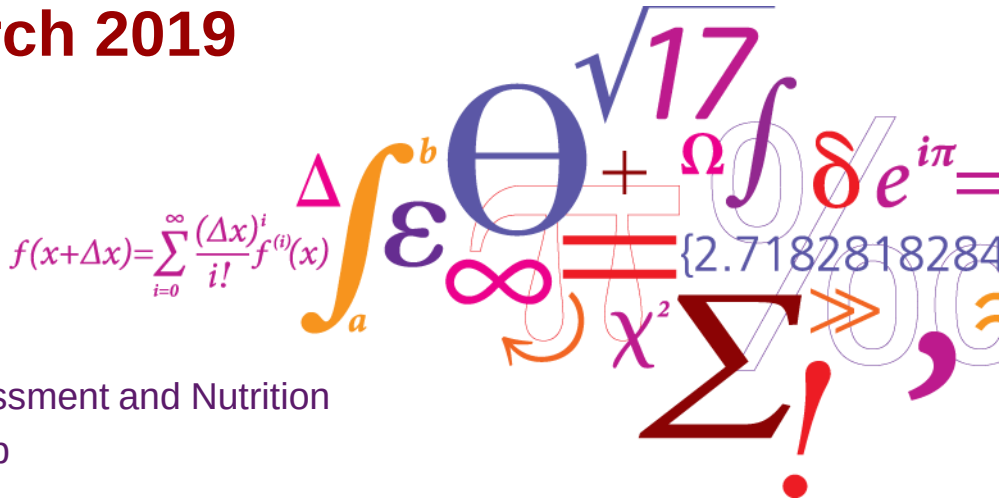
Introduction to DANMAP

Danish National System for Monitoring Antimicrobial Resistance and Antimicrobial Consumption

Lusaka, 4-6 March 2019



Flemming Bager, Head of division for Risk Assessment and Nutrition
Dr. Johanne Ellis-Iversen, Head of EpiRisk group
DTU National FOOD Institute

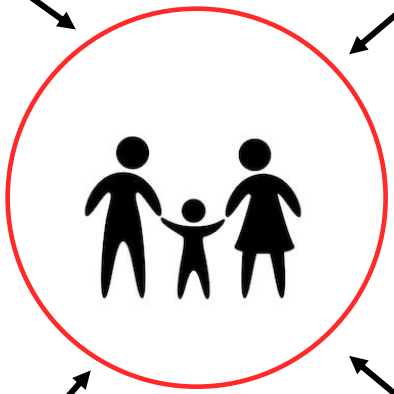
DTU Fødevareinstituttet

Drivers of AMR – generically One Health

Meat, milk, eggs

Use of antimicrobials

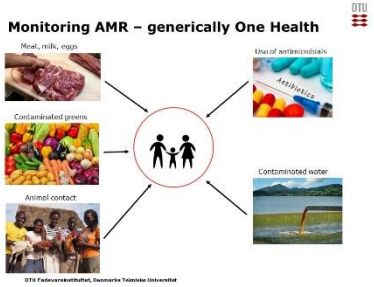
Contaminated greens



Contaminated water

Animal contact

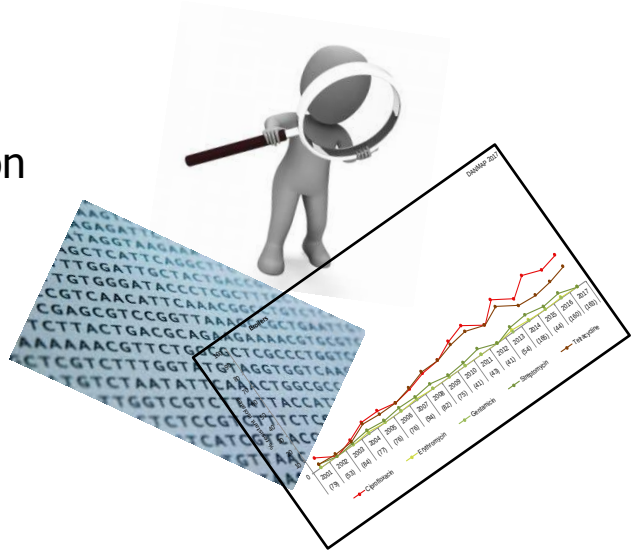
Designing an AMR monitoring system



- An appropriate design should consider
  - What are the most significant drivers of AMR in the local setting?
  - What are the most likely sources of AMR exposure in humans?
  - And focus on those or some of those
- DANMAP is an example of a monitoring system that fits the Danish setting, but needs adaptation for use in other locations with differerent infrastructures

Danmap
-Scientific objectives for surveillance

1. **Follow trends over time for AMR and AMU**
   To enable response at unusual events/increases
   To measure effect of interventions against AMR
2. **Spot new & emerging resistance**
   To enable early response/investigation
   As early warning between species
   To adjust suveillance design for new situation
3. **Maintain isolate & gene bank**
   For retrospective analysis and investigations
   For research



DANMAP – AMR in food animals

- Sampling unit is flock/herd
  - Herd/flock of origin is identifiable at slaughter

- Most samples are collected at slaughter
  - Sampling all months to avoid seasonal effects
  - **Systematic random sampling** approach
  - Requires knowledge of annual throughput of slaughterhouses participating
  - Coverage: 90-95 pct. of the national production of slaughter animals
  - Verification that a flock or herd is included only once

- Exception: samples for testing for Salmonella in broilers, layers and turkeys are collected on farm as part of AM meat inspection

- Exception: samples for Campylobacter collected only during summer

DANMAP – samples from food

- Random sampling

- Routinely, only fresh meat is sampled
  - Samples of beef, pork and chicken collected in retail outlets
    - 1-2 samples per outlet
  - All areas of country included
  - All months included

- Ready to eat greens: ad hoc as specific projects

- Note:
  - EU framework for monitoring AMR in animals and in food
    - Sampling
    - Lab methods

DANMAP – samples from humans

- Passive surveillance, based on diagnostic submissions
  - *Salmonella, Campylobacter*
    - Descrimination between domestic and imported cases
  - *E. coli* associated with disease
  - Other important (non-zoonotic) human pathogens

- Extraction of data from databases with national coverage
  - hospitals
  - general practice
  - All data included (ie no sampling)

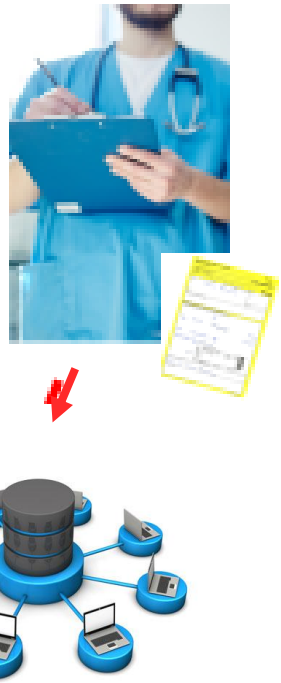
Monitoring use of antimicrobials

- Basic information required
  - Type of antimicrobial
    - Not all are equally potent by weight
    - Type needed to map to AMR
  - Quantity of active compound in formulation
  - Target – human or animals (and species if possible)

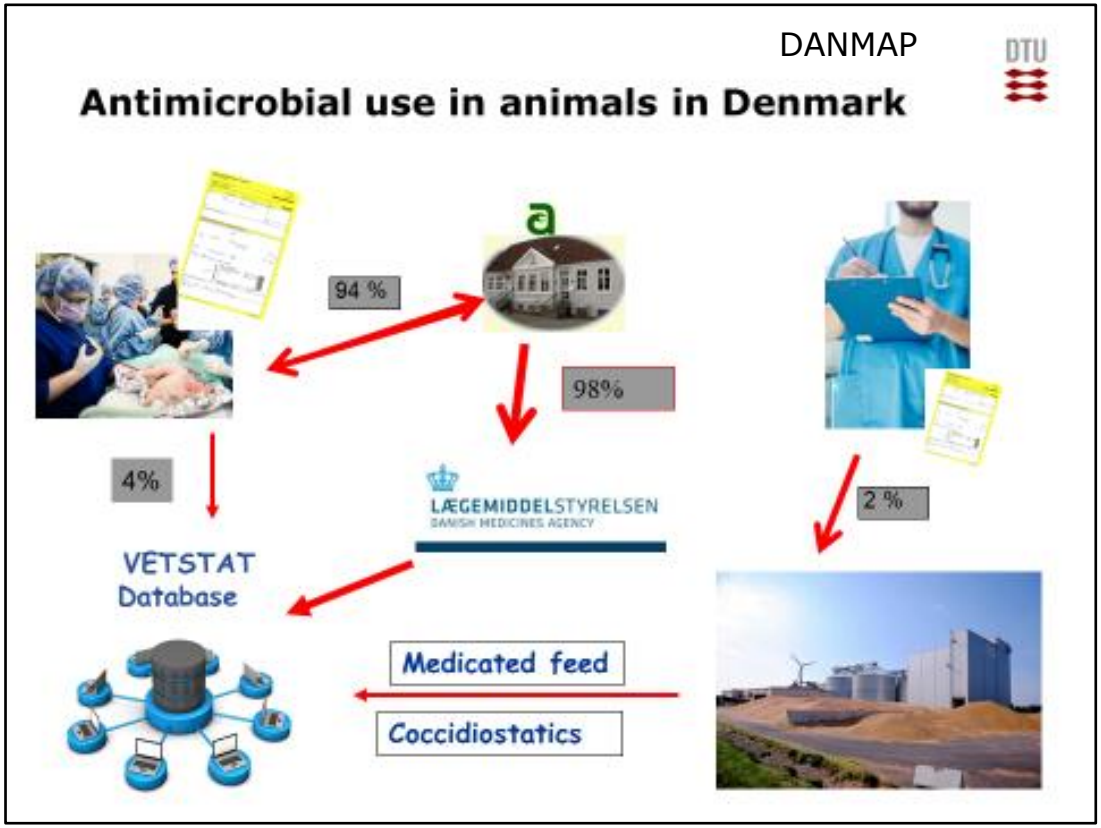
- NOTES:
- Knowledge of quantities of AM used is important, but the knowledge becomes really usefull if denominator information can be included

- Use of antimicrobials is an important driver for AMR, but horizontal spread of AMR microorganisms is highly important also

All antibiotics are sold through licensed outlets - data collected automatically at point-of-sale



Register of Medicinal product statistics



Overview of methods used in Denmark to control AMU

General: all antimicrobials are prescription only, available only through licensed outlets

Veterinary domain

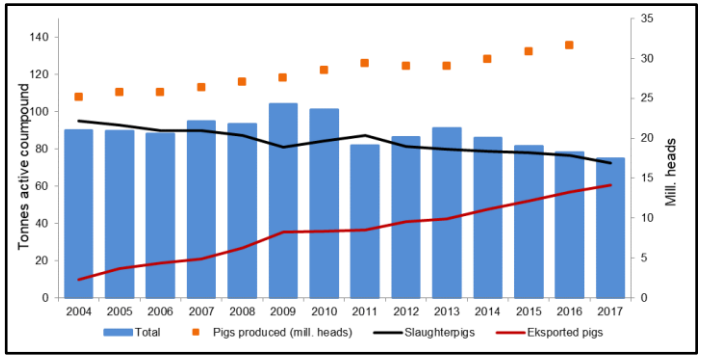
- No financial incentive to prescribe
- Banned antimicrobial growth promoters and prophylactic use
- Electronic Vetstat system captures AM use at farm level and prescribing history of individual vets – benchmarking!
- Differentiated taxes on veterinary medicines
- Treatment guidelines supported by stakeholders

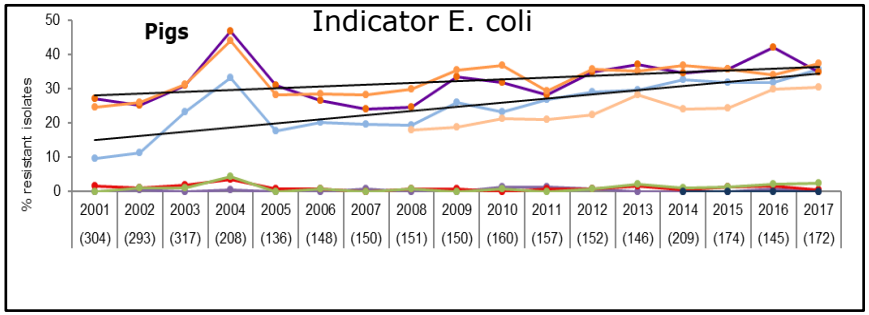
Medical domain

- No economic incentive for doctors to prescripe antimicrobials
- Treatment guidelines
- Education of the general public

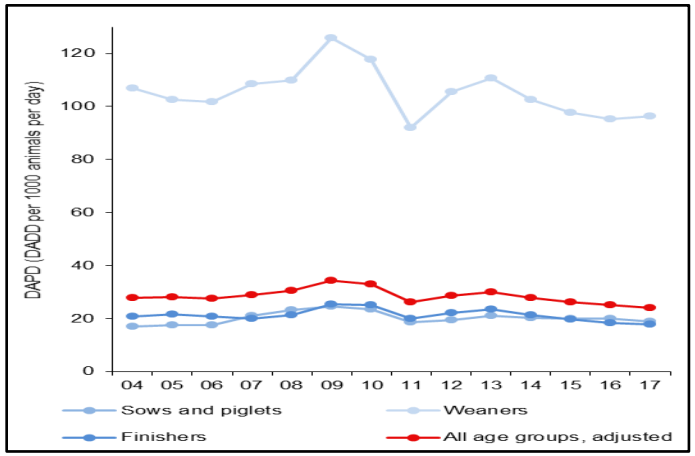
Does reduction of AMU work?

Well, sometimes apparently not



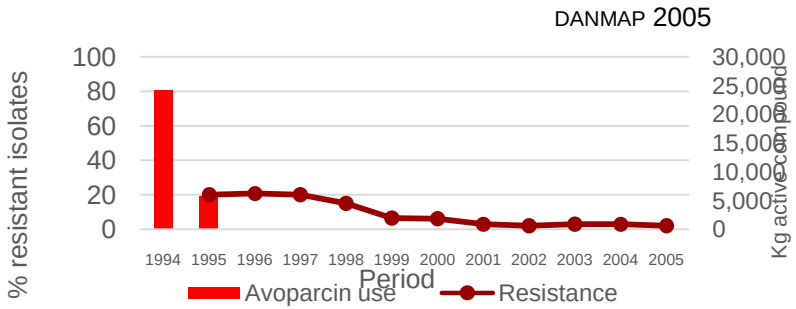


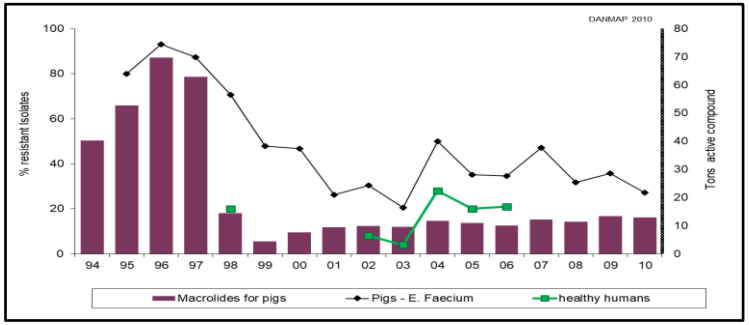
When it doesn't, there are sometimes good explanations



Does reduction of AMU work?

Fortunately, there can also be a very visible effect





In general, preventing excessive AMR through prudent use comes highly recommended !

Measurement of AMR - AST

Credit for the following slides on laboratory methods belongs to:

Prof. Rene Hendriksen

Dr. Valeria Botolaia

Prof. Frank Aarestrup

Centre for Genomic Epidemiology

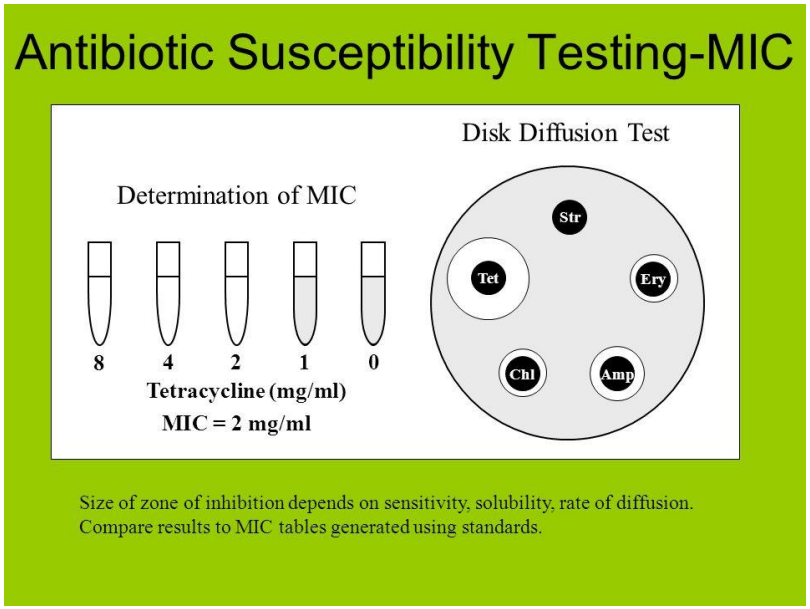
EU Reference Laboratory for AMR

WHO Collaborating Centre for AMR and WGS

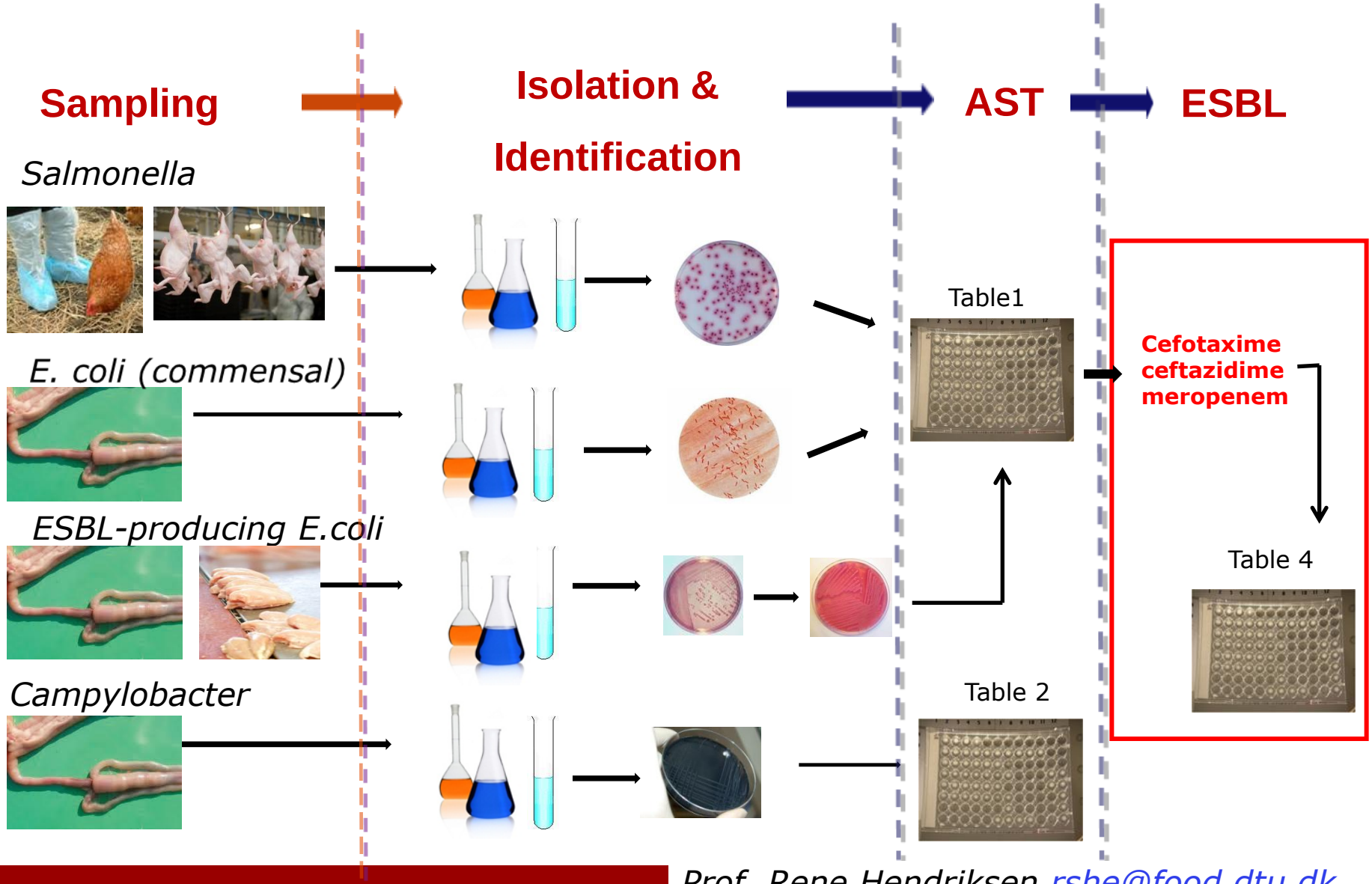
DTU National Food Institute

Measurement of antimicrobial susceptibility – classical AST

- Determination of antimicrobial susceptibility can be done with different methods
- Tablet or disc diffusion
- Microbroth dilution



- Disc diffusion is relatively easy to set up, but standardization can be challenging
- Microbroth dilution (MIC) lends itself to large through-puts and to some automation; allows recording of susceptibility distributions



Prof. Rene Hendriksen rshe@food.dtu.dk

Genetics based approach to AST

- Classical methods for AST measure phenotypic expression of resistance
- An alternative and more recent approach is to determine presence of resistance genes
  - Resistance genes are not always expressed as phenotypic resistance, however, in practice there is high concordance
- ResFinder 4.0 is a new online “AST method” - predicts phenotypic resistance on the basis of genotype
- Classical methods of AST, while considered the gold standard, do not measure AMR with 100 pct. specificity or sensitivity

In conclusion

- Monitoring AMR should be fit for purpose in the local setting
  - What are the most significant AMR reservoirs that needs monitoring?
  - What are the most likely hotspots?
  - How can they best be monitored within the economic constraints present?

- Monitoring AMU
  - How can you get a handle of quantities used?
    - Quantities imported + produced minus exports = use in country! Taxation?
    - Quantity of **active antibiotic** in formulations must be calculated
    - Break down in antibiotic groups is useful and necessary to account for differences in potency
    - Information about populations – denominator info

In conclusion

- Controlling AMU
  - Many knobs to tweak, eg.
    - Legislation to control availability – eg. licensing of outlets
    - Prudent use guidelines supported by stakeholders
    - Lay ‘guardians of antimicrobials’?
  - Prevent AMR from arising or from getting worse

- Measuring AST
  - Different methods with different pros and cons
  - In a monitoring context, stability of methods over time very important
  - Genetics based methods hold great promise

And finally

- AMR is a wicked problem!
  - An invisible foe, rarely apparent to users of antimicrobials
- The overriding concern is to change the perception of antimicrobials among end users to safeguard these potent chemicals that are so precious to human and animal health
- And while we have to combat AMR, in 2013, an estimated 5.7 mio. people globally died, because they did not have access to antibiotics!

Thank you for your attention!

Ressources on line

Susceptibility testing

http://www.genomicepidemiology.org/

- Training courses:
  - https://www.eurl-ar.eu/presentations/training-course-kgs-lyngby-whole-genome-sequencing-september-2017.aspx
  - www.effort-against-amr.eu/page/publications/public-deliverables.php
  - https://www.coursera.org/learn/antimicrobial-resistance

Monitoring AMU

www.aacting.org