





STATENS  
SERUM  
INSTITUT

# DANMAP Seminar

Danish Programme for surveillance of antimicrobial consumption and resistance in bacteria from food animals, food and humans


## Agenda

- Antibiotikaforbrug til dyr
- Antibiotikaforbrug til mennesker
- Antibiotikaresistens i zoonotiske bakterier og indikatorbakterier fra dyr og fødevarer
- Antibiotikaresistens i bakterier fra mennesker
- Antibiotikaresistens i patogene bakterier fra dyr





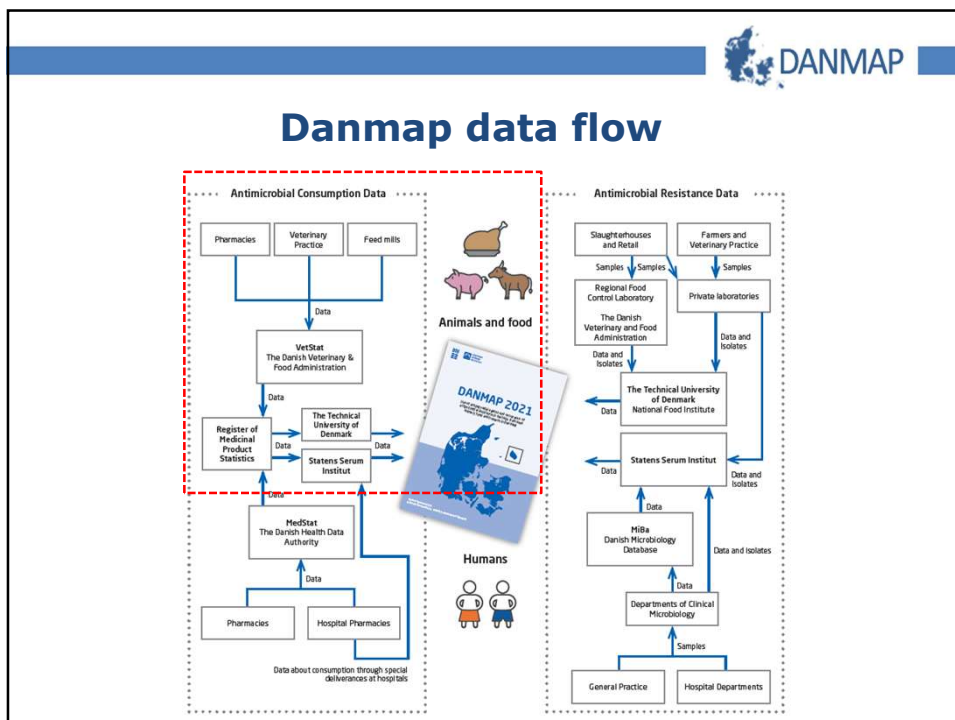

## FORBRUG AF ANTIBIOTIKA TIL DYR

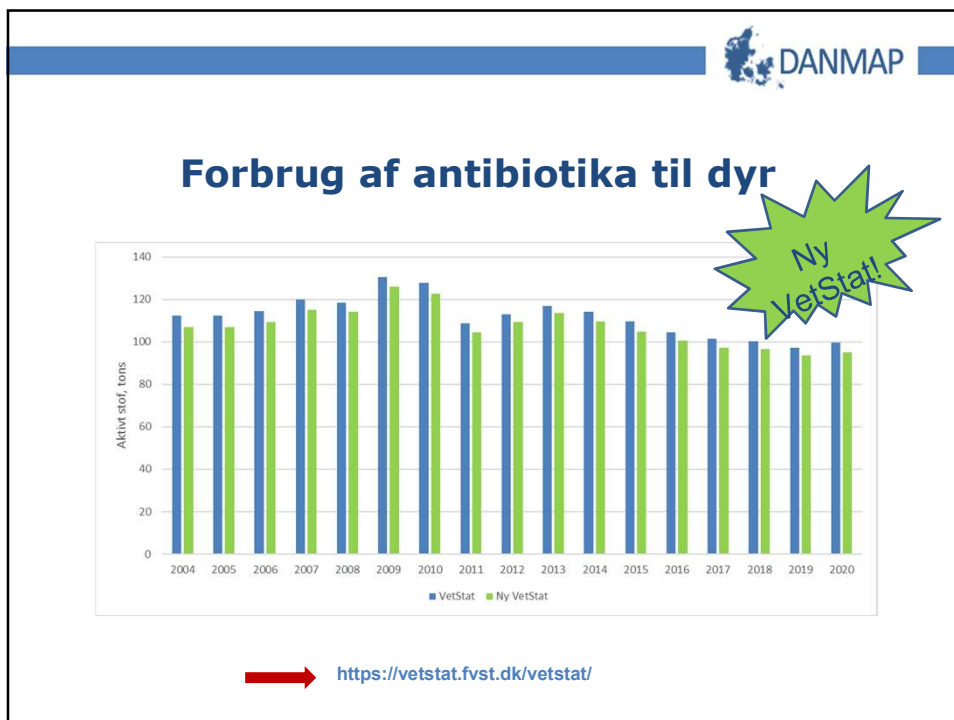
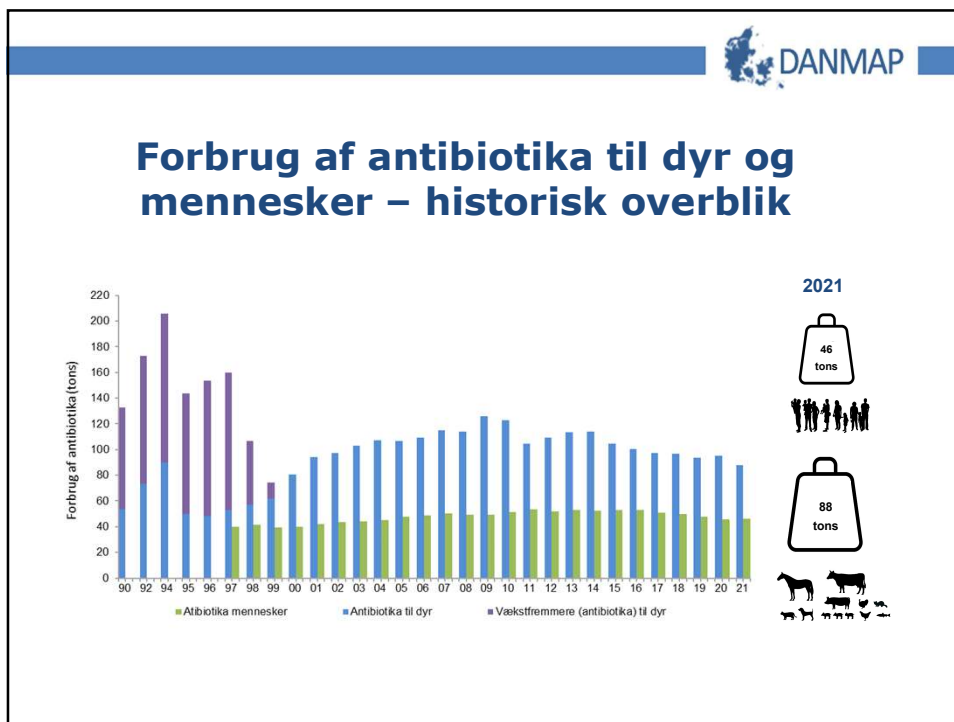


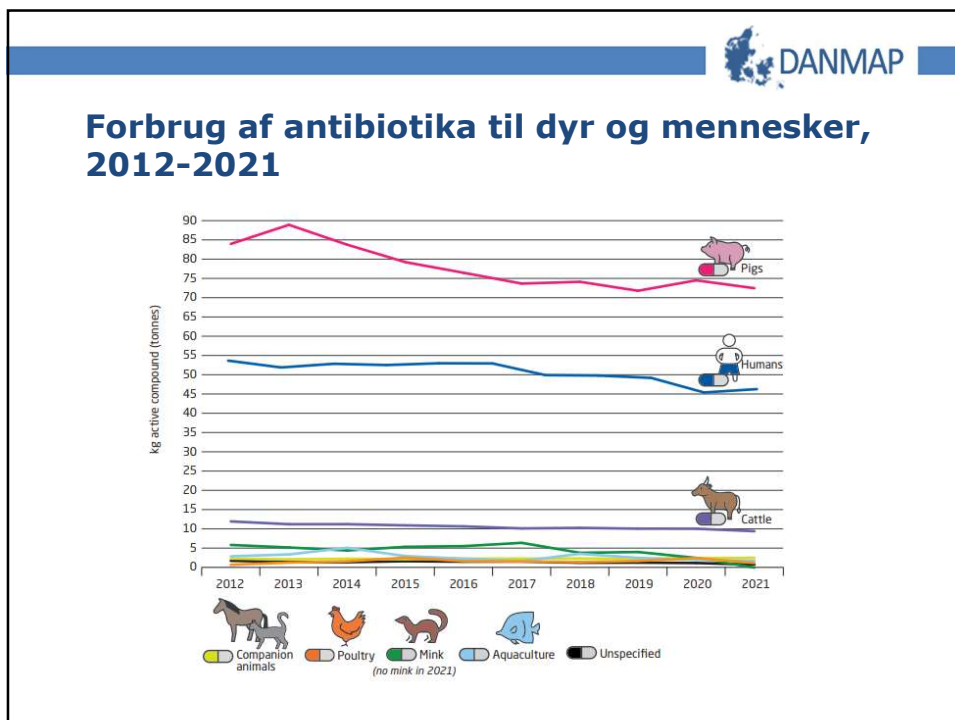
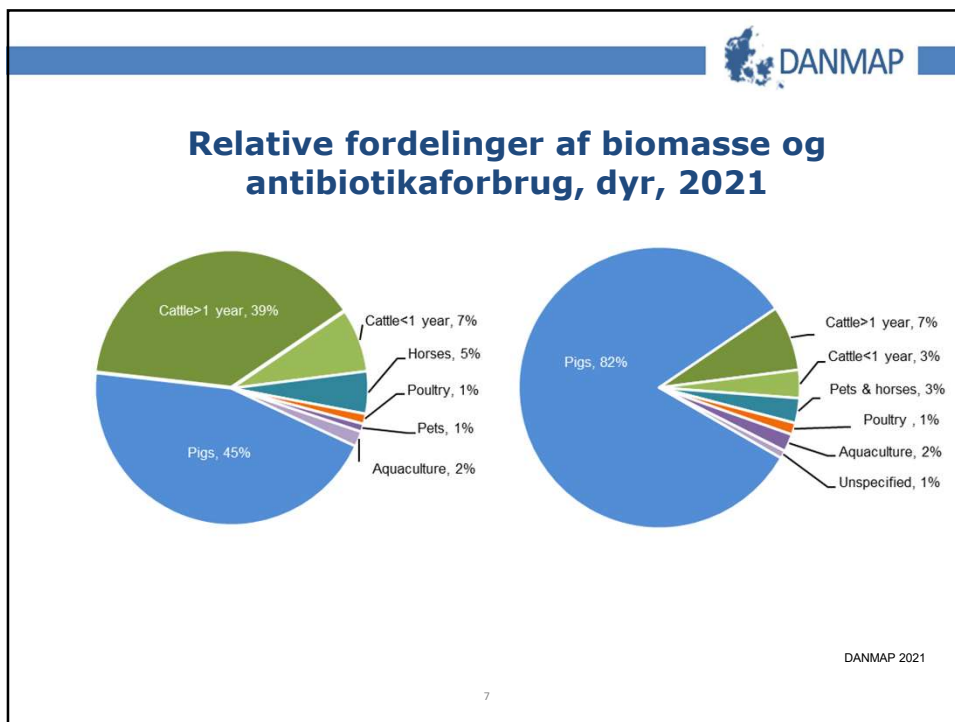
**Birgitte Borck Høg**  
 Dyrlæge, Fødevarestyrelsen  
 (Tidligere: Specialkonsulent, DTU Fødevareinstituttet)

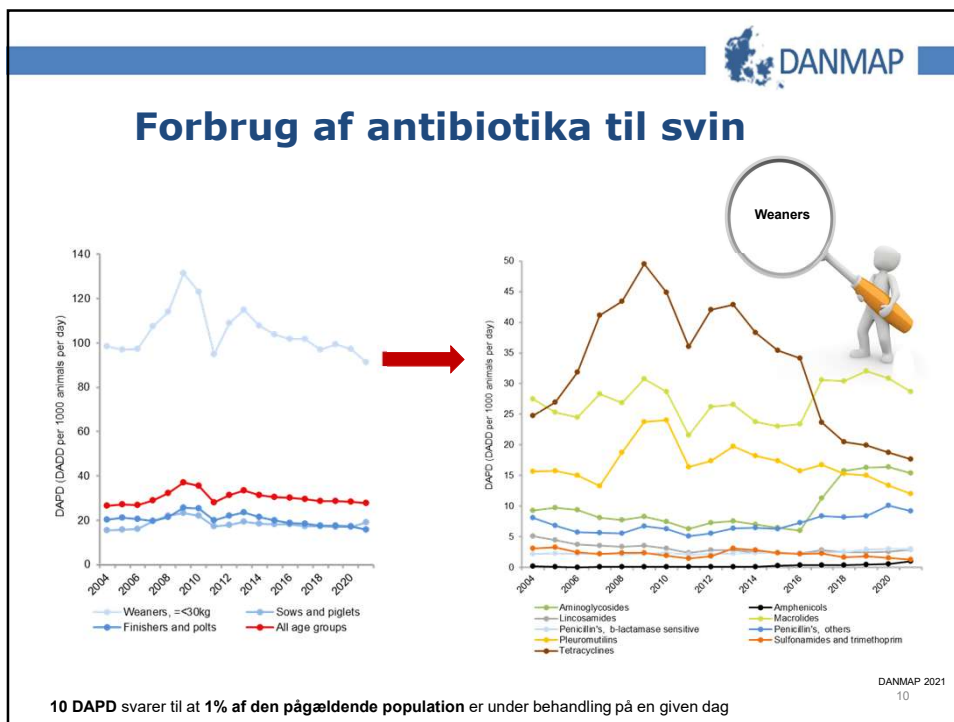
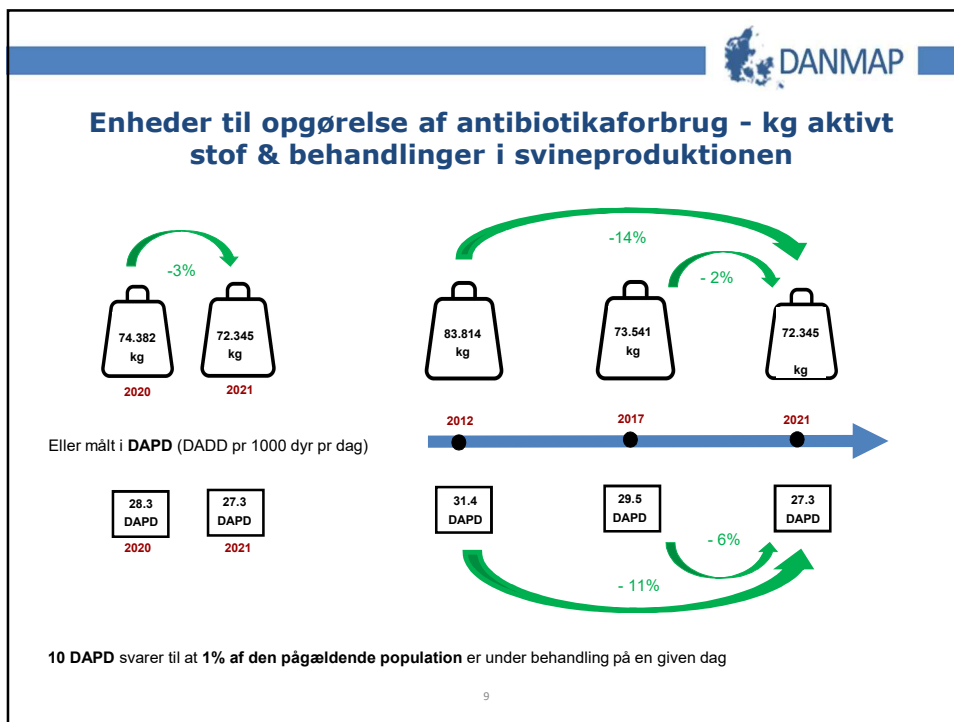
**Vibe Dalhoff Andersen**  
 Dyrlæge, Akademisk medarbejder, DTU Fødevareinstituttet

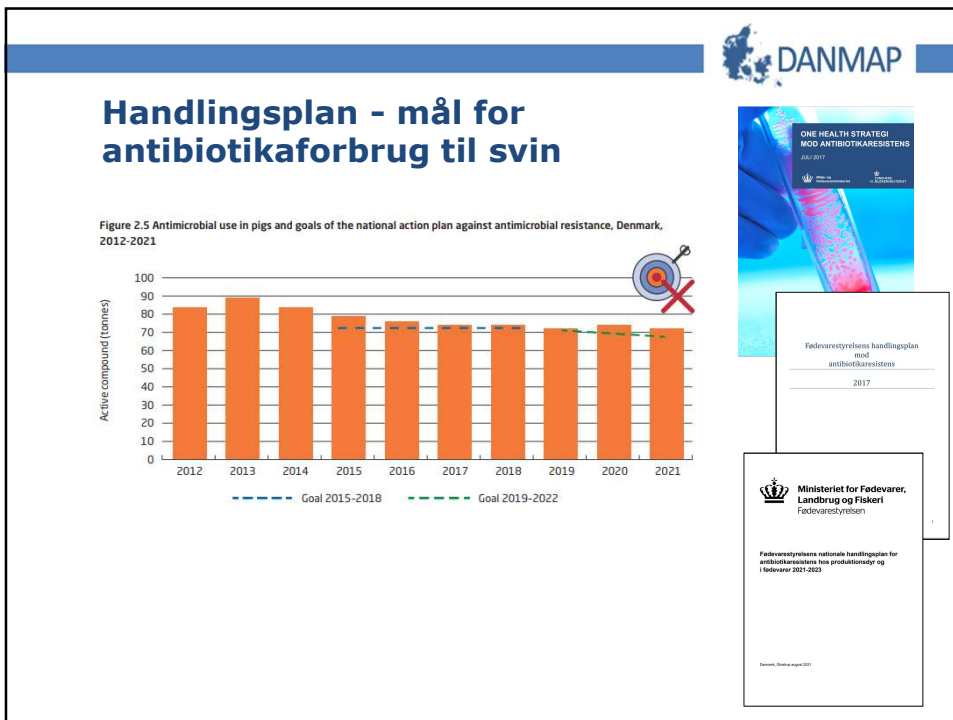
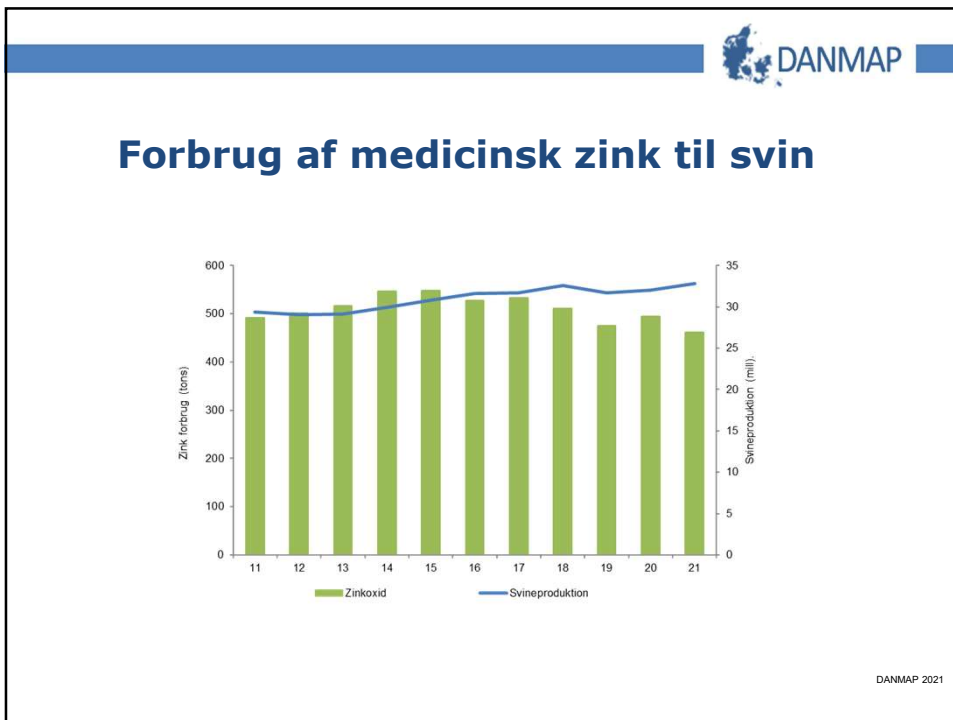


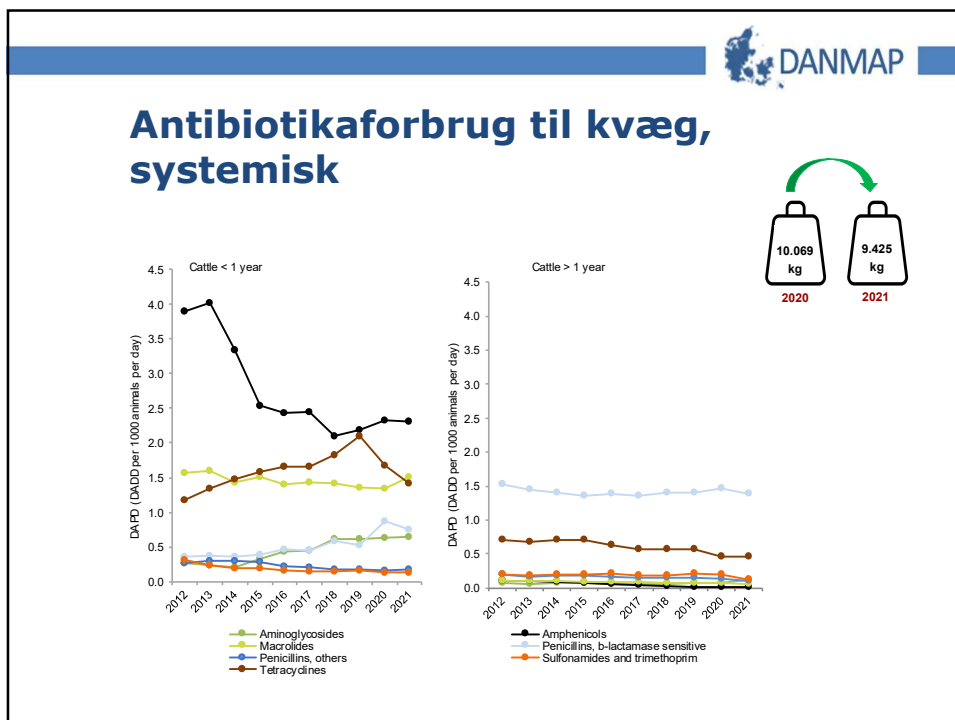
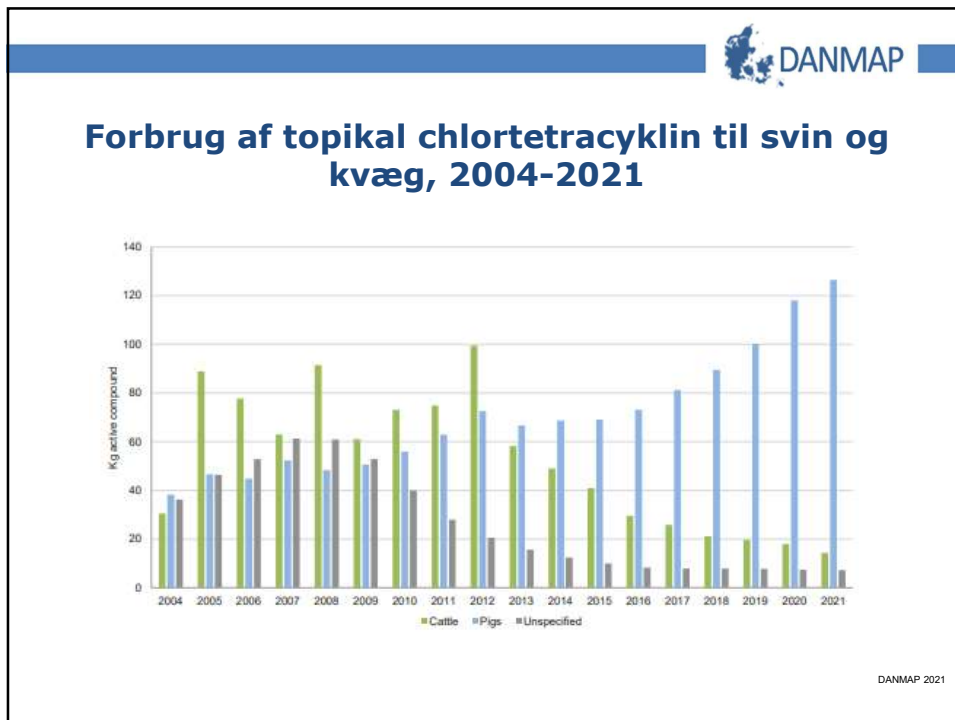


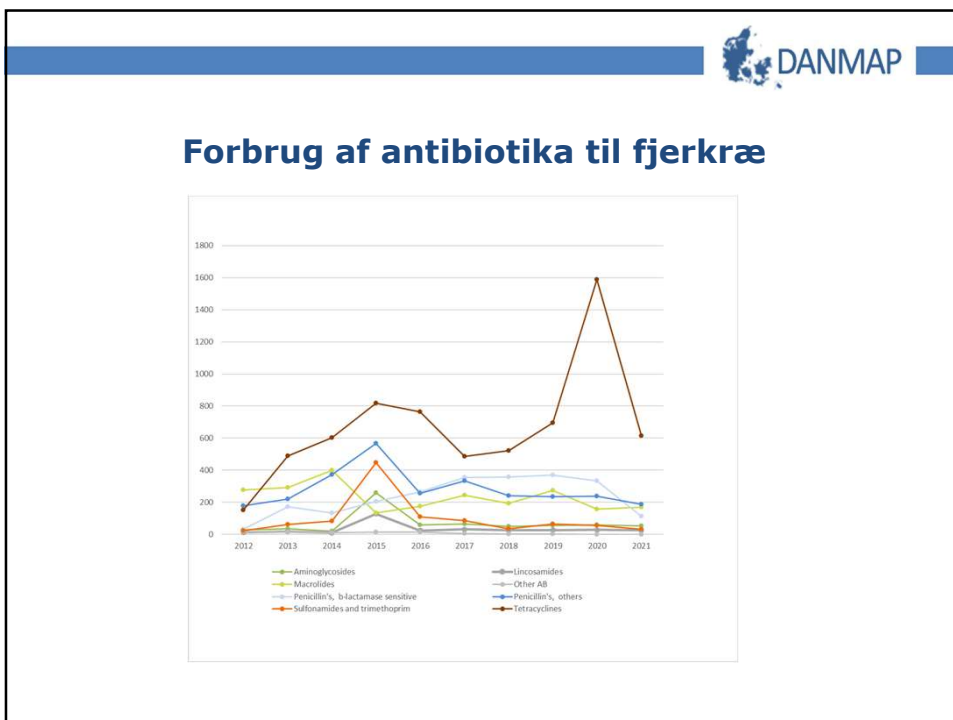
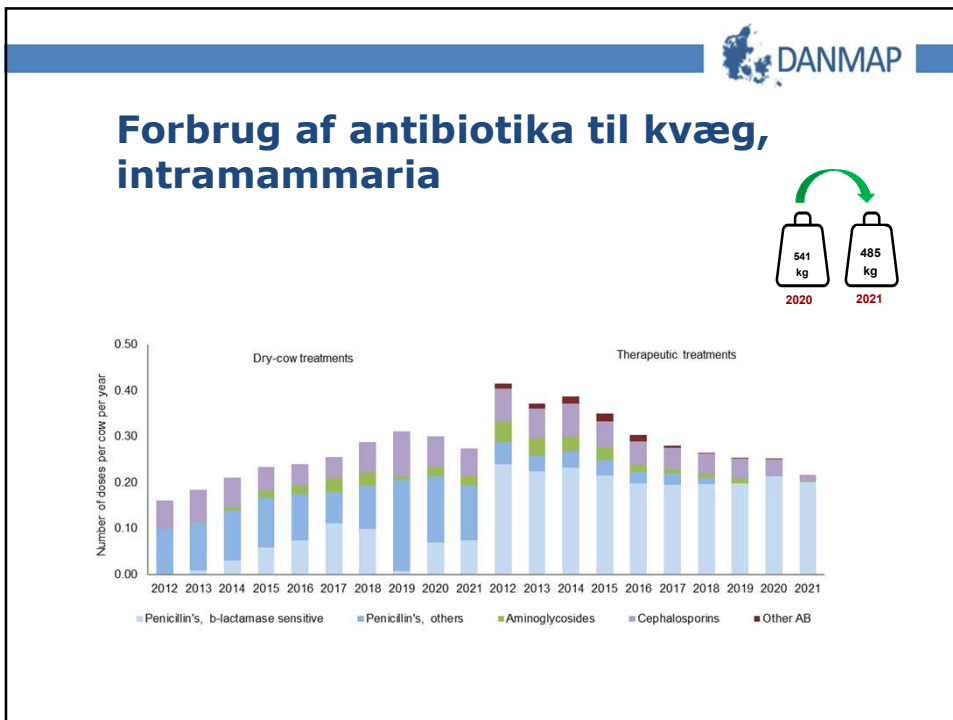




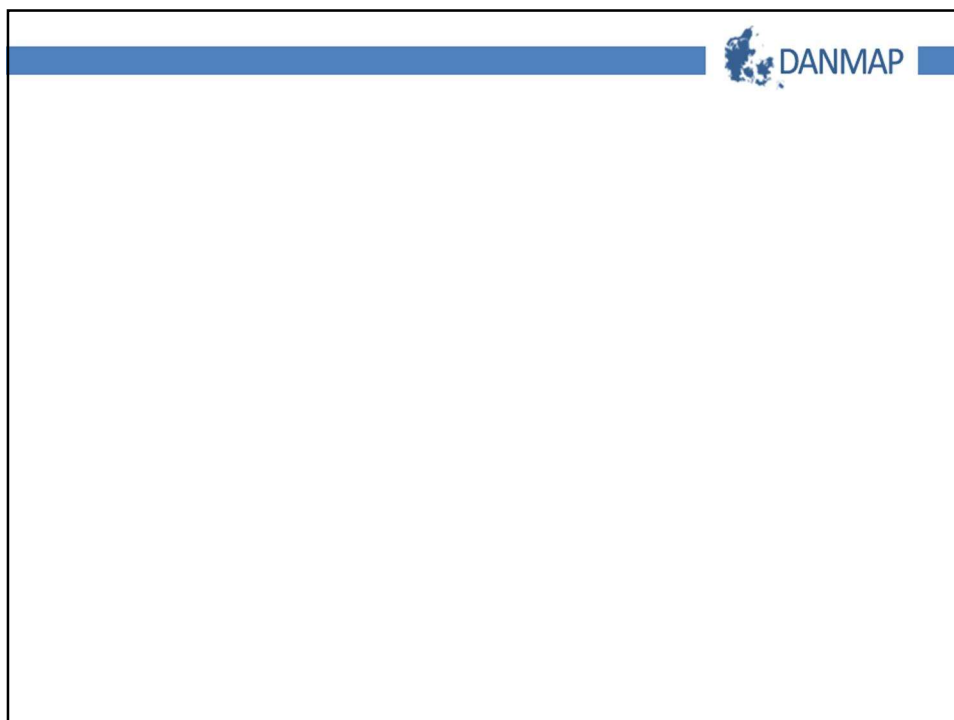
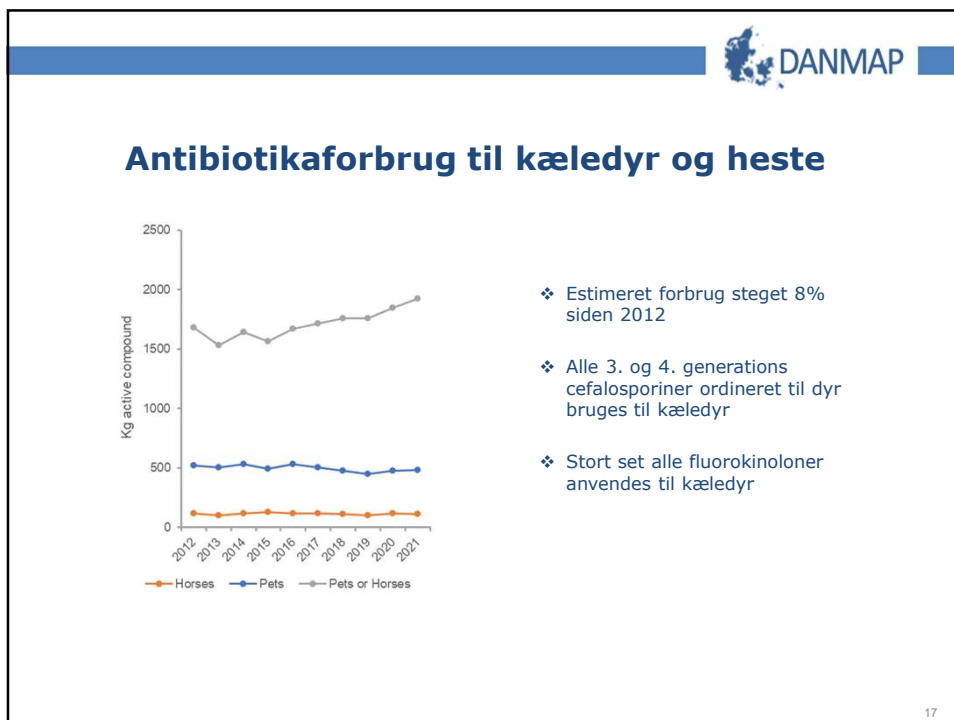















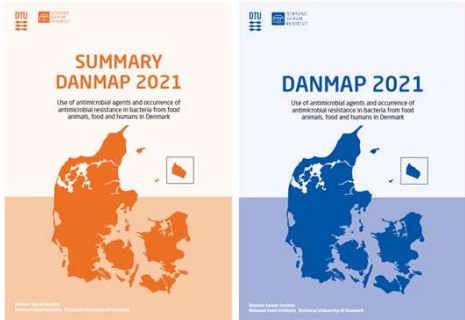


# DANMAP Seminar

## Overvågning af antibiotikaforbruget til mennesker

**Majda Attauabi**  
Cand.pharm

Referencelaboratoriet for Antibiotikaresistens  
Infektionsberedskabet  
Statens Serum Institut





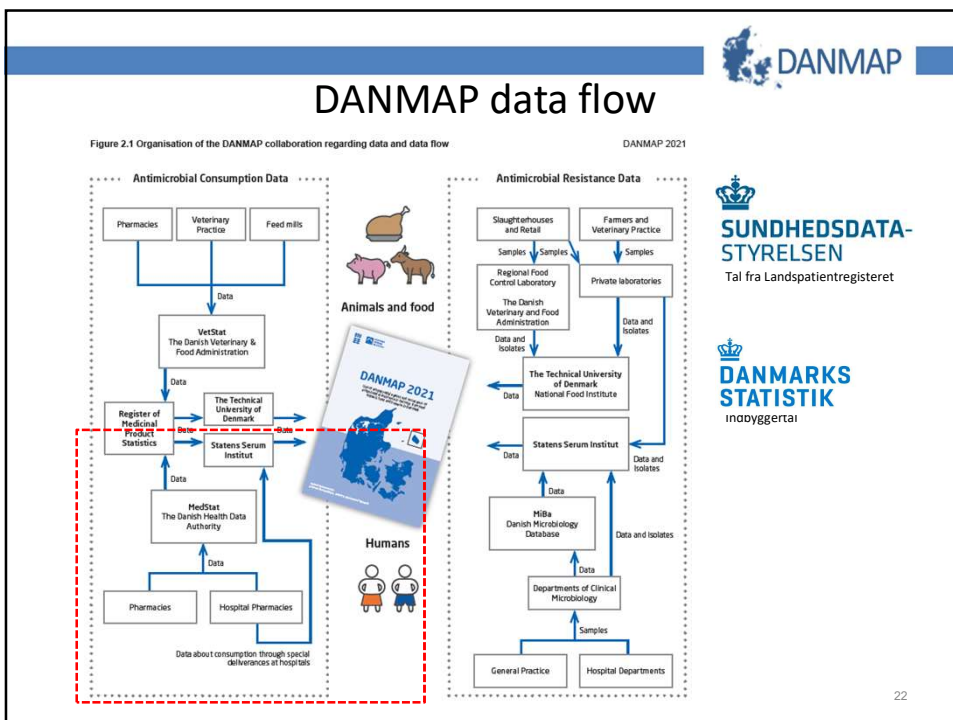
# Agenda

- Opgørelsesmetoder
- Antibiotika på landsplan
- Antibiotika i primærsektoren
- Antibiotika på plejehjemmene
- Antibiotika på hospitalerne
- Opsummering





## OPGØRELSESMETODER





## Forbrug kan måles på mange måder



Antal recepter



Antal behandlede

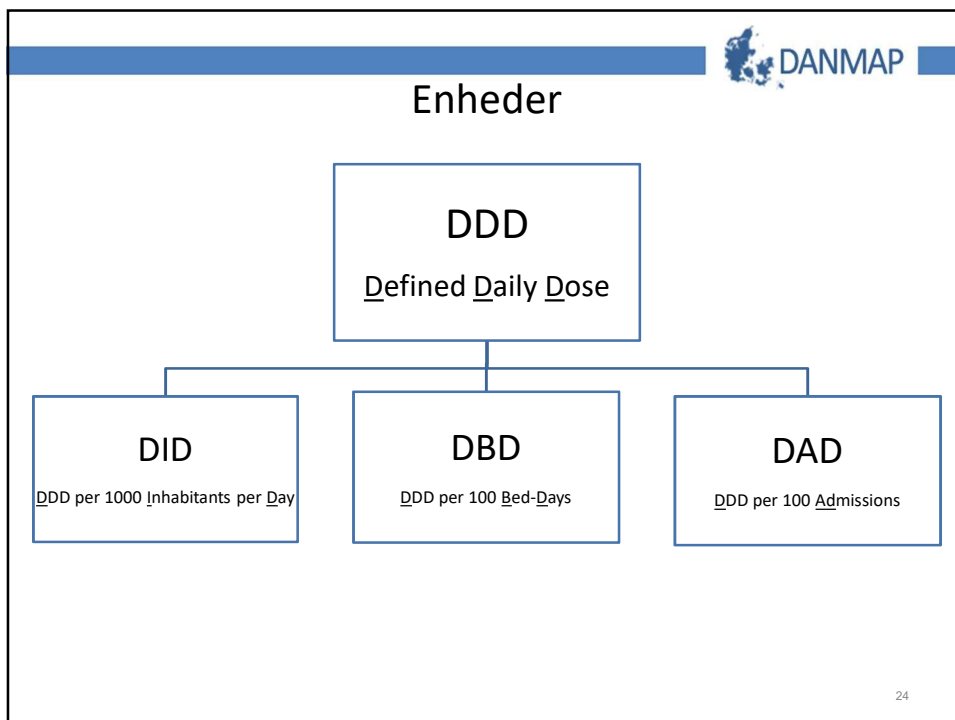


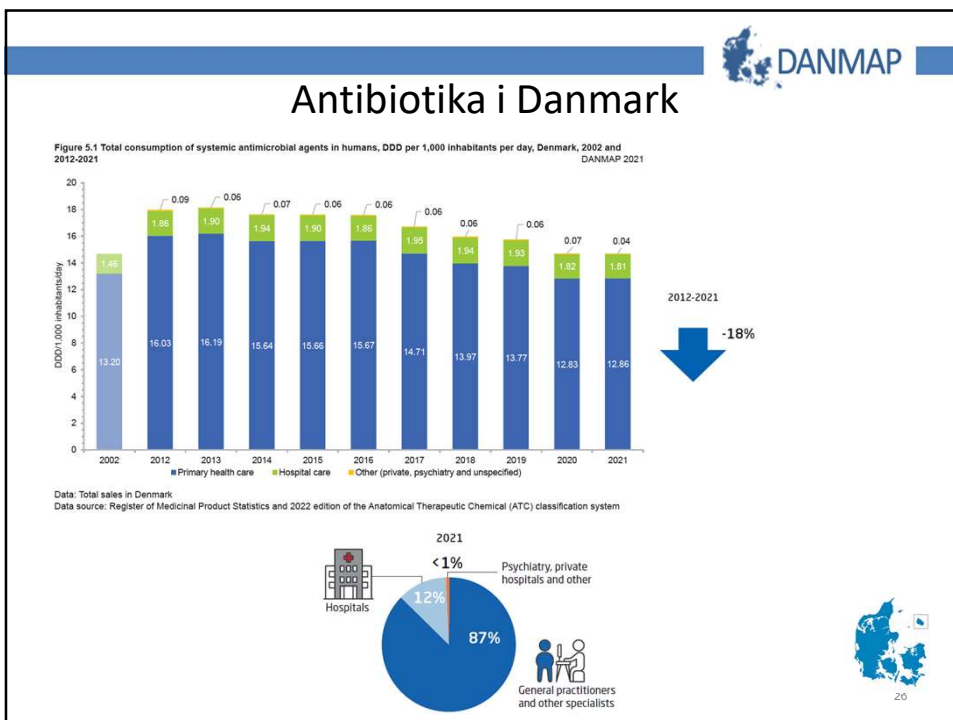
Definerede døgndoser (DDD)

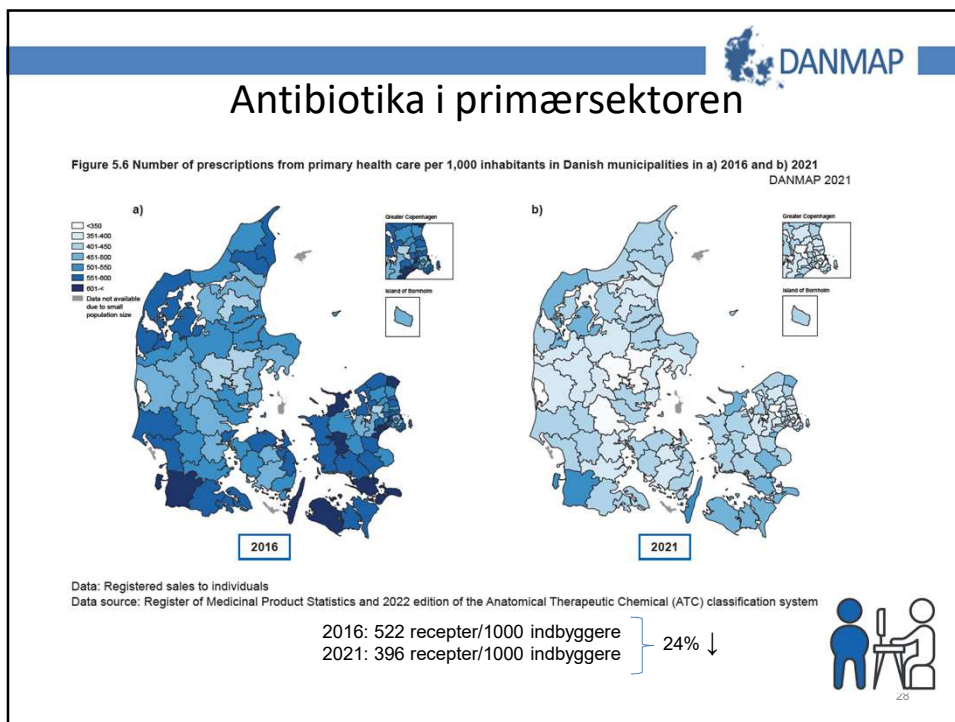
” DDD er den gennemsnitlige vedligeholdelsesdosis per dag for et lægemiddel, når det bruges til dets hovedindikation til behandling af voksne ”

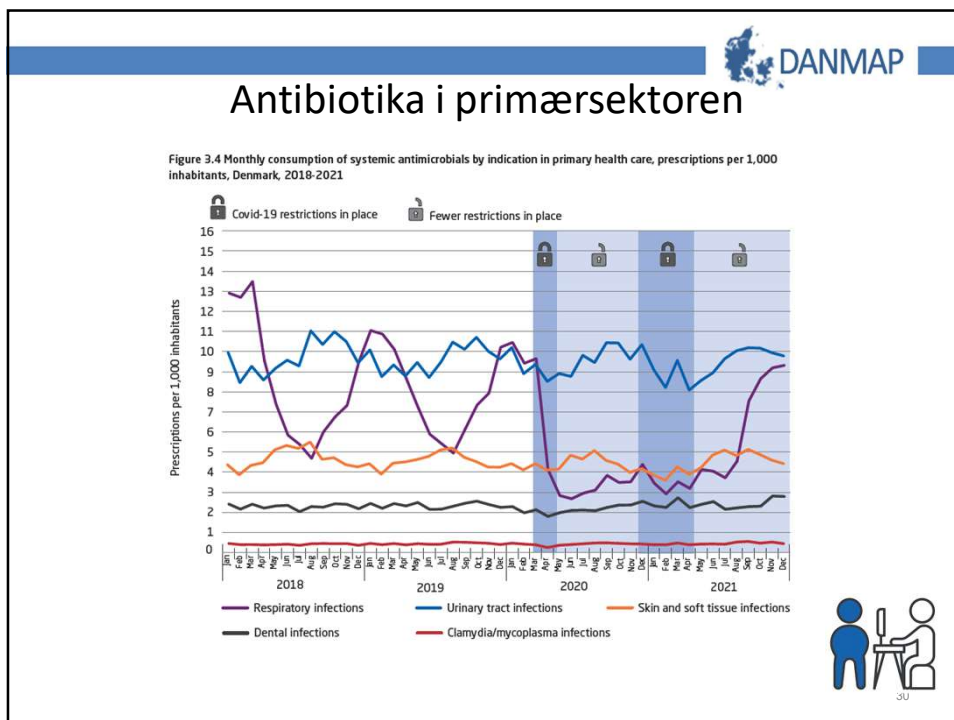
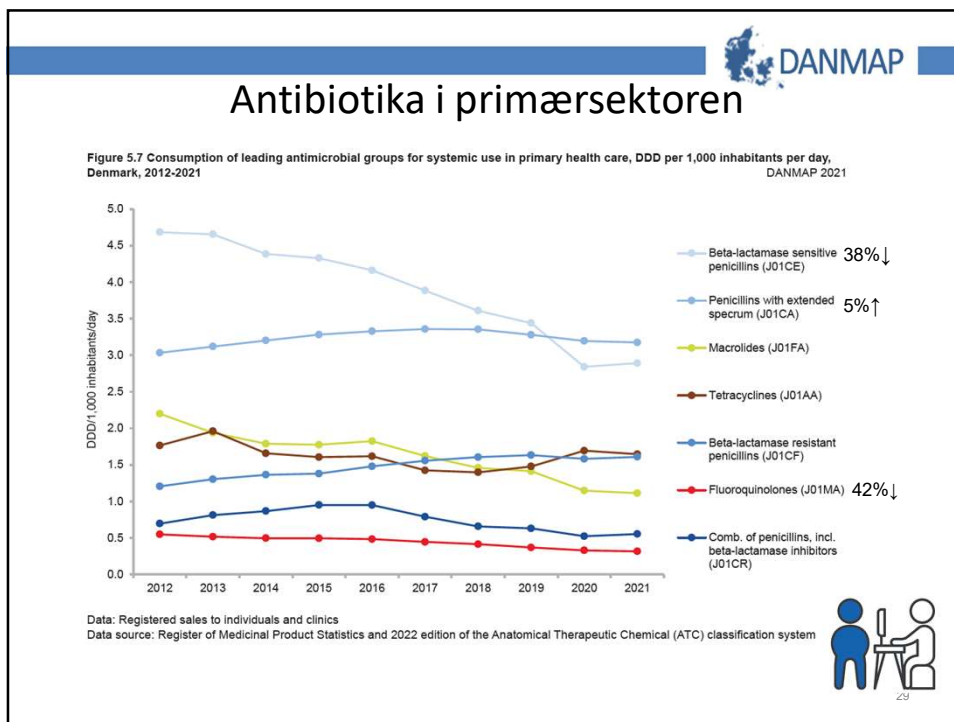


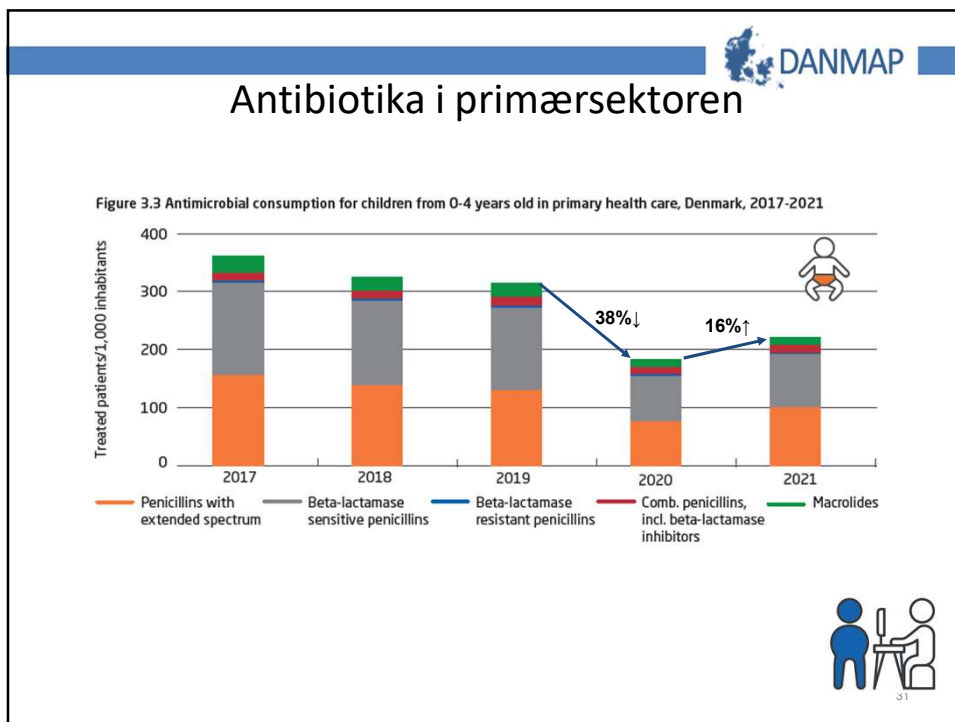
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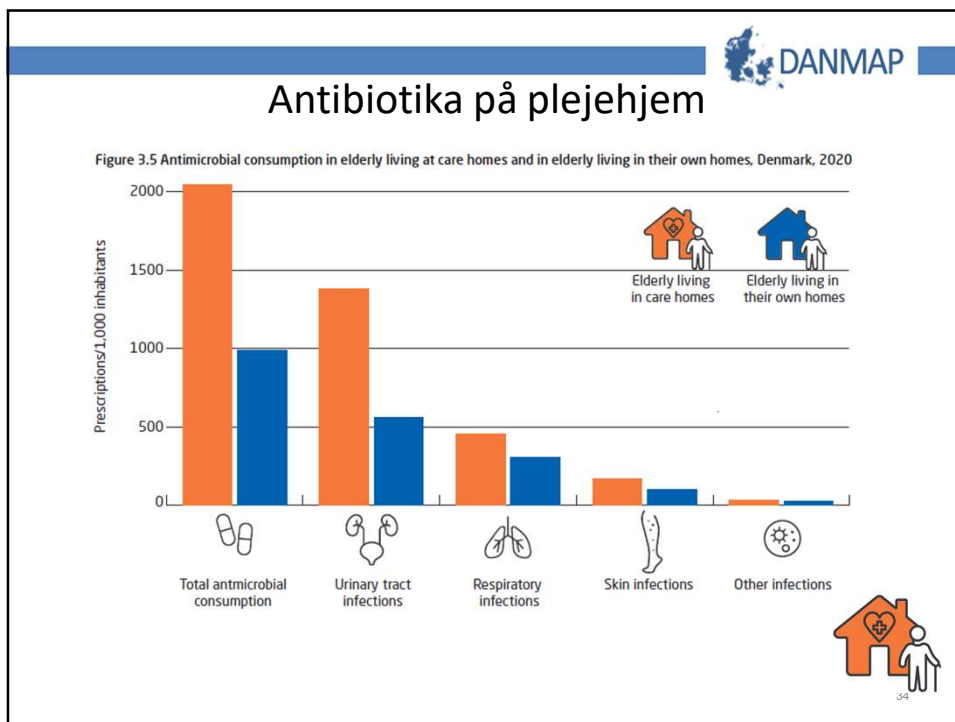
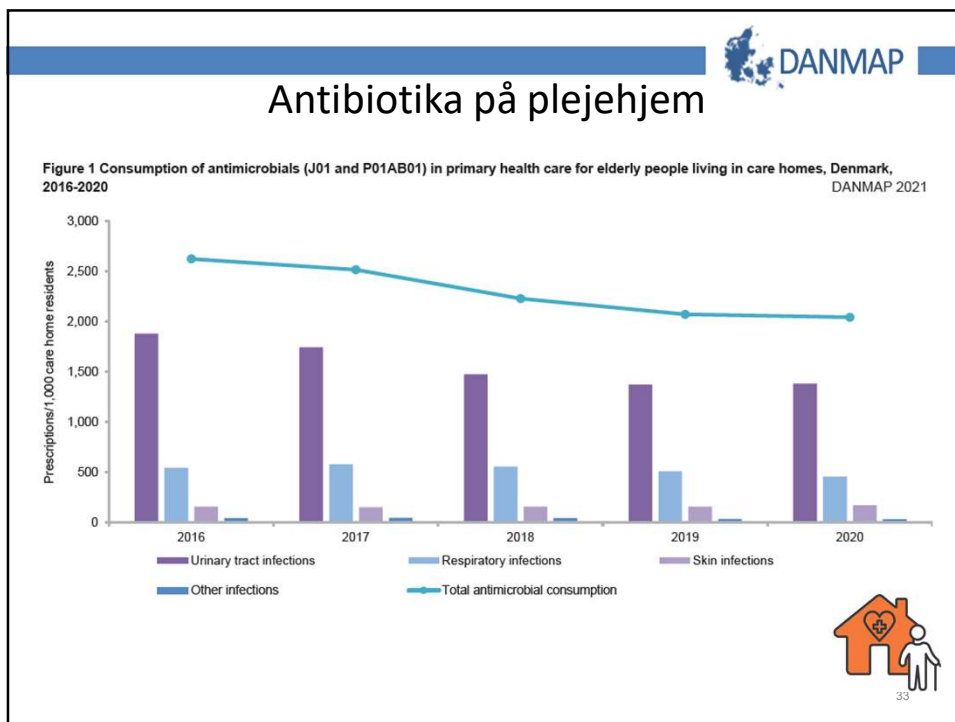


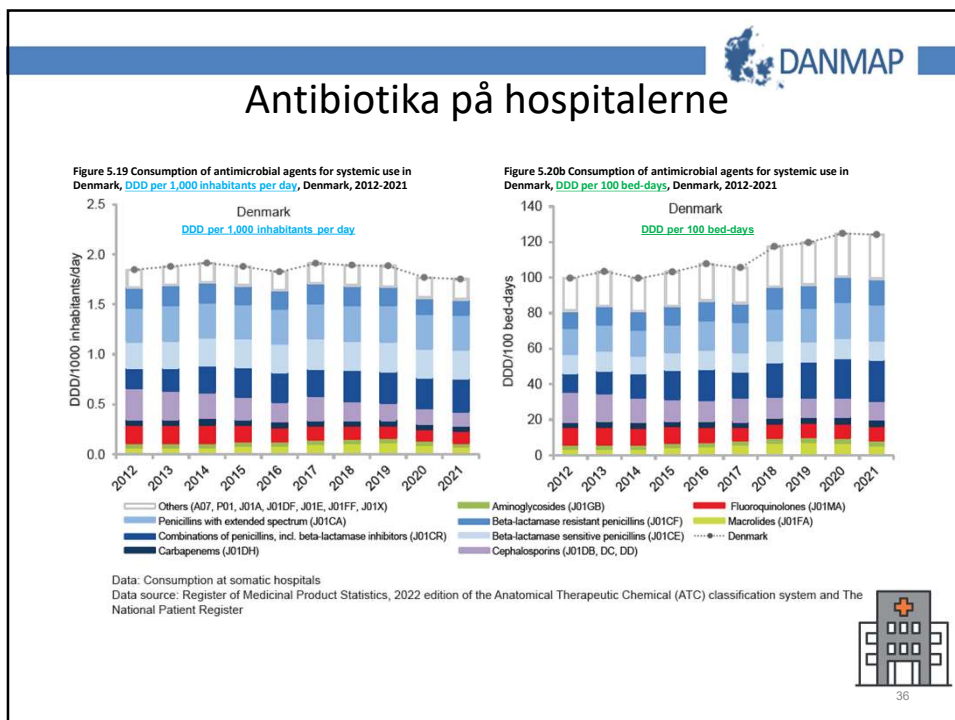


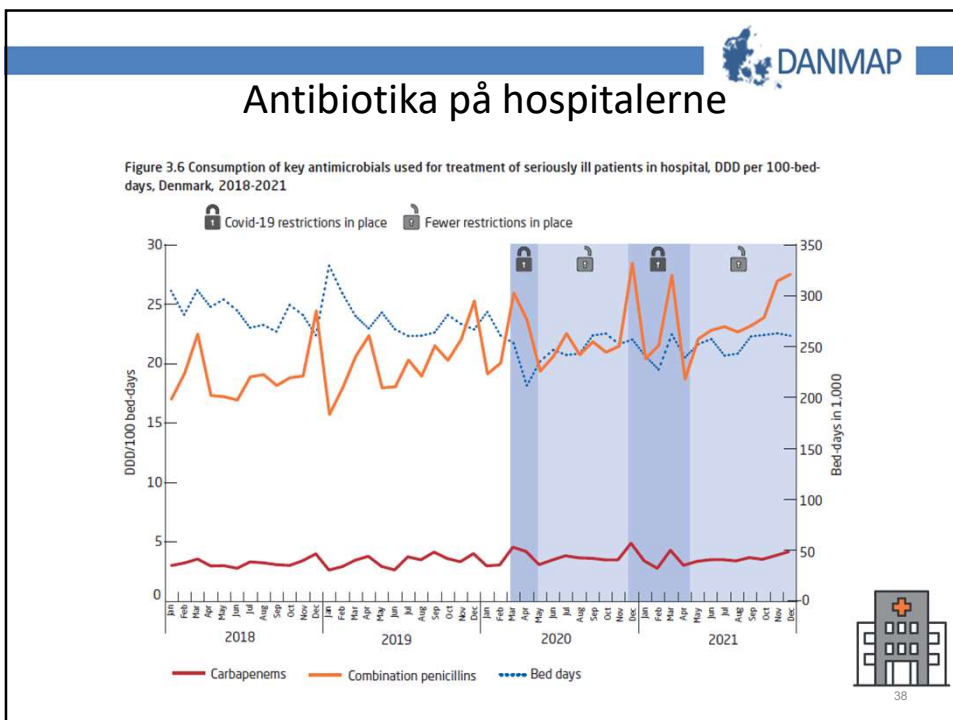
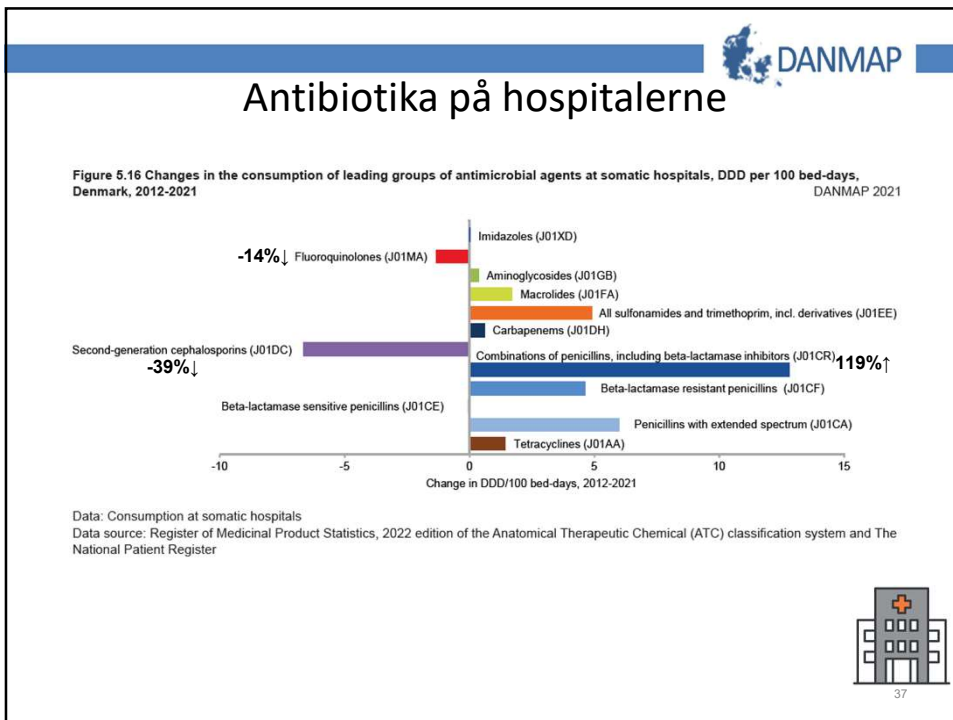


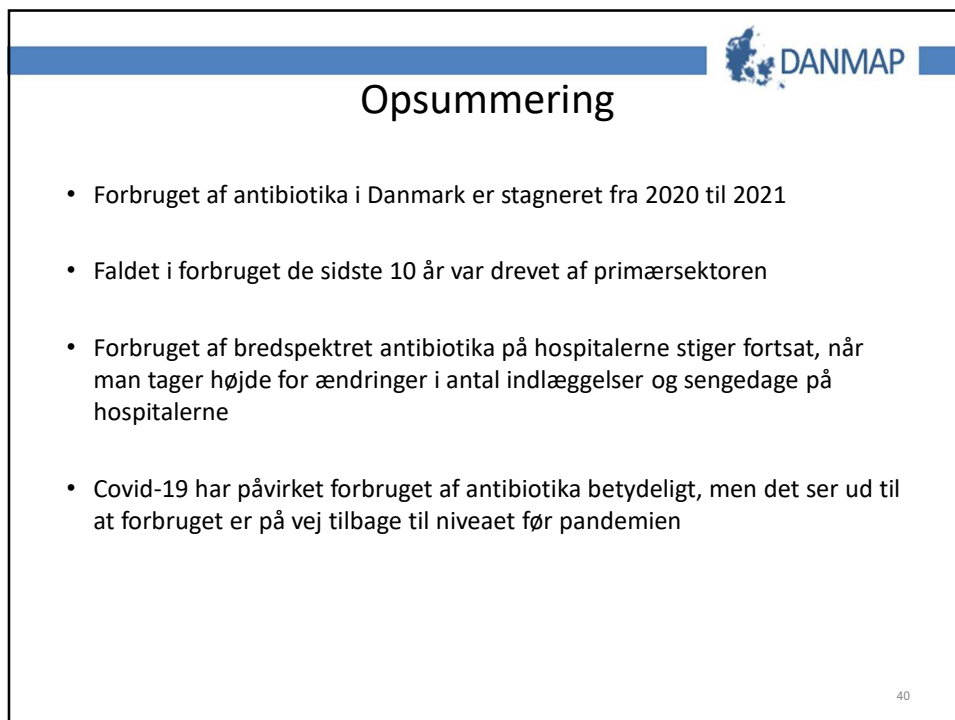
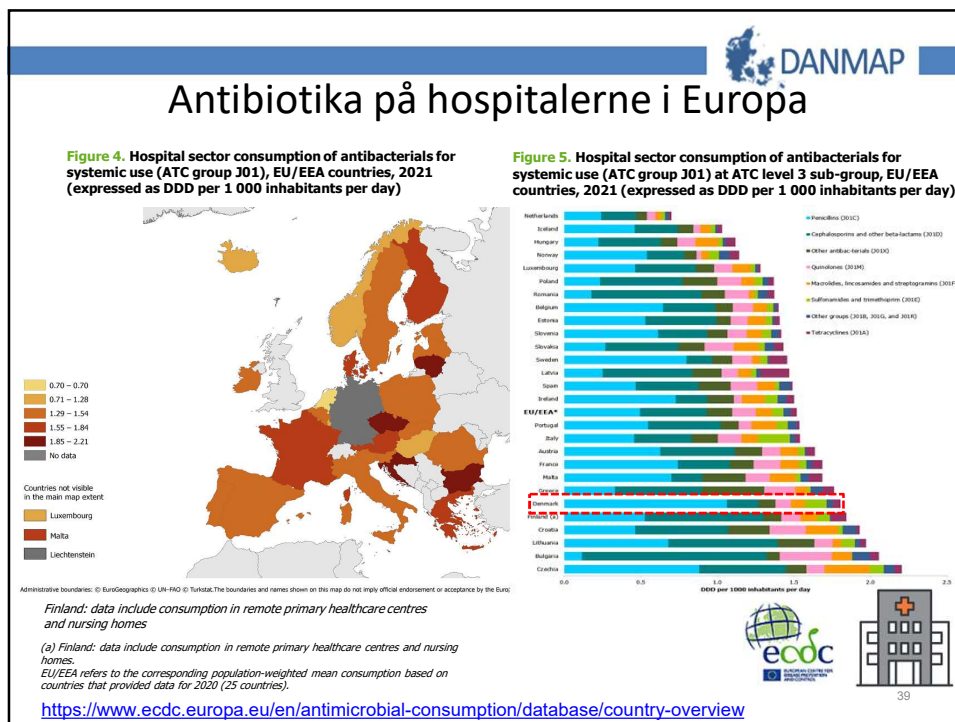









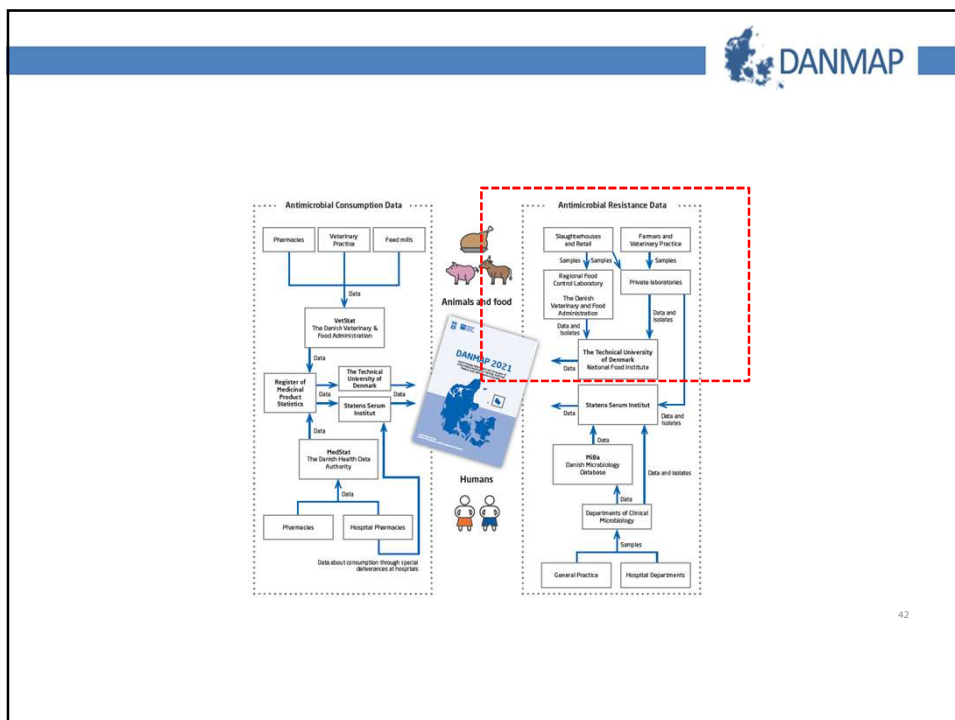





# Antimicrobial resistance in bacteria from food animals and food Denmark, 2021

Ana Sofia Ribeiro Duarte  
Senior Researcher  
DTU National Food Institute  
Foodborne Pathogens and Epidemiology






## New EU legislation for harmonized AMR monitoring

Decision 2020/1729/EU, 1 January 2021:

- Mandatory monitoring of:
  - *Campylobacter coli*
  - ESBL-, AmpC- or CP-producing *E. coli* in imported fresh meat sampled at Border Control Posts
  - ESBL-, AmpC- or CP-producing *E. coli* in fresh turkey meat sampled at retail and at BCPs
- Allows the use of WGS instead of AST for specific or confirmatory testing of ESBL-, AmpC- or CP-producing *E. coli*
- Changes in AST panels' substances and concentrations
- Changes in ECOFFs


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## Changes in AST panels and ECOFFs




- *Salmonella* and *E. coli*
  - » inclusion of amikacin
- *Campylobacter*
  - » removal of nalidixic acid and streptomycin
  - » inclusion of chloramphenicol and ertapenem
- Changes in ECOFFs
  - » Ampicillin (8 -> 4)
  - » Cefepime (0.125 -> 0.25)
  - » Ertapenem (0.064 -> 0.03)
  - » Meropenem (0.125 -> 0.06)
  - » Nalidixic acid (16 -> 8)
  - » Temocilin (32 -> 16)
  - » Tigecycline (1 -> 0.5)

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## Overview of animal isolates reported in DANMAP



**Caecal samples:**

- All samples: inc
- Pig and cattle s.....    coli
- Selection of pig samples: indicator *Enterococci* (*E. faecium*, *E. faecalis*; *E. faecalis* AST)

**Meat samples collected at retail/BCPs:**

- All samples: ESBL/AmpC/carbapenemase-DI    
- Retail samples: Salmonella

**Carcass swabs at the slaughterhouse:**

- Salmonella (national control program)  

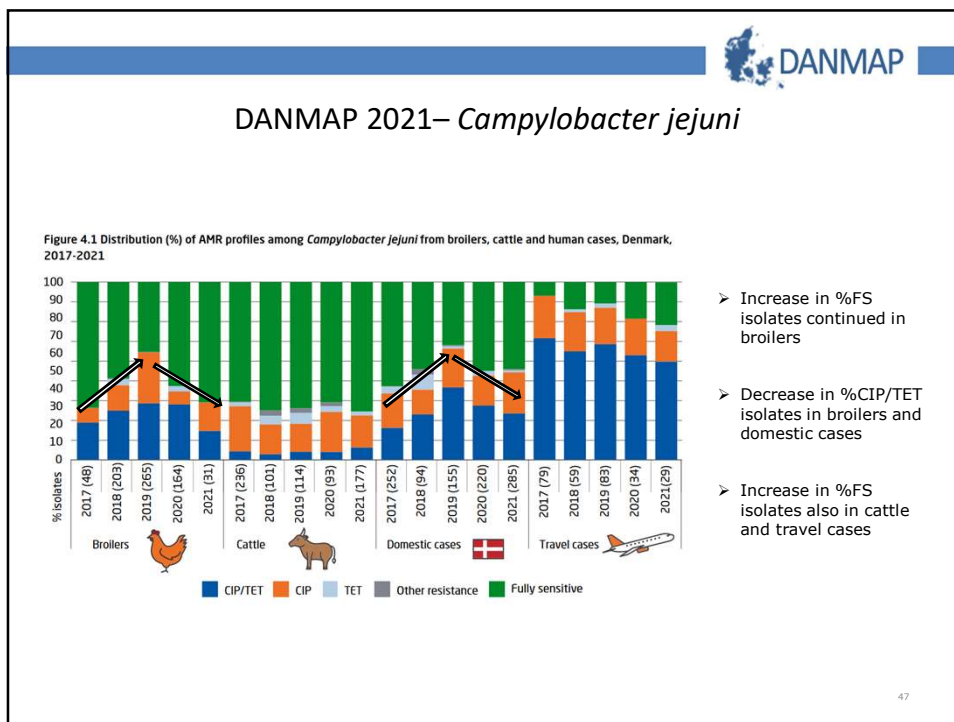
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## Resistance in zoonotic bacteria

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### DANMAP 2021– *C. jejuni* and *C. coli*

Table 4.1 Resistance (%) in *Campylobacter jejuni* isolates from broilers, cattle and human cases, Denmark, 2021

Antimicrobial agent	Broilers		Cattle		Human			Total %
	Danish %	Danish %	Danish %	Domestically acquired %	Travel abroad reported %	Unknown origin %	%	
Chloramphenicol	0	0	0	0	0	0	0	0
Ciprofloxacin	32	25	49	49	72	57	52	52
Ertapenem	0	0	4	4	14	6	5	5
Erythromycin	0	0	0	0	0	2	<1	<1
Gentamicin	0	0	0	0	0	0	0	0
Tetracycline	16	9	27	27	59	31	30	30
Fully sensitive (%)	68	73	49	49	24	41	46	46
Number of isolates	31	177	285	285	29	49	363	363

➤ Higher AMR occurrence in human isolates

➤ Common CIP and/or TET resistance

➤ Ertapenem resistance in *C. coli* from pigs, and *C. jejuni* from humans

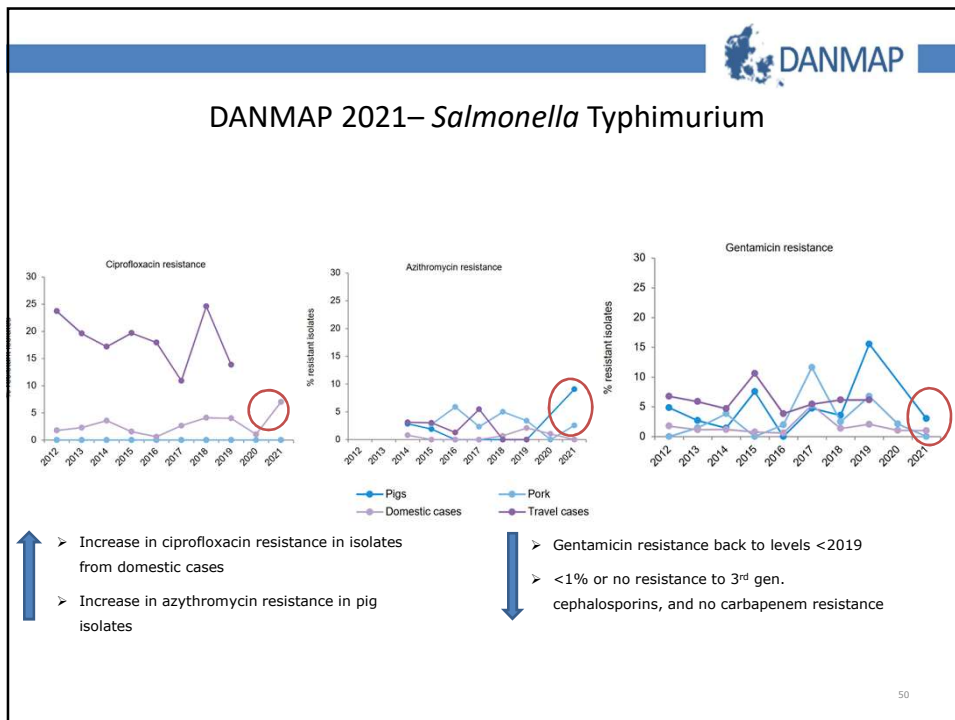
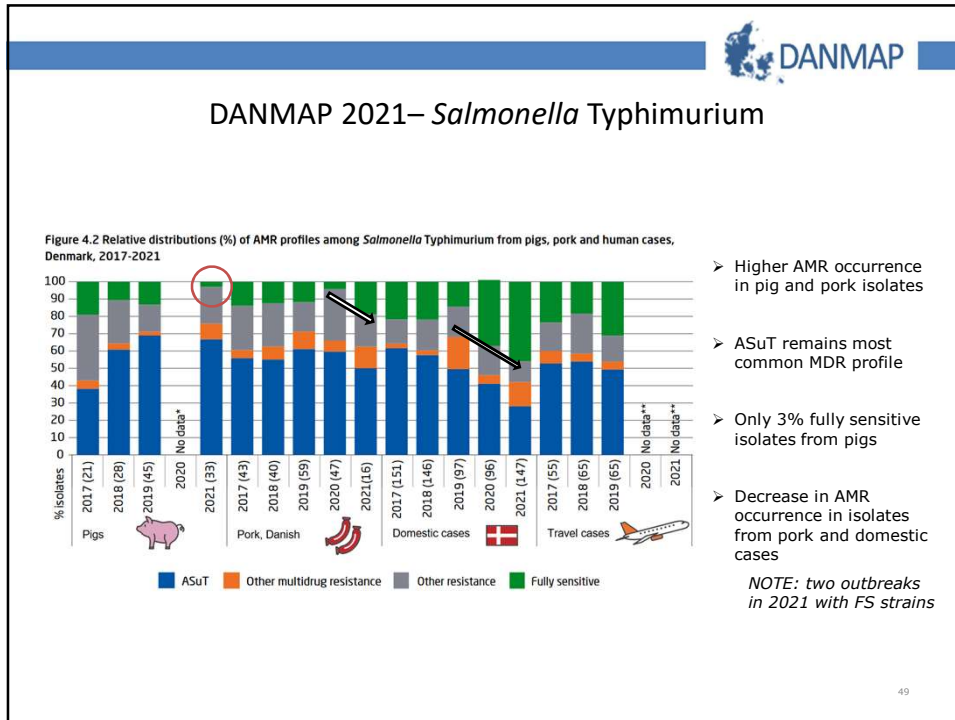
➤ Erythromycin resistance detected in *C. coli*

***Campylobacter coli*:**

- 20% and 26% resistant against ciprofloxacin and tetracycline
- Gentamicin and chloramphenicol resistance - not observed
- Erythromycin resistance: 6% (7 isolates)
- Ertapenem resistance: 1 isolate

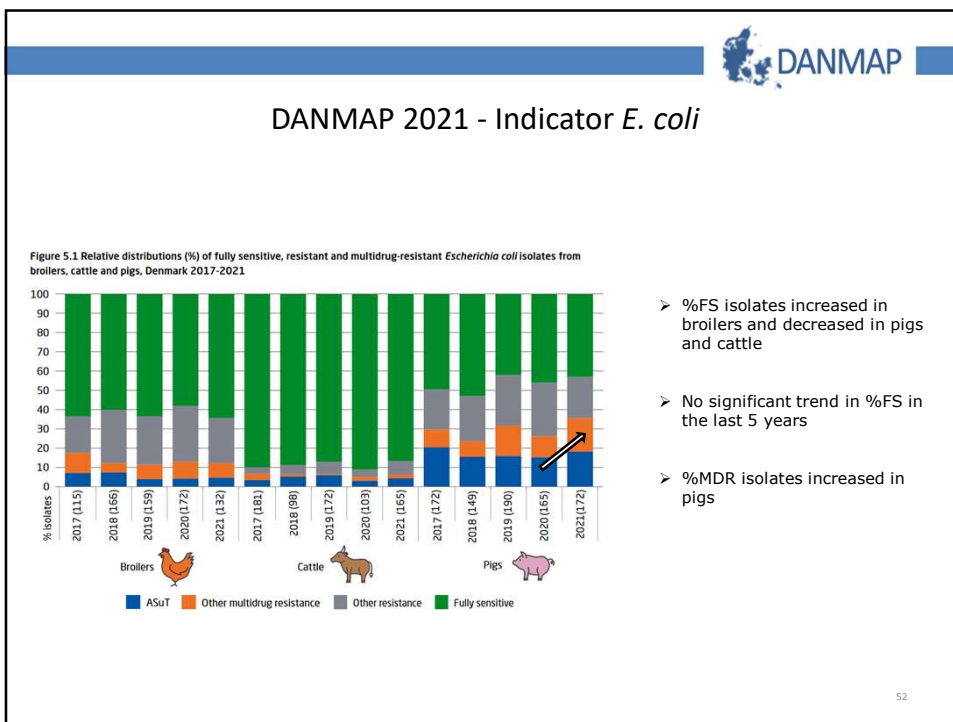
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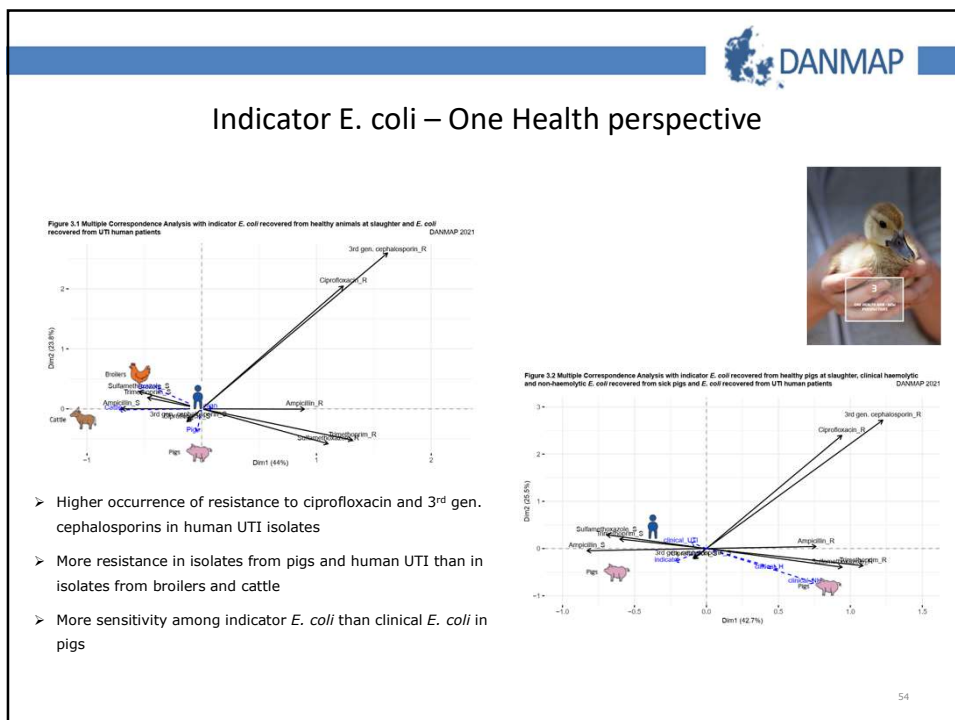
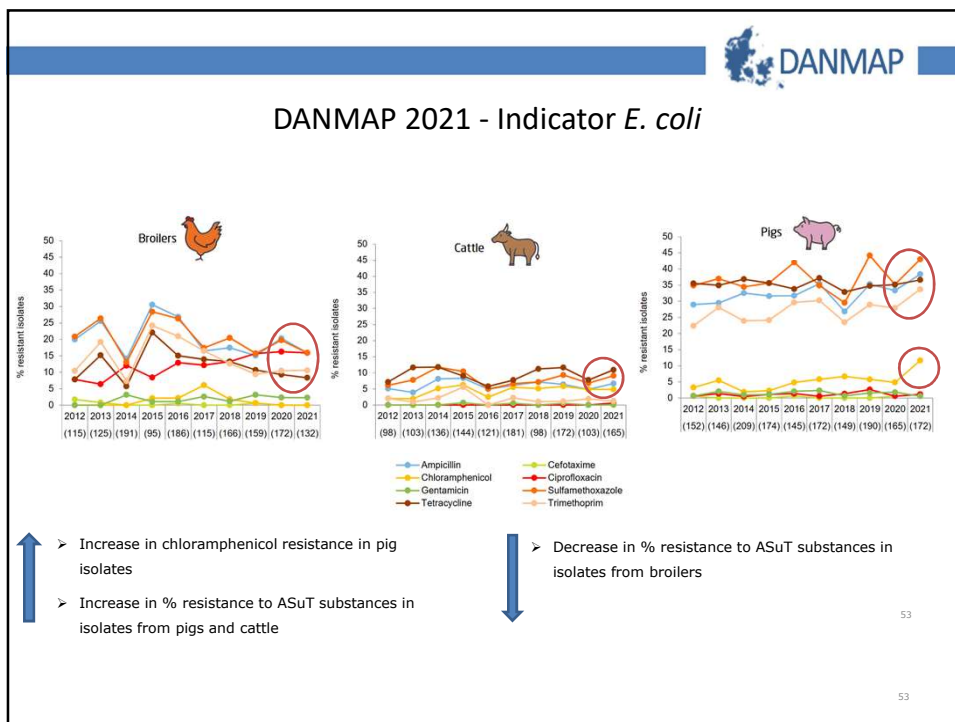


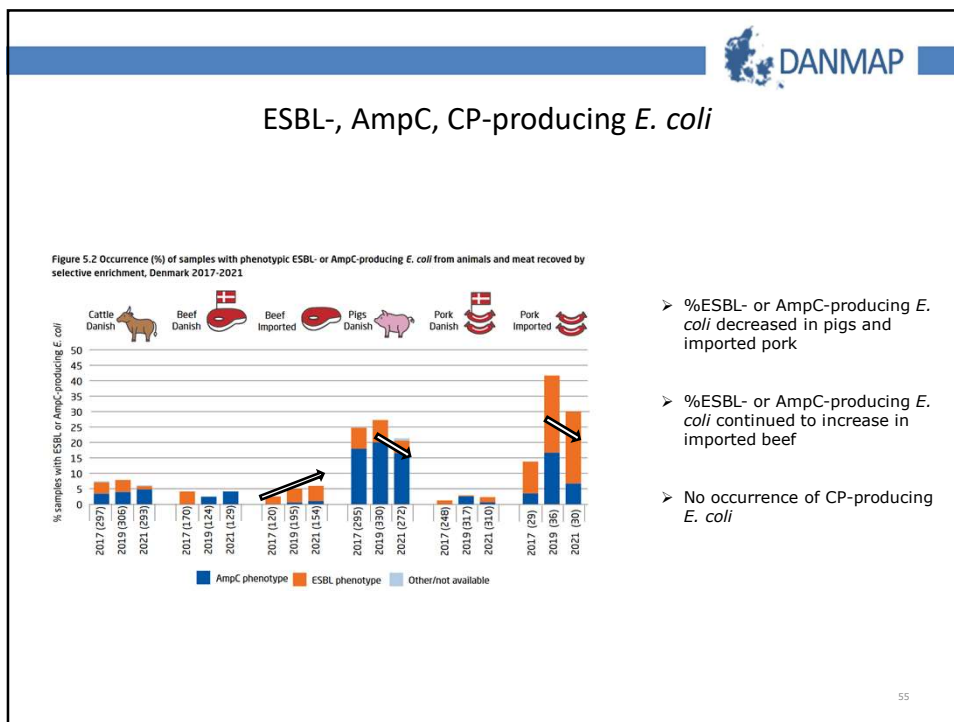



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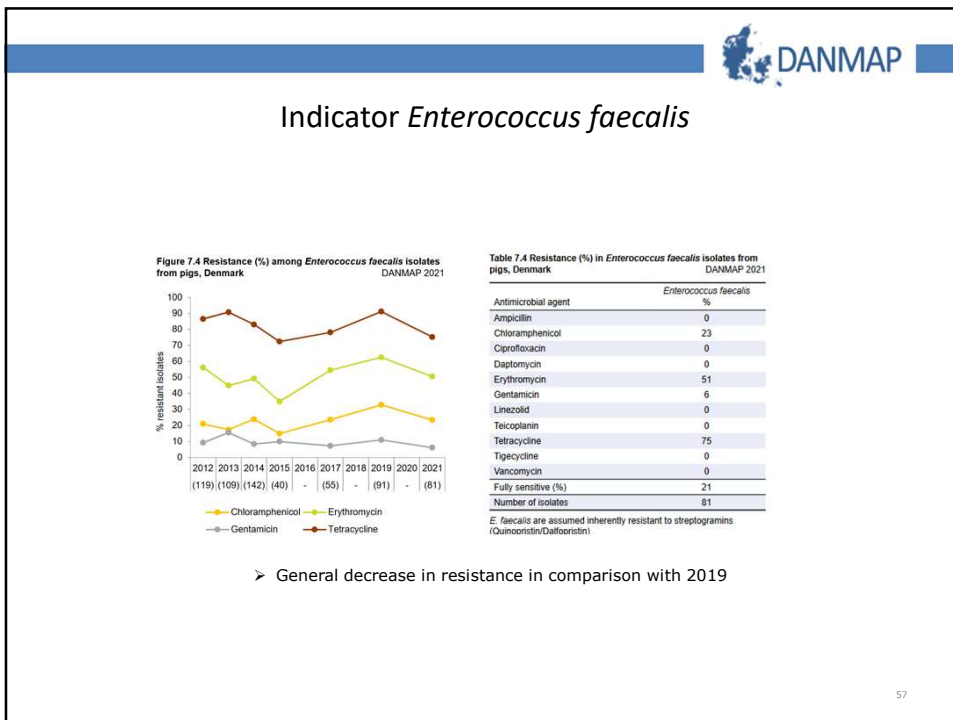
### ESBL-, AmpC, CP-producing *E. coli*

Table 5.2 Number of ESBL and AmpC enzymes detected in ESBL-producing *E. coli* isolates from animals and meat recovered by selective enrichment, Denmark, 2021

Genotypes based on AmpC/ESBL enzymes	Cattle		Beef		Pigs		Pork	
	Danish %	Danish %	Import %	Danish %	Danish %	Import %		
Number of AmpC genotypes	14	4	1	24	2	1		
Number of ESBL genotypes	3	0	8	9	4	5		
Number of AmpC+ESBL genotypes	1	0	1	14	0	1		
Not available	1	1	0	11	1	2		
Number (%) positive samples	18 (6%)	5 (4%)	10 (6%)	58 (21%)	7 (2%)	9 (30%)		
Number of tested samples	293	129	154	272	310	30		

- Phenotypic and genotypic profiles mostly in concordance
- WGS detected combined ESBL/AmpC encoding genes, but no combined resistance in AST
- Upregulated AmpC promotor C-42T mutations most common among AmpC-producing isolates
- Genes CTX-M-1 and TEM-1B most common among ESBL-producing isolates

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# Antibiotikaresistens i humane patogener

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resistens  
Statens Serum Institut




**SUMMARY  
DANMAP 2021**  
Use of antimicrobial agents and occurrence of  
antimicrobial resistance in bacteria from food  
animals, food and humans in Denmark




**DANMAP 2021**  
Use of antimicrobial agents and occurrence of  
antimicrobial resistance in bacteria from food  
animals, food and humans in Denmark





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RESISTANCE IN HUMAN  
PATHOGENS



## Datakilder

**Table 8.1 Summary of species/types, sampling and sources of isolates for national resistance surveillance in humans, Denmark, 2021** DANMAP 2021

Routine diagnostics from all 10 DCMs in Denmark. All data are directly identified and extracted in MiBa

Species	Sampling
<i>Escherichia coli</i>	First isolate per patient per year from blood or cerebrospinal fluid, from urine in hospitalised patients and from urine from primary health care
<i>Klebsiella pneumoniae</i>	
<i>Pseudomonas aeruginosa</i>	First isolate per patient per year from blood or cerebrospinal fluid
<i>Acinetobacter</i> species	
<i>Enterococcus faecalis</i>	
<i>Enterococcus faecium</i>	

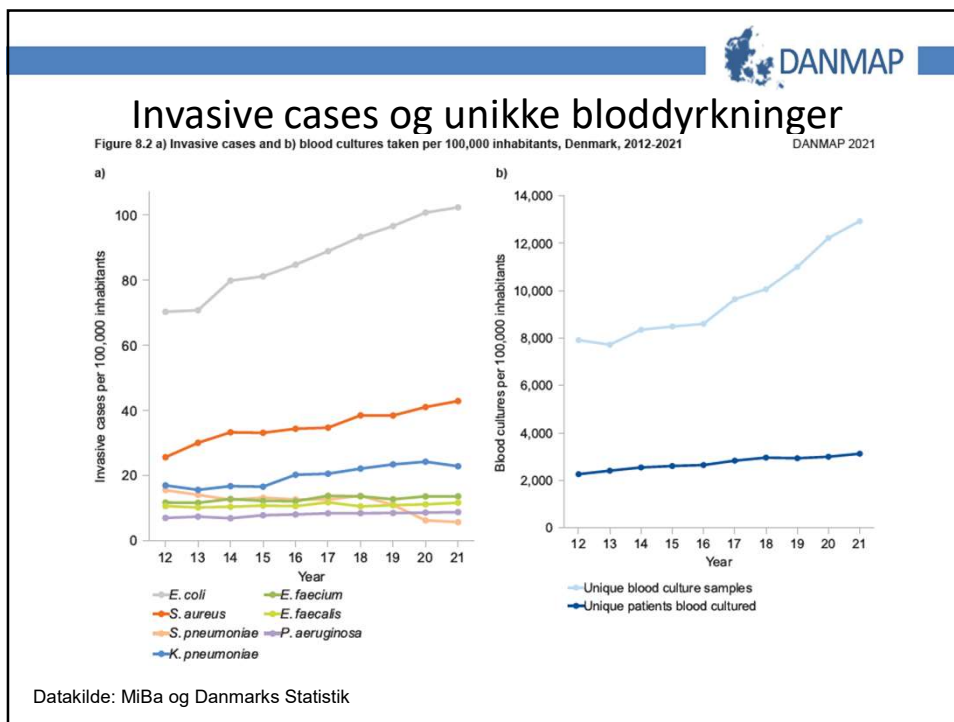
**Voluntary submissions of isolates to the reference laboratories at SSI**

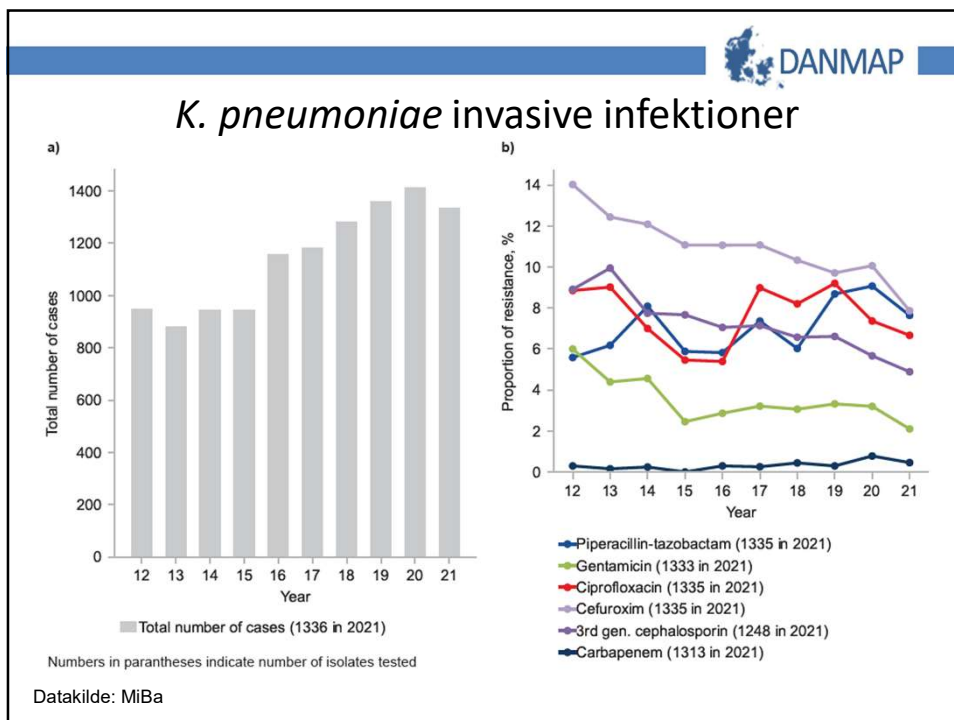
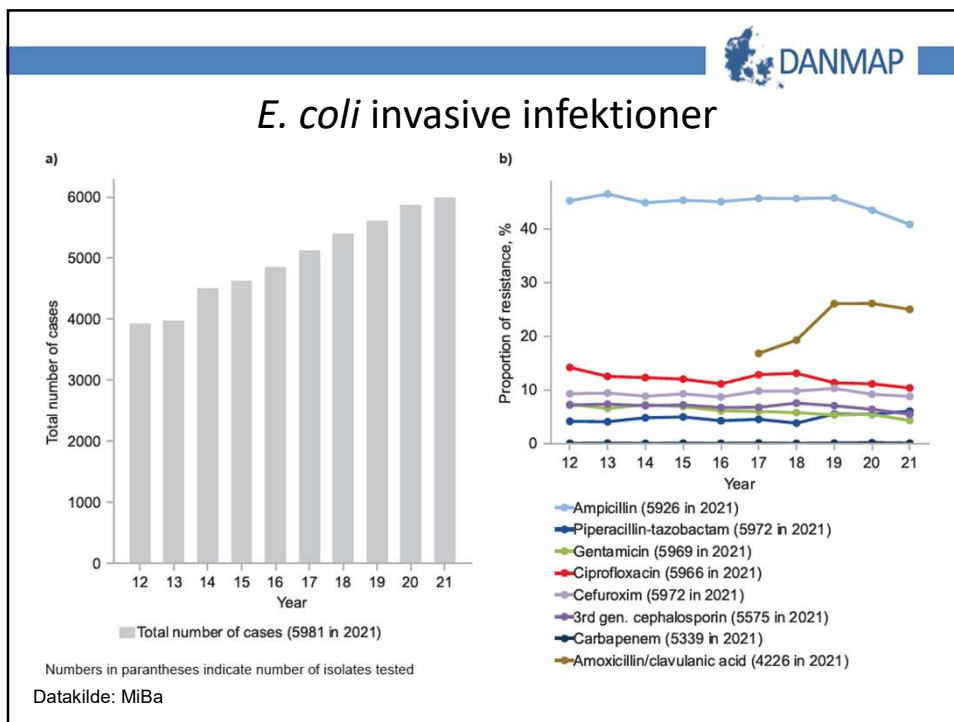
Species or type	Sampling
<i>Staphylococcus aureus</i>	One isolate per patient per episode from blood or cerebrospinal fluid
Beta-haemolytic streptococci	
<i>Neisseria gonorrhoeae</i>	One isolate per patient per episode from any sample site
3rd generation cephalosporin resistant <i>Escherichia coli</i>	First isolate per patient within 12 months from blood
Vancomycin-resistant enterococci	First isolate per patient within 12 months from any sample site (excluding screening samples)
Enterococci with exceptional phenotype (e.g. linezolid, daptomycin and tigecycline R)	First isolate per patient within 12 months from any sample site (clinical and screening samples)
All bacterial species with other exceptional phenotypes (e.g. acquired colistin resistance)	One isolate per patient per episode from any sample site

**Mandatory submissions of isolates to the reference laboratories at SSI**

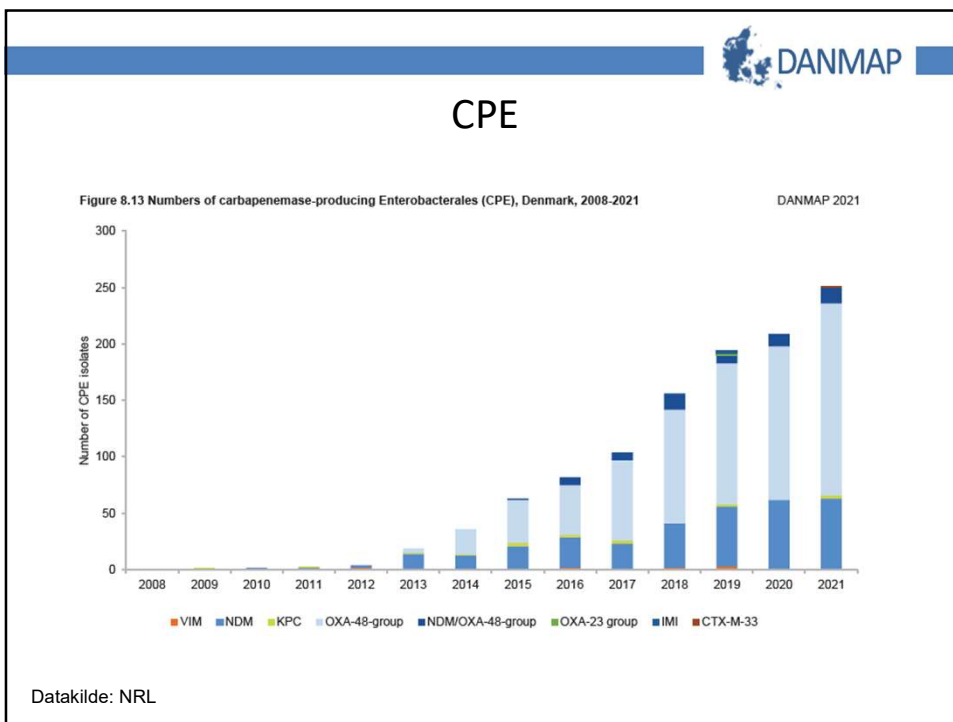
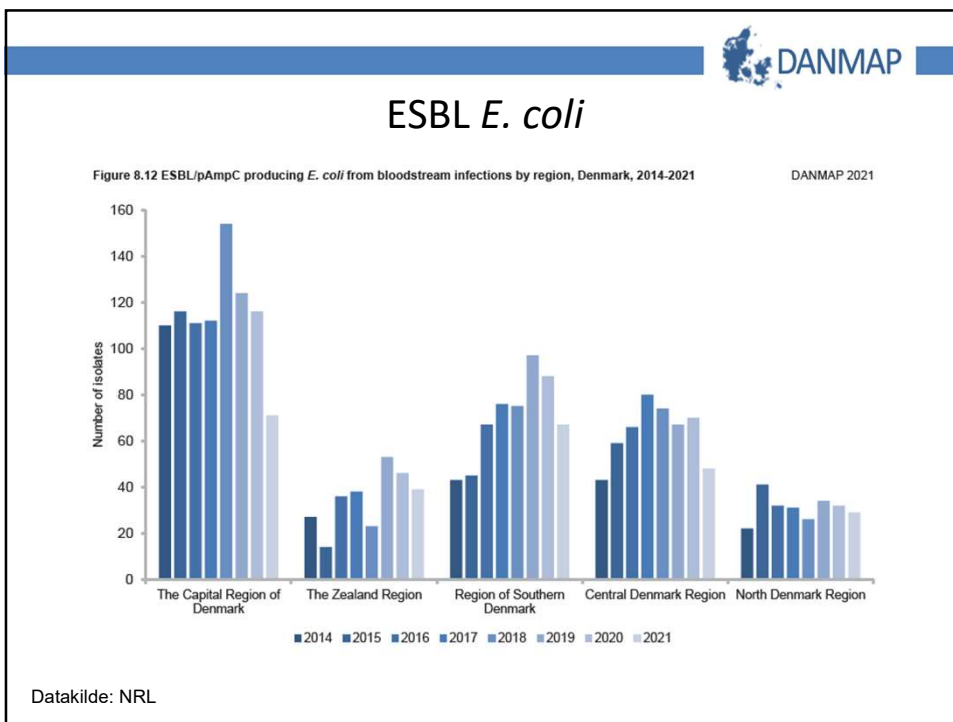
Species or type	Sampling
Carbapenemase-producing organisms	First isolate per patient within 12 months from any sample site (clinical and screening samples)
Methicillin-resistant <i>Staphylococcus aureus</i>	First isolate from all new cases of MRSA positive patients from any sample site (clinical and screening samples)
<i>Streptococcus pneumoniae</i>	One isolate per patient per episode from blood or cerebrospinal fluid
<i>Haemophilus influenzae</i> serotype b, Hib	All invasive isolates

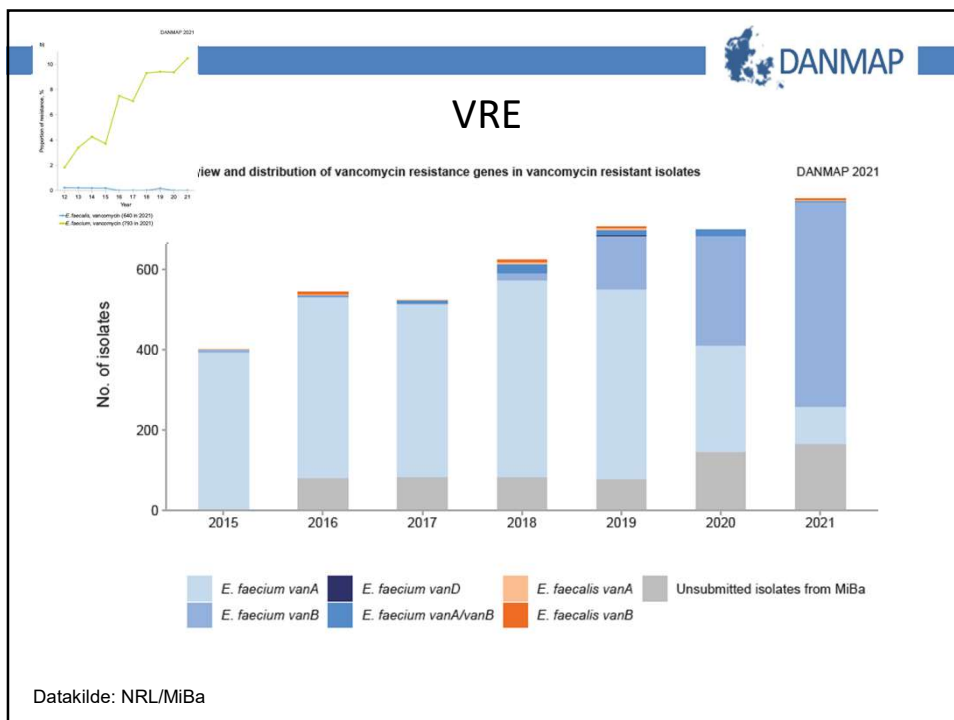
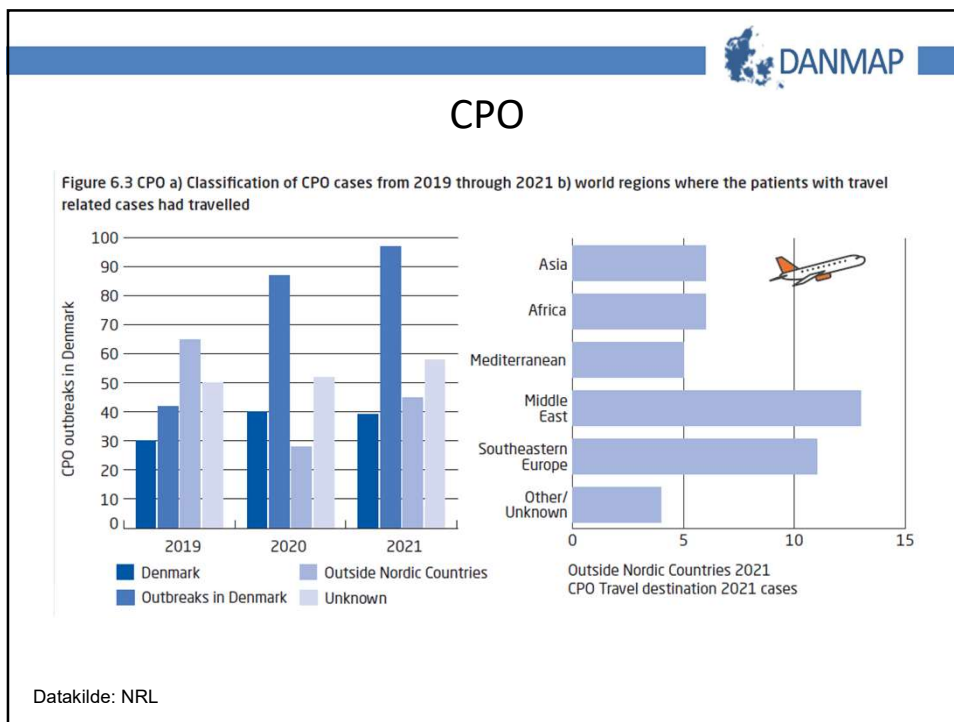
Regarding submissions of isolates to the reference laboratories normally more isolates are received, but for the statistics each patient is counted only once

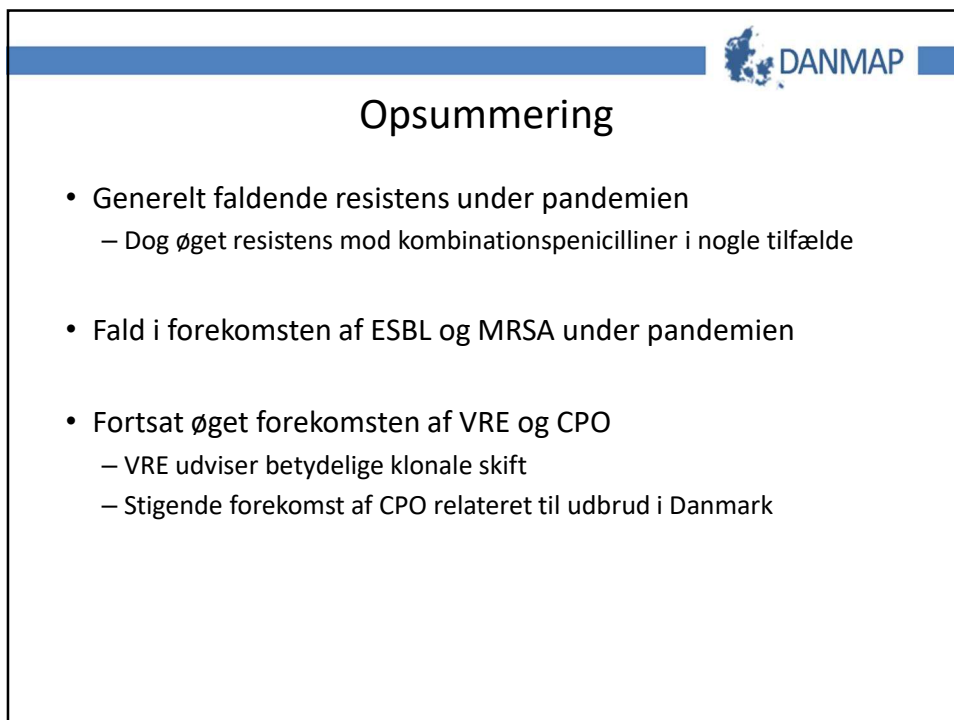
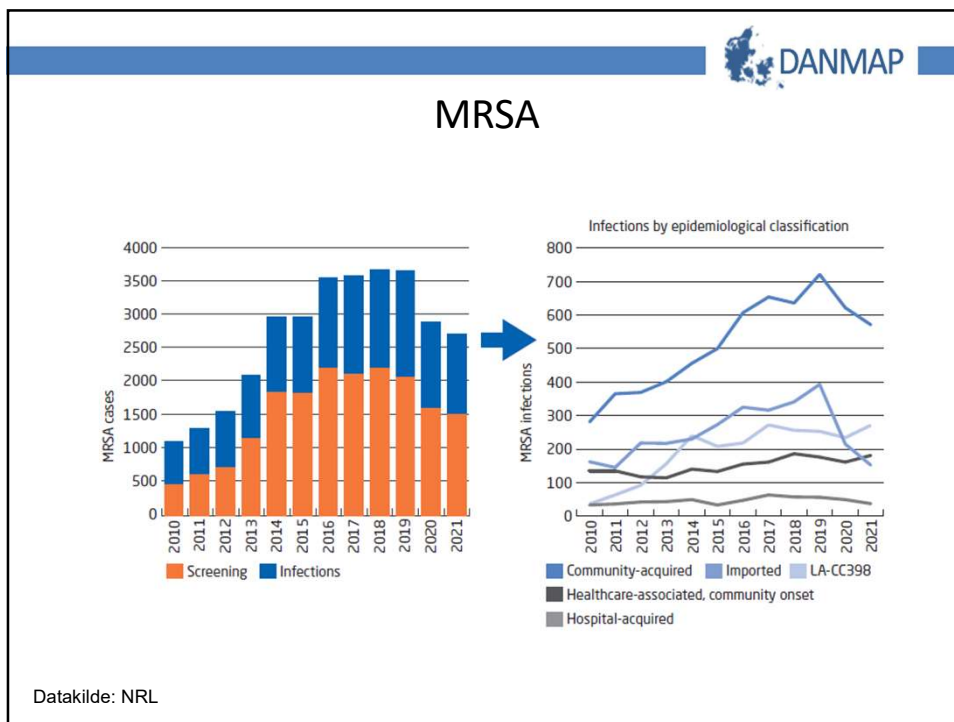
















## Resistens i patogene bakterier fra svin

**Jesper Larsen, Lina M. Cavaco & Pia T. Hansen**  
Bakterier, Parasitter og Svampe  
Statens Serum Institut

**Peter Damborg**  
Institut for Veterinær- og Husdyrvidenskab  
Københavns Universitet

**Charlotte M. Salomonsen & Svend Haugegaard**  
Veterinært Laboratorium, Landbrug & Fødevarer





## Resistensovervågning i svin

- Veterinært Laboratorium, Landbrug & Fødevarer
  - Modtager kliniske prøver fra svin
  - Udfører bakteriedyrkning, artsidentifikation og fænotypisk resistensbestemmelse
  - Publiceret i [DANMAP](#) siden 2015
    - *Actinobacillus pleuropneumoniae*
      - Ondartet lungesygge
    - Hæmolytisk *Escherichia coli*
      - Diarré i farestald og klimastald, septikæmi, toksæmi, ødemsyge
    - *Streptococcus suis*
      - Kan forårsage infektioner i mange organer, herunder hjerne, mellemøre, led eller hjerteklapper, ligesom den forårsager septikæmi
  - Fra 1. januar 2021 sendes udvalgte stammer til Dansk Veterinært Konsortium (n≈700 i 2021)

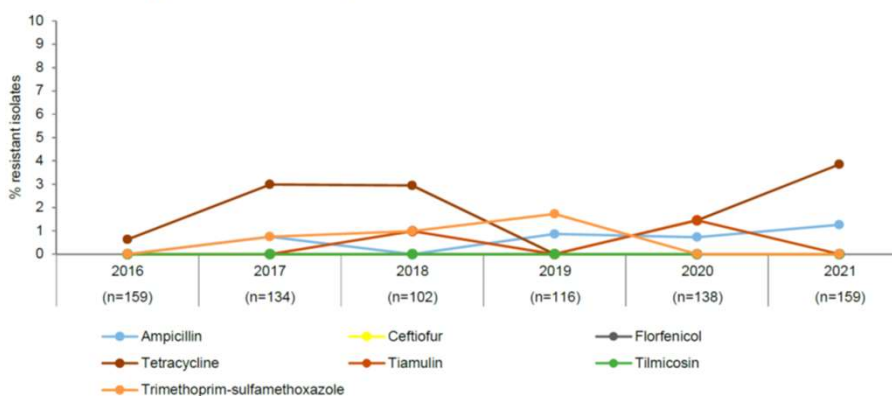
## Resistensovervågning i svin

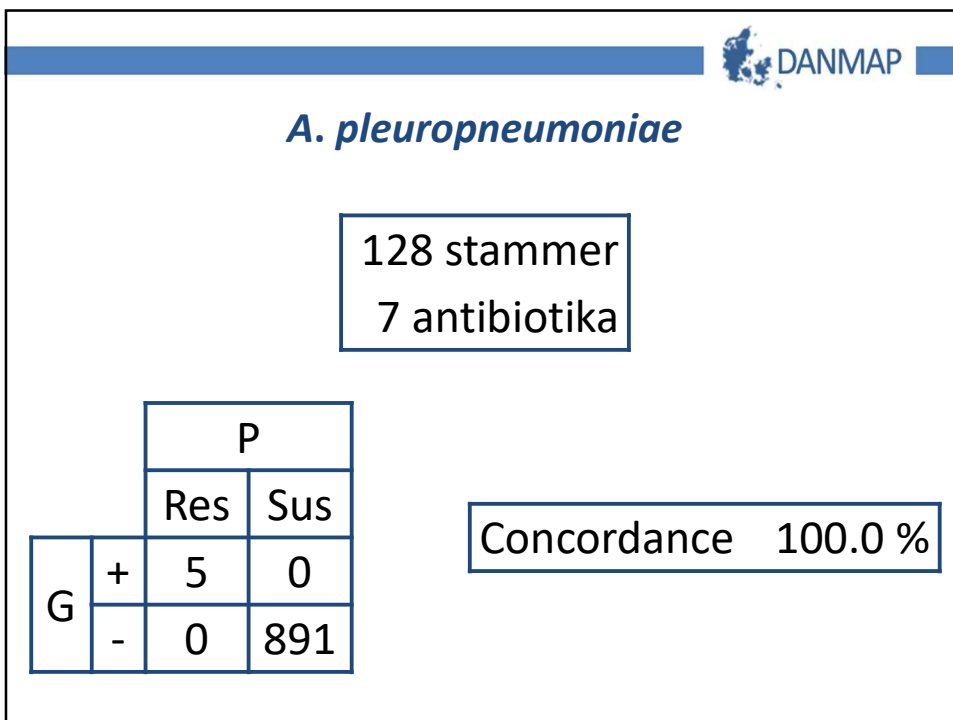
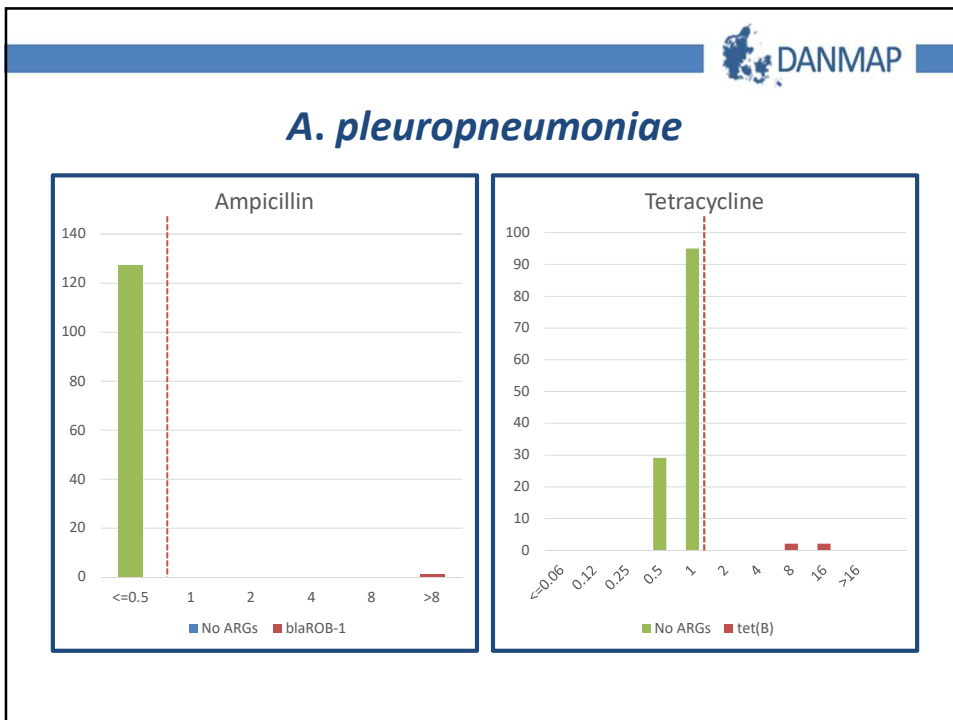
- Dansk Veterinært Konsortium (KU/SSI)
  - WGS
    - Forskellige Illumina-platformer
  - Identifikation af resistensgener og -mutationer
    - ResFinder og PointFinder
  - Sammenligning med fænotypiske resistensdata
    - ECOFFs, tentative ECOFFs, veterinære kliniske breakpoints, humane kliniske breakpoints

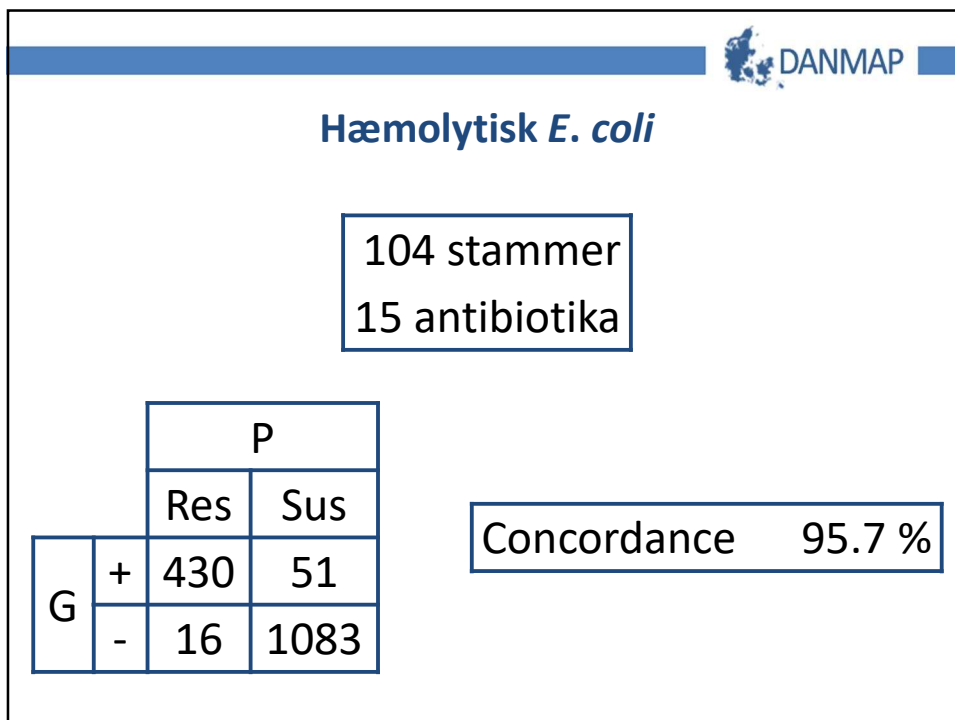
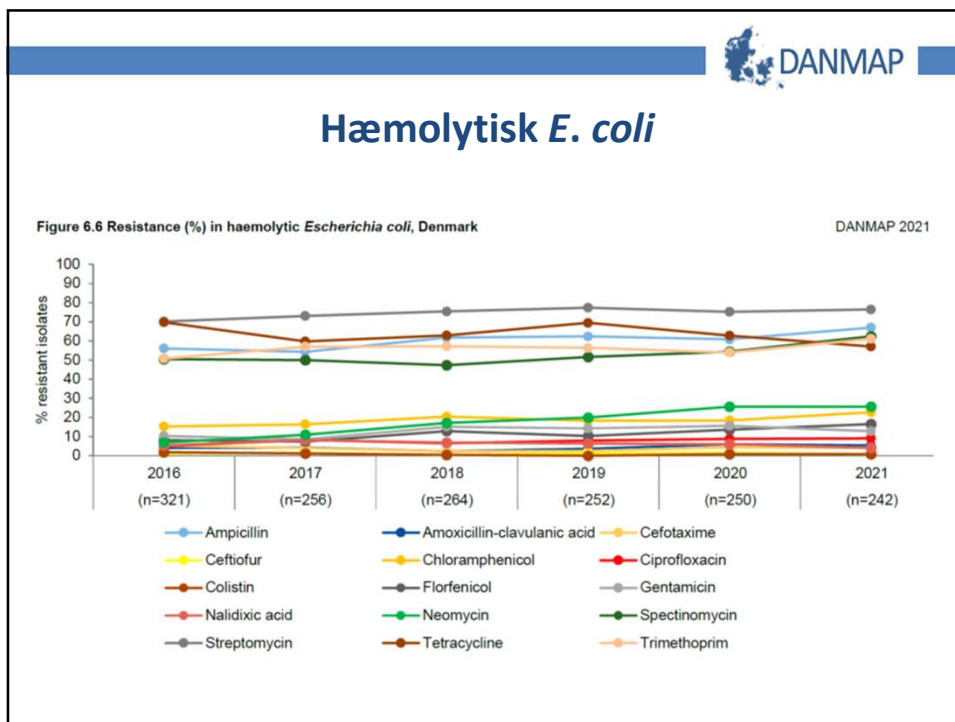
## *A. pleuropneumoniae*

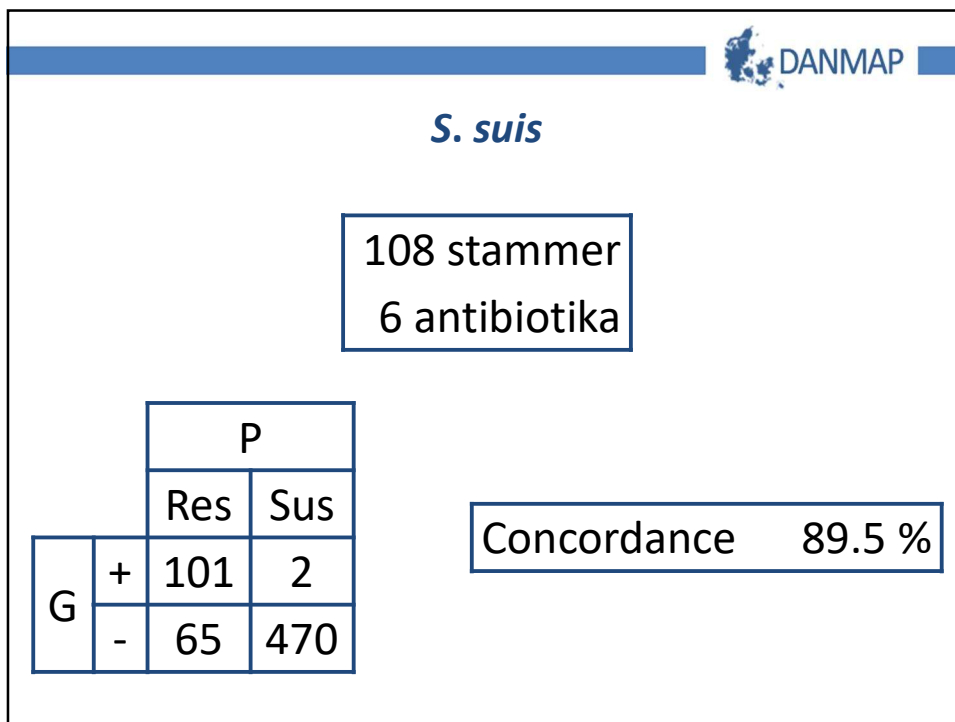
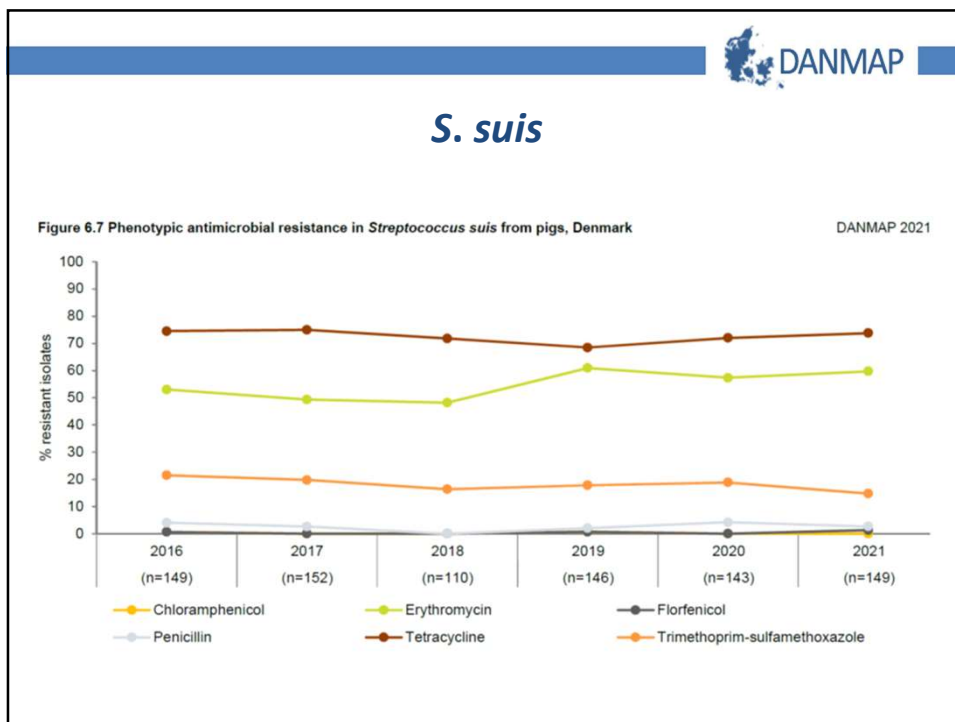
Figure 6.5 Resistance (%) in *Actinobacillus pleuropneumoniae*, Denmark

DANMAP 2021







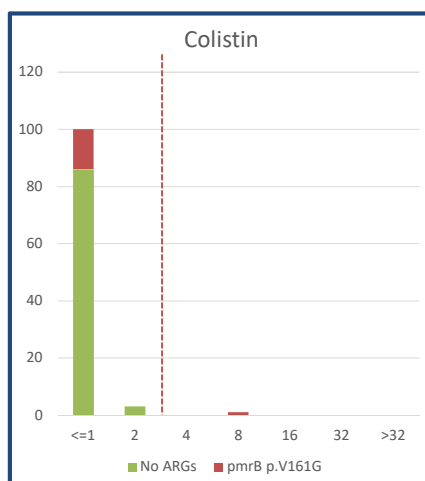




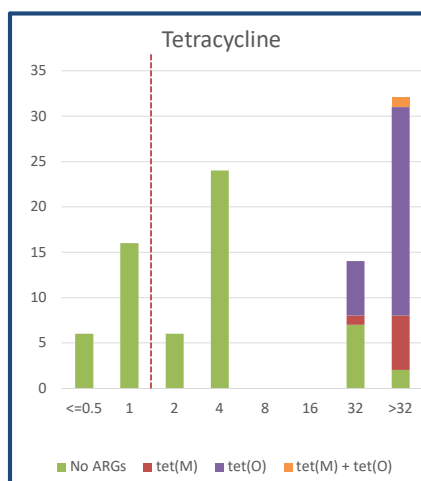
## Genotype vs. Fænotype

- Generel god overensstemmelse mellem genotype og fænotype
- De fleste uoverensstemmelser skyldes:
  - Tilstedeværelse af resistensgener/-mutationer associeret med resistens overfor colistin, spectinomycin og streptomycin i fænotypisk følsomme *E. coli* stammer
  - Manglende tilstedeværelse af resistensgener/-mutationer associeret med resistens overfor tetracyclin og trimethoprim-sulfamethoxazole i fænotypisk resistente *S. suis* stammer

### Hæmolytisk *E. coli*



### *S. suis*





## Human betydning

- Cefotaxim-resistens blev identificeret i 7 % af de hæmolytiske *E. coli* stammer og var altid forbundet med tilstedeværelse af enten *bla*<sub>CTX-M-1</sub> eller mutationer i *ampC* promoteren
- 14 % af de hæmolytiske *E. coli* stammer havde en mutation i *pmrB*, som er associeret med resistens overfor colistin. Dog var kun et af de 15 isolater med denne mutation fænotypisk resistent over for colistin.
- 2 % af *S. suis* stammerne var positive for *optrA*, som er associeret med resistens overfor linezolid (humant antibiotikum) og florfenicol (veterinært antibiotikum)



## Videre arbejde

- Undersøge uoverensstemmelser mellem genotype og fænotype
  - Identifikation af nye resistensgener/-mutationer
  - Evaluering af etablerede ECOFFs/kliniske breakpoints
- Bioinformatiske analyser med henblik på at undersøge spredning af patogene bakterier og resistensgener mellem svinebesætninger og mellem svin og mennesker





## Videre arbejde

- Resultater for andre bakterier er undervejs og vil blive lagt på Dansk Veterinært Konsortiums hjemmeside ([www.vetssi.dk/](http://www.vetssi.dk/)):
  - *Bordetella bronchiseptica*
  - *Clostridium perfringens*
  - *Erysipelothrix rhusiopathiae*
  - Non-hæmolytisk *E. coli*
  - *Haemophilus parasuis*
  - *Klebsiella pneumoniae*
  - *Salmonella enterica*
  - *Staphylococcus hyicus*



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