

DANMAP 2016

DANMAP 2016 - Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark



Statens Serum Institut
National Veterinary Institute, Technical University of Denmark
National Food Institute, Technical University of Denmark

Veterinært
antibiotikaforbrug i
Danmark (VetStat)

Zoonoser:
Salmonella
Campylobacter

Resistens i
Indikatorbakterier:
Enterokokker og
***E. coli*:**

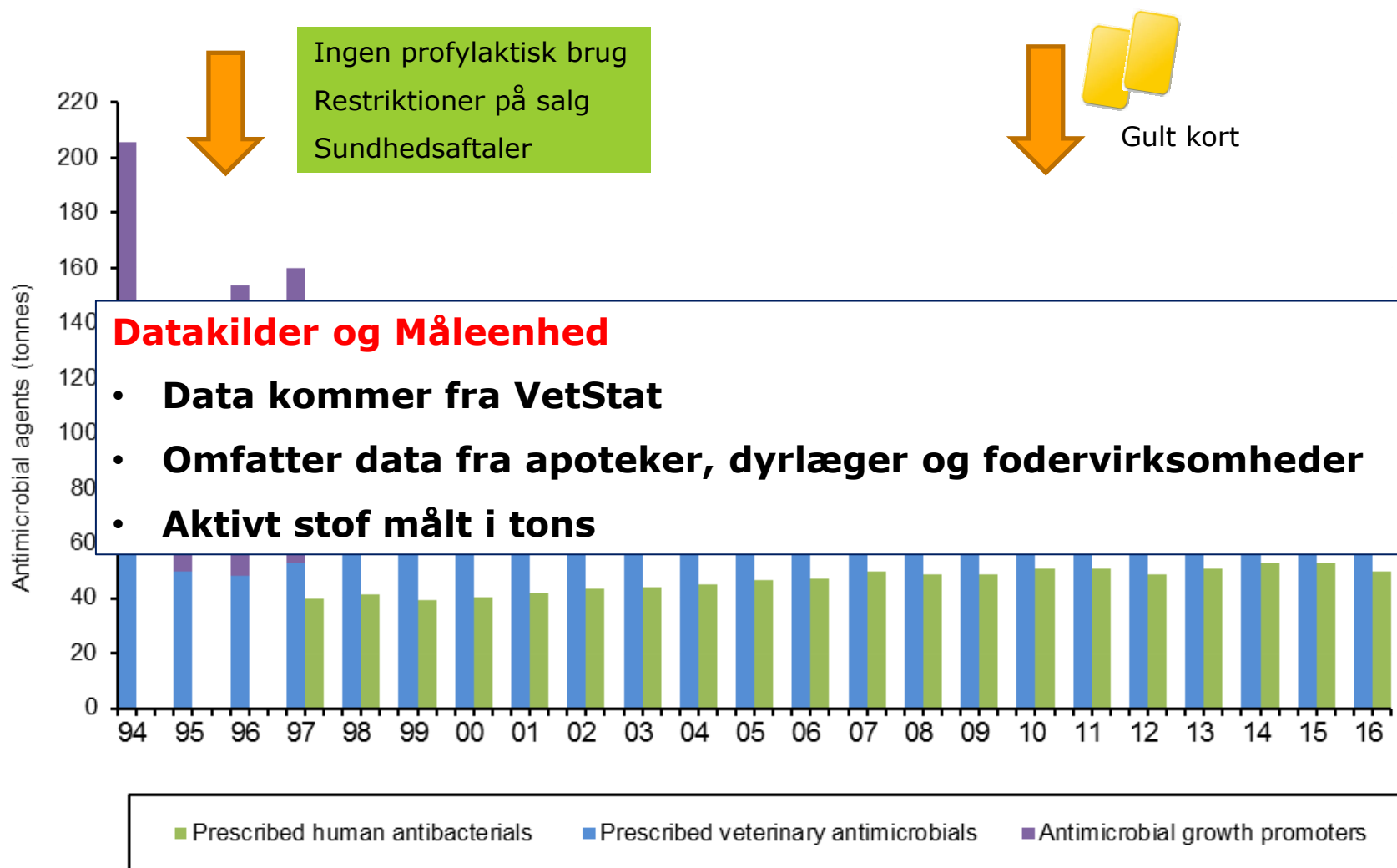
Resistensdata fra
Dyr og fødevarer

Tekstbokse i
samarbejde med SSI,
FVST, KU

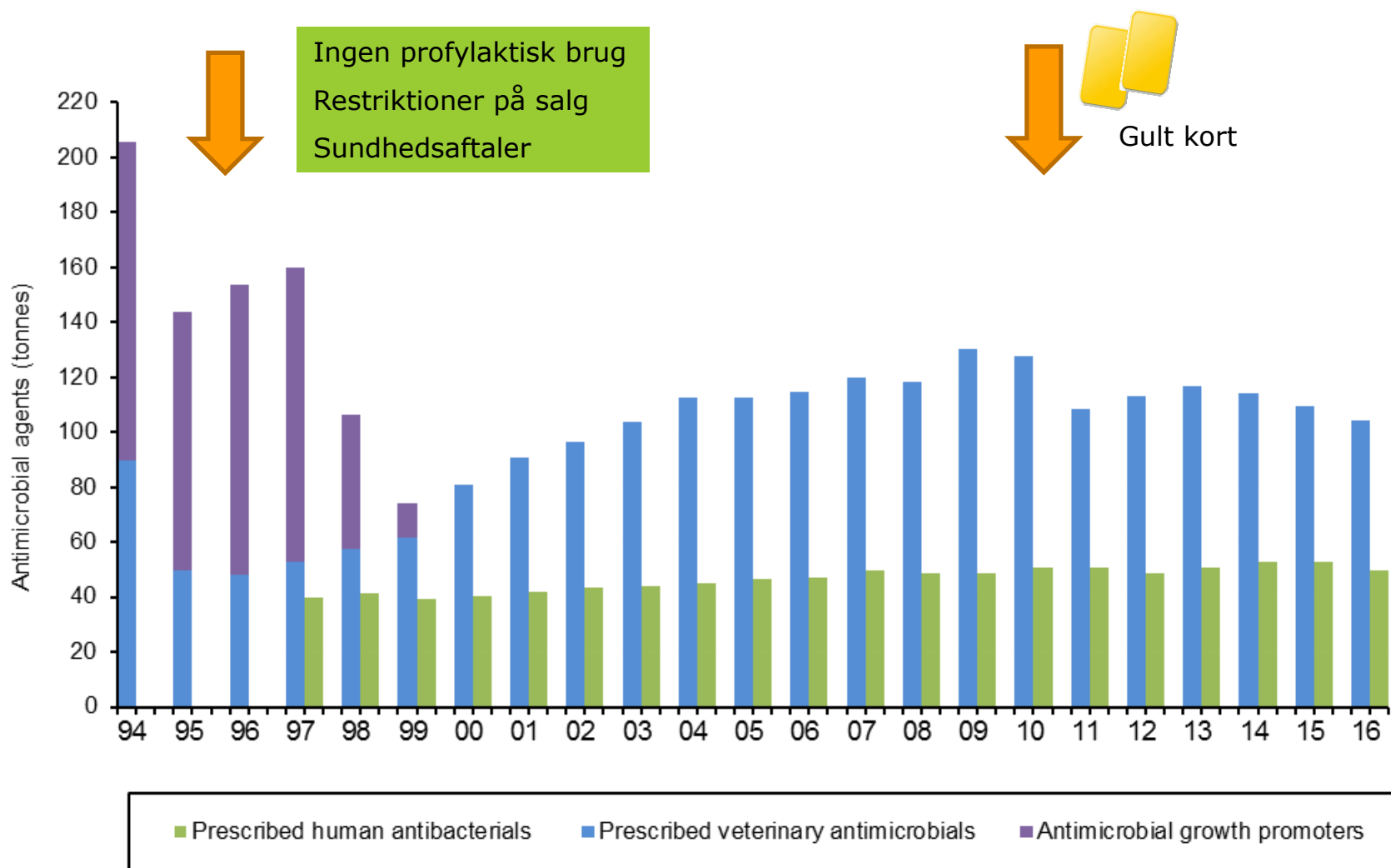
Brug af DANMAP rapporten



Antibiotika forbrug i Danmark 1994-2016

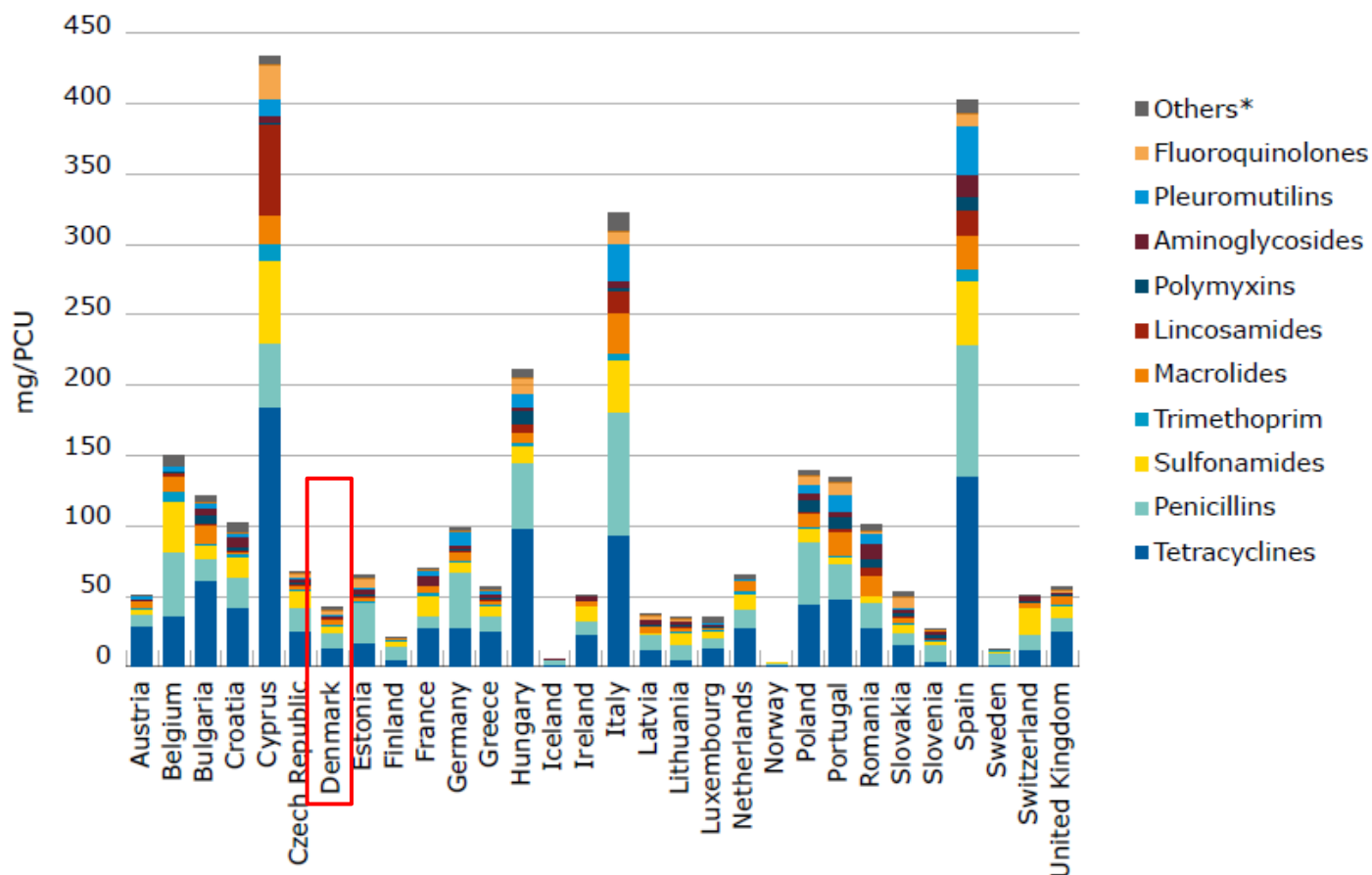


Antibiotika forbrug i Danmark 1994-2016



Fra ESVAC rapporten

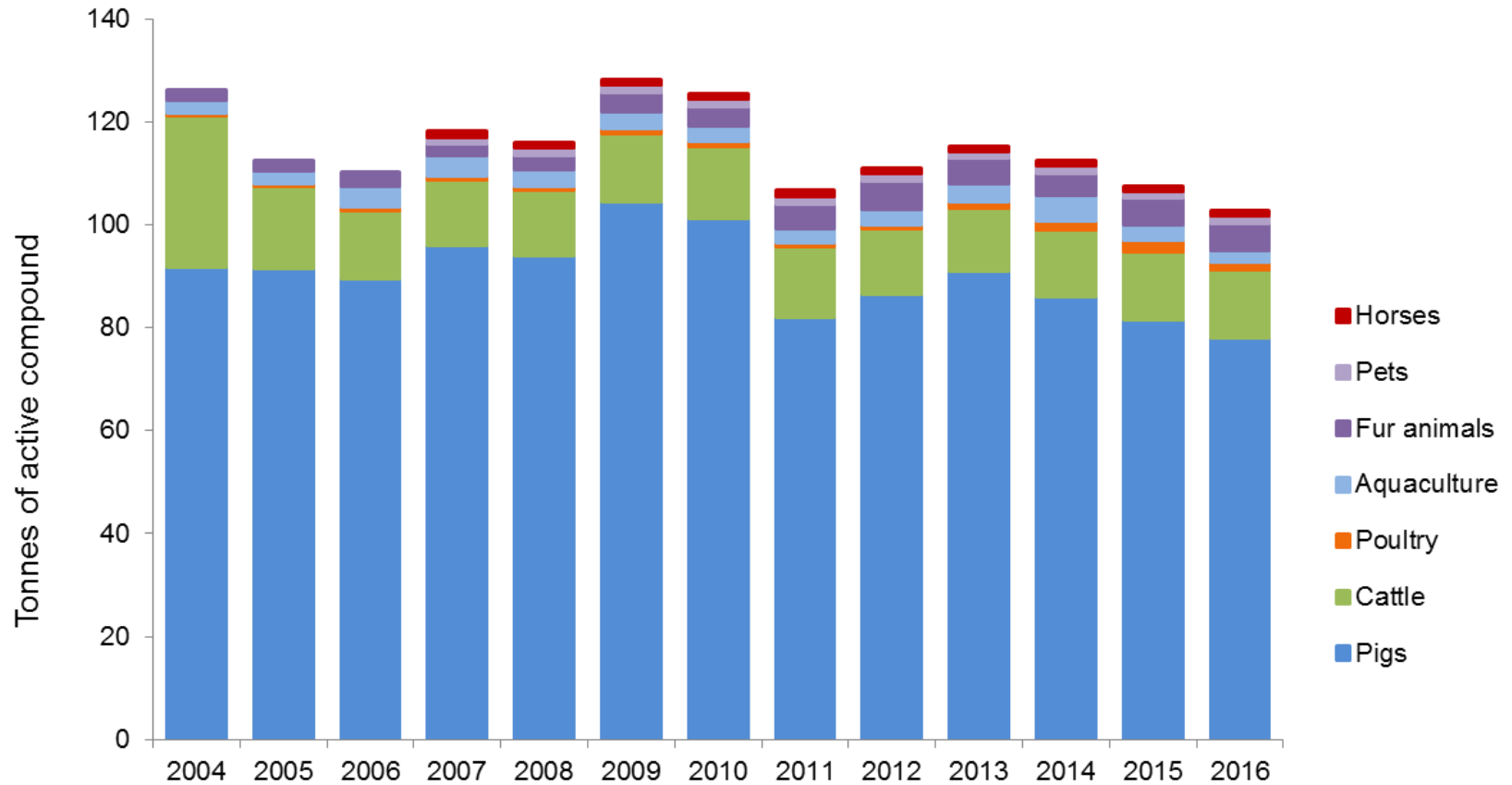
Figure 3. Sales for food-producing species, in mg/PCU, of the various veterinary antimicrobial classes, for 30 European countries, in 2015¹



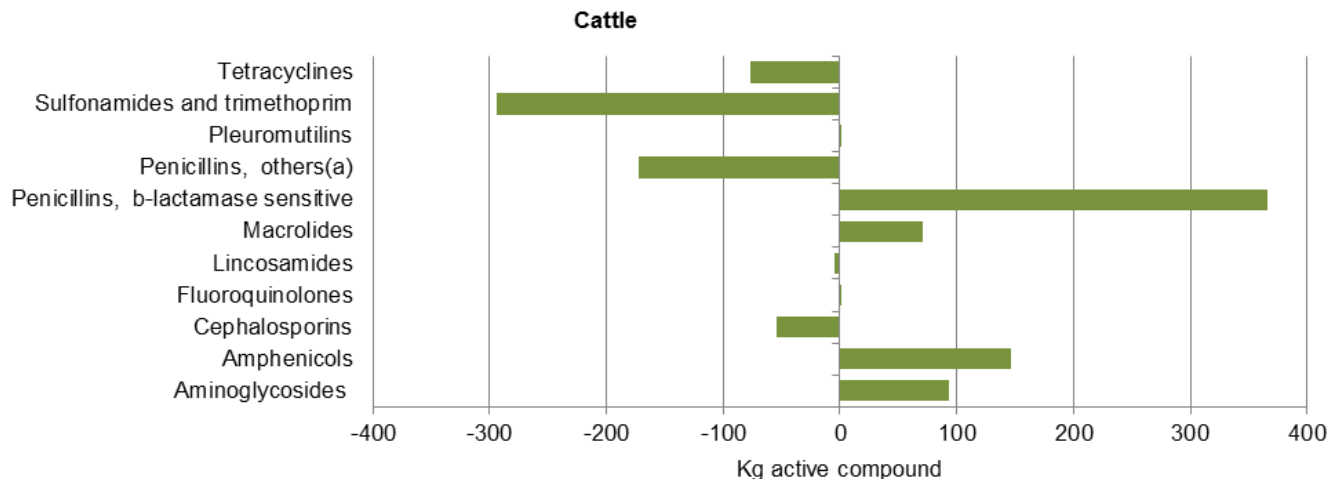
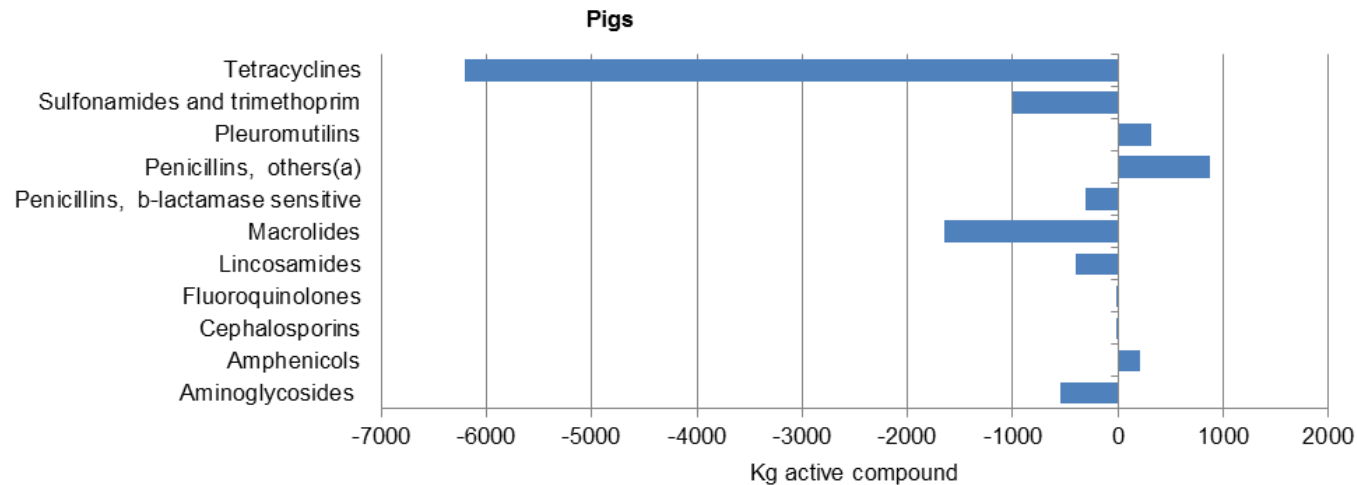
*Amphenicols, cephalosporins, other quinolones and other antibacterials (classified as such in the ATCvet system).

¹ Differences between countries can be partly explained by differences in animal demographics, in the selection of antimicrobial age in dosage regimes, in type of data sources, and veterinarians prescribing habits and prices.

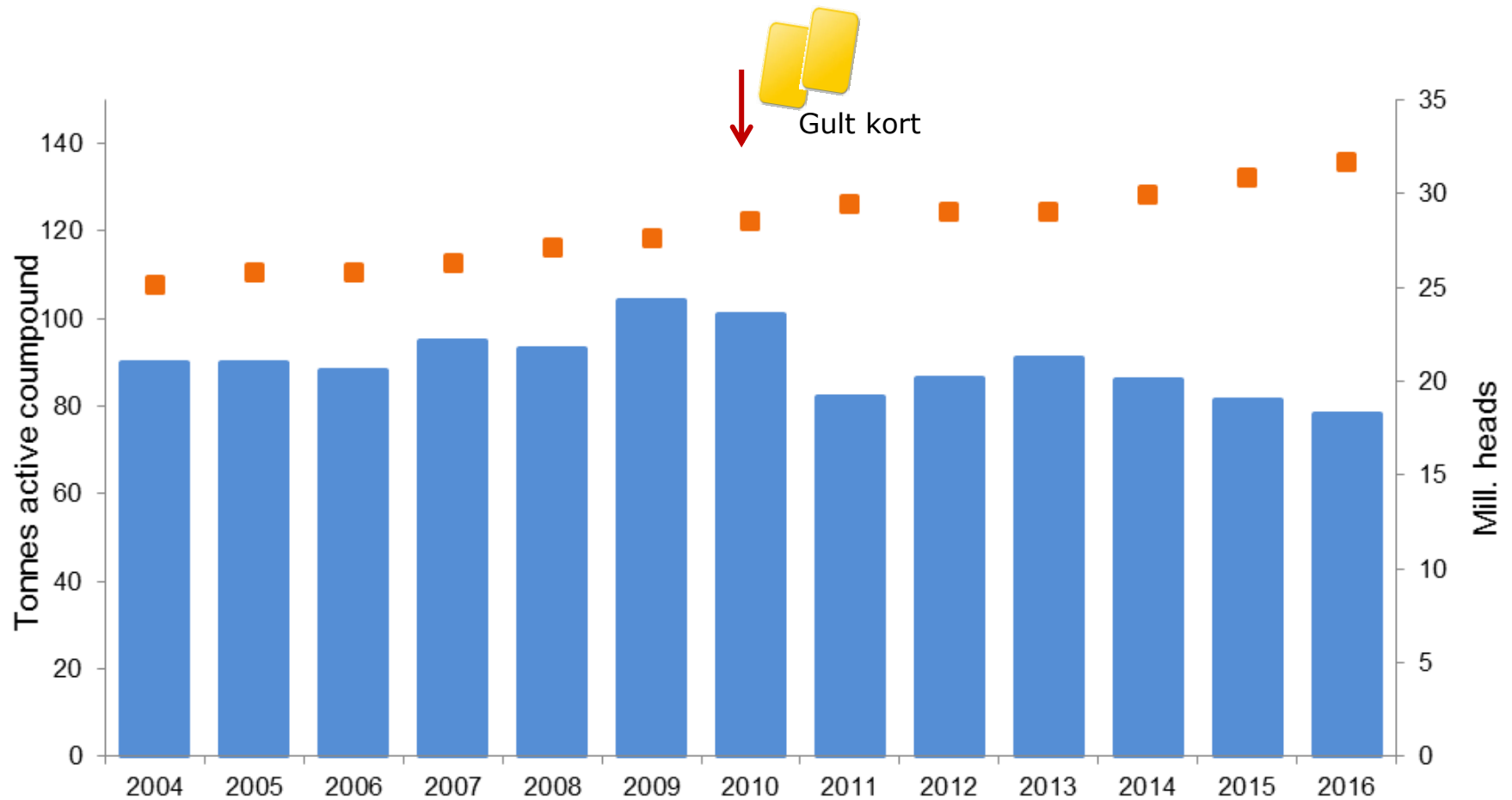
Antibiotika forbrug til dyr i Danmark



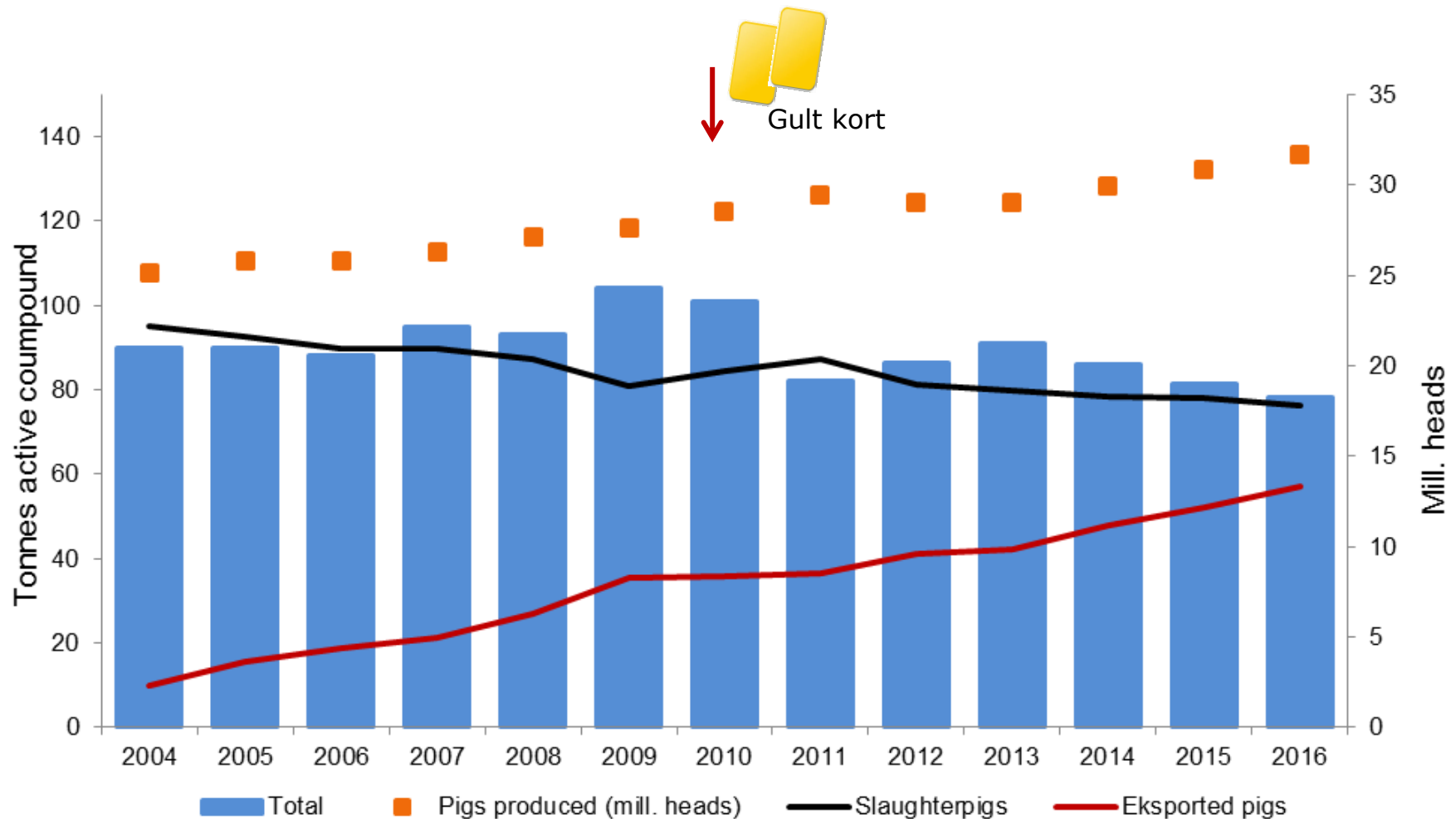
Antibiotikaforbrug til dyr – ændring 2012-2016



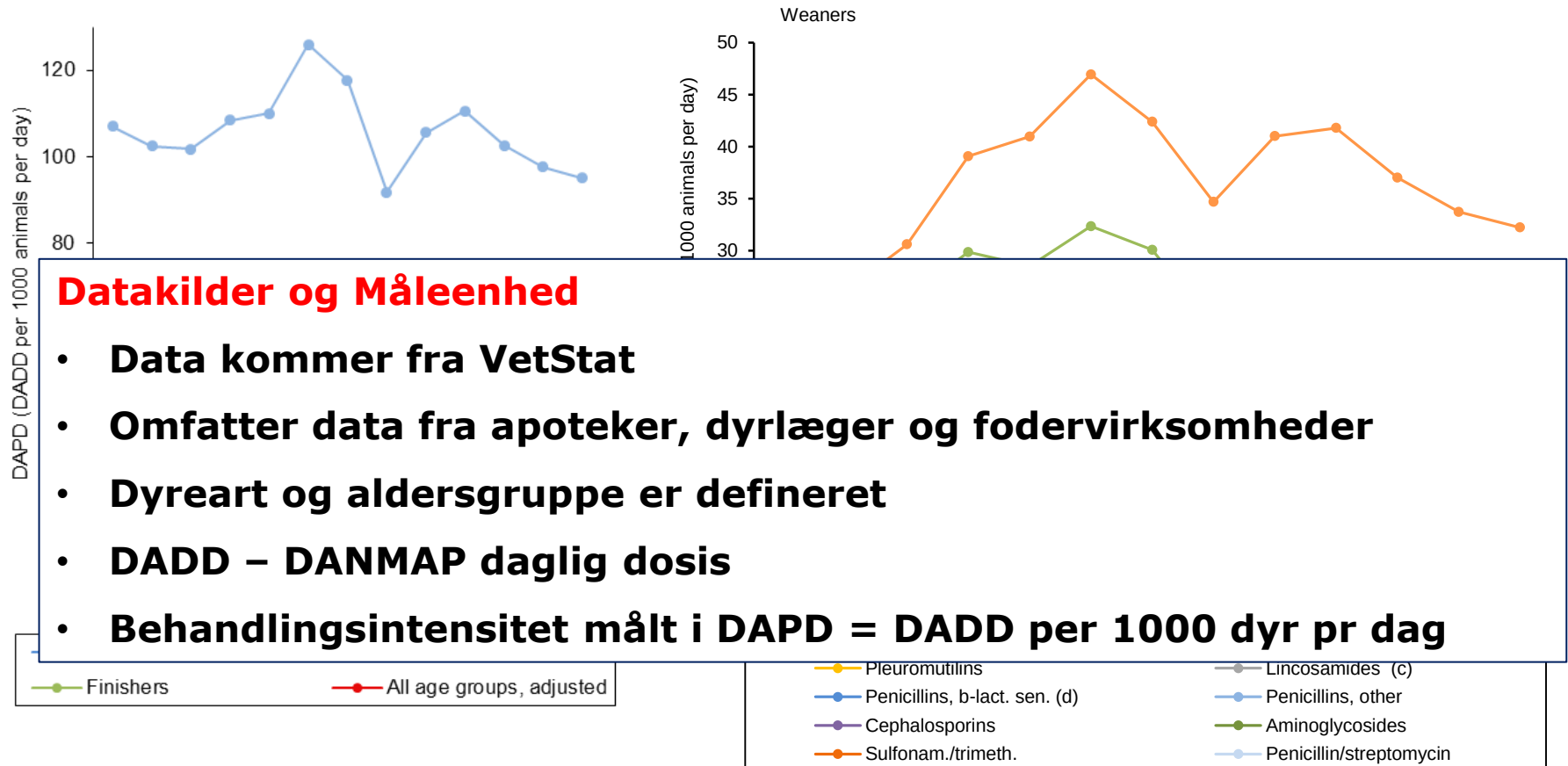
Faldende forbrug til svin



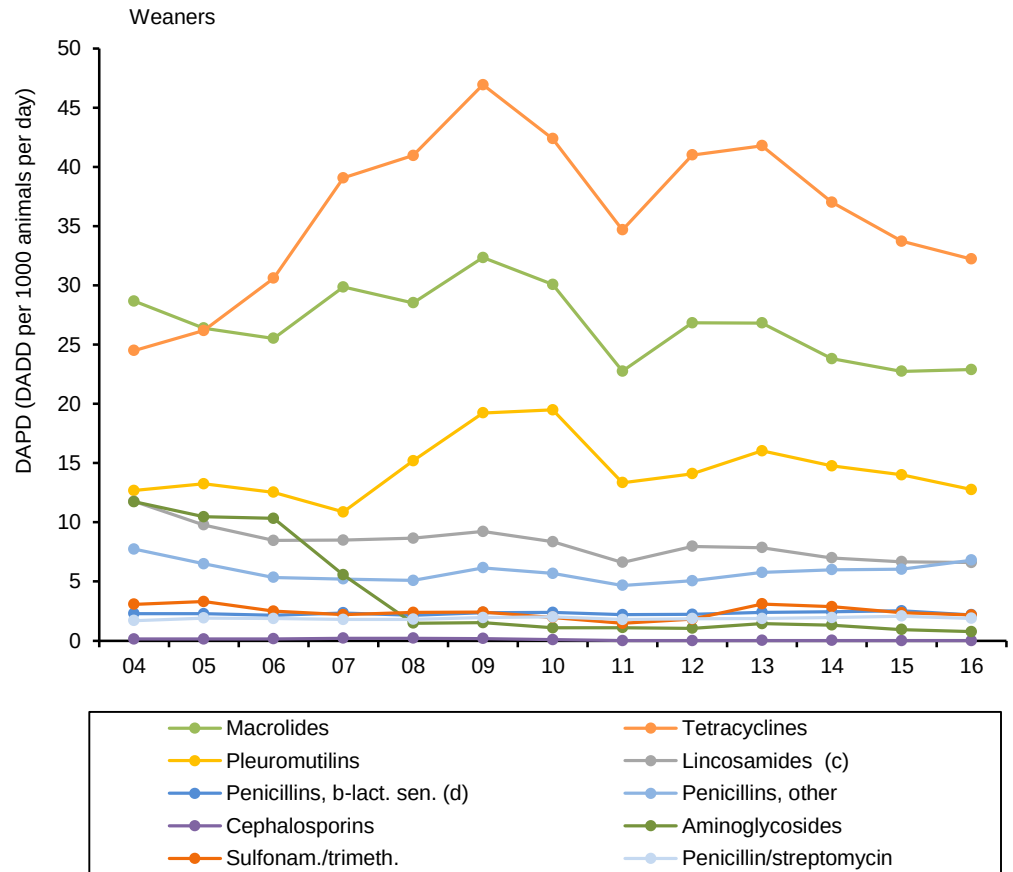
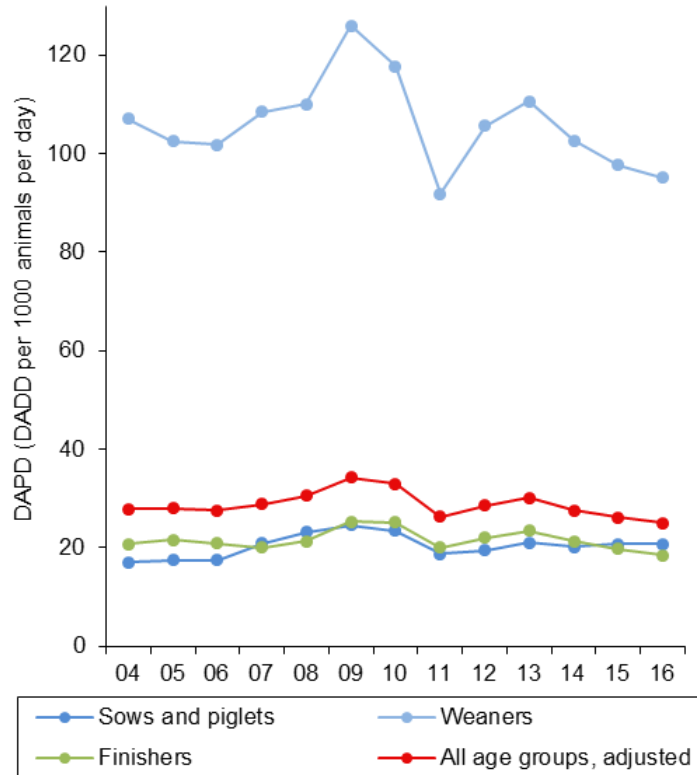
Faldende forbrug til svin



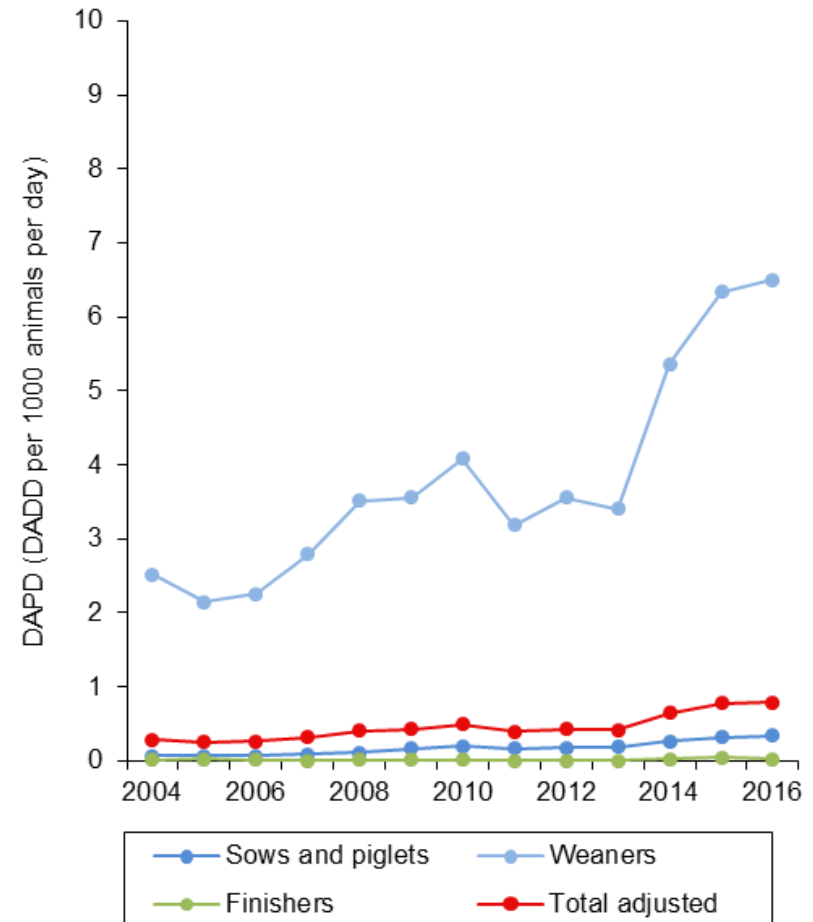
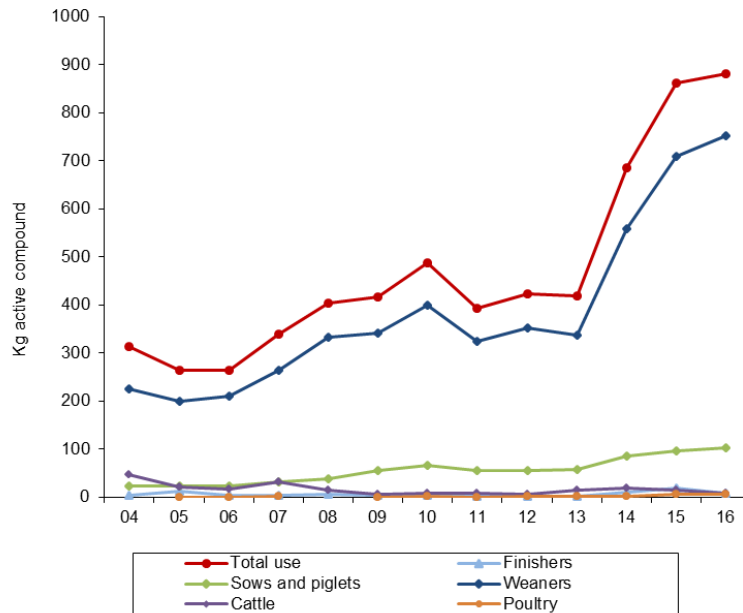
Forbrug til fravænningsgrise



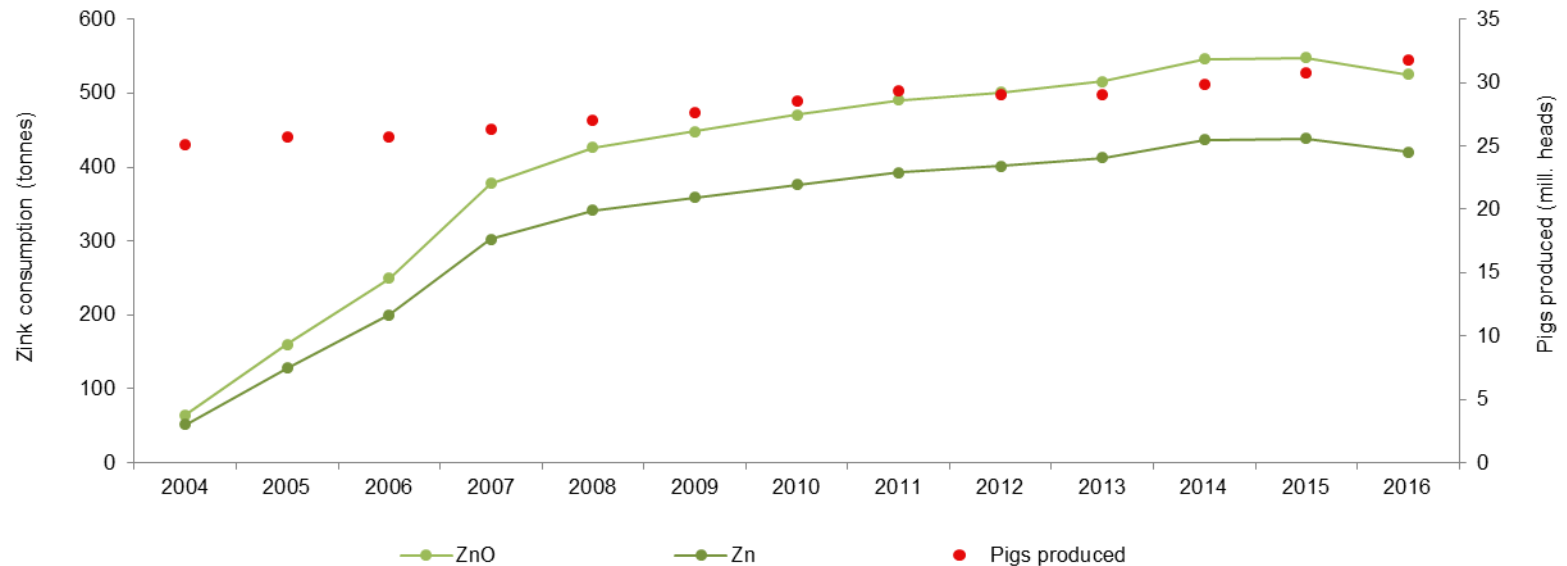
Forbrug til fravænningsgrise



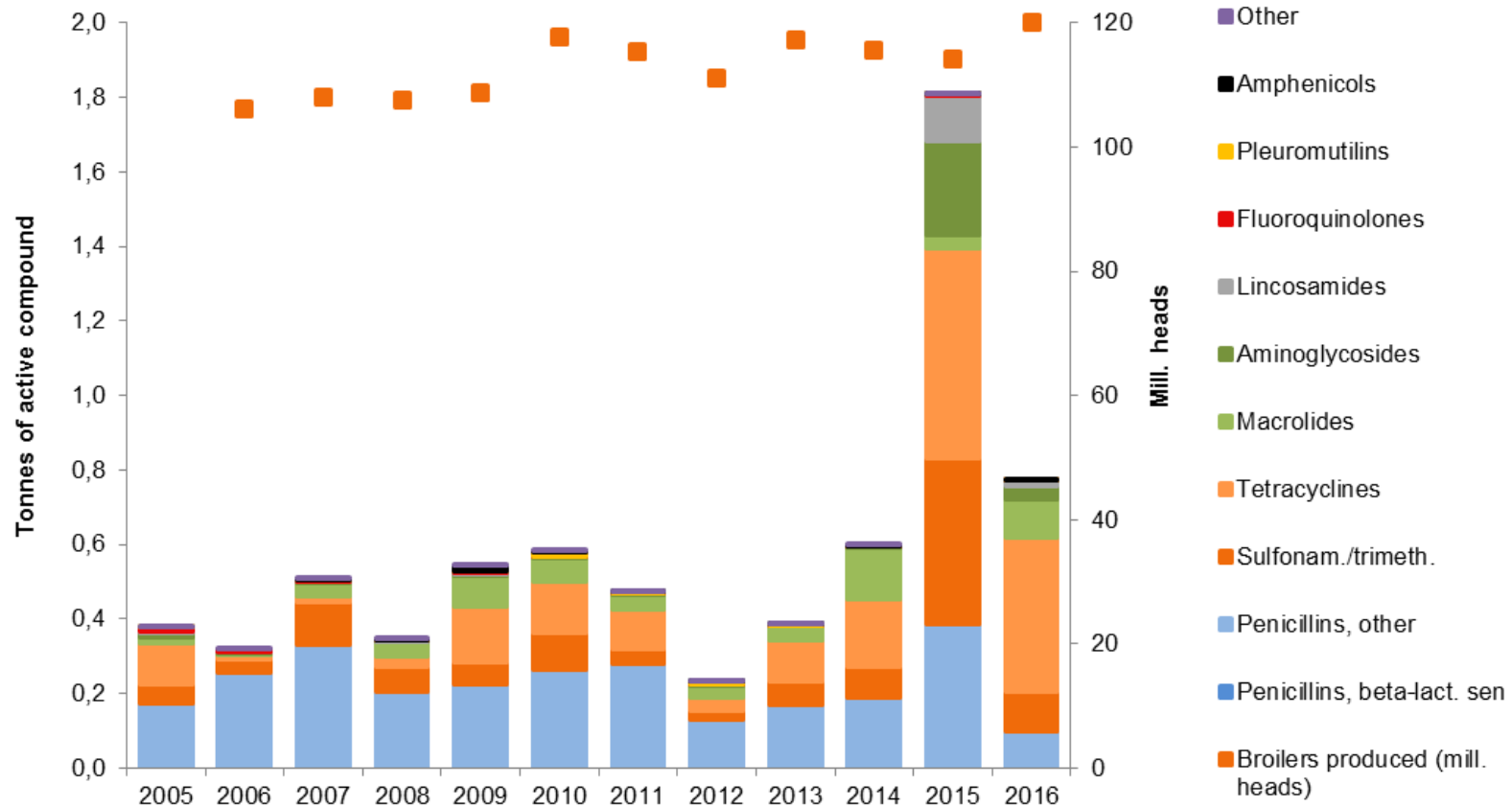
Forbrug af colistin



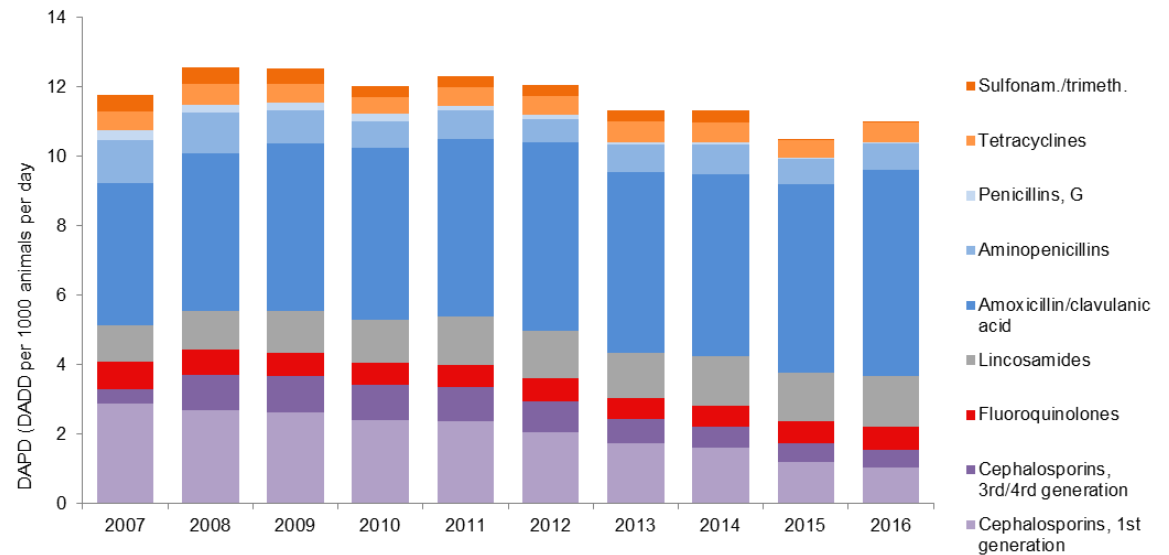
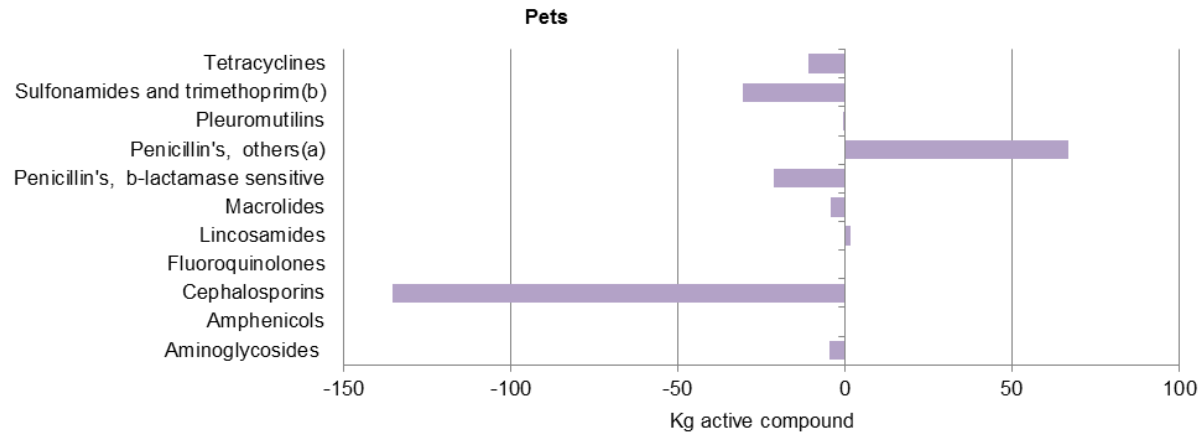
Forbrug af medicinsk zink til svin



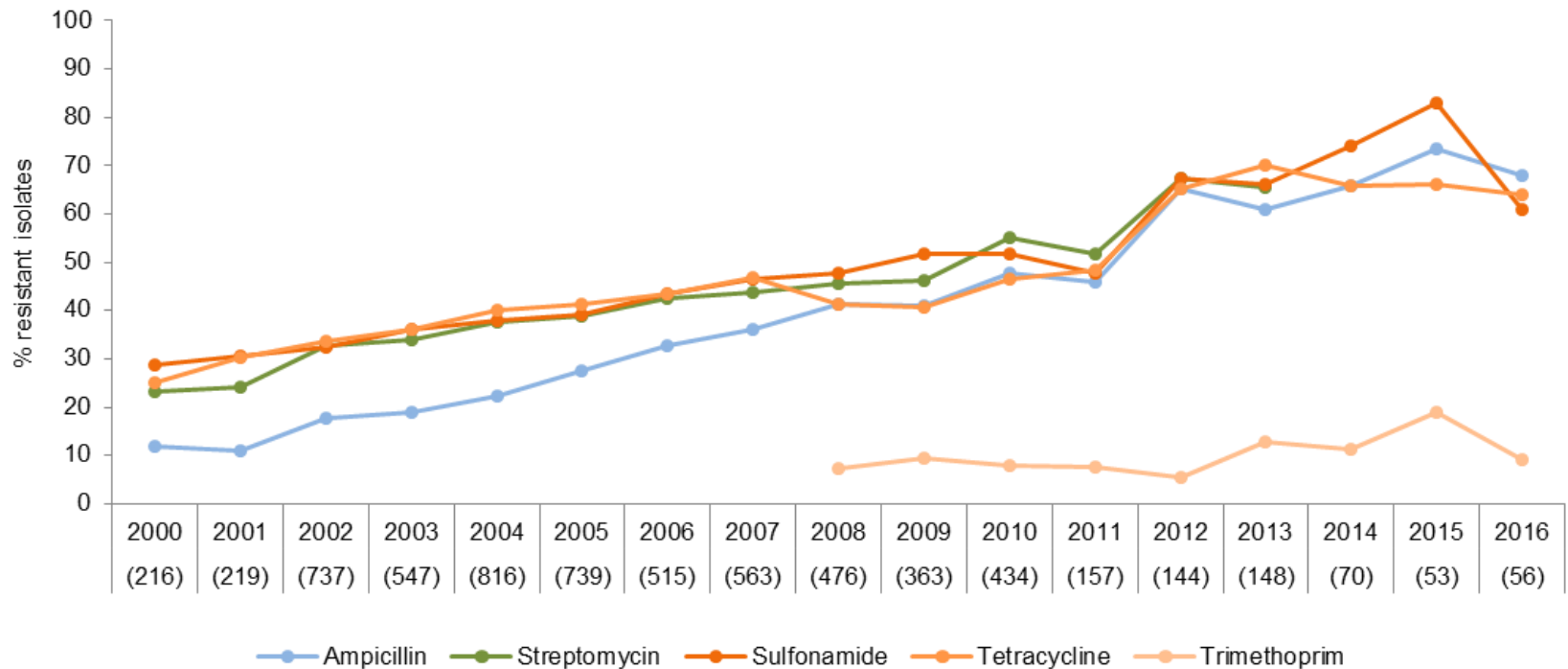
Fald i forbrug til fjerkræ (ekskl. kalkun)



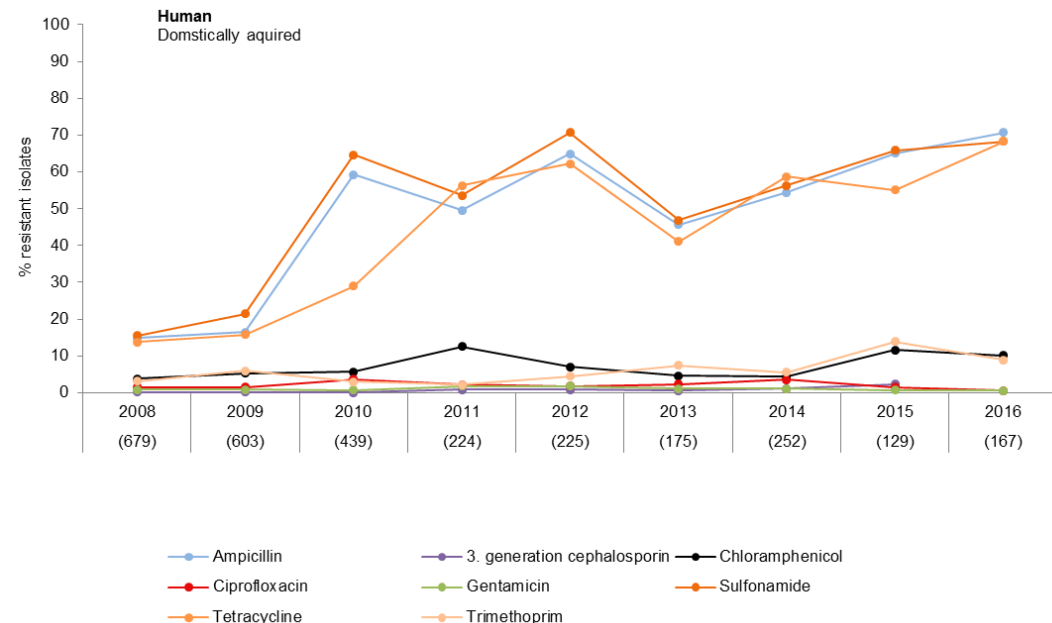
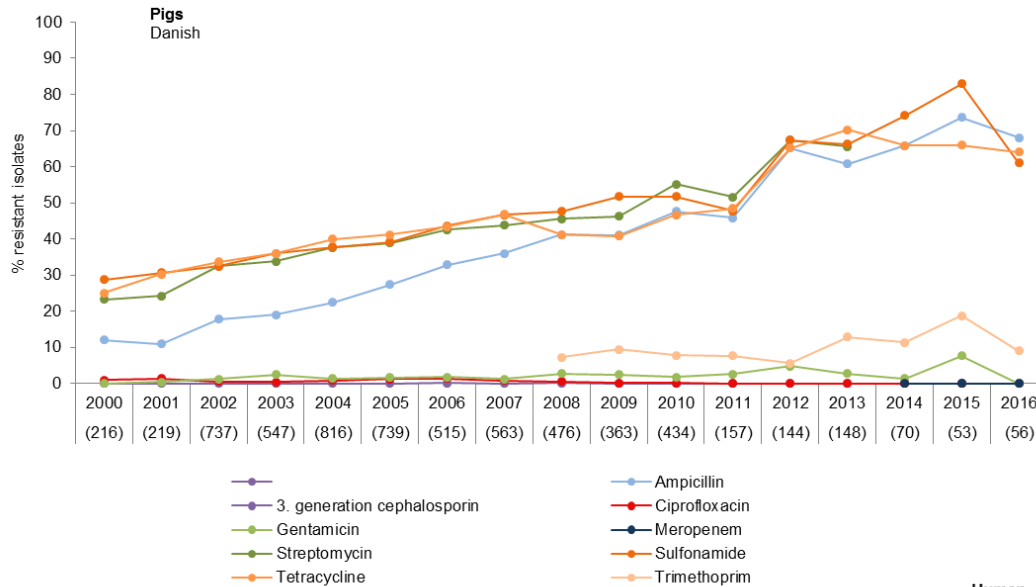
Forbrug hos kæledyr



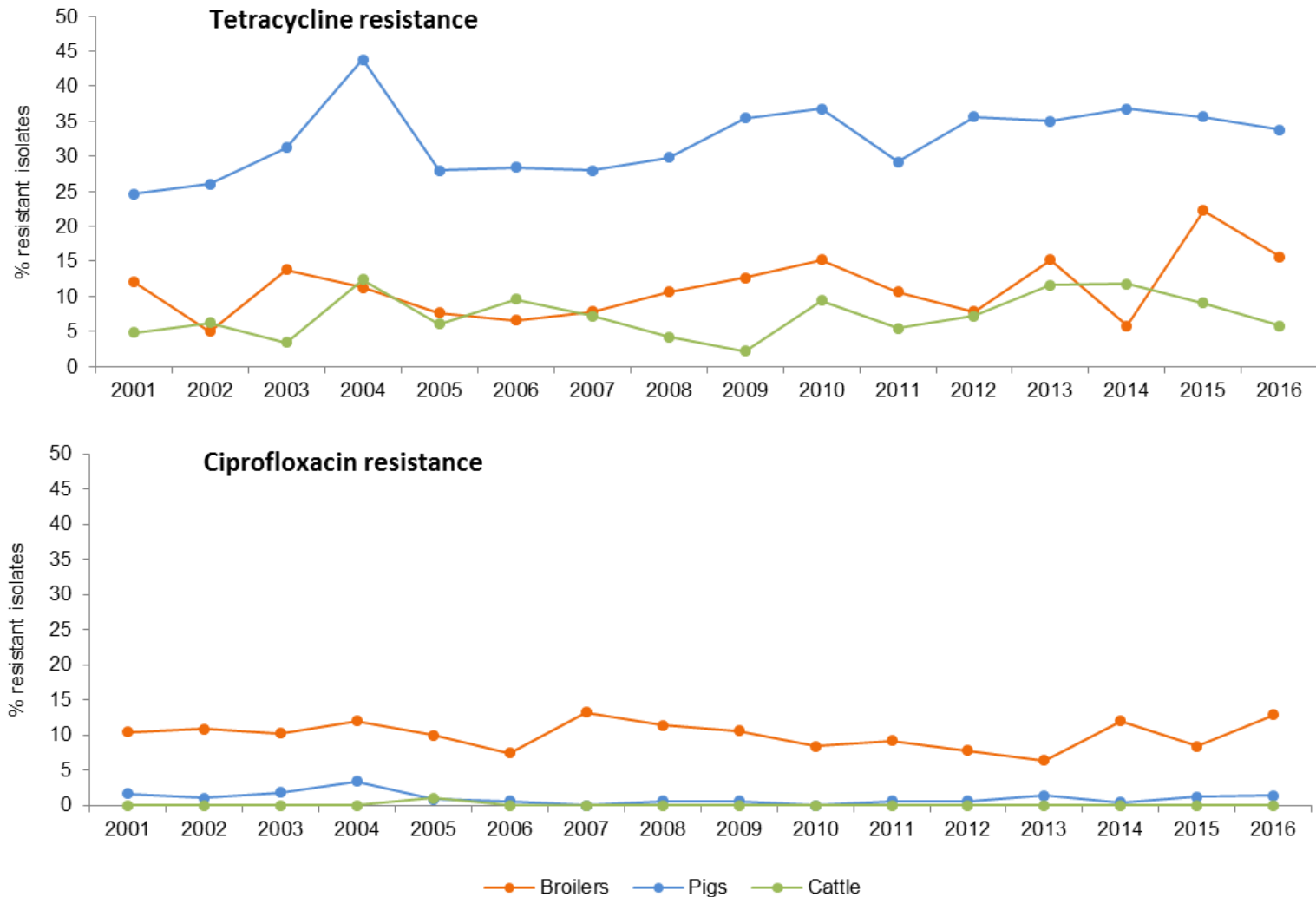
Resistens i *Salmonella* Typhimurium fra svin



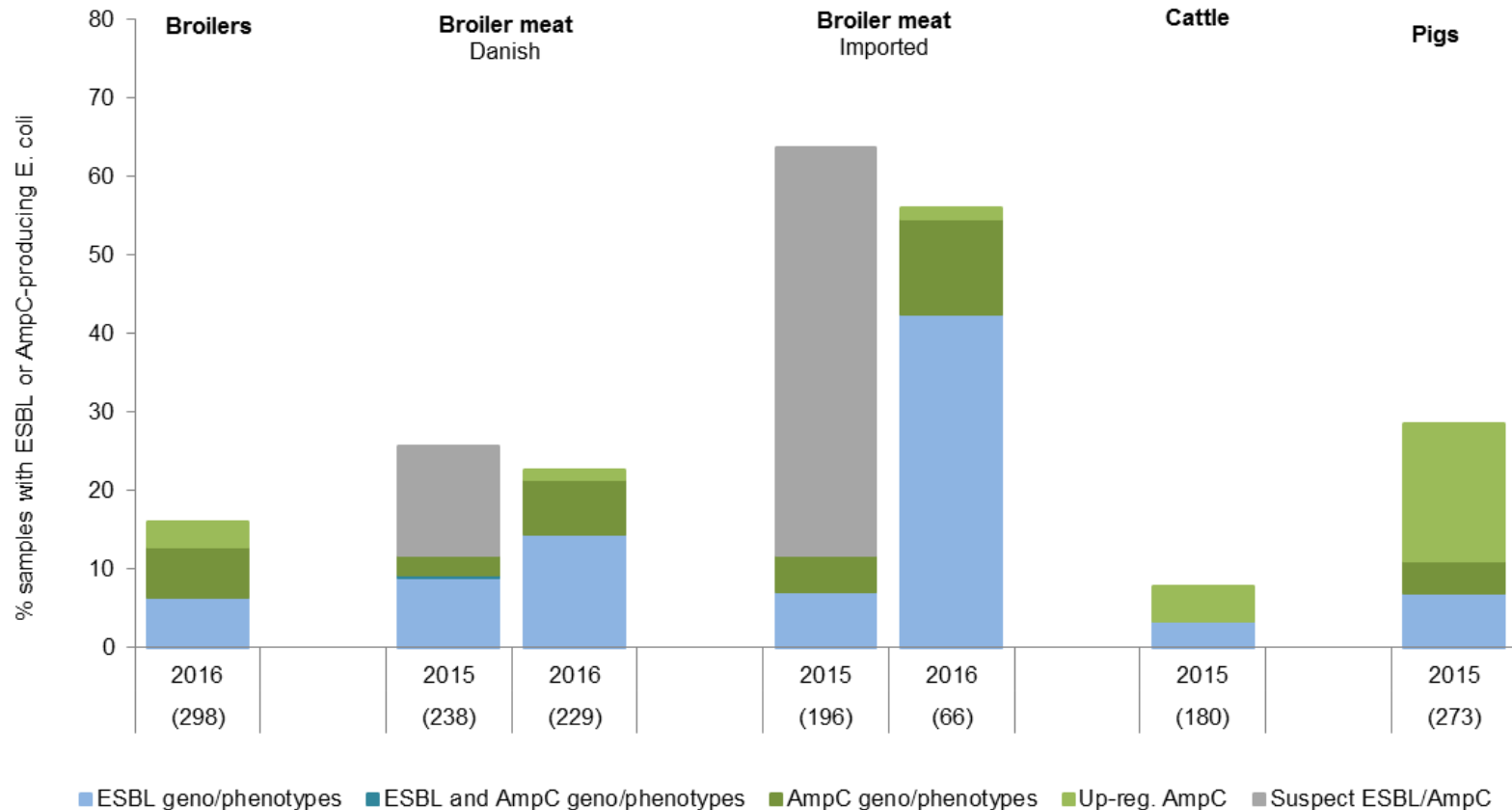
Resistens i *S. Typhimurium* fra svin og mennesker



Tetracyclin og ciprofloxacin resistens i indikator *E. coli*



ESBL/AmpC-producerende *E. coli*



Note: Number of tested samples each year is presented in the parenthesis. Samples were processed according to the EURL-AR laboratory protocol (October 2015). Distribution is based on WGS data, supplemented with data from presumptive isolates when not available (Phenotype included when available)

Måleenheder

Praksis:

- DDD/1000 indbyggere/dag (DID)
- Pakker/1000 indbyggere
- Ordinationer/1000 indbyggere
- Antal behandlede personer/1000 indbyggere

Hospitaler:

- DDD/1000 indbyggere/dag (DID)
- DDD/1000 (100) sengedage (DBD)
- DDD/1000 (100) udskrivelser (DDA)

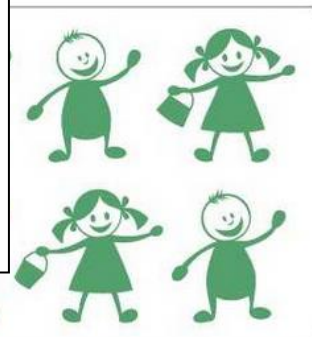
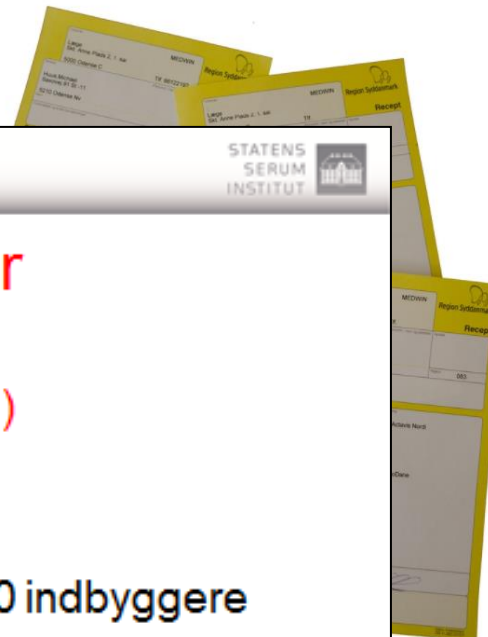


Figure 5.1 Total consumption of systemic antimicrobial agents in humans in primary health care vs hospital care. Denmark

DANMAP 2016

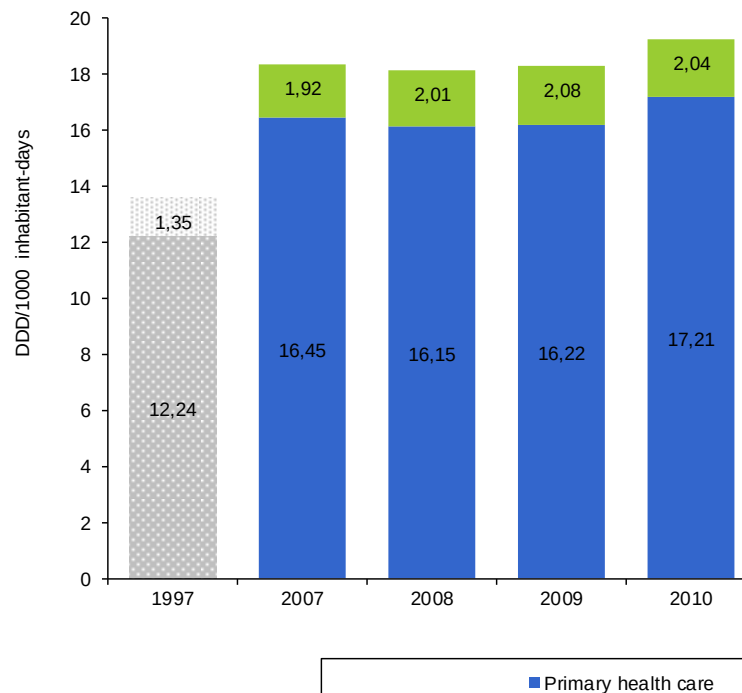
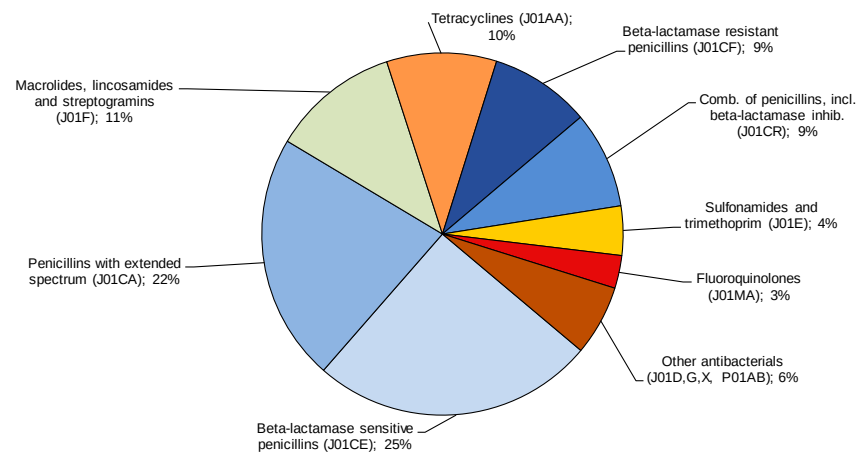


Figure 5.3. Distribution of the total consumption of antimicrobial agents in primary health care, Denmark

DANMAP 2016



Consumption of antibiotics for systemic use (ATC group J01) in the community, EU/EEA, 2015

Figure 1. Consumption of antibiotics for systemic use in the community by antibiotic group, EU/EEA countries, 2015 (expressed in DDD per 1 000 inhabitants and per day)

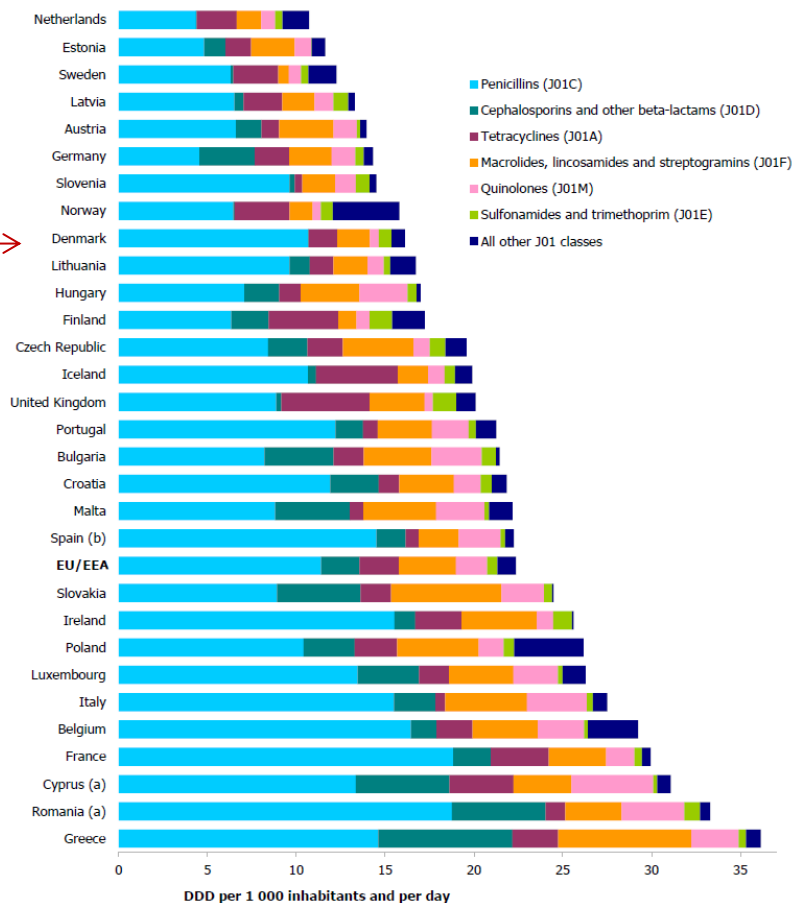


Figure 2. Consumption of antibiotics for systemic use in the community by antibiotic group, EU/EEA countries, 2015 (expressed as packages per 1 000 inhabitants and per day)

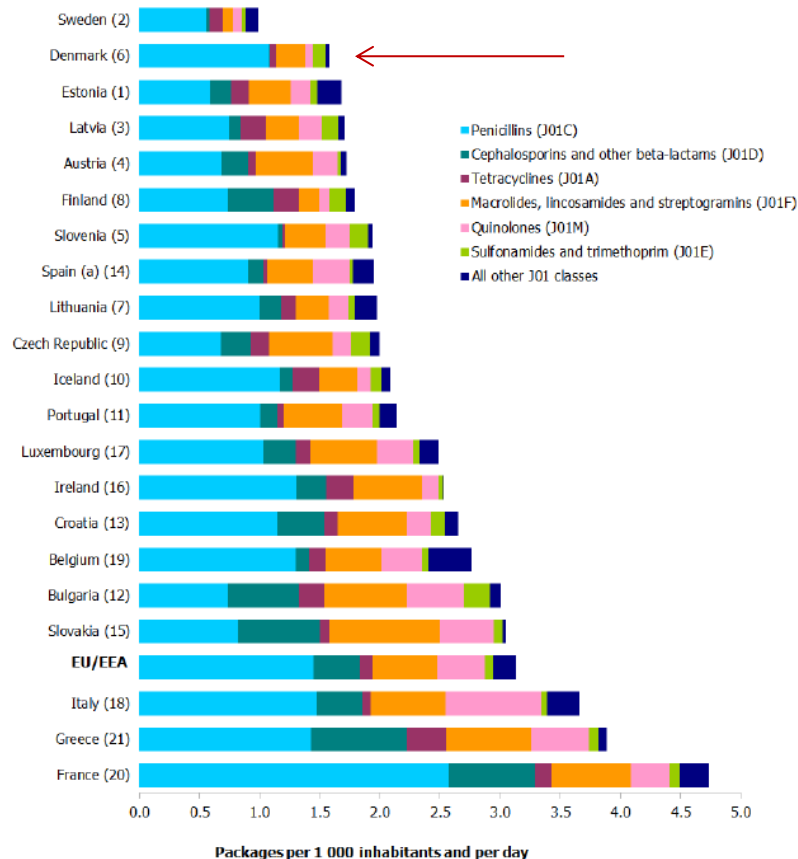
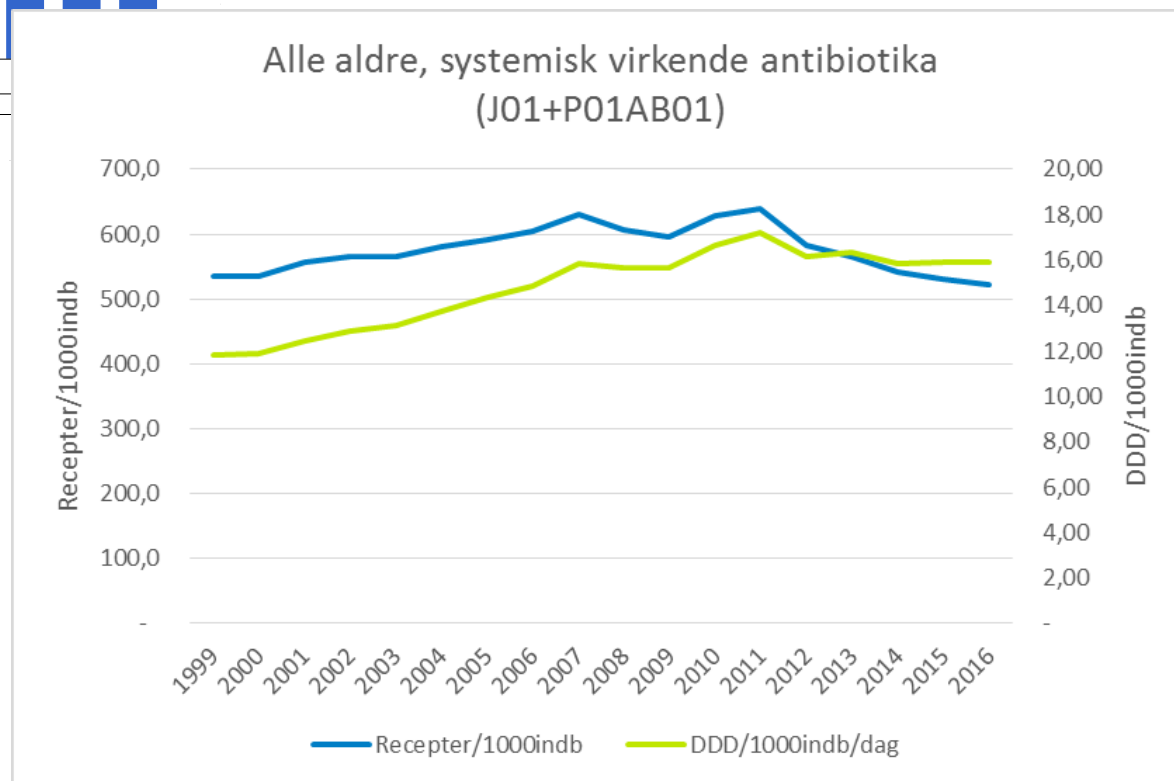
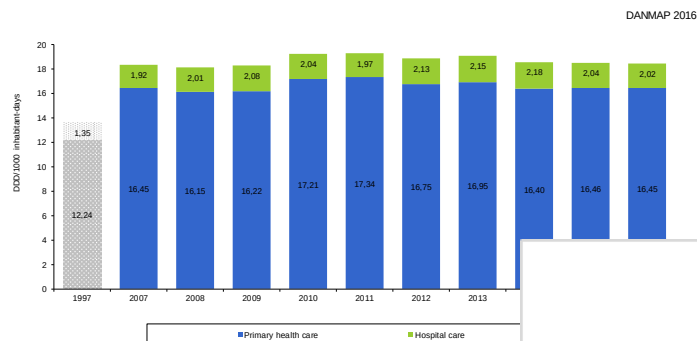
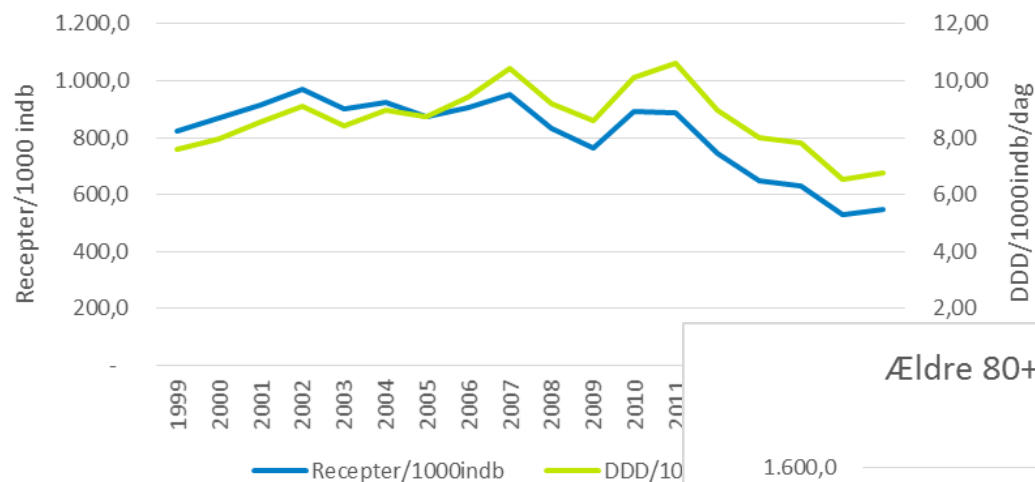


Figure 5.1 Total consumption of systemic antimicrobial agents in humans in primary health care vs hospital care. Denmark





Børn 0-4 år, Systemisk virkende antibiotika (J01+P01AB01)



Ældre 80+ år, systemisk virkende antibiotika (J01+P01AB01)

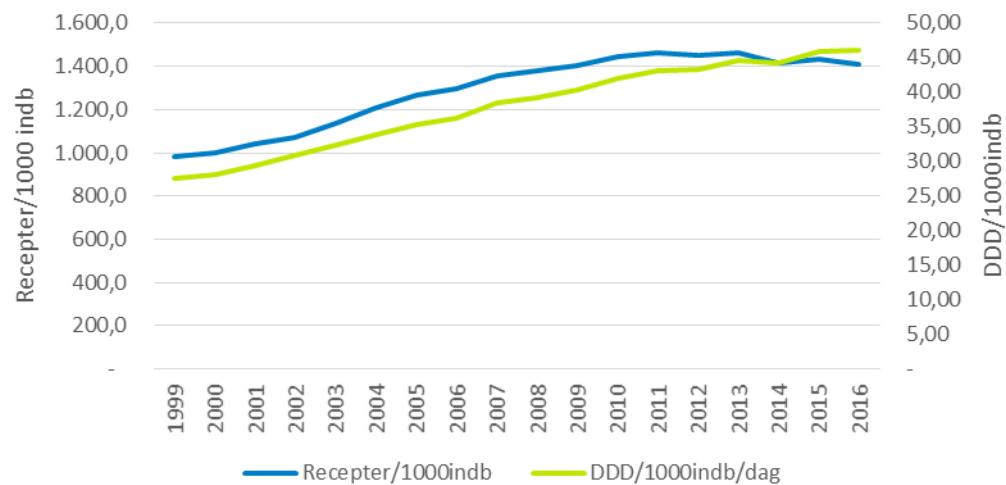
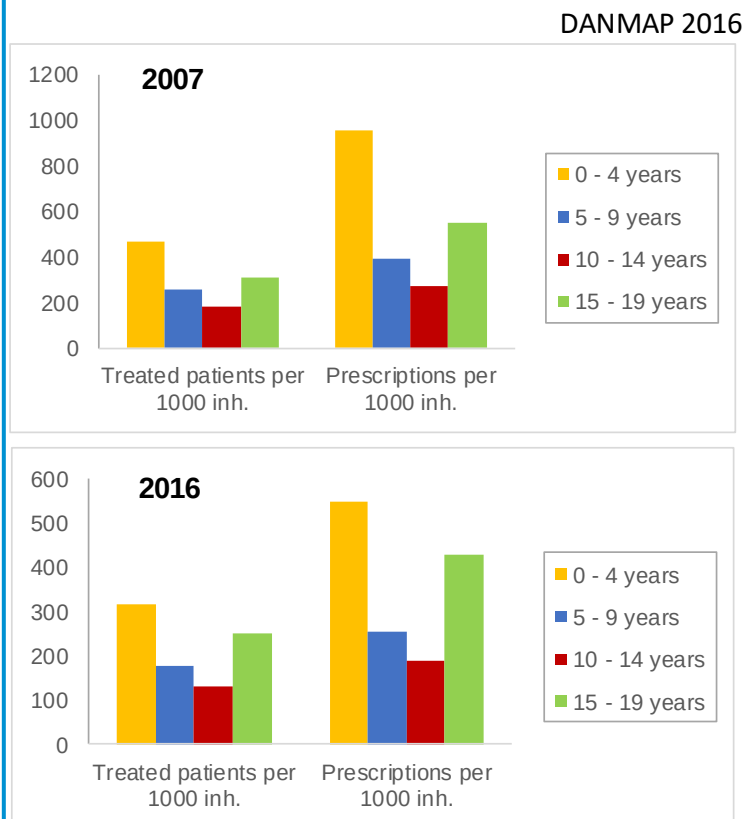
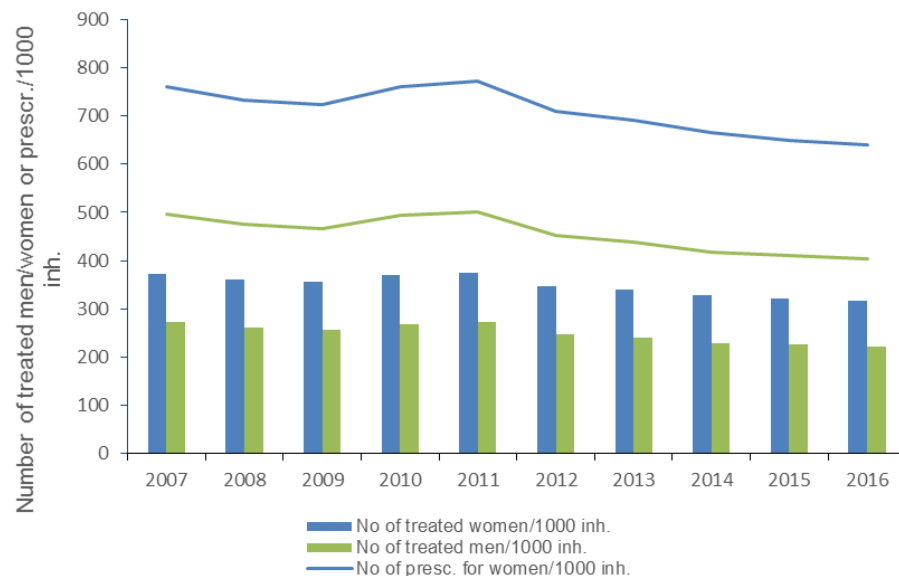


Figure 5.6b. Number of prescriptions and treated patients per 1000 inhabitants aged 0-19 in 2007 and 2016, Denmark

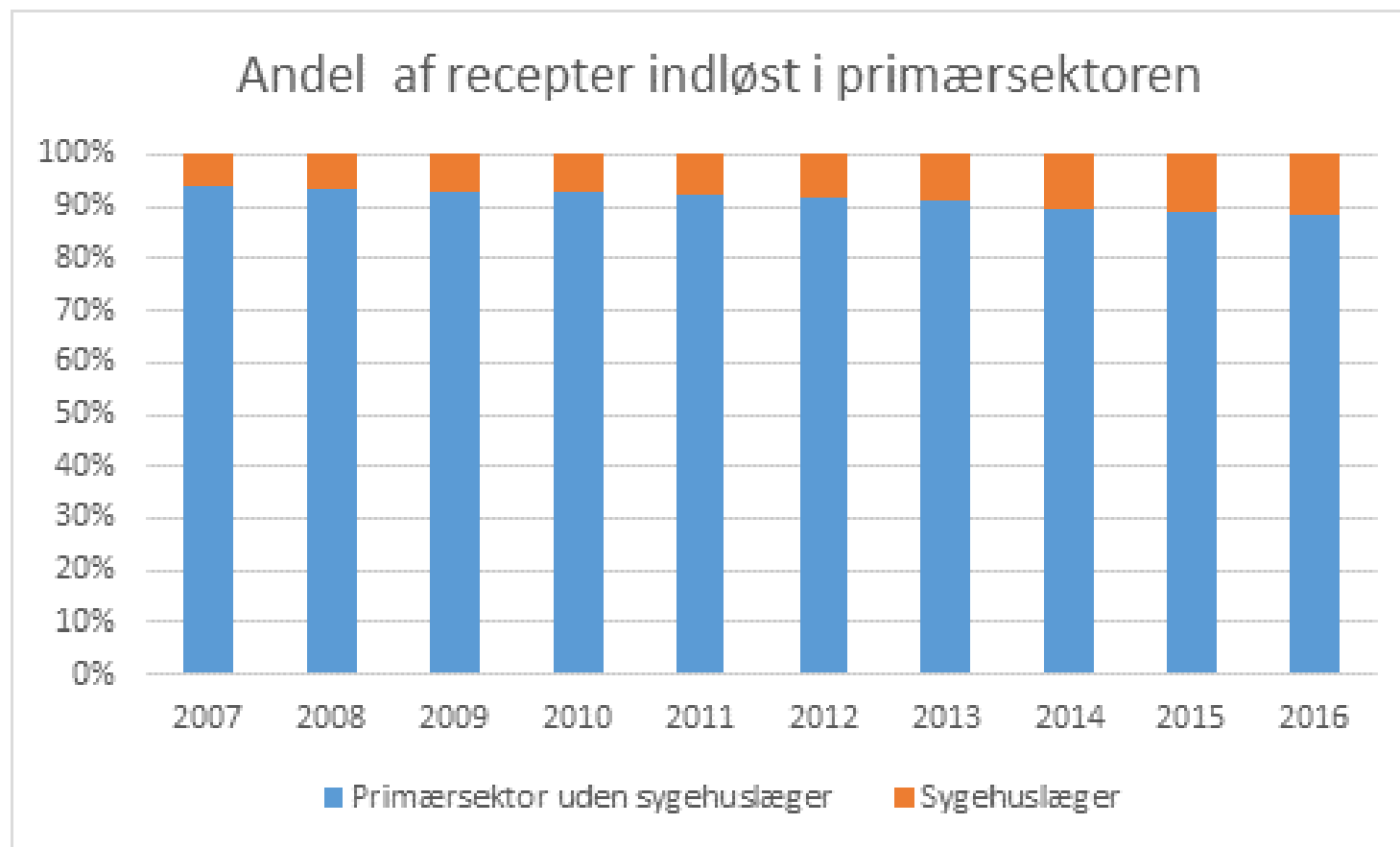


Figur 5.7b. Number of treated men/women and of prescriptions per gender per 1000 inhabitants, 2007-2016



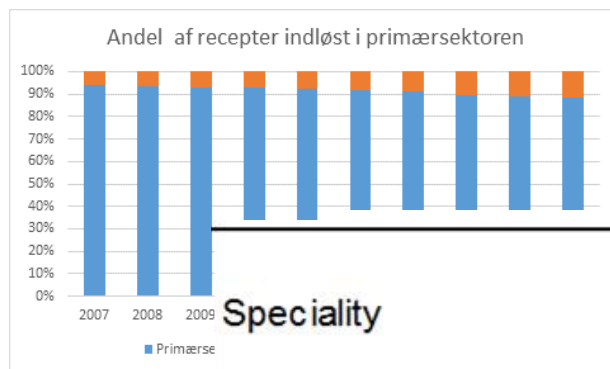
Børn, ældre og kvinder bruger mest
Og har derfor været målgruppe
For den Nationale
antibiotikakampagne de seneste år

Den Danske Handlingsplan 2017



Den Danske Handlingsplan 2017

Fordelingen af receptudskrivning på de forskellige faggrupper/specialer



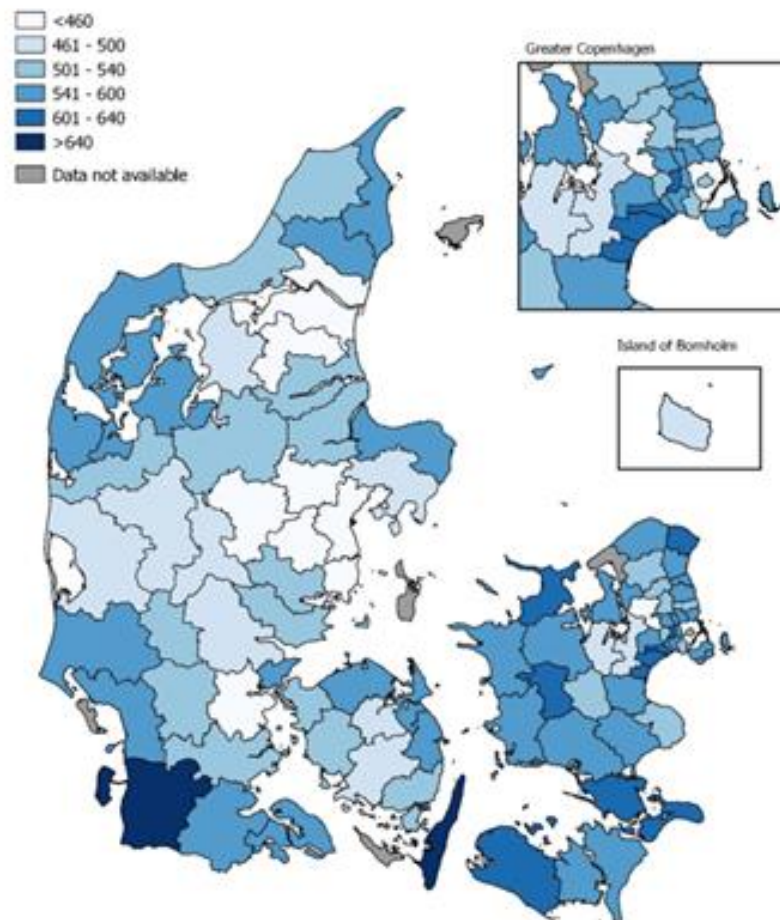
DANMAP 2016

Speciality	Prescriptions/ 1000 inhabitants	2016 Prescriptions/ user	DDD/prescription
General practitioners	391	1.8	10.7
Dentists	36	1.4	8.5
Ear/nose/throat specialists	9	1.3	9.0
Dermato-venerologists	6	1.5	29.9
Other specialists	5	1.4	11.4
All	462	2.0	10.8



Figure 5.8 Number of primary health care prescriptions/1000 inhabitants in Danish municipalities, 2016

(National average=522 prescriptions/1000 inhabitants)





Total somatic hospital consumption (DBD) by leading groups of antimicrobial agents (J01), Denmark

DANMAP 2016

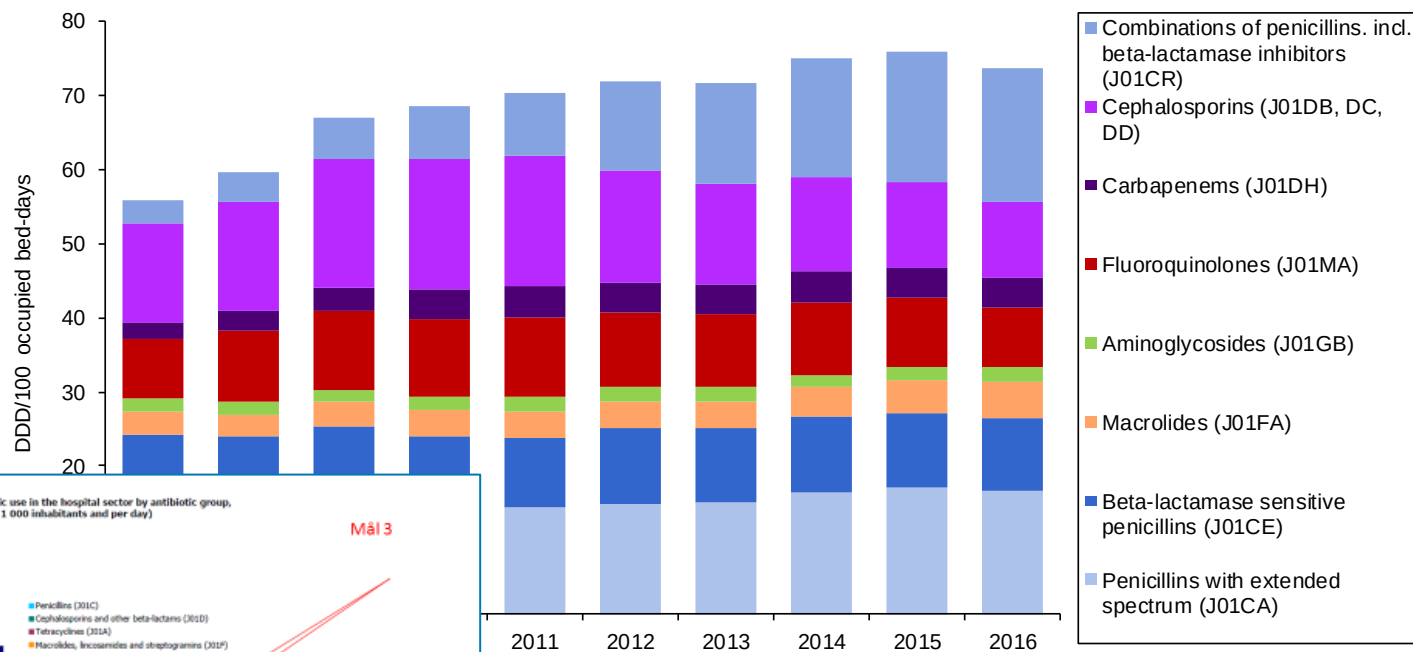
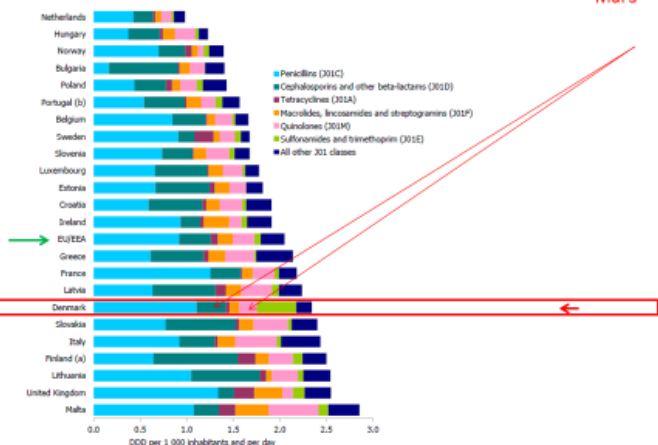


Figure 3. Consumption of antibiotics for systemic use in the hospital sector by antibiotic group, EU/EEA countries, 2015 (expressed as DDD per 1 000 inhabitants and per day)



Jenny Dahl Knudsen november 2017

Reduktion i andelen af forbruget af de kritisk vigtige - cefalosporiner, fluorkinoloner og carbapenemer: 32 % i 2007, 22 % i 2016



Figure 5.9. Number of bed-days and admissions in somatic hospitals, Denmark
DANMAP 2015

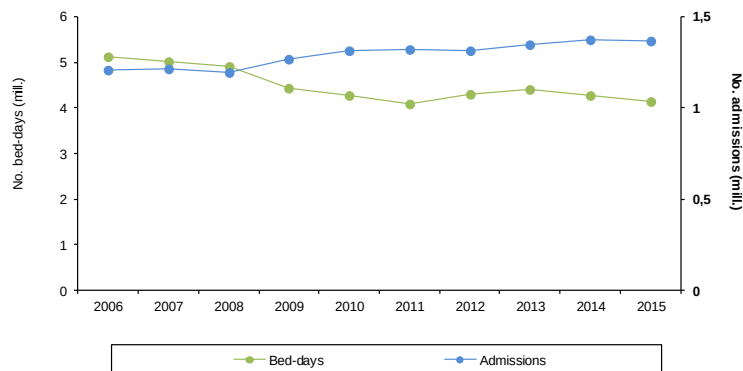
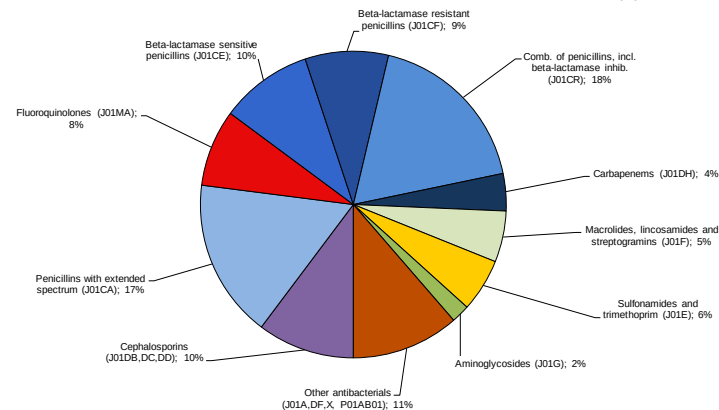


Figure 5.9. Distribution of the total consumption of antimicrobial agents in somatic hospitals, Denmark
DANMAP 2016



		DANMAP 2016									
ATC group ^(a)	Therapeutic group	Year									
		2007	2008 ^(b)	2009	2010	2011	2012	2013	2014	2015	2016
J01 DBD	Antibacterial agents for systemic use (total)	74.33	80.14	90.87	93.67	97.08	98.94	99.88	104.30	103.02	99.98
J01 DAD	Antibacterial agents for systemic use (total)	306.9	328.3	317.8	304.3	301.9	322.7	325.2	324.1	313.38	310.53

+ 36 %

+ 1,2 %

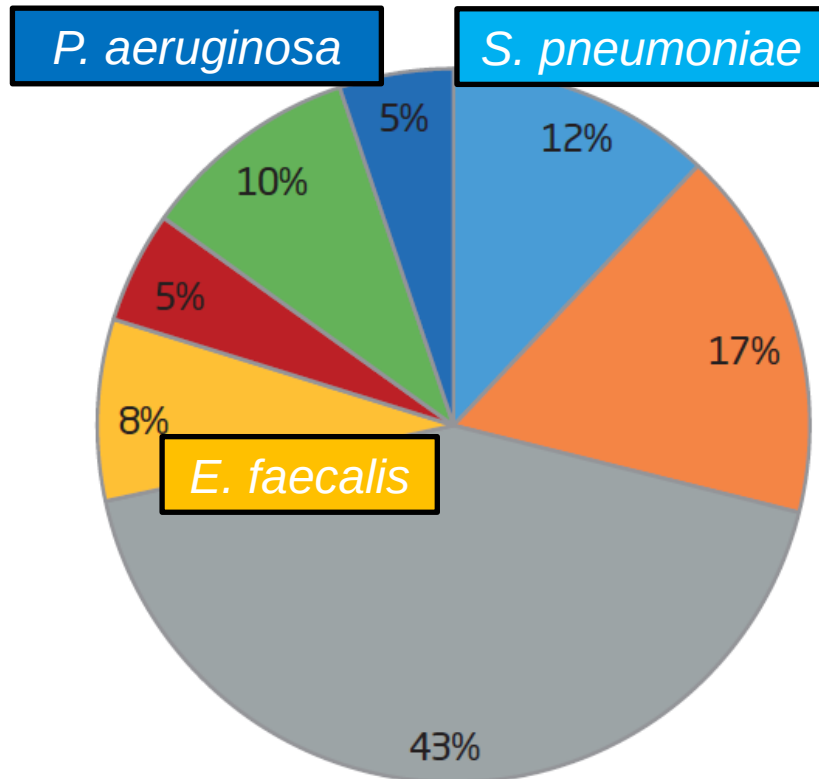
RESISTENSDATA FRA DE KLINISK MIKROBIOLOGISKE AFDELINGER



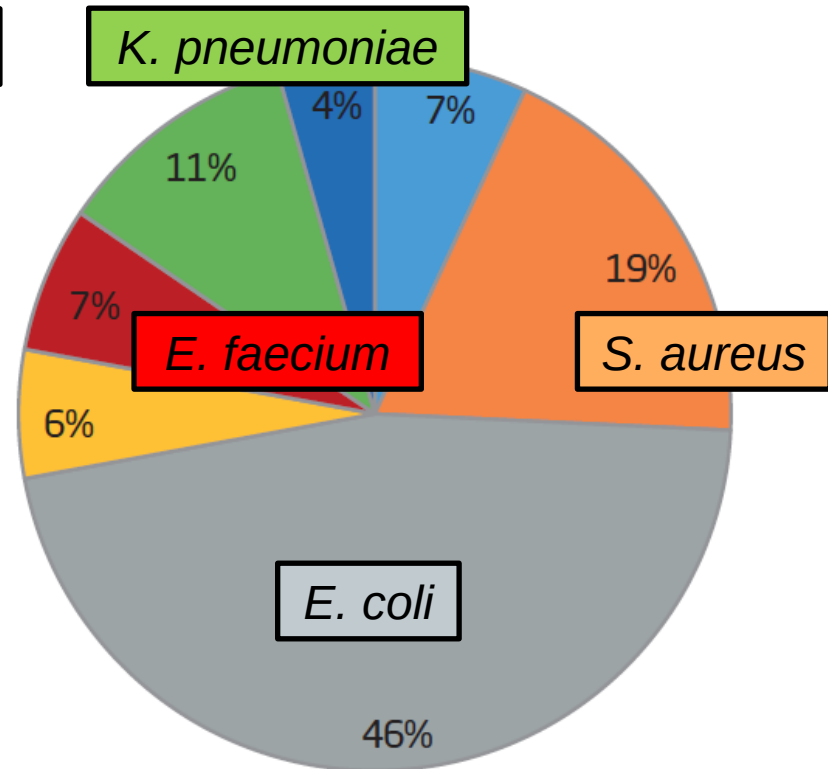
Positive bloddyrkninger



2009
N = 8277

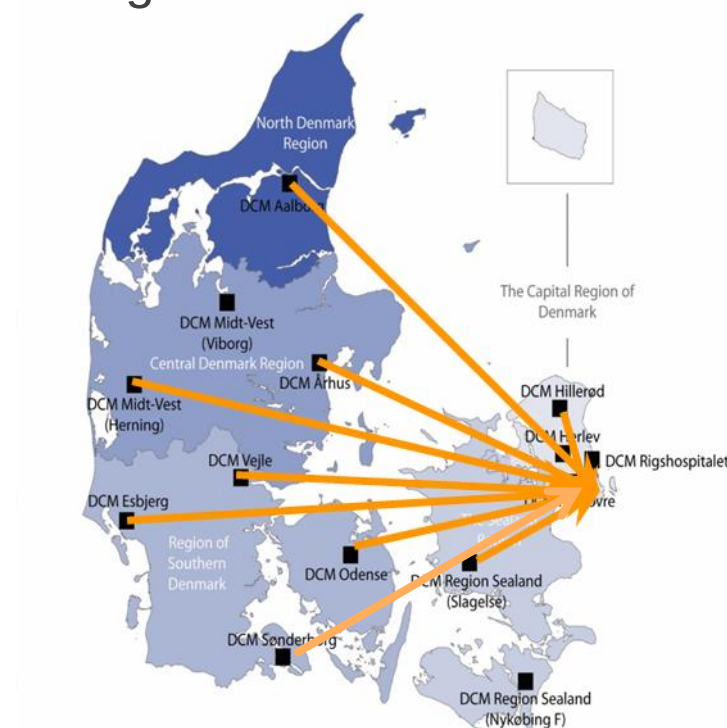


2016
N = 10.442

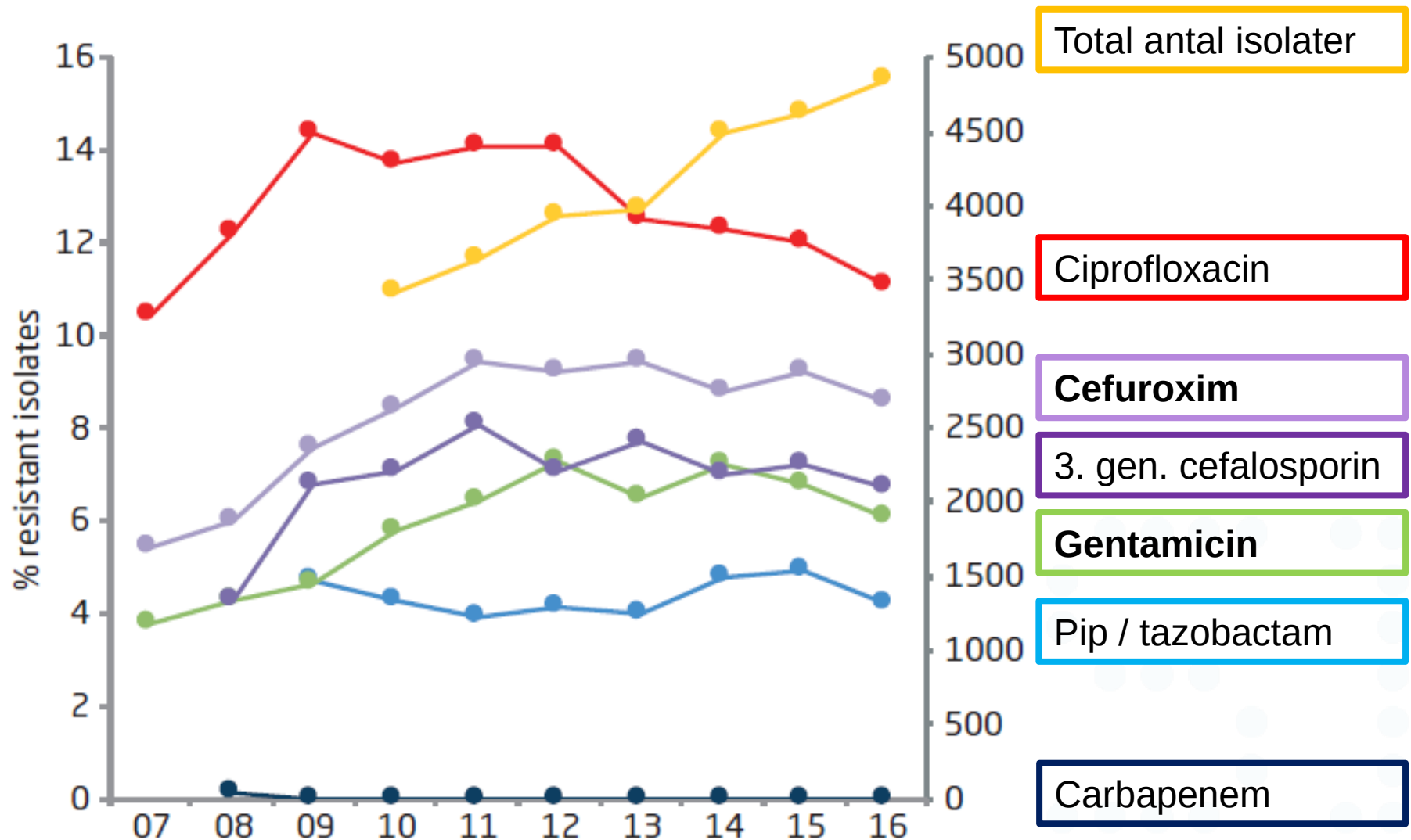




- ❖ Data modtaget fra alle klinisk mikrobiologiske afdelinger i Danmark
- ❖ De mikrobiologiske afdelingers egne fortolkninger af resistensdata
- ❖ Første isolat pr. patient pr. år
- ❖ Ingen data for udvikling af resistens under behandling

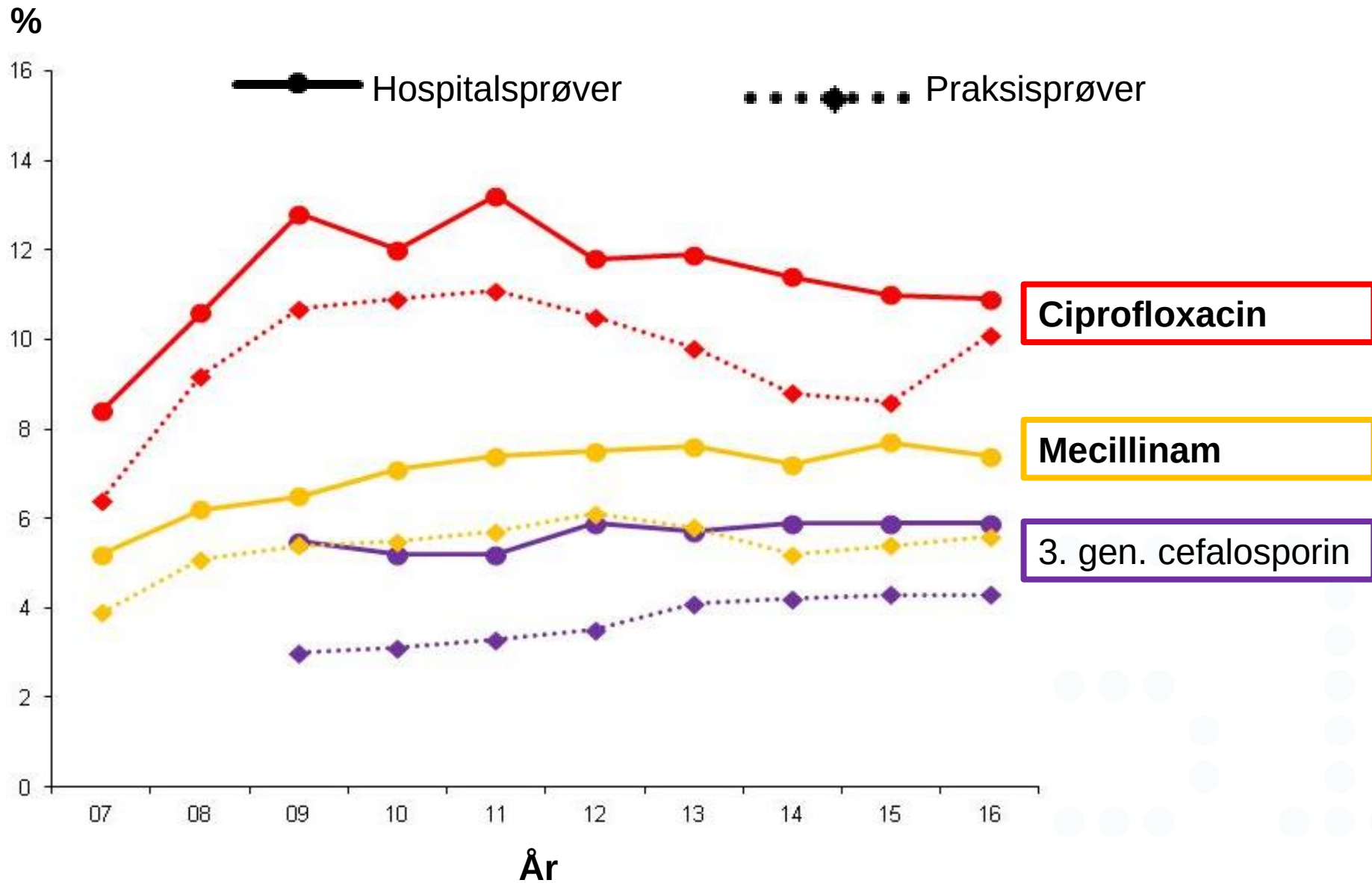


Resistente, invasive *E. coli*

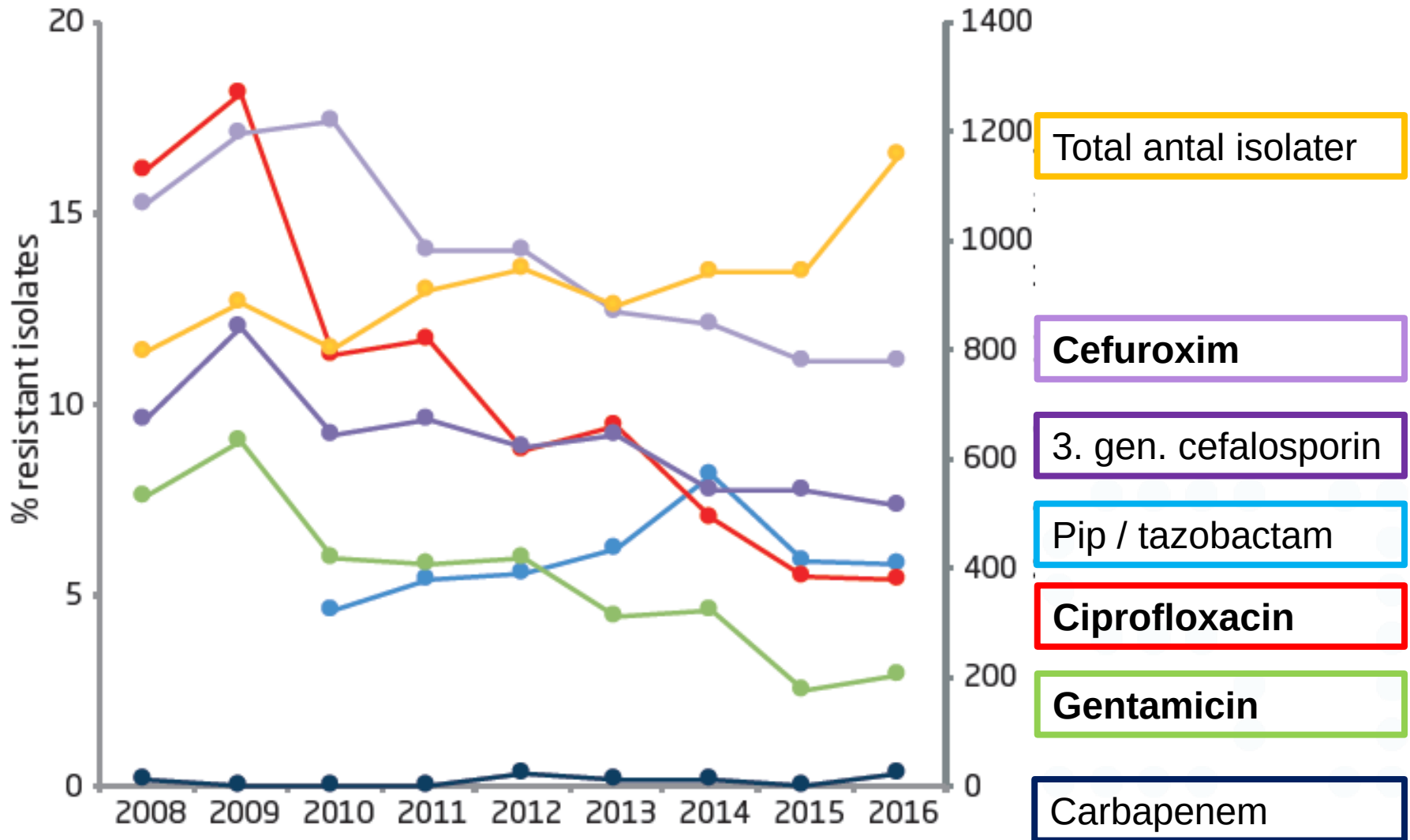


	2007	2016
Pip / tazobactam	-	4 %
Cefuroxim	5 %	9 %
3. gen. cefalosporin	-	7 %
Ciprofloxacin	11 %	11 %
Gentamicin	4 %	6 %
Carbapenem	-	< 1 %
Multiresistent	-	2 %
<i>Max antal testet (N)</i>	3398	4838

Resistente *E. coli* i urin

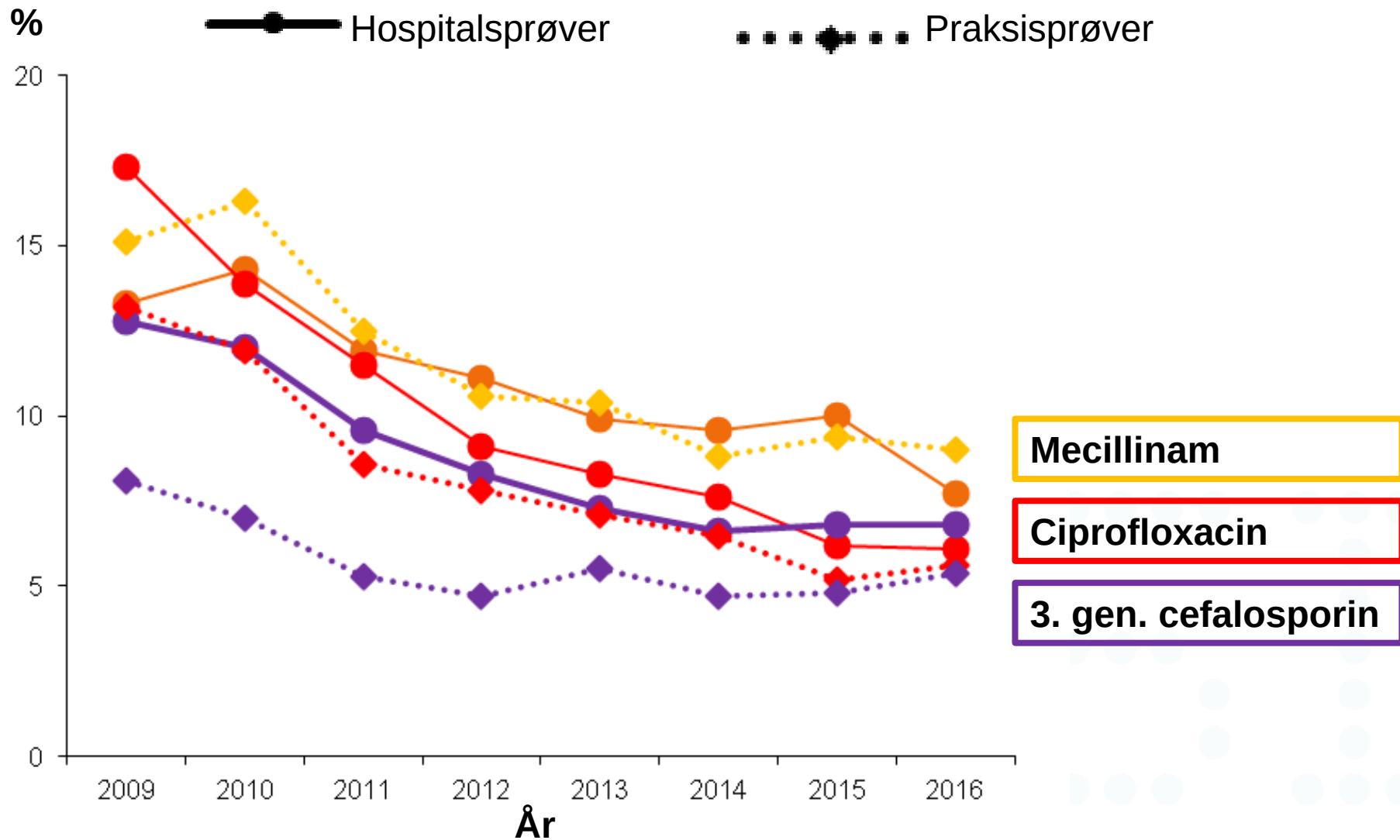


Resistente, invasive *K. pneumoniae*

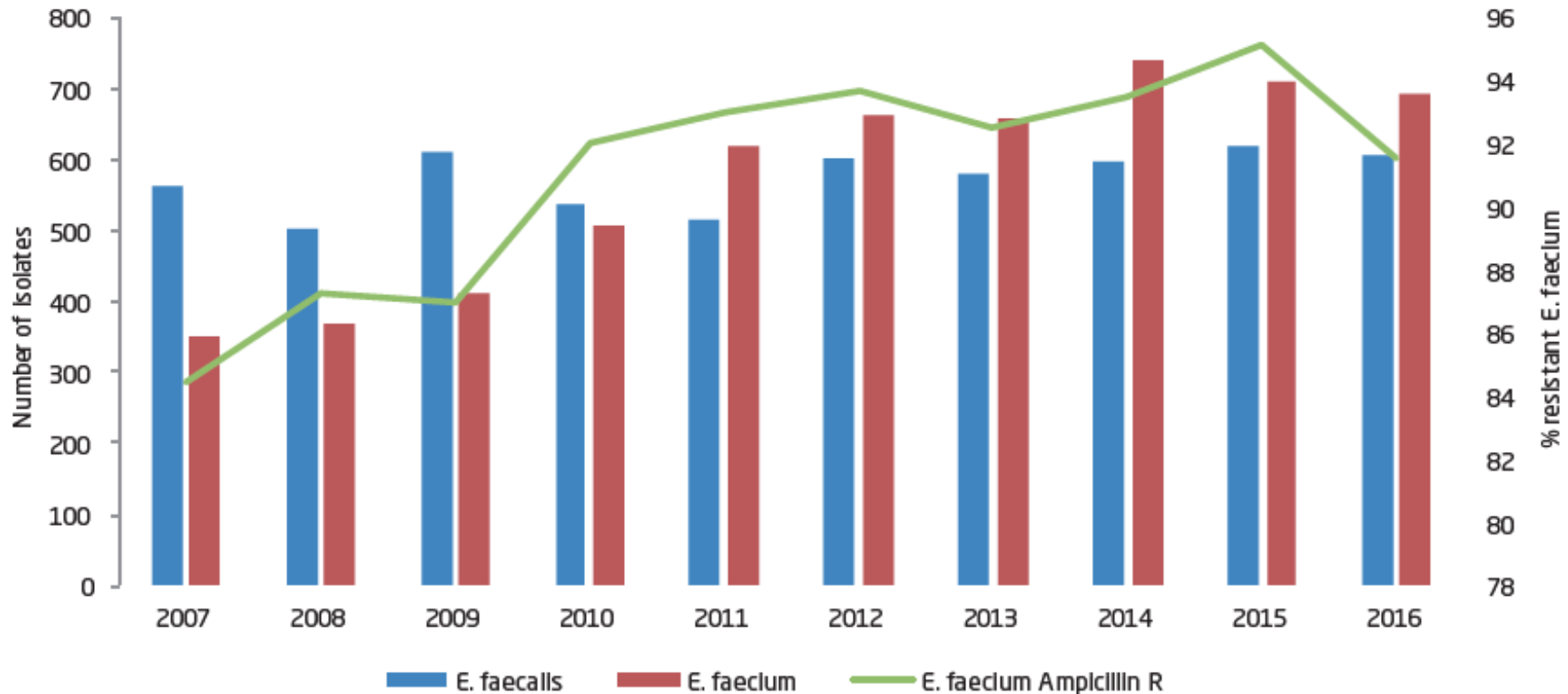


	2008	2016
Pip / tazobactam	-	6 %
Cefuroxim	15 %	11 %
3. gen. cefalosporin	10 %	7 %
Ciprofloxacin	16 %	5 %
Gentamicin	8 %	3 %
Carbapenem	-	< 1 %
Multiresistent	-	2 %
<i>Max antal testet (N)</i>	788	1152

Resistente *K. pneumoniae* i urin



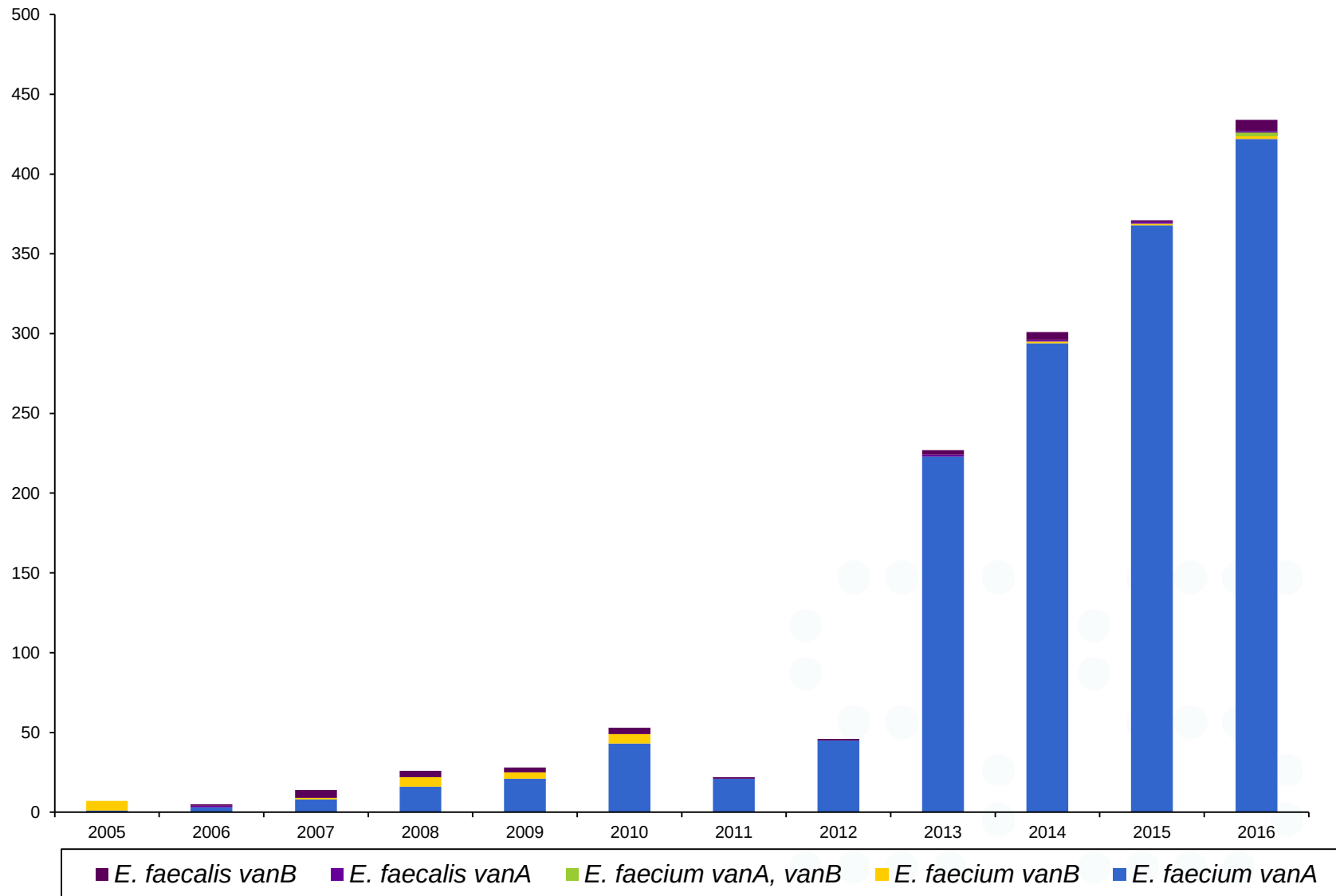
Invasive *E. faecium* og *E. faecalis*



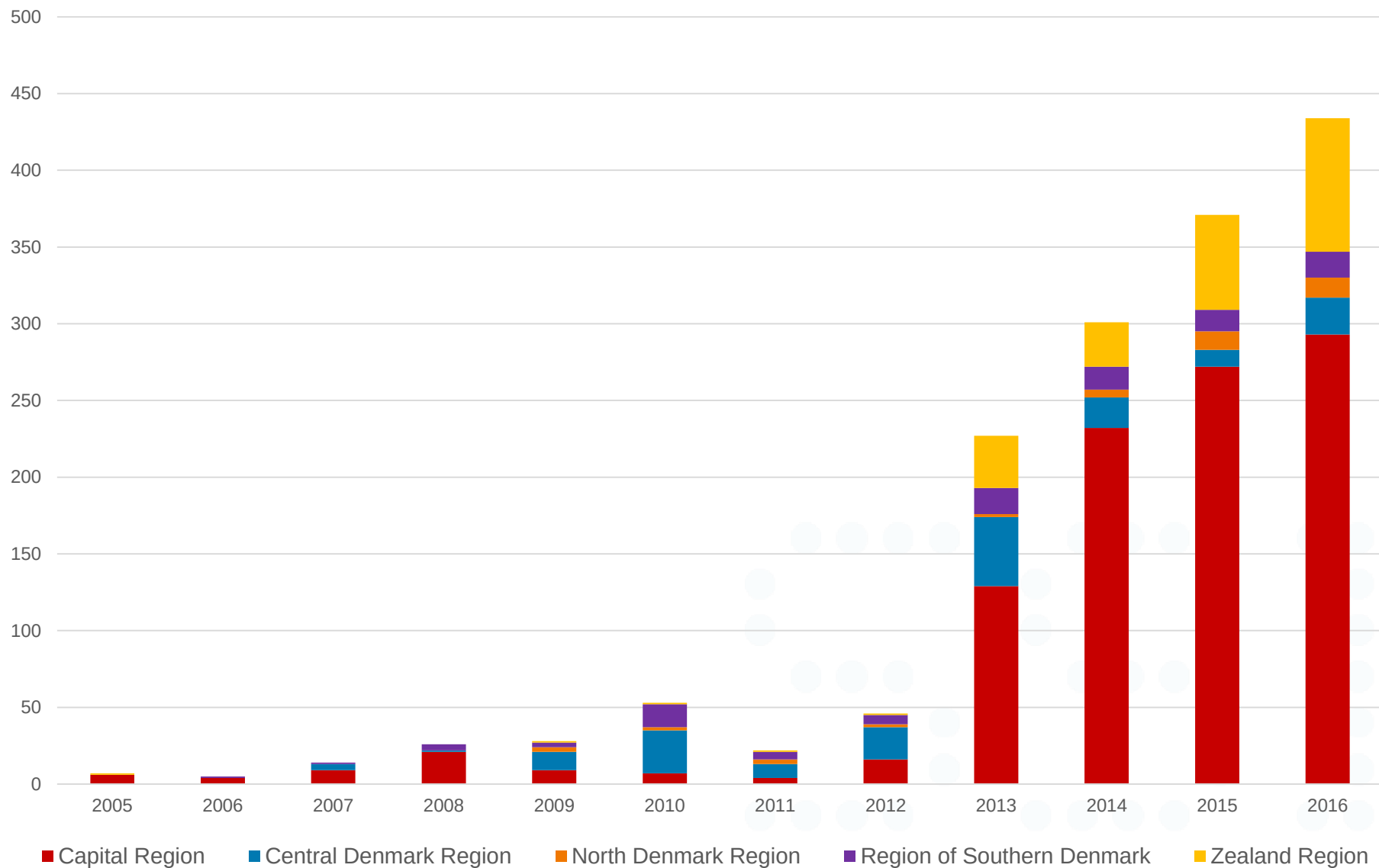
	E. faecalis		E. faecium	
	2007	2016	2007	2016
Ampicillin	1 %	2 %	84 %	92 %
Vancomycin	1 %	0 %	1 %	7 %
Linezolid	-	< 1 %	-	< 1 %
<i>Max antal testet (N)</i>	511	593	284	681

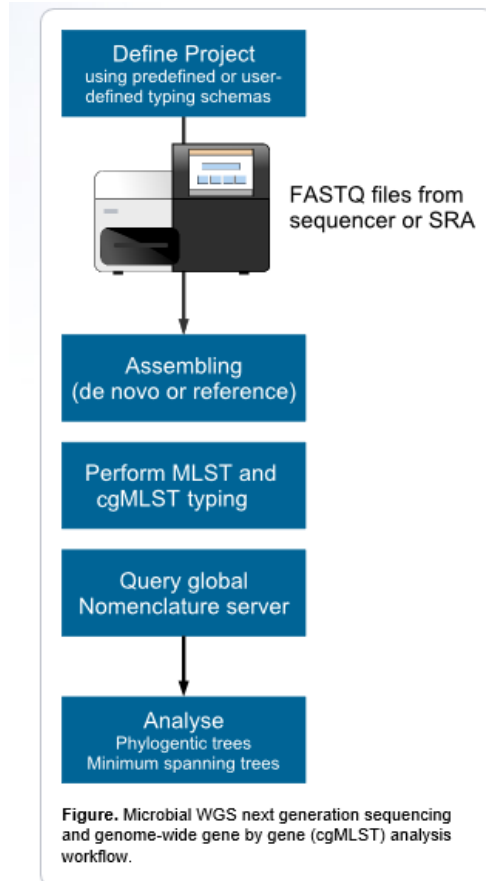
OVERVÅGNING AF SÆRLIGE RESISTENSMEKANISMER/RESISTENTE BAKTERIER BASERET PÅ HELGENOMSEKVENTERING

Kliniske VRE (2005-2016)



Distribution of the clinical VRE isolates according to the five Danish regions, 2005-2016

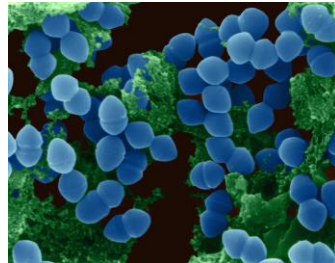




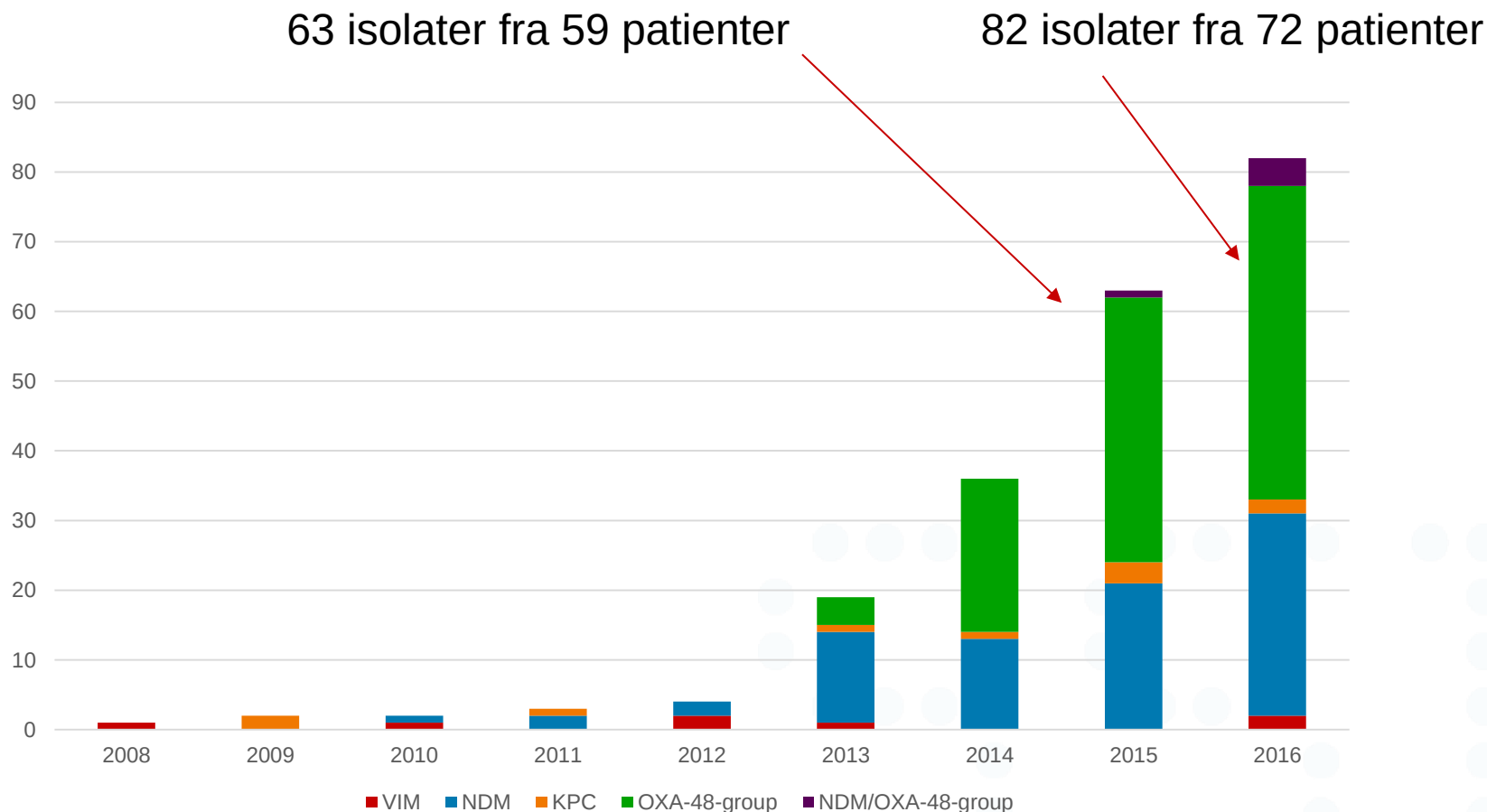
- I 2016 har vi indført subtypning med SeqSphere (nyt kommercielt software)
- Sammenligning af variation i 1423 gener
- Kan opdele én ST type i mange Cluster typer (CT)
- Nemt at kommunikere f.eks. CT859
- Sammenholdes med andre isolater i databasen (også internationalt)



- ❖ I 2016, blev de 422 *vanA E. faecium* isolater opdelt i 42 cluster typer (CTs) med cgMLST
- ❖ Der var en dominerende type ST203-CT859
- ❖ 64% af *vanA E. faecium* isolater tilhørte ST203-CT859 i 2016 (51% i 2015)

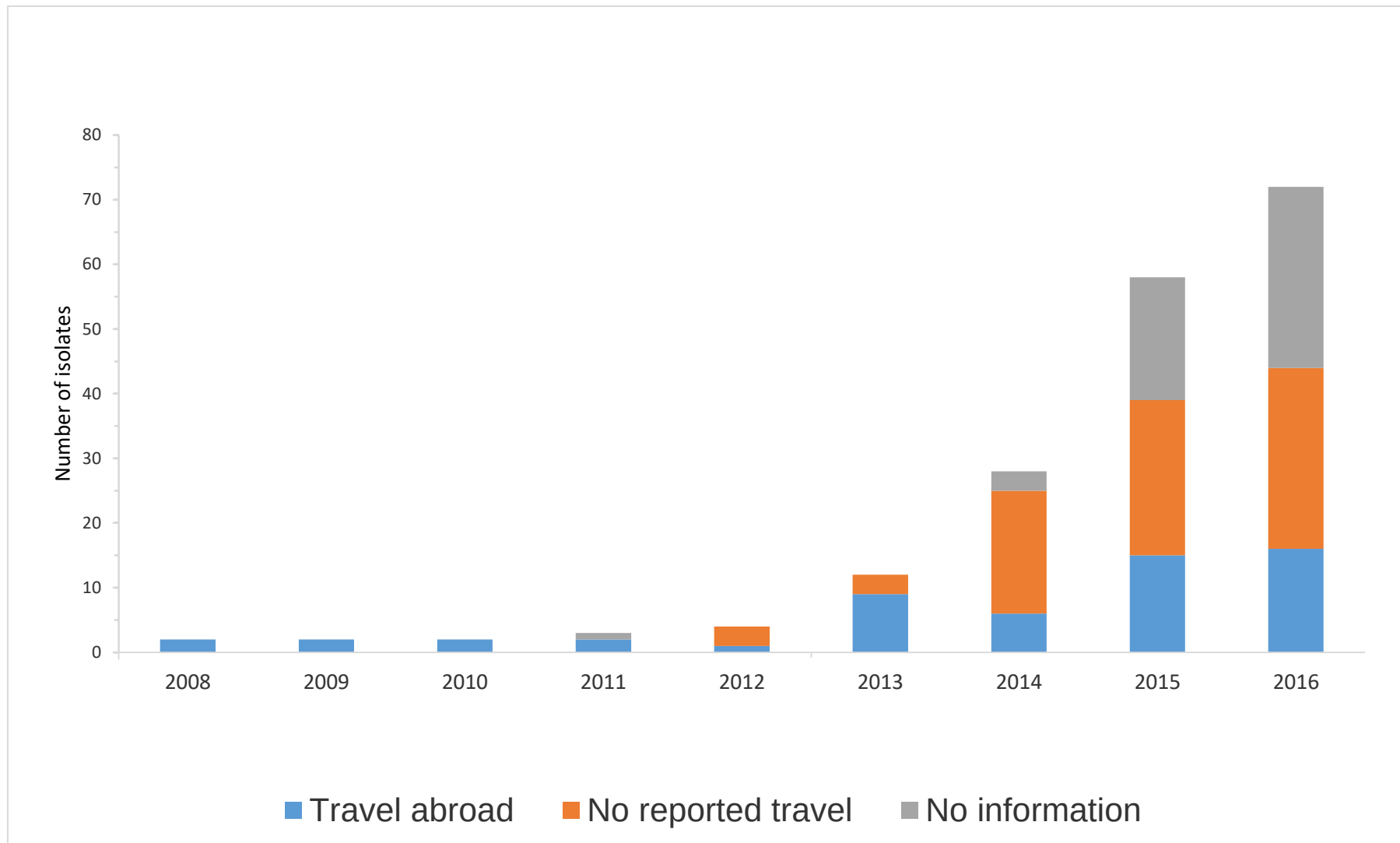


Carbapenemase producerende enterobakterier (CPE)



More than one isolate was included from the same patient, if the isolates belonged to different bacterial species and/or harboured different carbapenemases

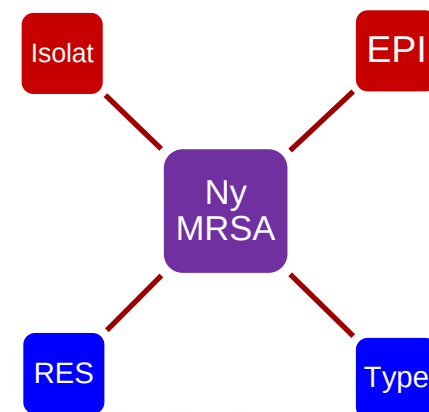
Travel information for patients with Carbapenemase-producing *Enterobacteriaceae* (CPE) during 2008-2016



Staphylococcus aureus - DANMAP2016



- ❖ Referencelaboratoriet modtager
 - *S. aureus* fra bakteriæmier (SAB) – frivillig siden 1957
 - MRSA – anmeldelsespligtigt siden nov. 2006
 - Infektioner/ raske bærere, import/ hospital/ samfund/ dyrekontakt mm.
- ❖ mPCR (Stegger M, et al. CMI 2011)
 - *spa*, *mecA/C*, *lukF-pv* (PVL), *scn*, *hsdCC398*
- ❖ *spa*- type bestemmes (og CC)
 - - undtagen husdyr MRSA CC398
- ❖ Resistensbestemmelse på (ca. 1/4 af MSSA og alle non-CC398 MRSA)
- ❖ WGS: MRSA udbrud, samt ca. 10% øvrige MRSA (SAB)
- ❖ Alt gemmes



- ❖ 1981 nye tilfælde i 2016
 - Ældre med underliggende sygdomme (kræft, diabetes, dialyse)
 - 425 (21 %) døde indenfor 30 dage
- ❖ Stigende diversitet: 578 forskellige *spa* typer (28 CC grupper), 10 hyppigste udgør 31%
 - 22 (1,1%) havde PVL genet (6 var MRSA)
- ❖ Resistens: Penicillin 71%, fald i fusidin resistens (12%)
- ❖ 40 (2,1%) MRSA
 - 6/40 (15%) døde indenfor 30 dage



Surveillance Atlas of Infectious Diseases

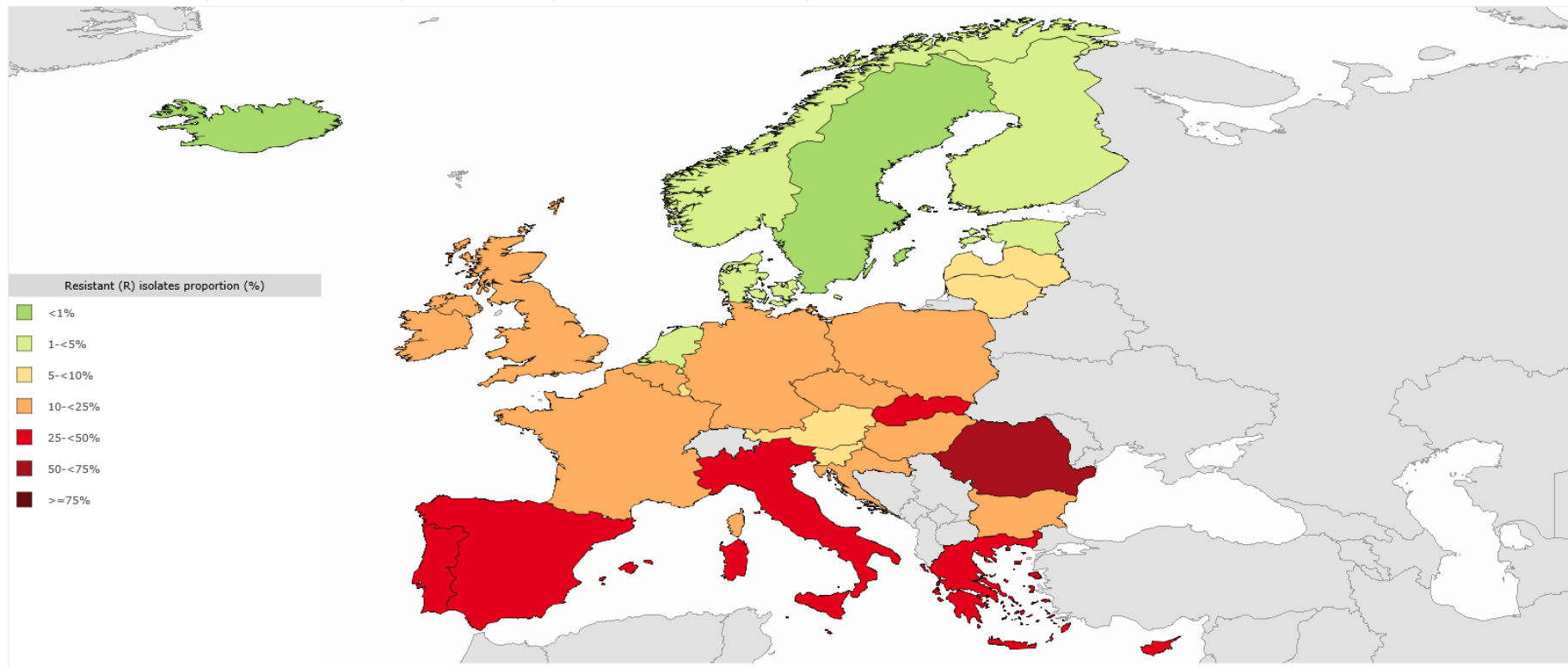
Antimicrobial resistance

Staphylococcus aureus

Meticillin (MRSA)

Resistant (R) isolates proportion

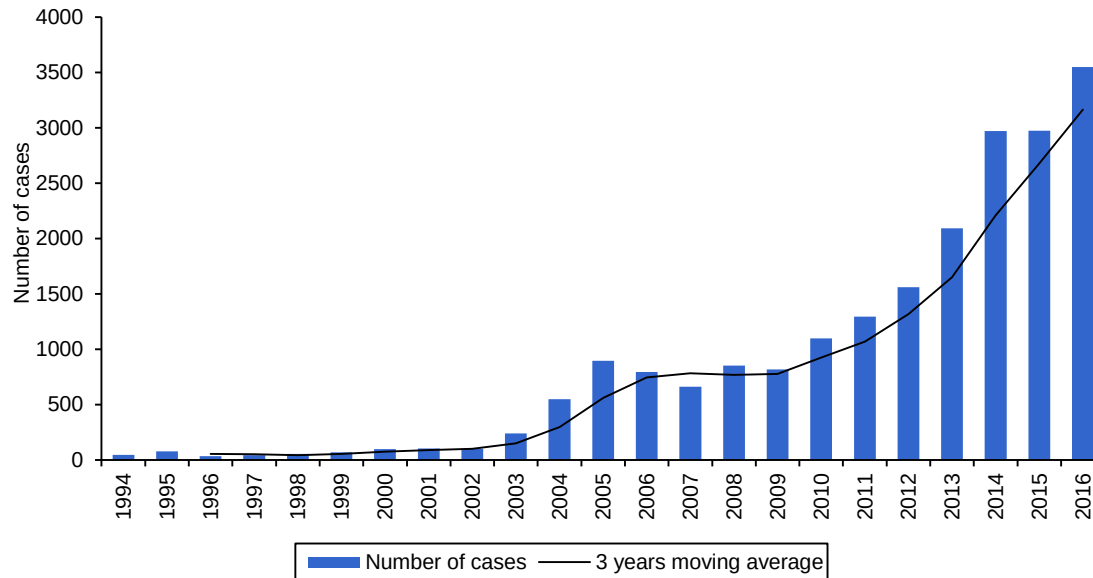
2015





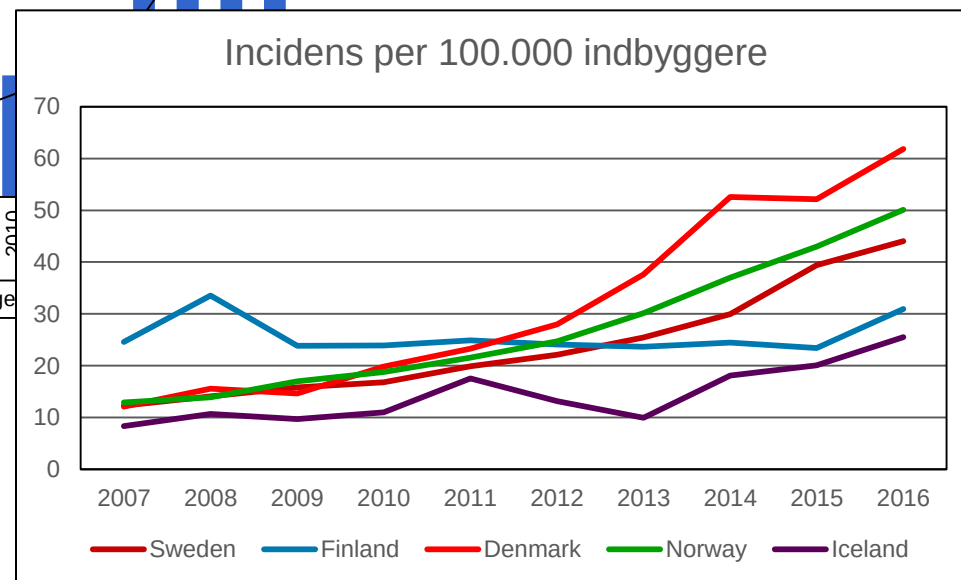
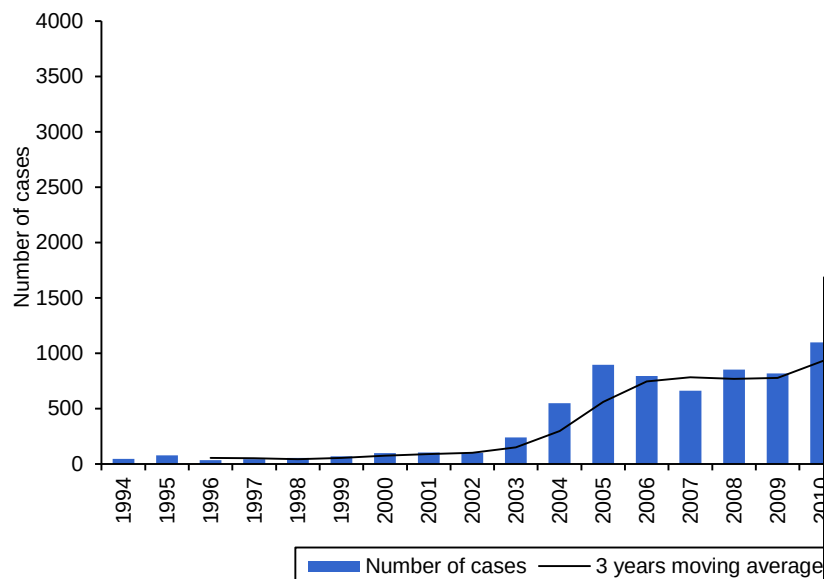
✚ 3,550 førstegangstilfælde

- 20 % stigning ifht. 2015
- Heraf 1,249 (35%) husdyr MRSA CC398 LA-MRSA

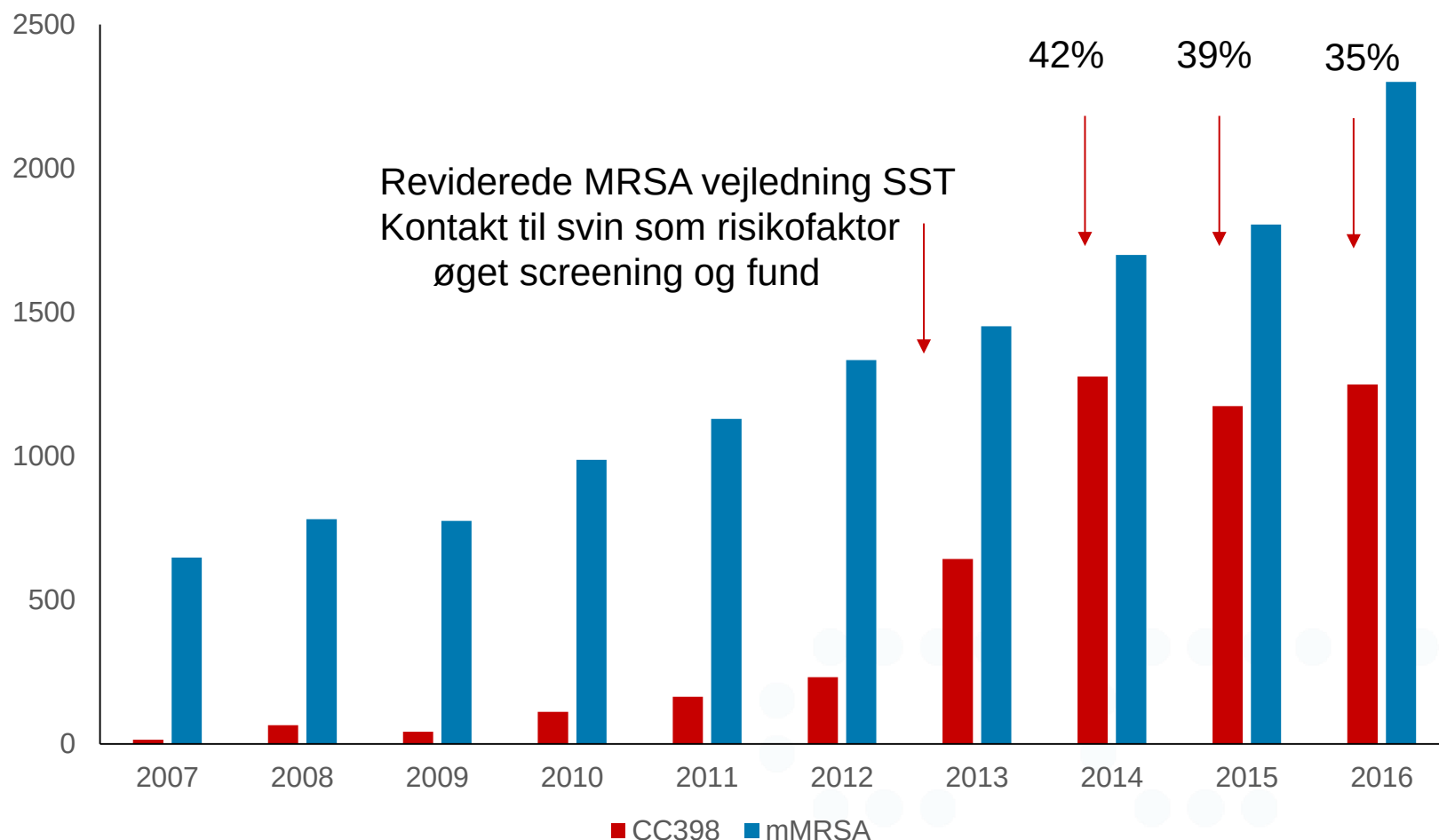


✚ 3,550 førstegangstilfælde

- 20 % stigning ifht. 2015
- Heraf 1,249 (35%) husdyr MRSA CC398 LA-MRSA



Husdyr MRSA CC398 vs. andre MRSA

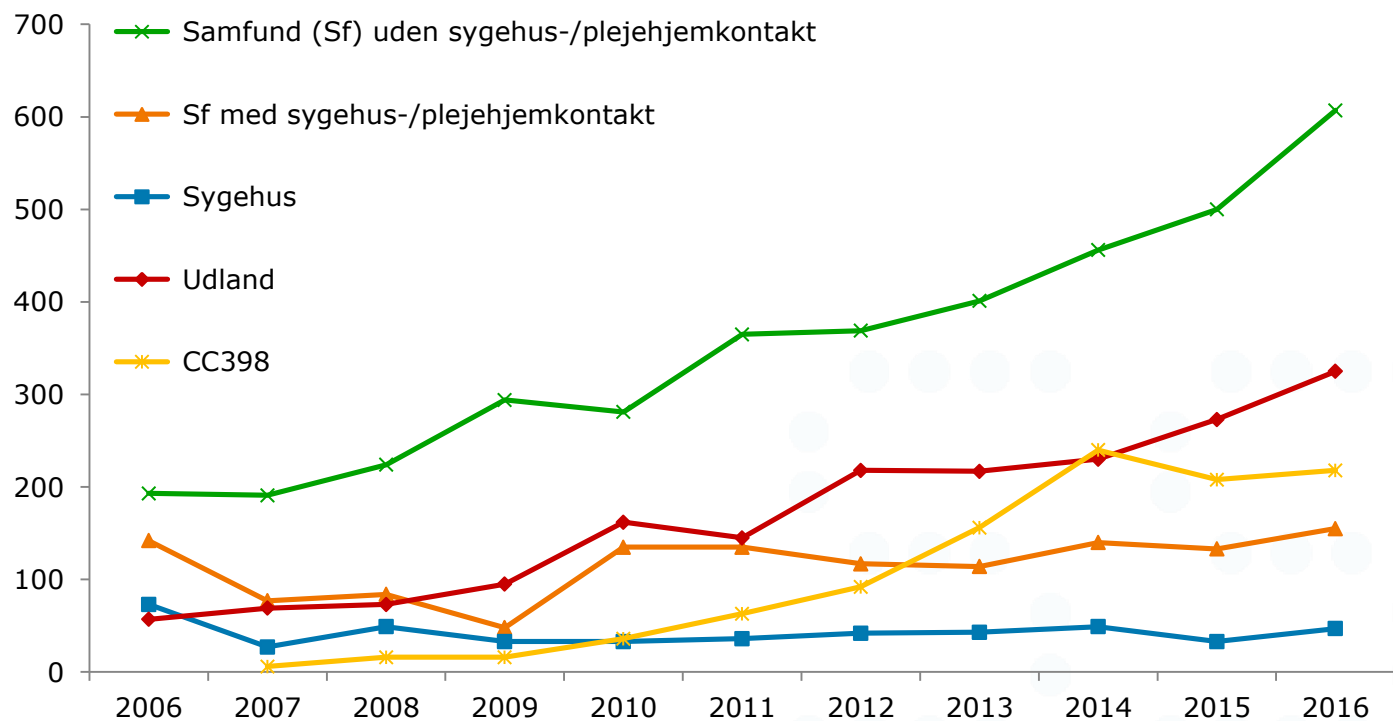


Stagning af antallet af nye tilfælde med Husdyr MRSA CC398

83 % af Husdyr MRSA CC398 tilfælde havde direkte kontakt til husdyr (eller i husstand)



MRSA-infections according to epidemiological classification, 2006-2016



- ✧ Stor diversitet: 322 *spa* typer
- ✧ De 10 hyppigste non-CC398 *spa* typer udgjorde 33% (1164 / 3350),

2016

spa type	MRSA		
	CC group ^(a)	No. of cases	No. causing infections (%)
t304	CC6/CC8	223	69 (31)
t223	CC22	212	64 (30)
t002	CC5	188	98 (52)
t127	CC1	135	58 (43)
t008	CC8	105	72 (69)
t019	CC30	96	69 (72)
t044	CC80	84	44 (52)
t437	CC59	46	30 (65)
t005	CC22	39	22 (56)
t657	CC97	36	20 (56)

- Hyppigste MRSA typer er t304 og t223, *pv*/ negative, få tilfælde med infektioner- mange importerede tilfælde (hhv. 35 og 43%)

2016

MRSA			
spa type	CC group ^(a)	No. of cases	No. causing infections (%)
t304	CC6/CC8	223	69 (31)
t223	CC22	212	64 (30)
t002	CC5	188	98 (52)
t127	CC1	135	58 (43)
t008	CC8	105	72 (69)
t019	CC30	96	69 (72)
t044	CC80	84	44 (52)
t437	CC59	46	30 (65)
t005	CC22	39	22 (56)
t657	CC97	36	20 (56)

2015

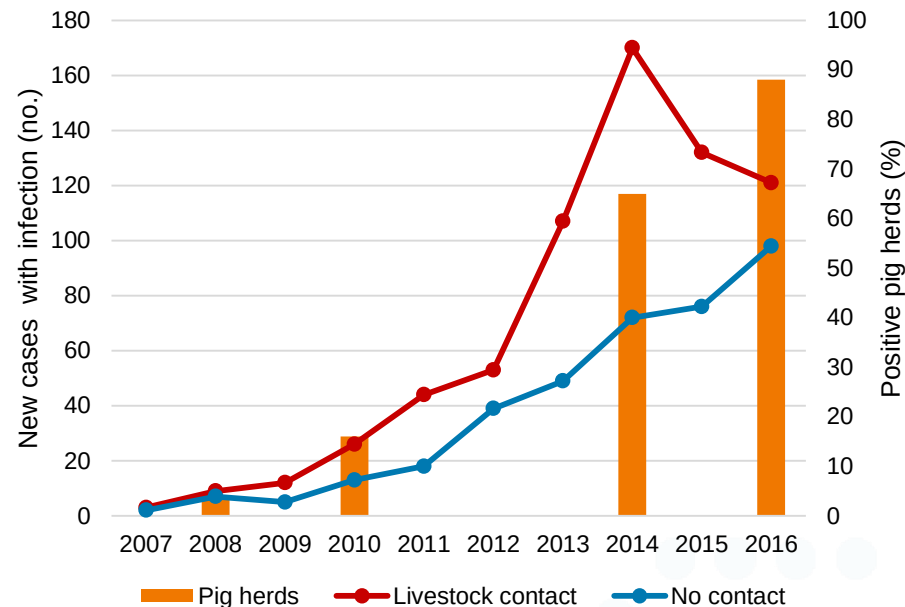
MRSA			
spa type	CC group ^(a)	No. of cases	No. causing infections (%)
t002	CC5	173	94 (54)
t127	CC1	148	75 (51)
t008	CC8	122	79 (65)
t304	CC6/CC8	112	46 (41)
t019	CC30	90	60 (67)
t223	CC22	87	37 (43)
t044	CC80	48	22 (46)
t437	CC59	44	31 (70)
t032	CC22	40	21 (53)
t843	CC130	38	21 (55)

Husdyr MRSA CC398 i forskellige reservoirs Human, veterinære og fødevare





- ⌘ Stigning i positive besætninger (3% i 2008, 15% i 2010, 68% i 2014, 88% i 2016)
- ⌘ 218 kliniske tilfælde, 98 uden dyre kontakt

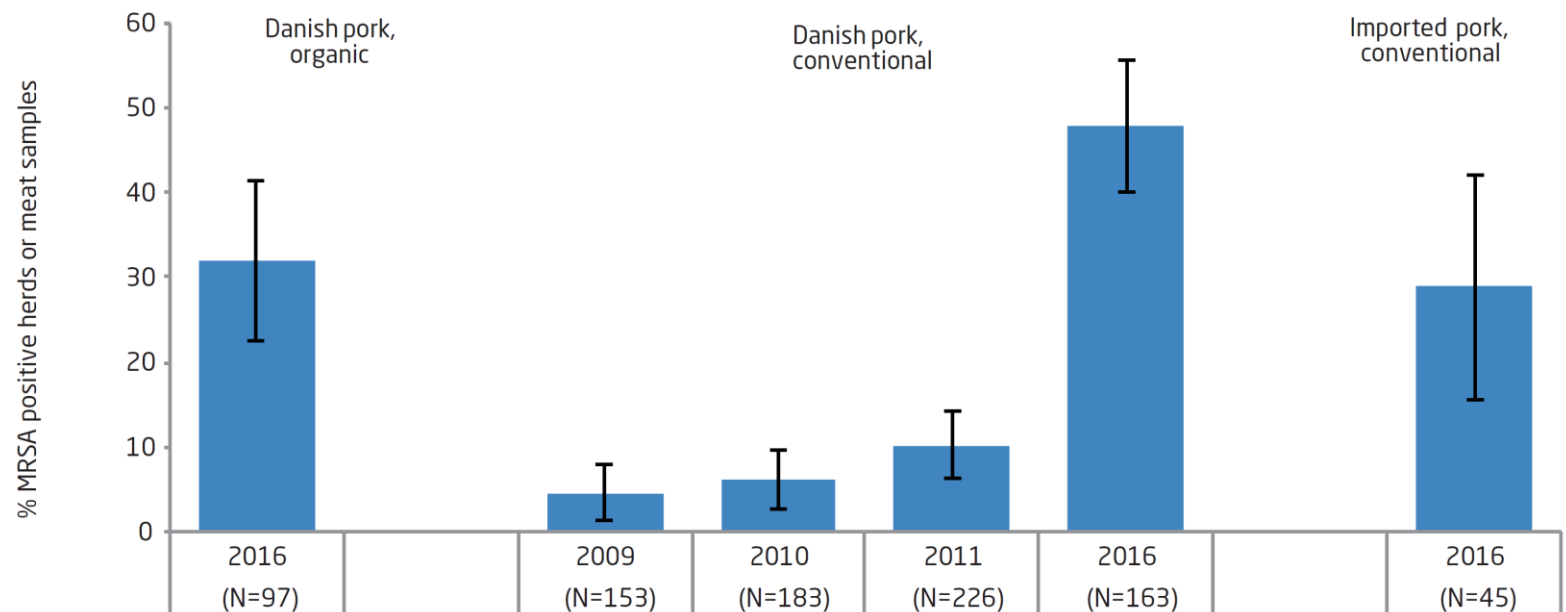


- ⌘ Antallet af LA-MRSA i **personer uden dyrekontakt fortsætter med at stige**- primært i områder med stor tæthed af svin
 - SAB med husdyr MRSA CC398 findes fortrinsvis hos personer uden dyre kontakt
 - 7 SAB tilfælde (uden dyrekontakt), 1 dødsfald
- ⌘ **Sygdomsbyrden er forholdsvis lav** - Healthy worker effect



- ❖ Mink: 30/89 (34%) var positive for Husdyr-MRSA Hansen JE, et al. Vet Microbiol. 2017
- ❖ Heste: 17/401 (4,3%) – heste assoiceret MRSA Islam et al., Front. Microbiol. 2015
- ❖ Mælkeprøver: 7/236 (3%)
- ❖ Økogrise: 6%

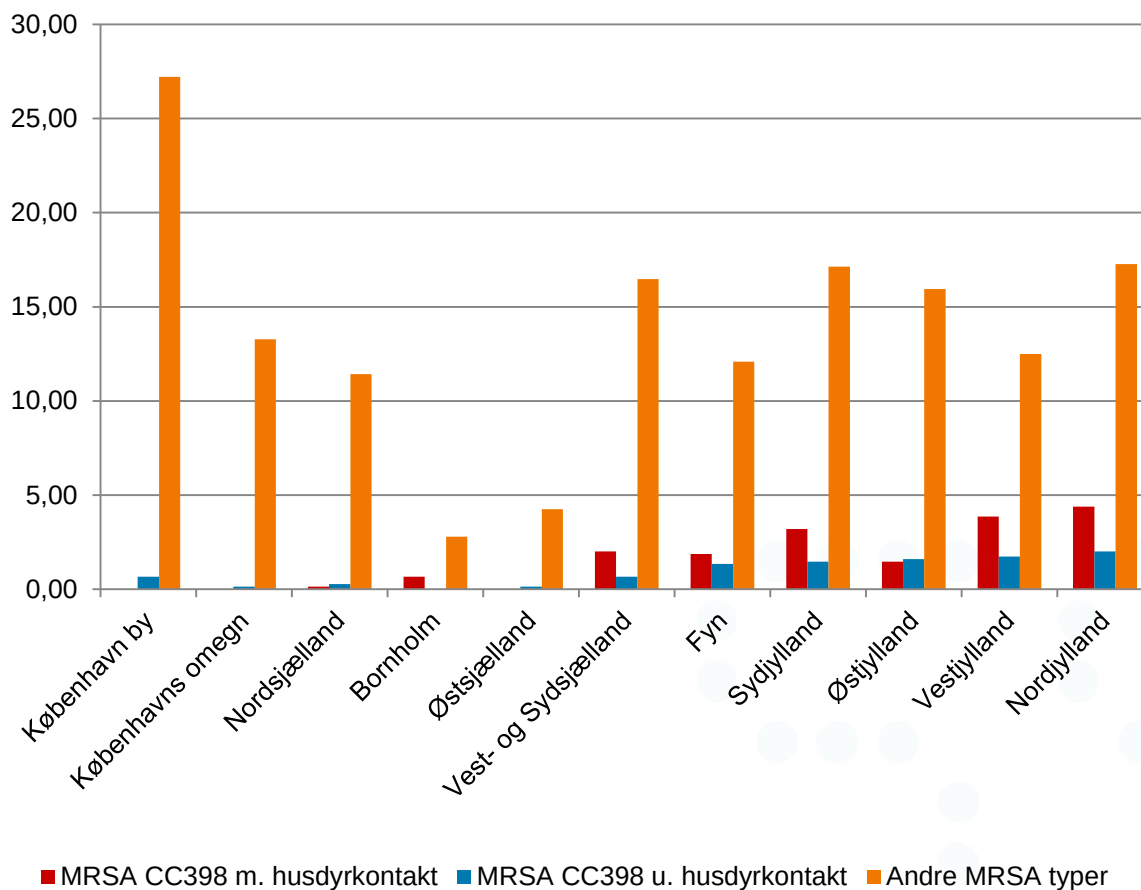
Figure 2. Occurrence (%) of MRSA in pork, Denmark



Note: Confidence intervals are calculated as 95% binomial proportions presenting Wilson intervals.

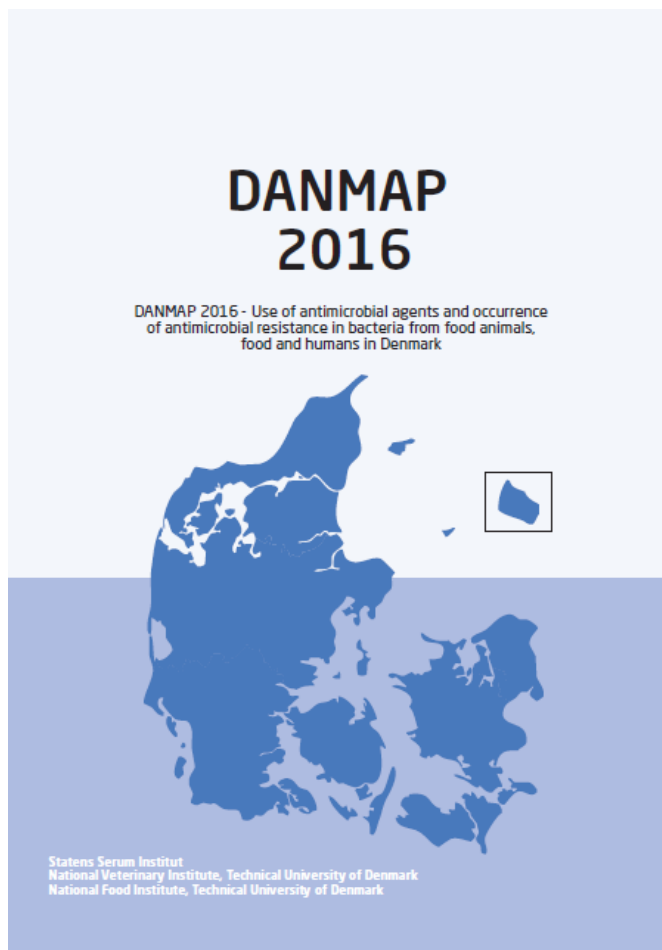


Antal MRSA infektioner per 100.000
indbyggere



- ✚ Stigning i samlet antal, **flere CA- og Imp-, få HA- tilfælde**
 - **Husdyr CC398 MRSA stagnerer**, muligvis pga. **mætningseffekt**
- ✚ Flere tilfælde af Husdyr MRSA CC398 hos personer **uden dyrekontakt**
 - Når det også en mætning?
 - **Nye reservoirs** i andre dyrearter end svin?
 - **Kød** antages **ikke** at bidrage væsentligt til spredning af CC398 MRSA
- ✚ Fortsat epidemiologisk udvikling i LA-MRSA
 - **Bakteriel evolution**
 - CC398 dominerende genotype i husdyr **men andre typer** er også fundet
- ✚ **Finmasket overvågning af humane, såvel som dyre- og fødevare-associerede tilfælde er nødvendig**

Tak for opmærksomheden!



En særlig tak til de kliniske mikrobiologiske afdelinger og laboratorierne på SSI, DTU og FVST

DTU Fødevareinstituttet

Flemming Bager
Valeria Bortolaia
Johanne Ellis-Iversen
Rene S. Hendriksen
Birgitte Borck Høg
Lars Bogø Jensen
Helle Korsgaard

DTU Veterinærinstituttet

Karl Pedersen

Statens Serum Institut

Tine Dalby
Kristina Træholt Franck
Anette M. Hammerum
Henrik Hasman
Steen Hoffmann
Katrin Gaardbo Kuhn
Anders Rhod Larsen
Jesper Larsen
Eva Møller Nielsen
Stefan Schytte Olsen
Andreas Petersen
Louise Roer
Sissel Skovgaard
Ute Wolff Sönksen
Mia Torpdahl
Veronika Vorobieva Solholm Jensen