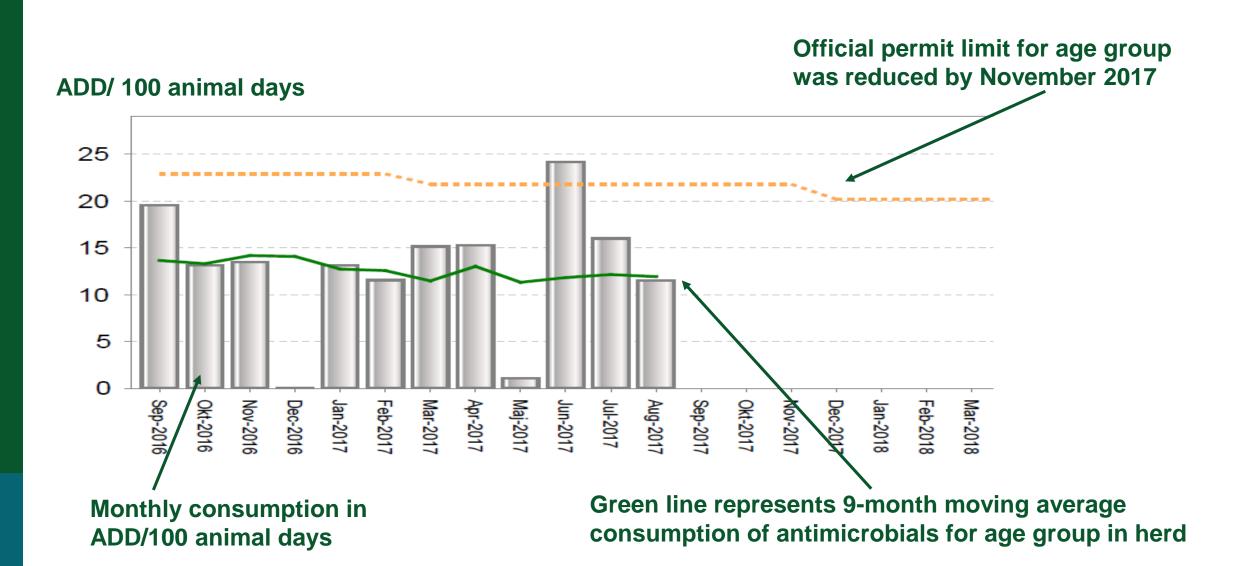
Implemented to eliminate very high use seen on individual farms

- Later, limits have been reduced further
 - Take care not to reduce too much!

Age group	Permit limits*
	initial (current)
Sows and piglets	5.2 (3.2)
Weaners	28 (17.2)
Finishers	8 (4.4)
	0 (4.4)

^{*} Animal daily doses (ADD) per 100 animal days

Evaluation of antimicrobial consumption in weaner herd



Herd health contracts between farmer and vet

Danish vet are only allowed to profit up to 5% from sales of medicine

 Instead, vet and individual farmer make contracts about veterinary advisory service in the herd

Contracts introduced in 1995 - Became mandatory for large herds in 2010

- ≥ 300 Sows, ≥ 3,000 Finishers and ≥ 6,000 Weaners
- Involves frequent visits
 - During visits vet gives advice with focus on disease prevention, production and responsible use of AM
 - Reports written after each visit
 - Quarterly report provides details about AMU and productivity

Together, farmer and vet decide on actions to initiate

- Focus on limiting need for treatment
 - Final decision and responsibility lies upon farmer



Treatment guidelines and risk assessments

Needs to be based on both effect of treatment and risk of resistance

Else, the vets will not comply with the guidelines

Risk of resistance should be based upon risk assessment

 European Medicines Agency (EMA) has developed guidelines for how to make risk assessment

DK experience using EMA guidelines:

Possible, but cumbersome!





PREVENTIVE VETERINARY MEDICINE

Preventive Veterinary Medicine 83 (2008) 115-129

www.elsevier.com/locate/prevetmed

A human health risk assessment for macrolide-resistant Campylobacter associated with the use of macrolides in Danish pig production

Lis Alban*, Elisabeth Okholm Nielsen, Jan Dahl



ORIGINAL RESEARCH published: 26 May 2017



Assessment of the Risk to Public Health due to Use of Antimicrobials in Pigs—An Example of Pleuromutilins in Denmark

Lis Alban^{1*}, Johanne Ellis-Iversen², Margit Andreasen³, Jan Dahl¹ and Ute W. Sönksen⁴

¹ Risk Assessment Group, Department for Food Safety and Veterinary Issues, Danish Agriculture and Food Council, Copenhagen, Denmark, ² National Food Institute, Technical University of Denmark, Kongens Lyngby, Denmark, ³ Danish Association of the Veterinary Pharmaceutical Industry, Copenhagen, Denmark, ⁴ Department for Bacteria, Parasites and Fungi, Statens Serum Institut, Copenhagen, Denmark

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Categorisation of AM

European Medicines Agency has just come out with a categorisation of AM

Dividing AM into 4 groups:

A (avoid)

B (restrict)

C (caution)

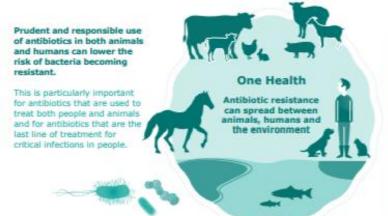
D (prudence)

Route of administration also important

- Lowest risk: Local treatment of individual animal
- Highest risk: group treatment via feed, premix or water



Categorisation of antibiotics for use in animals for prudent and responsible use



The Antimicrobial Advice Ad Hoc Expert Group (AMEG) has categorised antibiotics based on the potential consequences to public health of increased antimicrobial resistance when used in animals and the need for their use in veterinary medicine.

The categorisation is intended as a tool to support decision-making by veterinarians on which antibiotic to use.

Veterinarians are encouraged to check the AMEG categorisation before prescribing any antibiotic for animals in their care. The AMEG categorisation does not replace treatment guidelines, which also need to take account of other factors such as supporting information in the Summary of Product Characteristics for available medicines, constraints around use in food-producing species, regional variations in diseases and antibiotic resistance, and national prescribing policies.

Avoid

- antibiotics in this category are not authorised as veterinary medicines in the EU
- · should not be used in food-producing animals
- may be given to companion animals under exceptional circumstances

Caution

- for antibiotics in this category there are alternatives in human medicine
- for some veterinary indications, there are no alternatives belonging to Category D
- should be considered only when there are no antibiotics in Category D that could be dinically effective

Restrict

- antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health
- should be considered only when there are no antibiotics in Categories C or D that could be clinically effective
- use should be based on antimicrobial susceptibility testing, wherever possible

Category D

Prudence

- should be used as first line treatments, whenever possible
- as always, should be used prudently, only when medically needed

Full agreement in categorisation between guidelines made by different parties cannot be expected

C = Caution

EMA: Macrolides

D = Prudence

EMA: Tetracyclines

WHO is more conservative than EMA – because WHO does not differentiate between use in poultry and pigs

Danish authorities are more conservative than EMA

Evaluation of monitoring for AM use and resistance

Necessary to evaluate monitoring programmes at regular intervals

- To ensure that they provide value for money
- That the latest news/methodology is part of the programme

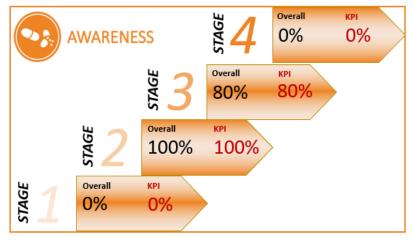
Different tools are in place to evaluate monitoring programmes

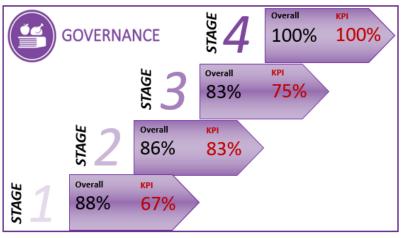
FAO's Progressive Management Pathway tool for AMR (AMR-PMP) is one example

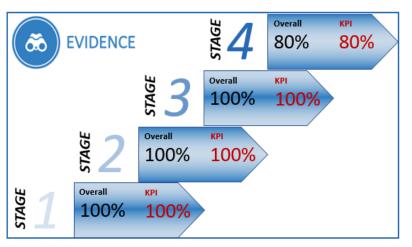
- Can be used as a management tool to evaluate a country's National Action Plan for AMR
- Hereby, countries and individual sectors can evaluate their current status and document areas working well
- Structure is based on four focus areas:
 Awareness, Evidence, Governance & Practices

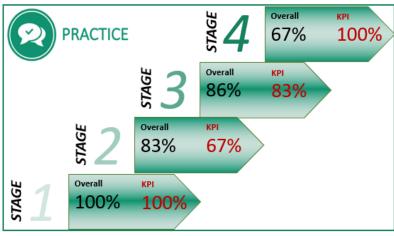


An example of an output from use of FAO's AMR-PMP tool









Nielsen et al., 2020. Clin Microbiol Inf.

Summing up

To ensure a change, actions should be taken at different levels

To understand what will work at which level, use Systems Thinking

Legislative frames should be set at national level

Will ensure equal conditions for all producers

At sector level and preferably in a public-private partnership

• Eradication of disease e.g. dysenteria or PRRS

Measures to be taken by the individual farmer

- Biosecurity (also because of African Swine Fever)
- Targeted vaccination / knowledge about infection status
- Feed we still have a lot to learn
- Easy access to own data + benchmarking?

Will ensure that the productivity of production can be maintained, while having prudent use of AM

Challenge: How do we improve AMR stewardship further?

- When and which animals to treat?
- Which antimicrobials to use?
- Way of administration?

Antimicrobial use

- Which vaccines to apply and when?
- Usefulness of status for infections in the herd?
 - Tradication of infection

Manage-

ment

Vaccination eradication

And how do we involve pig producers and their vets more actively?

Effect of feeding

Weaning weight more important than age?

Biosecurity

- Effect of external
- and internal biosecurity
- Where are the weak points in biosecurity?

Exercise

- 1. Where is your country located regarding mg antimicrobials per PCU on the ESVAC comparison figure? please see European Medicines Agency (2021) in the reference list
- 2. Has there been a change in the location on the figure during the last 6 years?
- 3. Is monitoring for AMU in place in you country for the livestock species you have selected?
- 4. If yes, since which year
- 5. Is it a monitoring programme or a surveillance programme, where the latter means that actions are in place if use is above a certain threshold?
- 6. Is the use in the species subdivided into age groups? And if so, how many groups are there?
- 7. Are certain legal veterinary antimicrobials prohibited or limited in use for the species of interest?
- 8. Which requirements or actions are set at the livestock producer level?
- 9. Is AMU by prescription only?
- 10. Are veterinarians earning parts of their income on selling antimicrobials?
- 11. Which actions have been taken at the sectorial level?
- 12. Which are set at the national level?
- 13. What are three most important barriers against reduction in AMU in your country? these should be divided into underlying structures and mental models
- 14. Which 6 actions do you think should be put in place at individual, sectorial and national level, respectively, to effectively reduce the AMU in the species of interest? again having in mind the underlying structures and mental models
- 15. For each of the 6 actions, please insert them in a x-y-coordinate system, where x is impact and y is feasibility including costs.

Suggestion:

Q1-Q12 fill in for your own country (1 hour)

Q13-Q15 provide general answers for the group (1 hour)

Focus presentation for Wednesday on addressing Q13-Q15 (0.5 hour)