NORM / NORM – VET 2018

Antibiotikabruk og resistens i Norge

Gunnar Skov Simonsen

NORM – UNN HF

Norsk overvåkingssystem for antibiotikaresistens hos mikrober (NORM)

Dagbladet

Måndag 6. september 2010 Nr. 243. Uke 36. 142. årgang. Løssalg kr 15,00 € 3 utenfor Norden

NDM-

(New Dehli

FORSKERNE FRYKTER PAND

SUPE

BAKTE

SPRER

ER ALLEREDE

I NORGE

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Scanpix

Invasjon av

SUPERBAKTERIE

- ADVARER mot HELSEREISER
- FRYKTER UTBREDELSE i NORGE
- VIKTIG med RESTRIKTIV ANTIBIOTIKABRUK

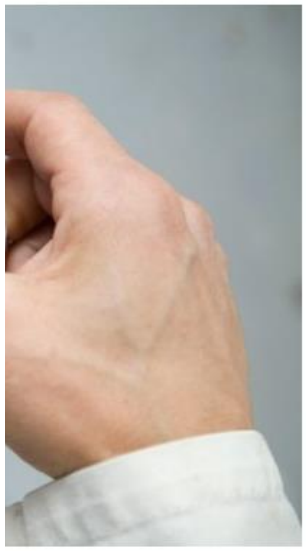
NDM-1

(New Dehli

Hospitals on alert after superbug outbreak in Tuscany

A superbug outbreak has been reported in the Italian region of Tuscany. Photo: Depositphotos

Authorities in Tuscany, home to some of Italy's most visited tourist attractions, have stepped up hospital controls after a deadly outbreak of the New Delhi superbug.



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Aftonbladet › Hälsa

Publicerad: 2011-01-21 9 kommentarer

Superbak frammars

Hotar att göra antibioti värdelöst

Den resistenta superbakterieg NDM-1 frodas i avlopp och kranva runt om i New Dehli. Det visar en som kommer att publiceras i välrenommerade The Lancet, skr Svenska Dagbladet.

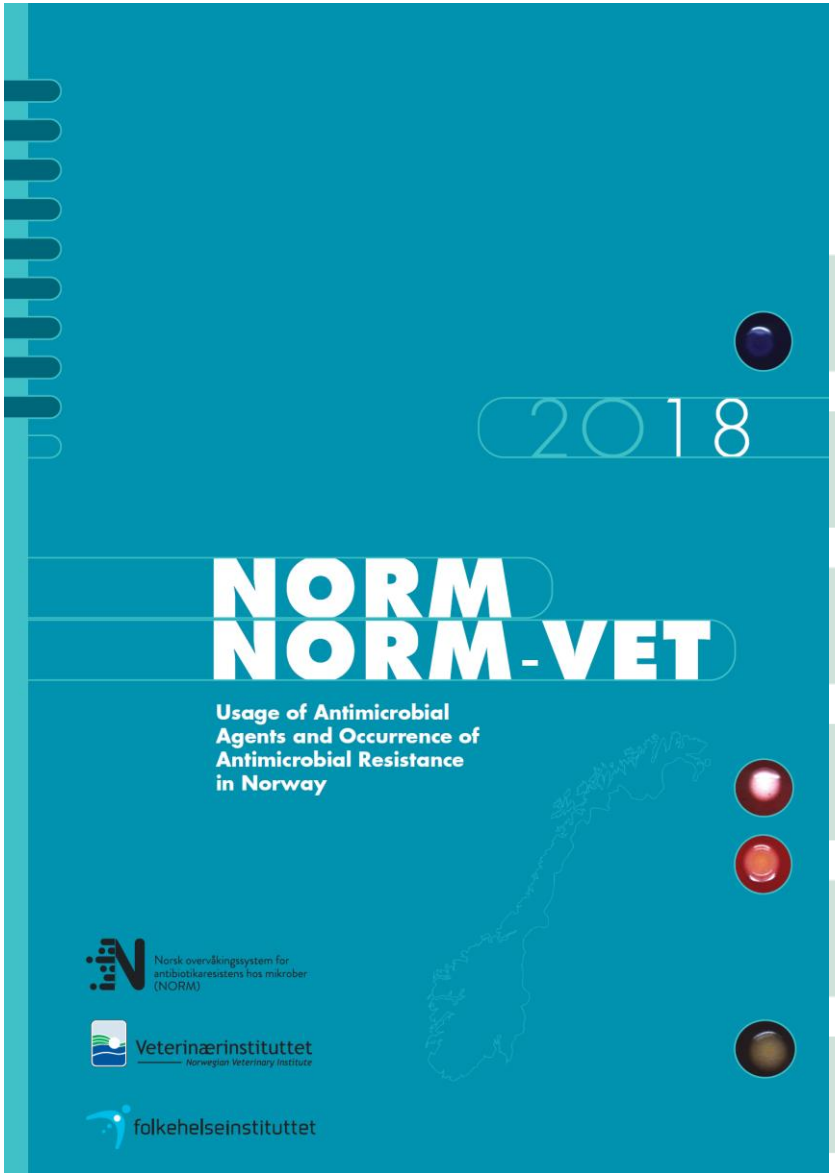
Genen gör bakterier motståndskraftiga mot nästan all antibiotika som finns i dag. Nu varnar forskare för att den kan komma att spridas snabbt över världen.

ffisere tilfelle-deretter isoler e pasienter.

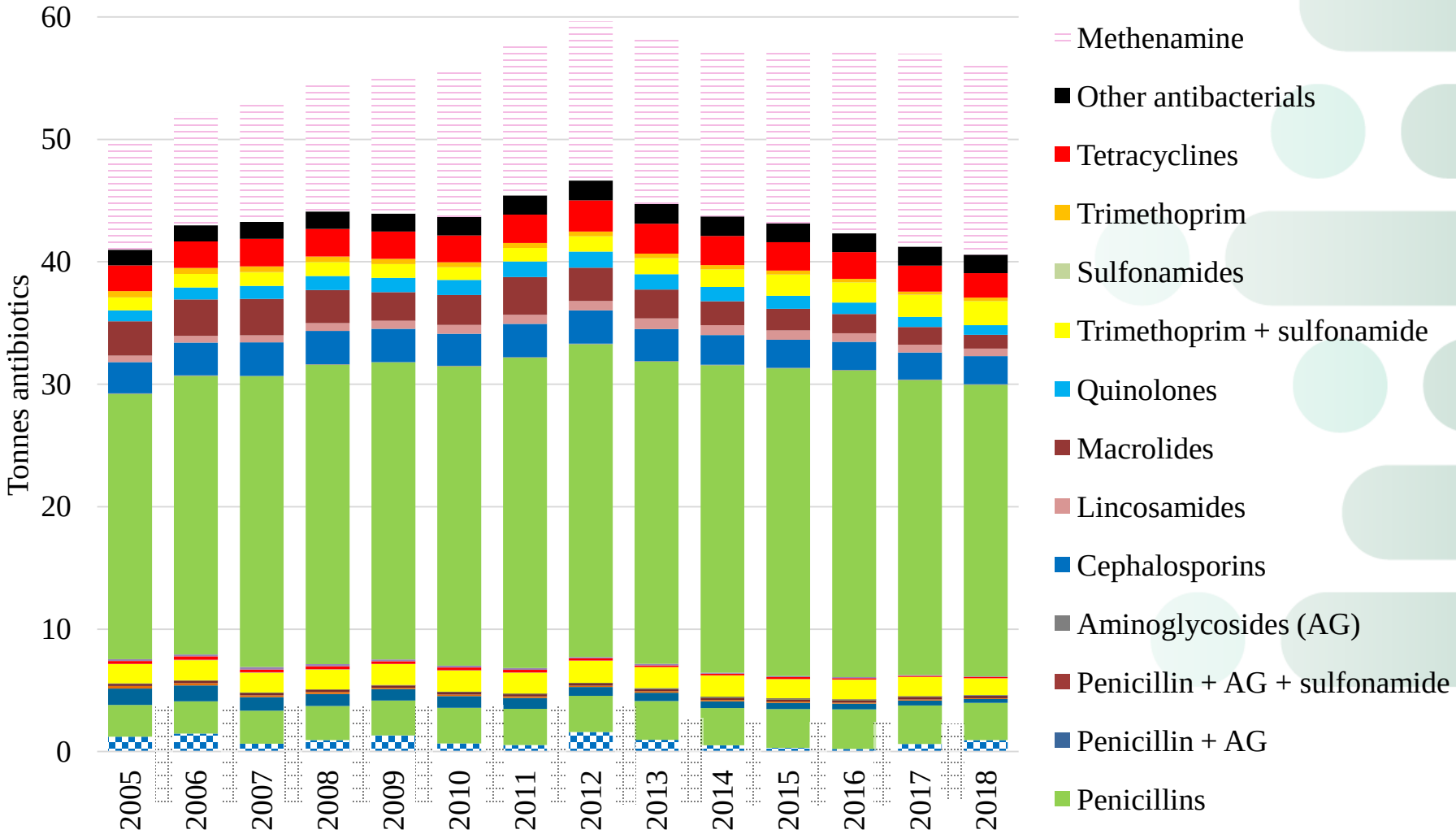
kterie

set for første gang i Danmark

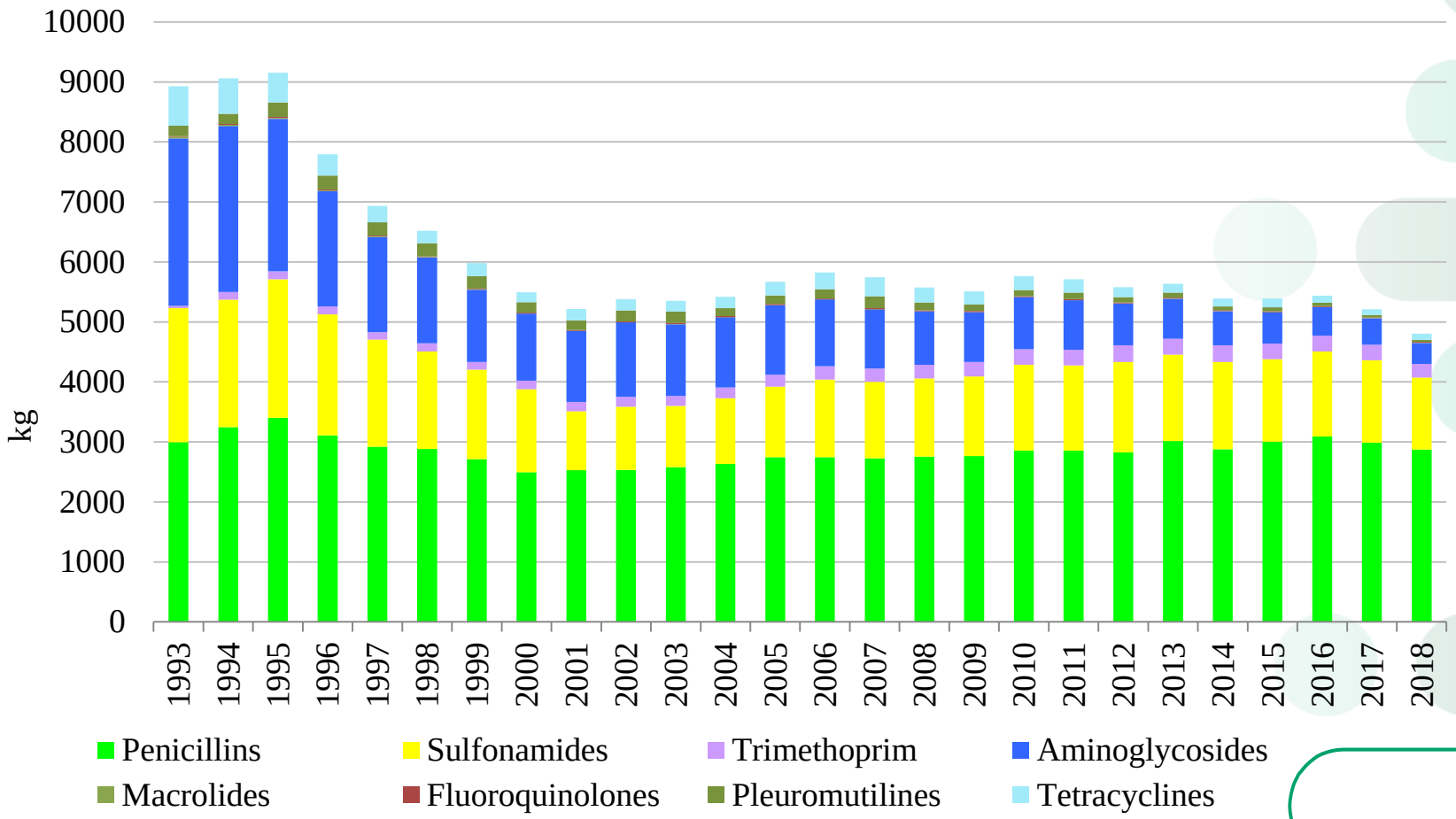
- Antibiotikaforbruket i Norge 2018
- Antibiotikaresistens i Norge 2018
- Mennesker og dyr
- Artikler om aktuelle tema



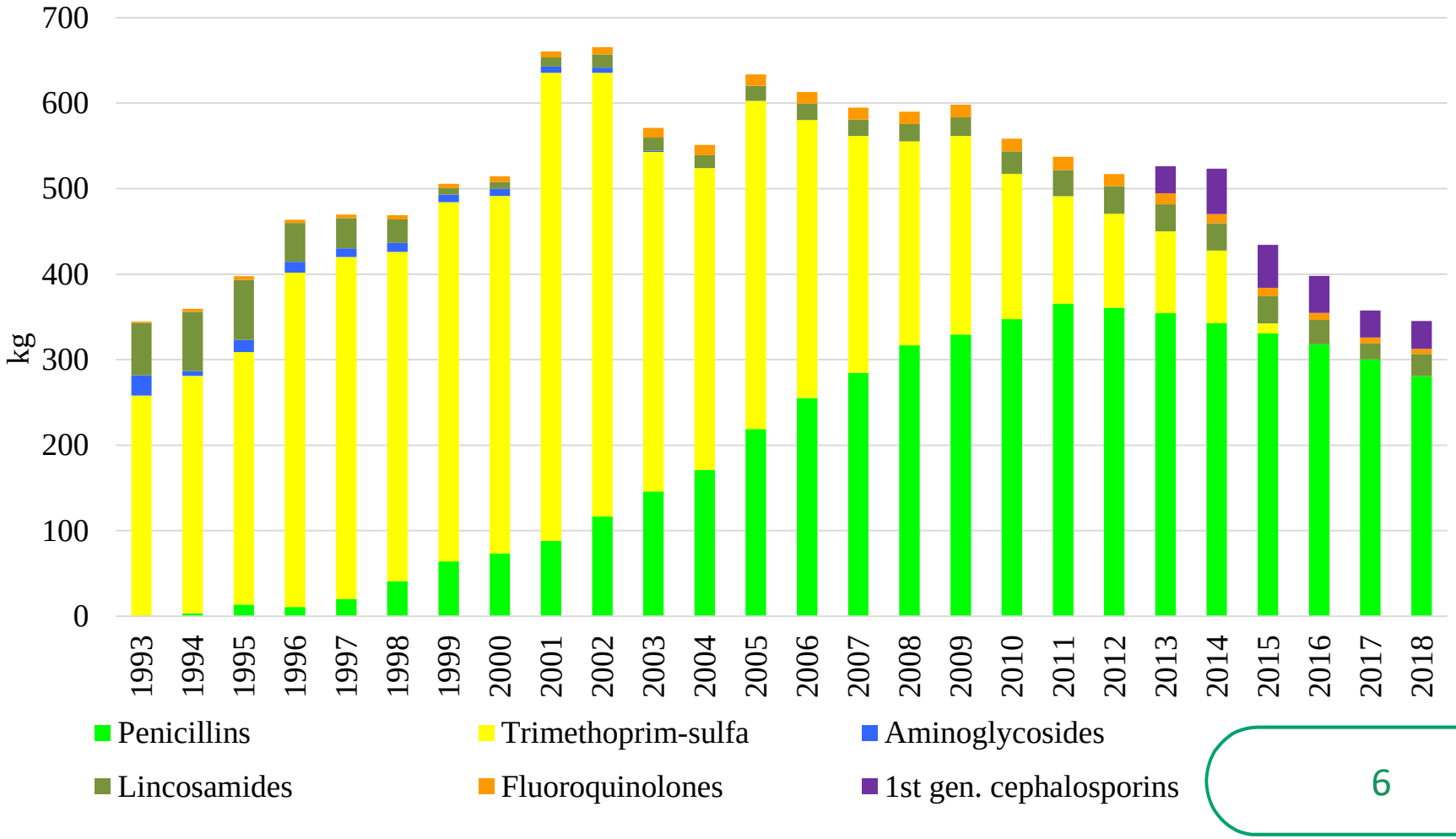
Samlet bruk av antibiotika i Norge



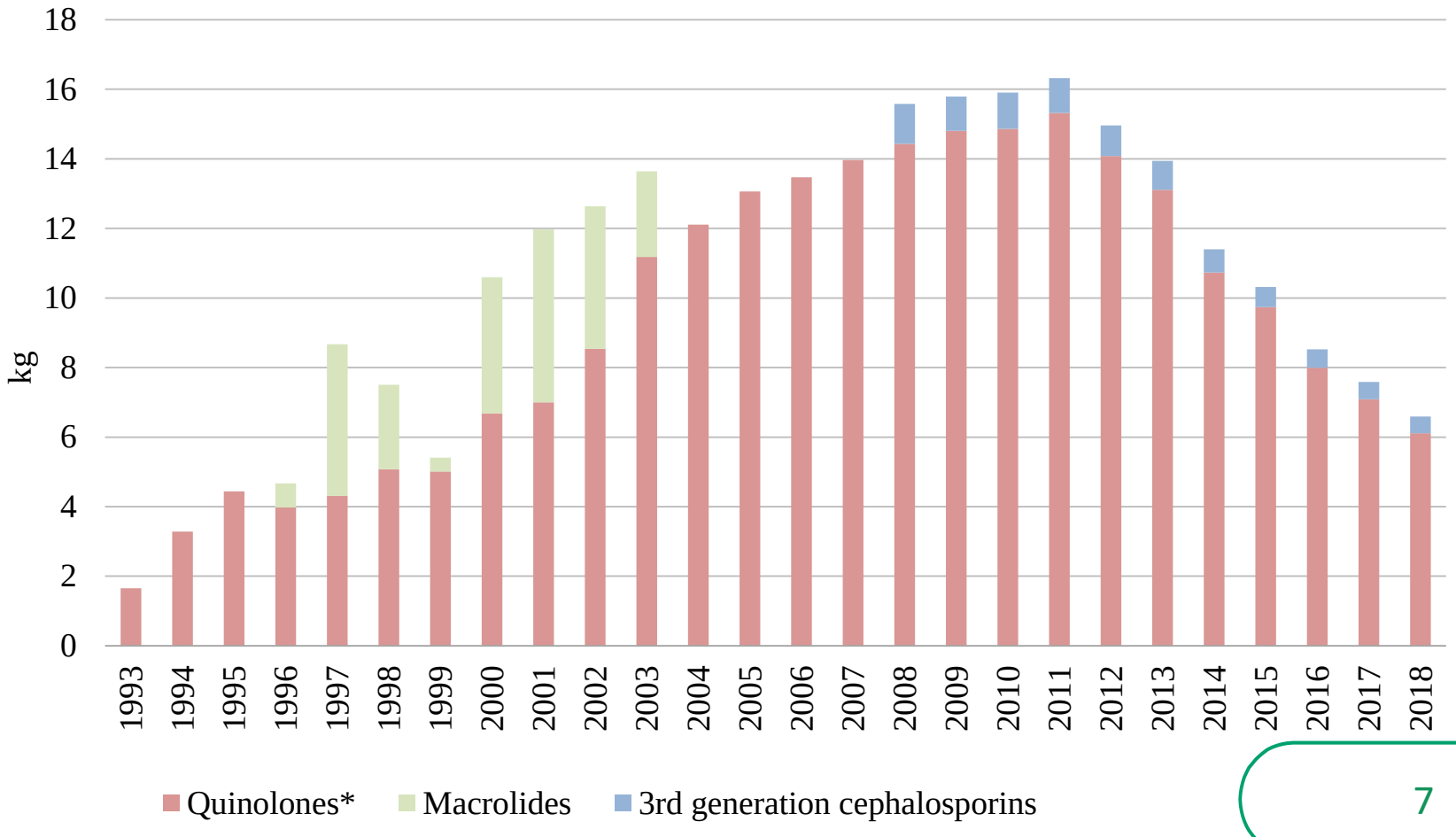
Bruk av antibiotika til produksjonsdyr



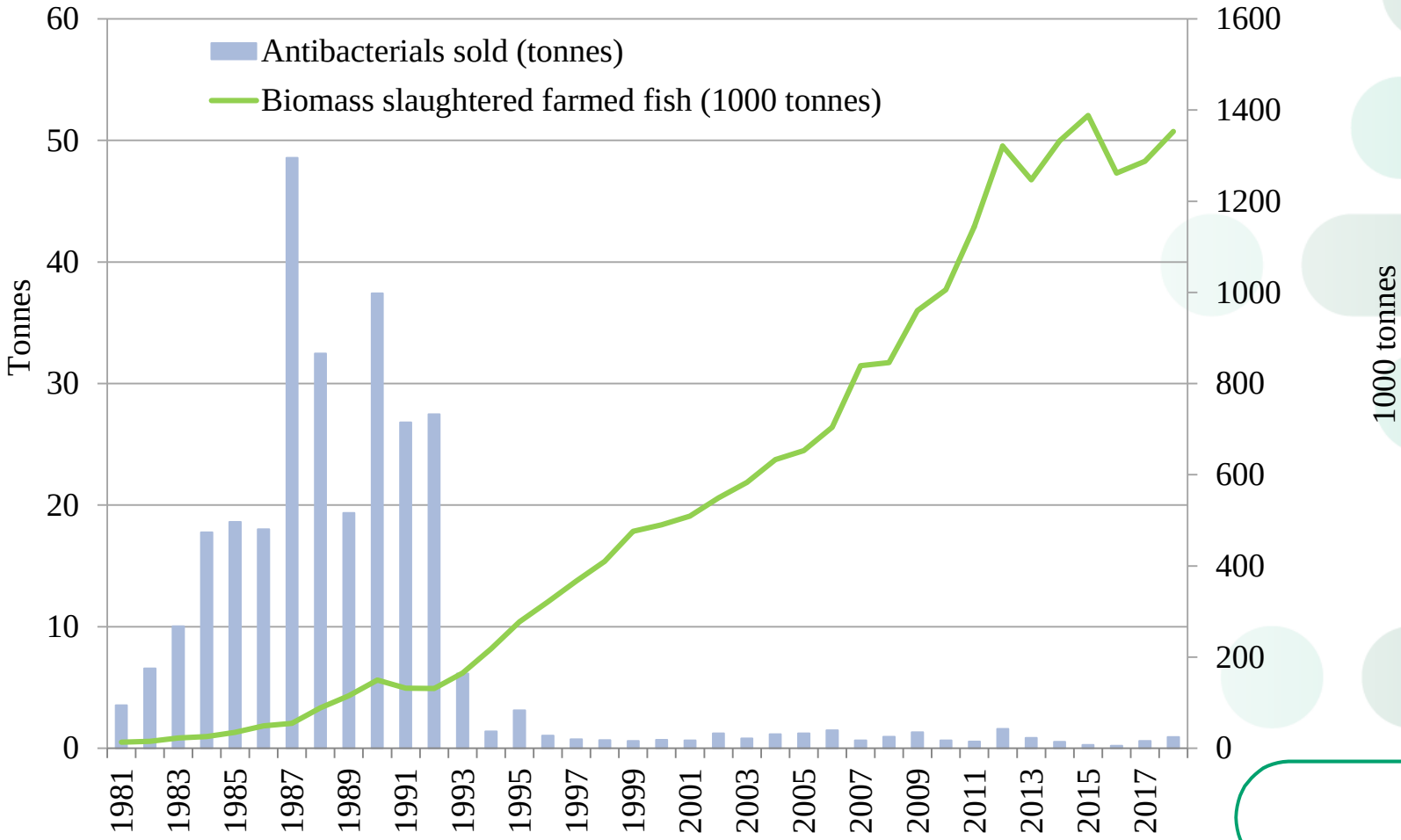
Bruk av antibiotika til sports- og kjæledyr



Bruk av «kritisk viktige» antibiotika til sports- og kjæledyr



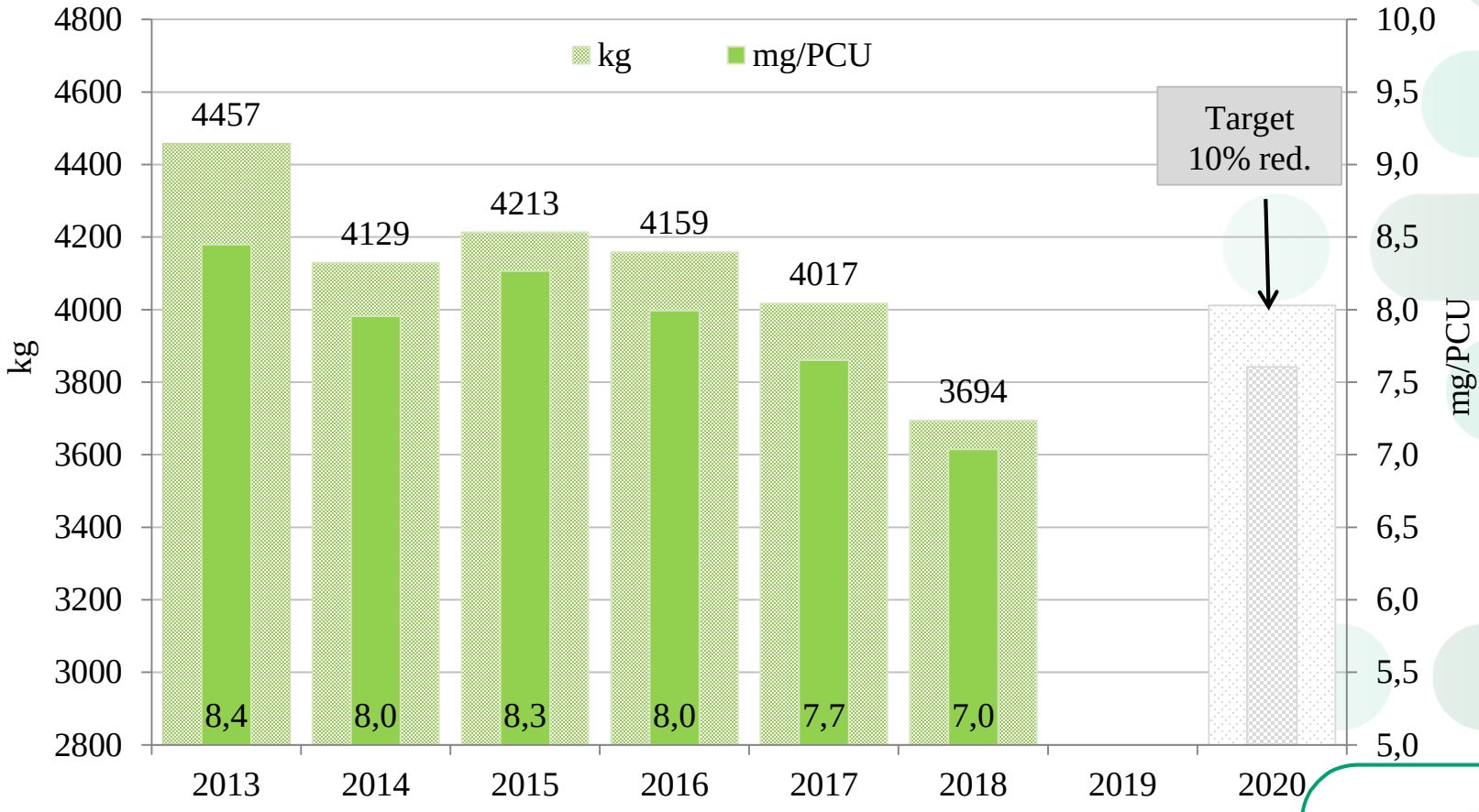
Bruk av antibiotika i akvakultur



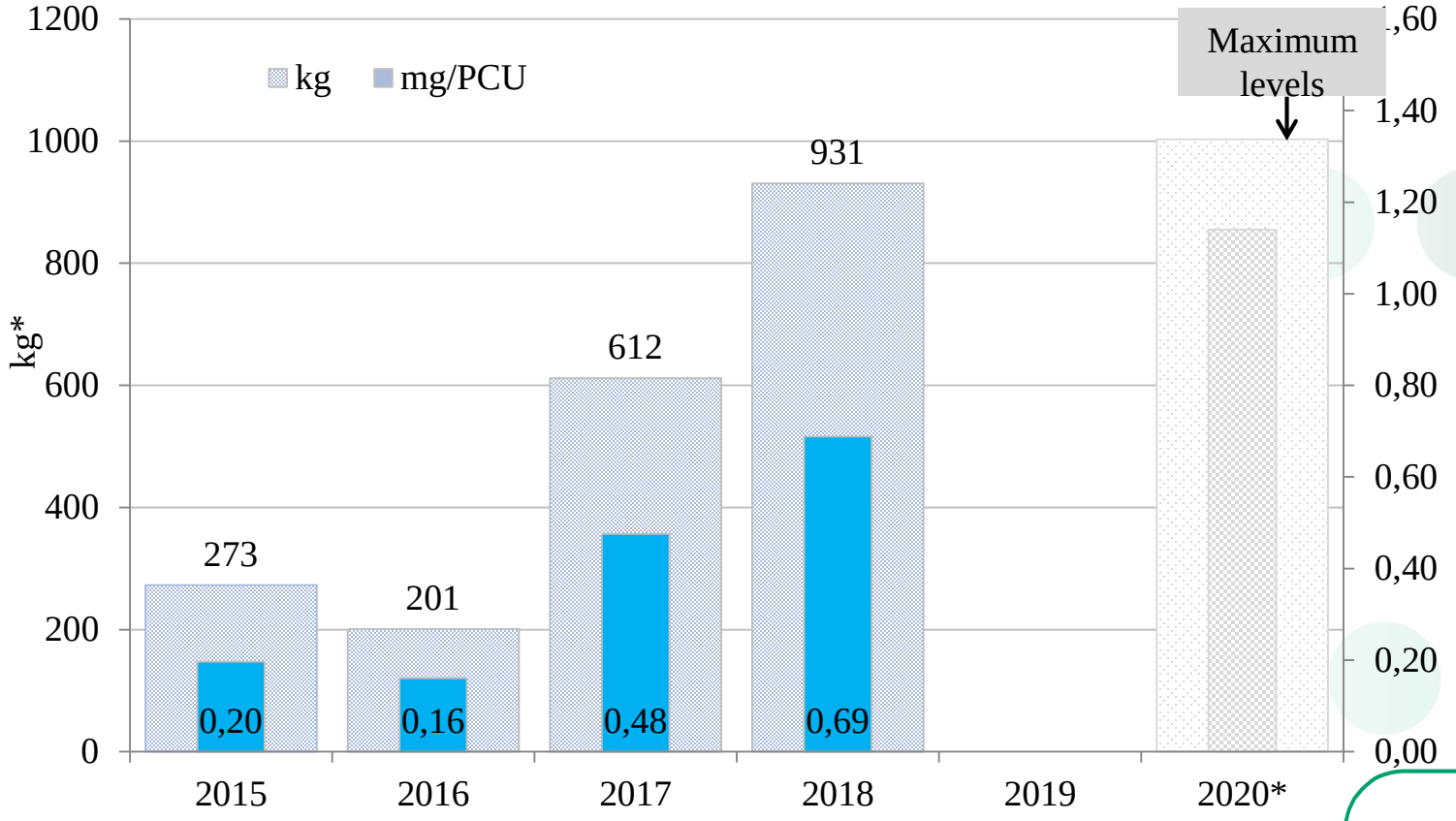
Mål for veterinær antibiotikabruk i Nasjonal strategi 2015 - 2020

- Antibakterielle midler til produksjonsdyr redusert 10 % 2013 - 2020
- Forbruket av antibakterielle midler til oppdrettsfisk på samme nivå eller lavere i 2020 enn gjennomsnittet for 2004 – 2014
- Antibakterielle midler til sports/kjæledyr redusert 30 % 2013 - 2020
- Koksidiostatika med antibakteriell effekt ut av broilerproduksjonen
  - Uten skadevirkninger for dyrehelsa
  - Uten økning av terapeutisk bruk av antibakterielle midler

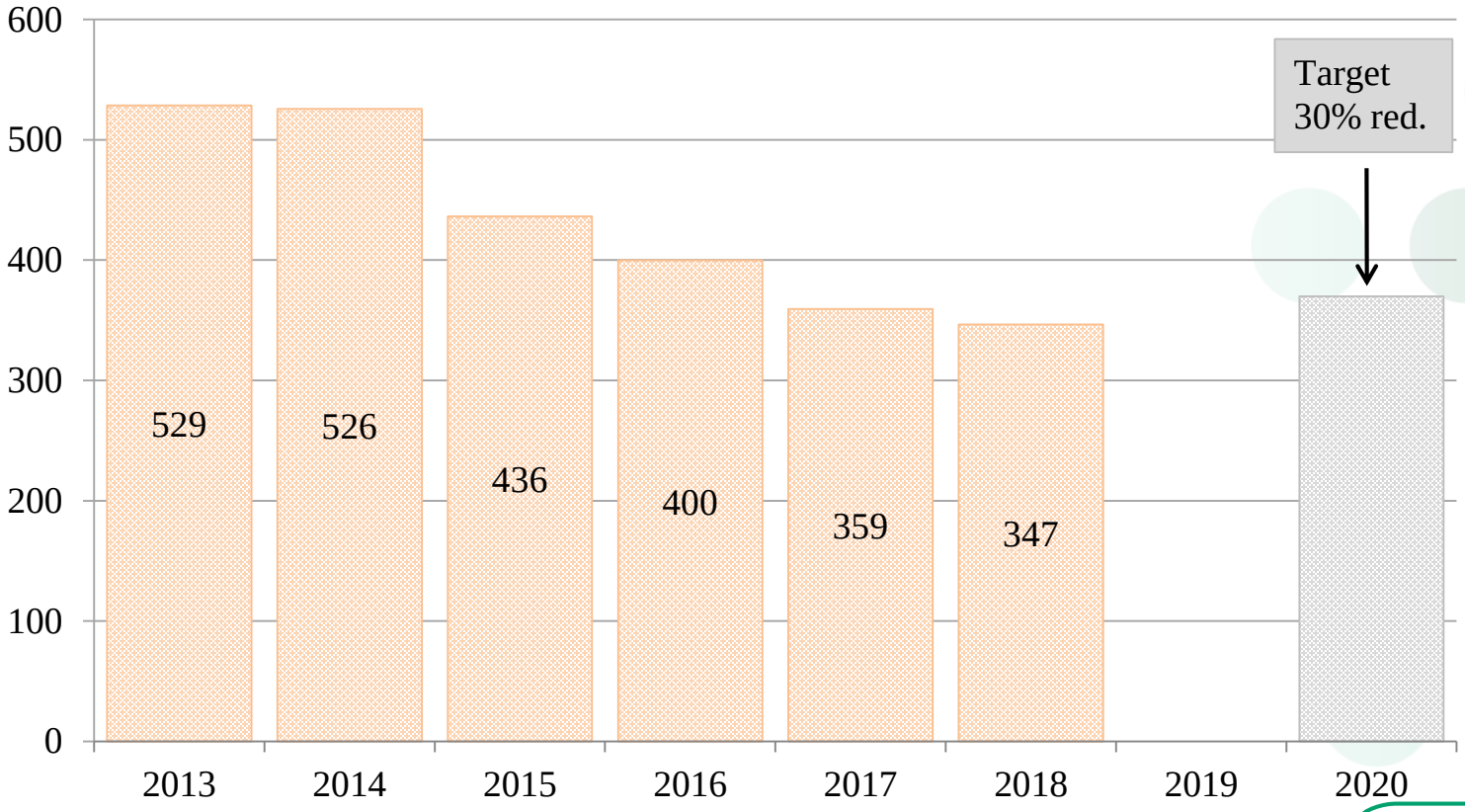
10 % redusert bruk av antibakterielle midler til produksjonsdyr



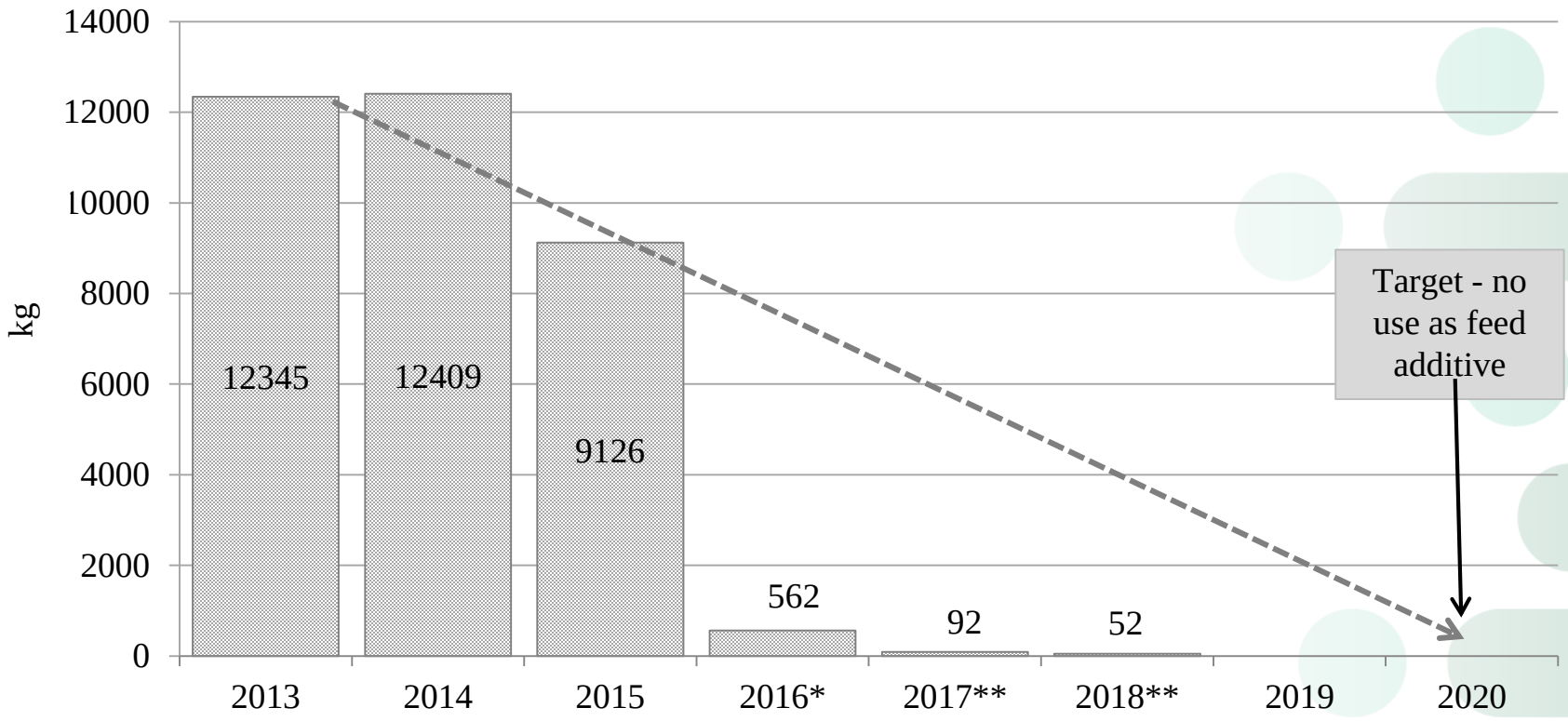
Forbruk til oppdrettsfisk likt eller lavere enn gjennomsnitt 2004 - 2014



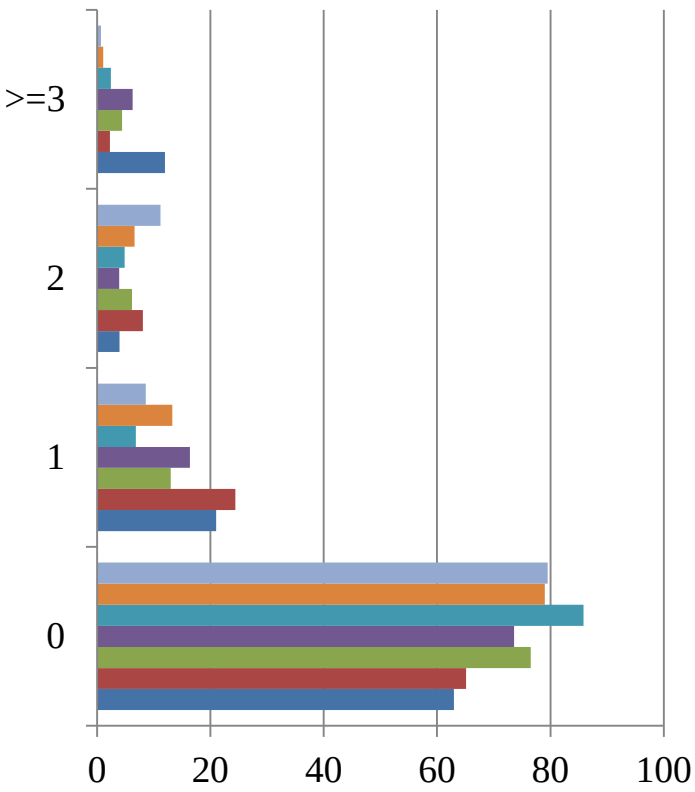
30 % redusert bruk av antibakterielle midler til sports- og kjæledyr

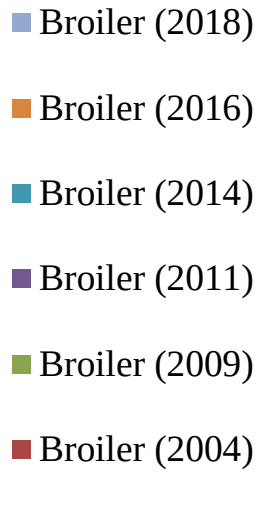


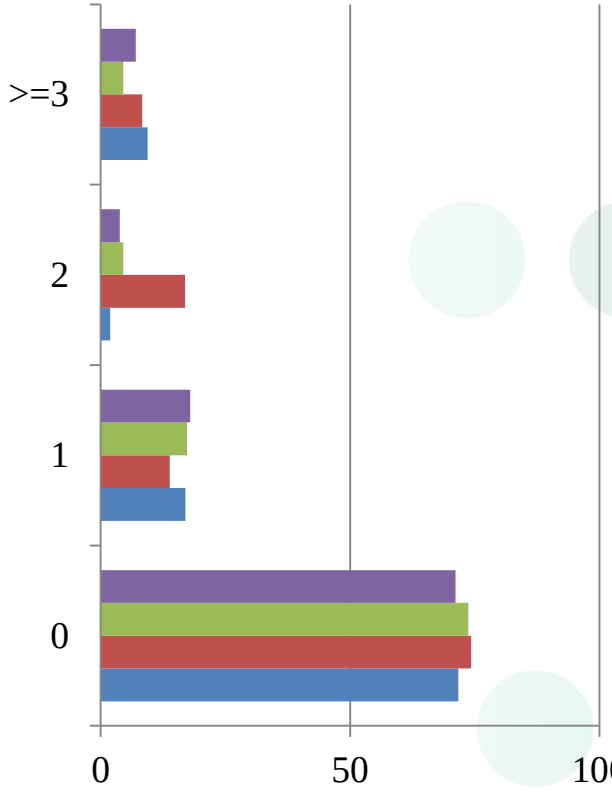
Utfasing av narasin og andre koksidiostatika i broilerproduksjon



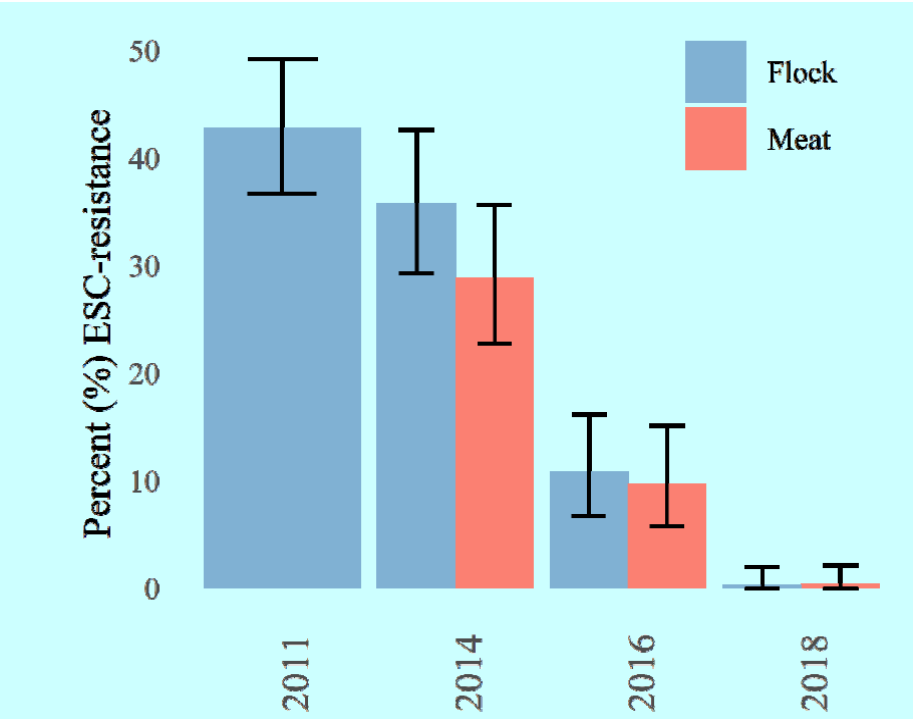
Indikatorbakterier fra dyr og mat – *E. coli*

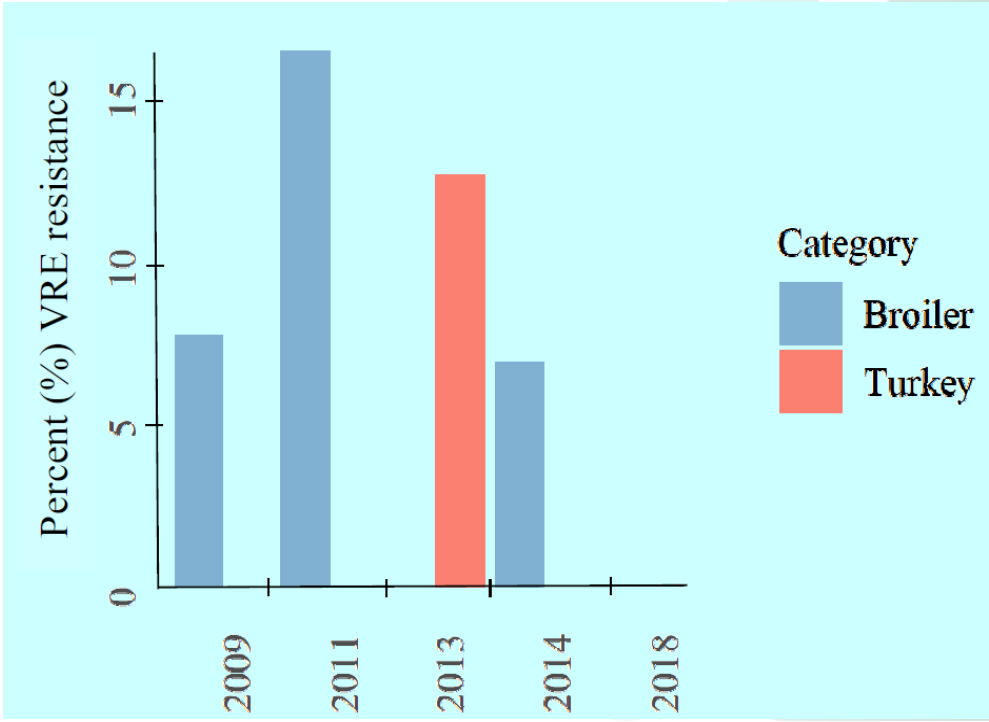






Indikatorbakterier fra dyr og mat – *E. coli* og *Enterococcus* spp.





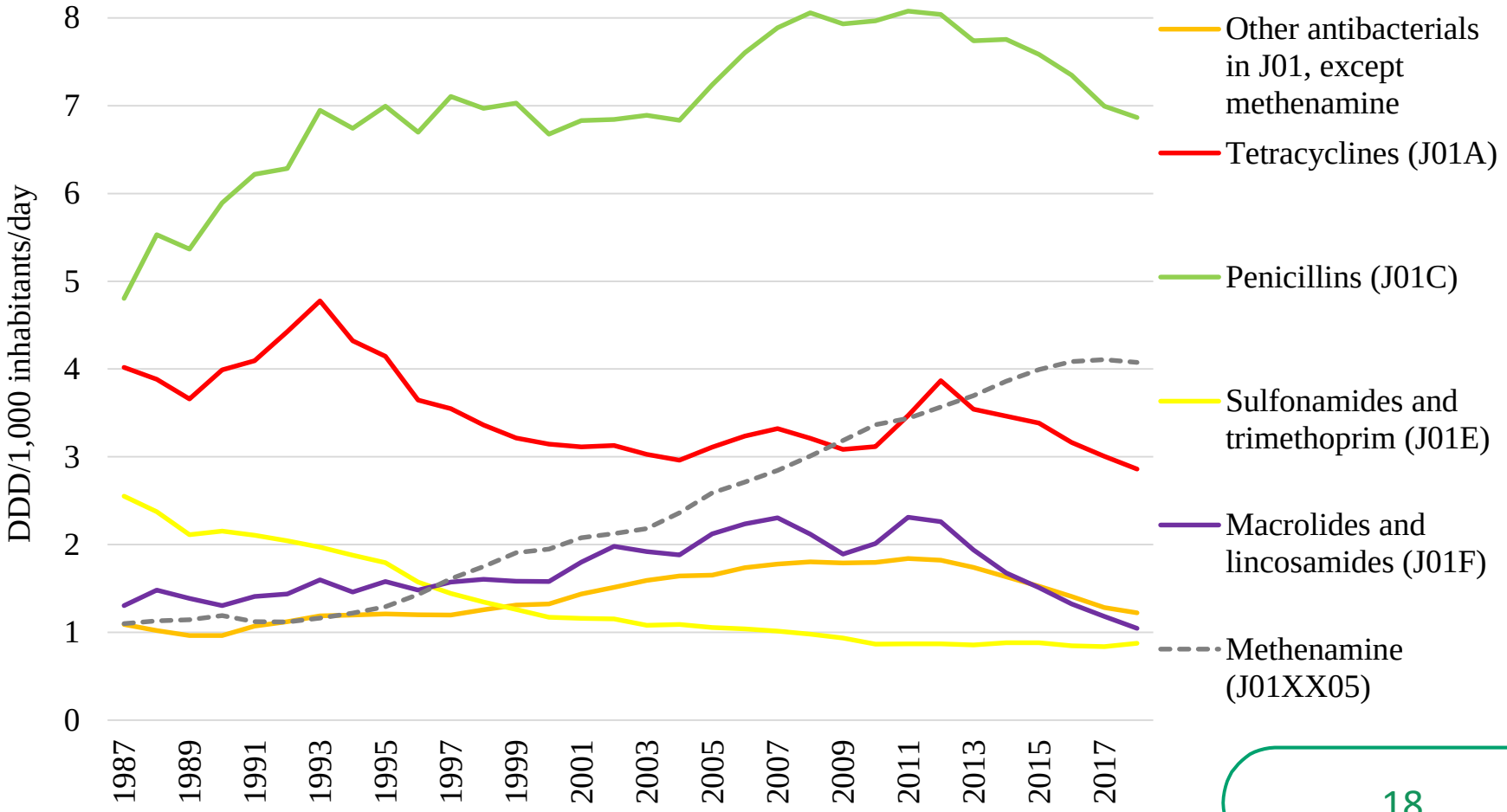
Bruk av antibiotika til mennesker

ATC	Groups of substances	2011	2012	2013	2014	2015	2016	2017	2018	Change (%) 2017-8017
J01A	Tetracyclines	3.47	3.87	3.54	3.46	3.38	3.16	3.01	2.86	- 5
J01B	Amphenicols	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	-
J01CA	Penicillins with extended spectrum	2.69	2.79	2.82	2.90	2.73	2.62	2.47	2.46	-
J01CE	Beta-lactamase sensitive penicillins	4.47	4.30	4.09	3.88	3.88	3.73	3.61	3.43	- 5
J01CF	Beta-lactamase resistant penicillins	0.88	0.90	0.79	0.91	0.89	0.90	0.84	0.90	+ 7
J01CR	Combination of penicillins	0.03	0.04	0.05	0.07	0.08	0.10	0.07	0.08	-
J01D	Cephalosporins, monobactams, carbapenems	0.54	0.53	0.50	0.46	0.43	0.42	0.38	0.39	+ 3
J01E	Sulfonamides and trimethoprim	0.87	0.87	0.86	0.88	0.88	0.85	0.84	0.88	+ 5
J01F	Macrolides, lincosamides and streptogramins	2.31	2.26	1.94	1.68	1.51	1.33	1.18	1.05	- 11
J01G	Aminoglycosides	0.07	0.08	0.07	0.08	0.08	0.08	0.09	0.09	-
J01M	Quinolones	0.74	0.74	0.71	0.67	0.69	0.53	0.45	0.42	- 7
J01X*	Other antibacterials	0.49	0.47	0.45	0.43	0.41	0.38	0.36	0.32	- 11
J01	**Total excluding methenamine**	**16.6**	**16.9**	**15.8**	**15.4**	**14.9**	**14.1**	**13.3**	**12.9**	**- 3**
J01XX05	Methenamine	3.44	3.57	3.70	3.86	3.99	4.09	4.11	4.08	- 1
J01	**Total all antimicrobial agents**	**20.0**	**20.4**	**19.5**	**19.3**	**18.9**	**18.2**	**17.4**	**16.9**	**- 3**

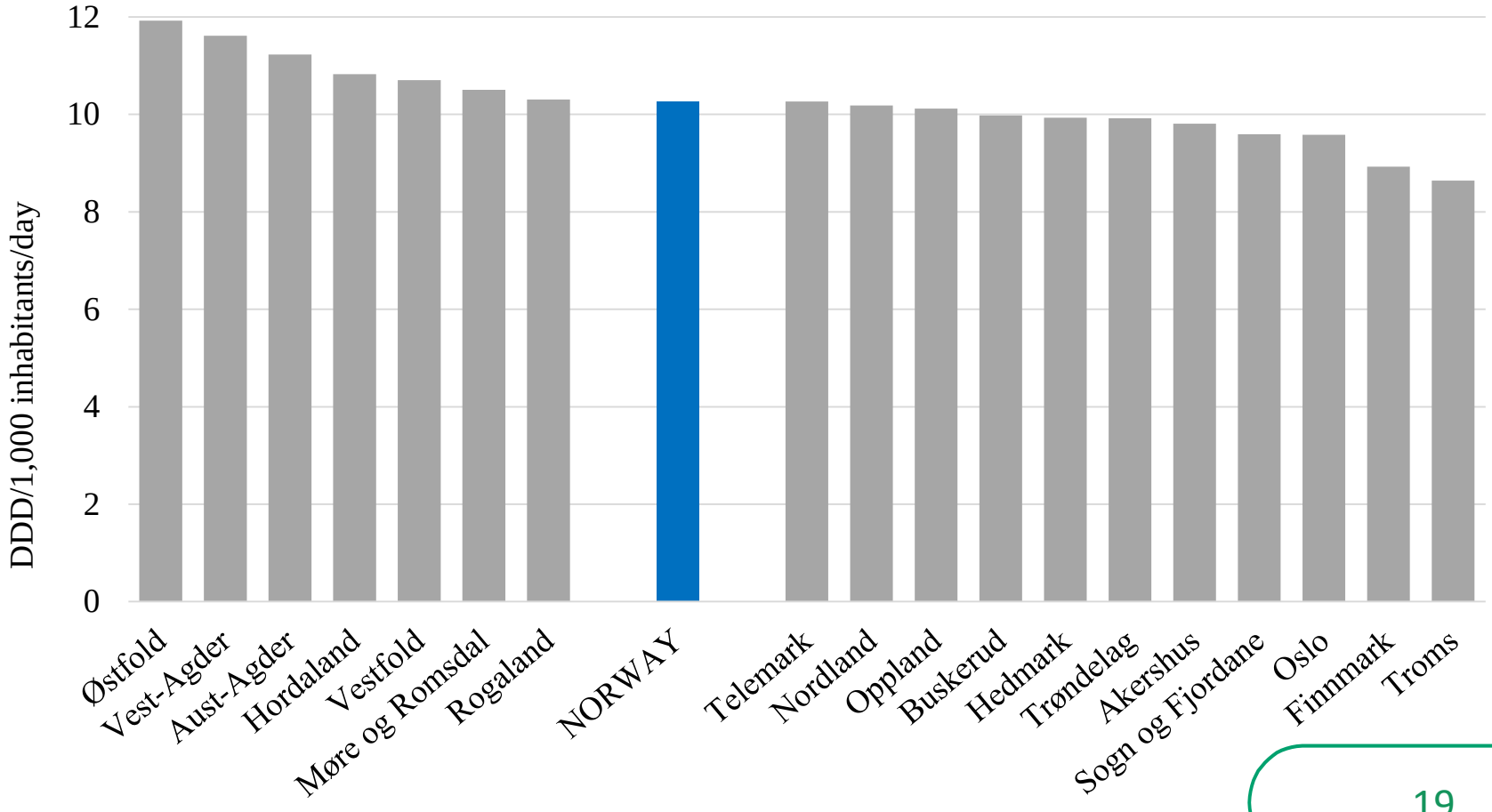
Endrede definisjoner av DDD´er i legemiddelstatistikken

ATC code	Active ingredient	Form	Old DDD	New DDD (2019)
J01CA01	Ampicillin	P	2 g	6 g
J01CA04	Amoxicillin	O	1 g	1.5 g
J01CA04	Amoxicillin	P	1 g	3 g
J01CA17	Temocillin	P	2 g	4 g
J01CR02	Amoxicillin/beta-lactamase inhibitor	O	1 g	1.5 g
J01DE01	Cefepime	P	2 g	4 g
J01DH02	Meropenem	P	2 g	3 g
J01MA02	Ciprofloxacin	P	0.5 g	0.8 g
J01XB01	Colistin	P	3 MU	9 MU

Bruk av antibiotika til mennesker



Geografisk fordeling av antibiotikabruk



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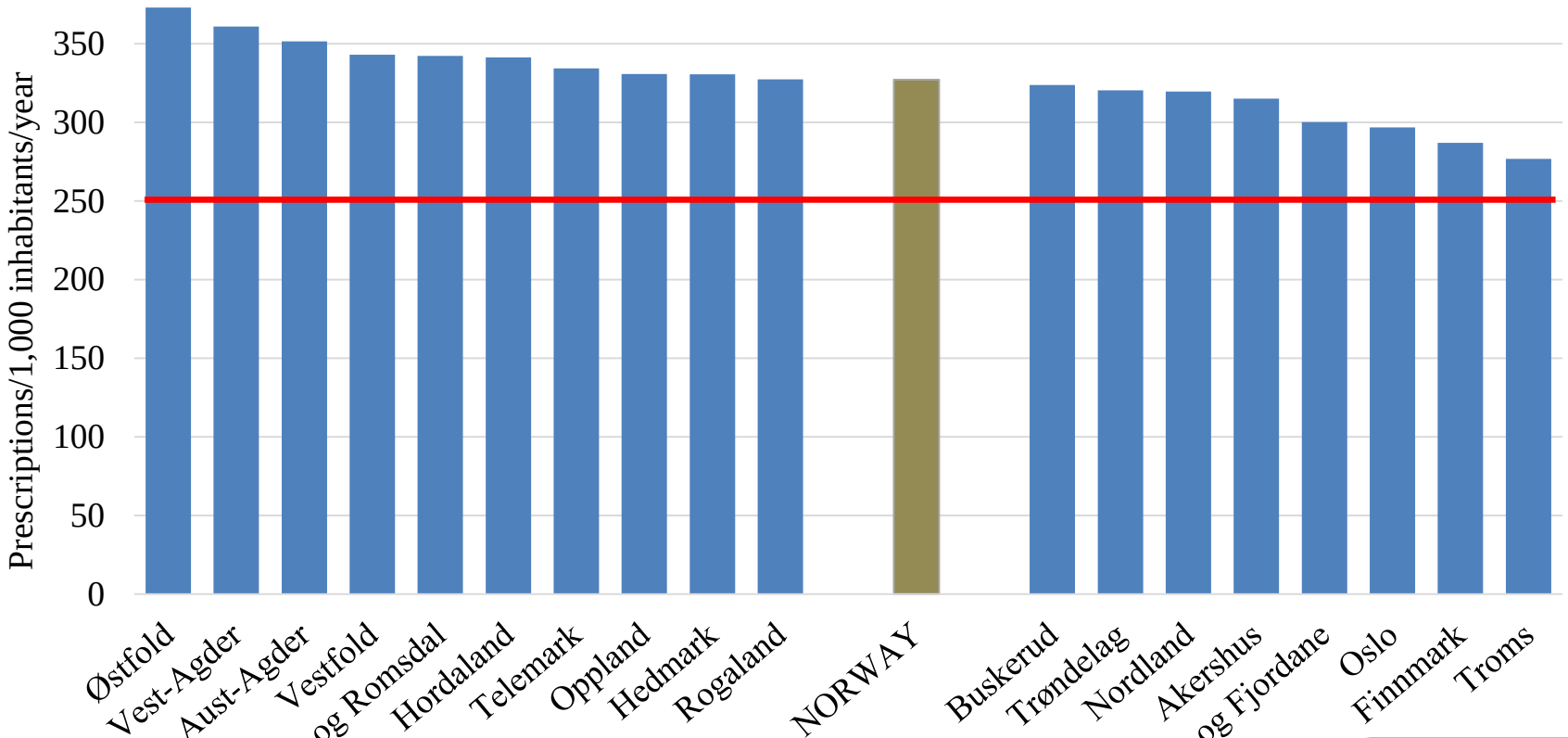
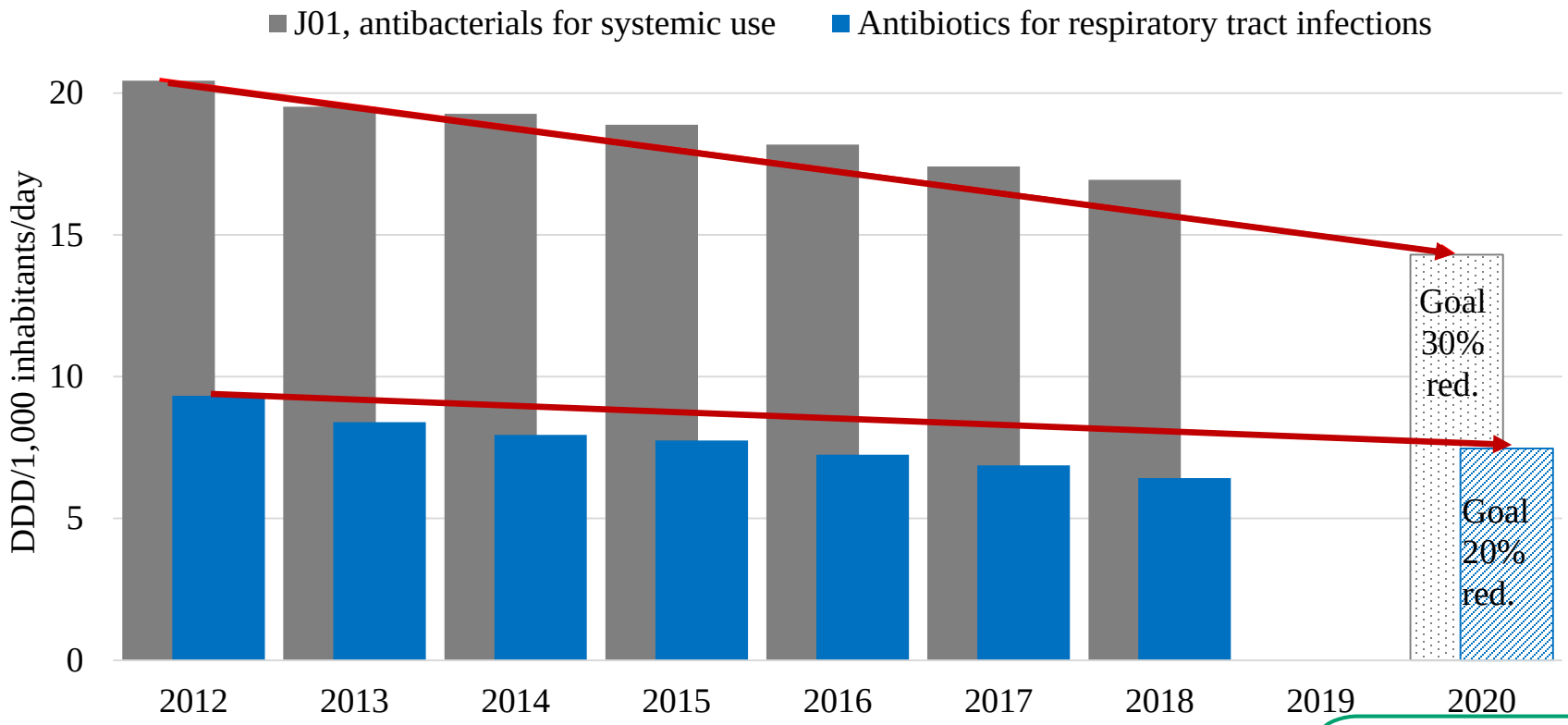
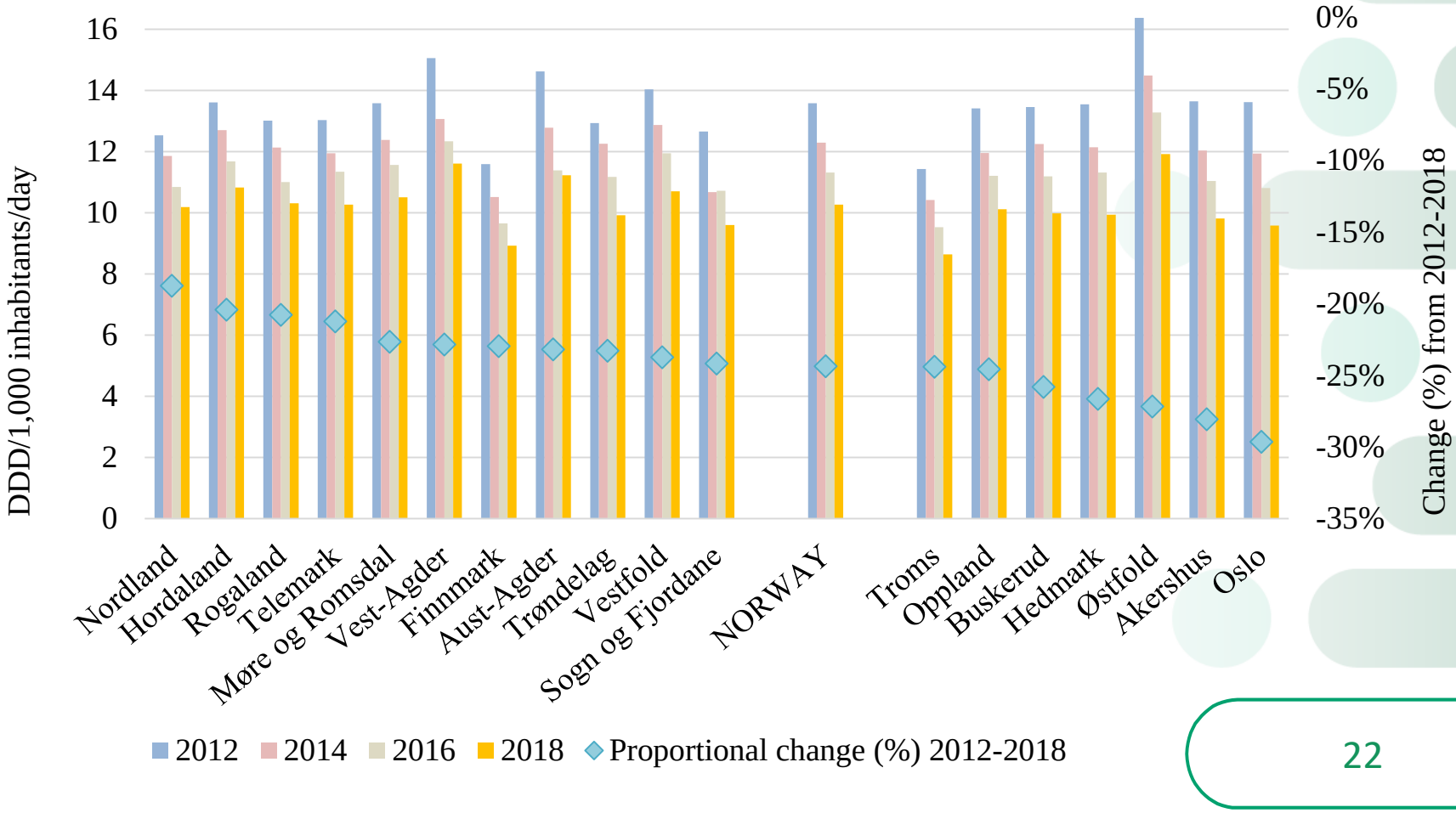


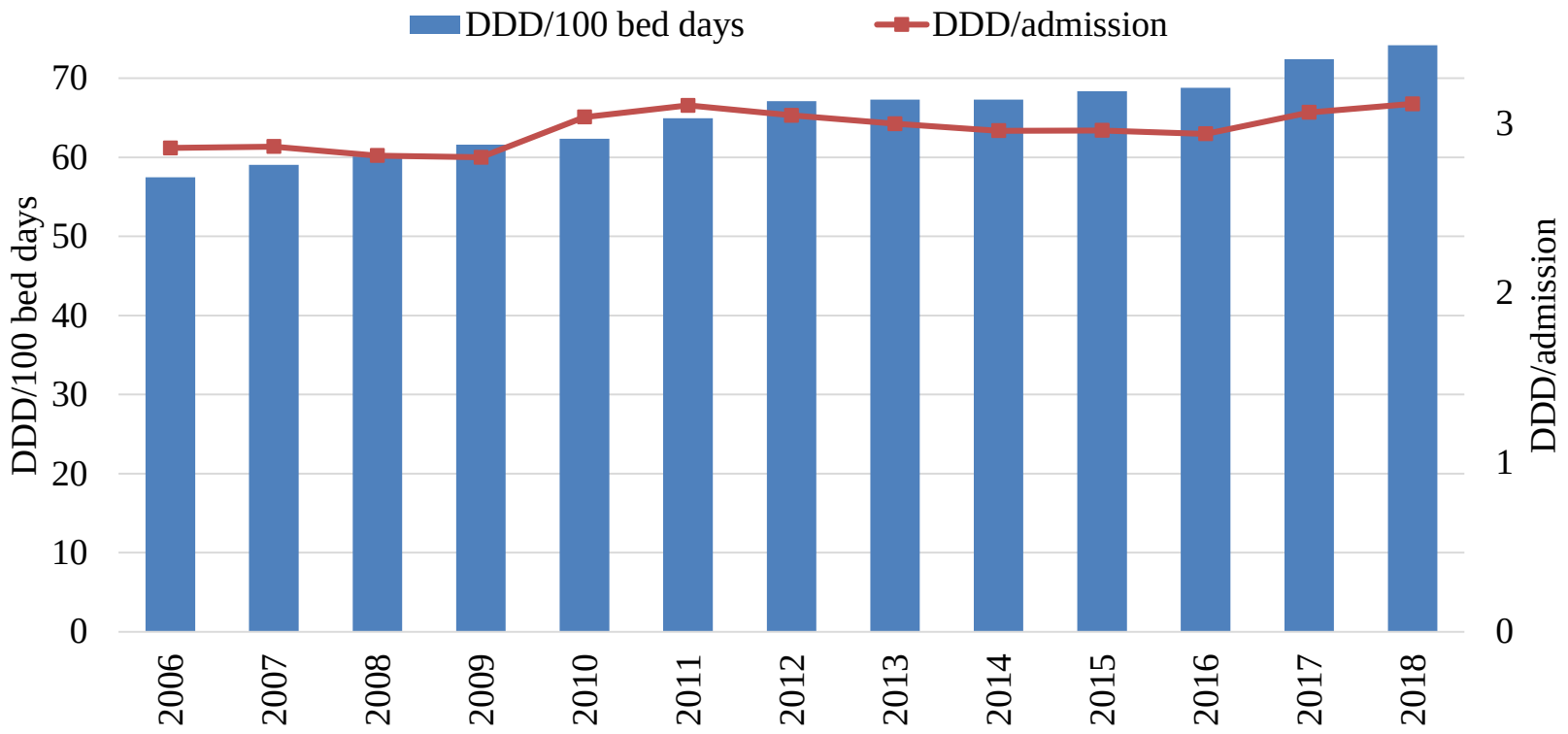
Regjeringens mål om reduksjon av antibiotikabruk



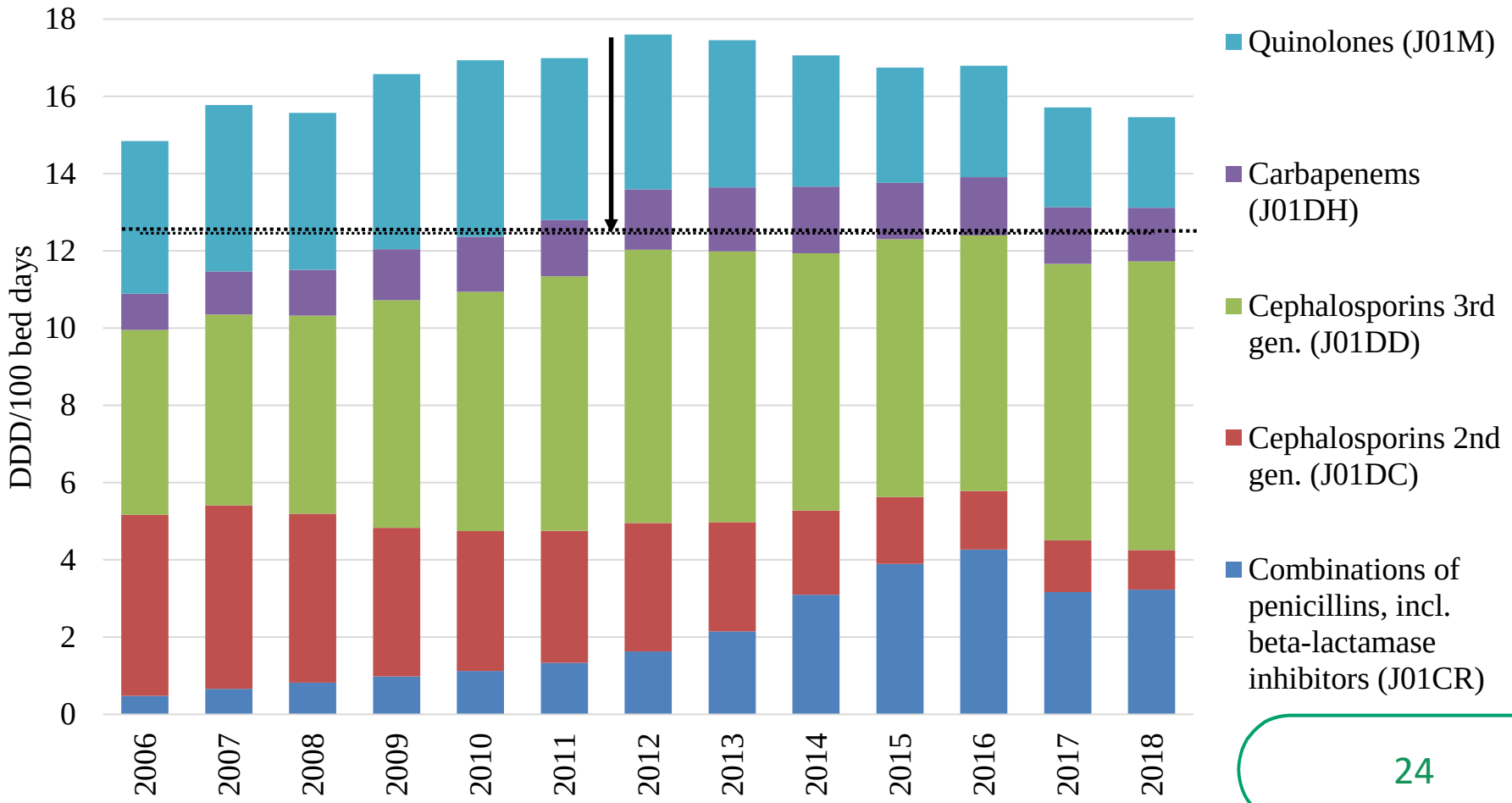
Geografisk fordeling av antibiotikabruk



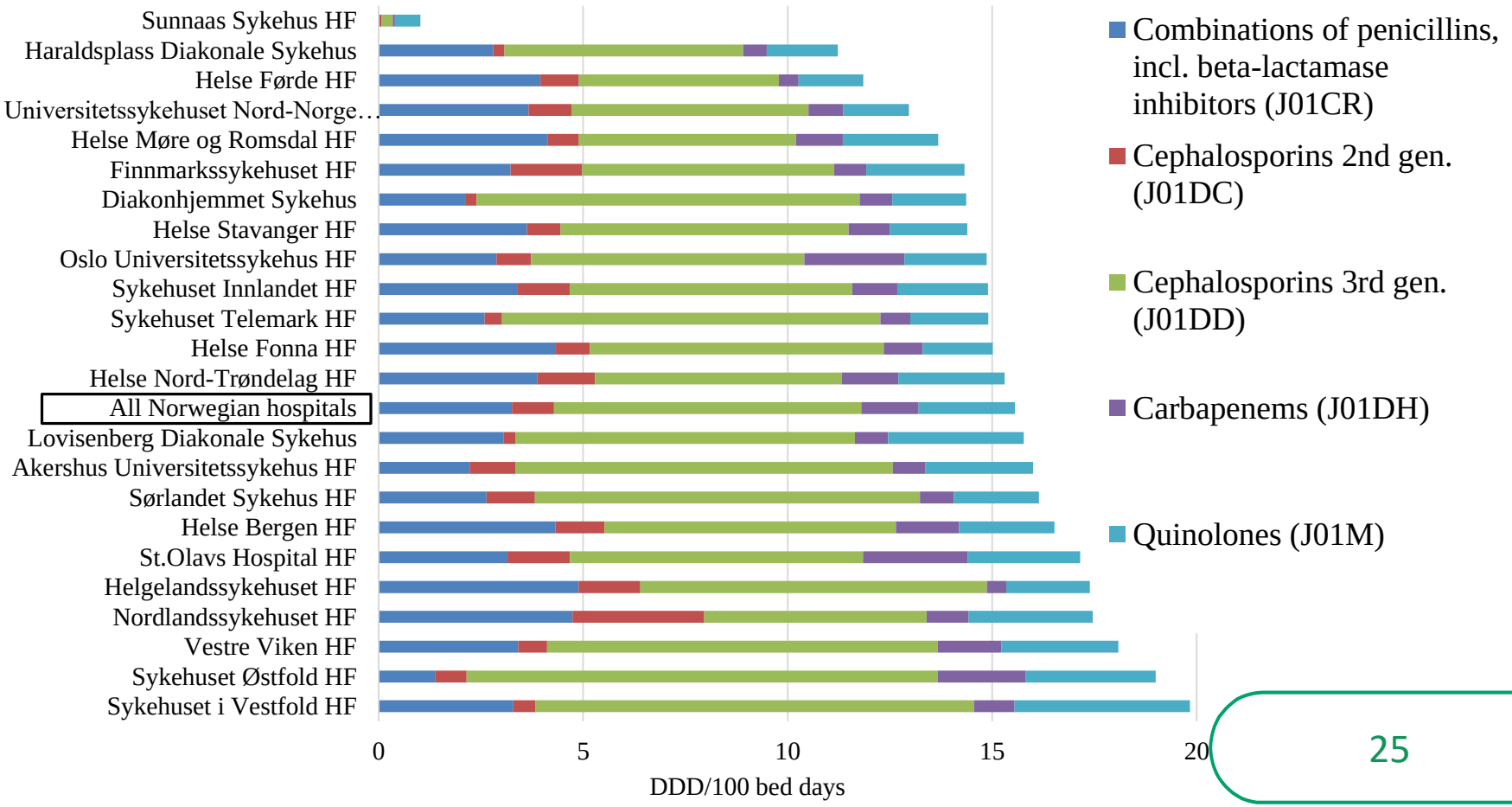
Antibiotikabruk på sykehus



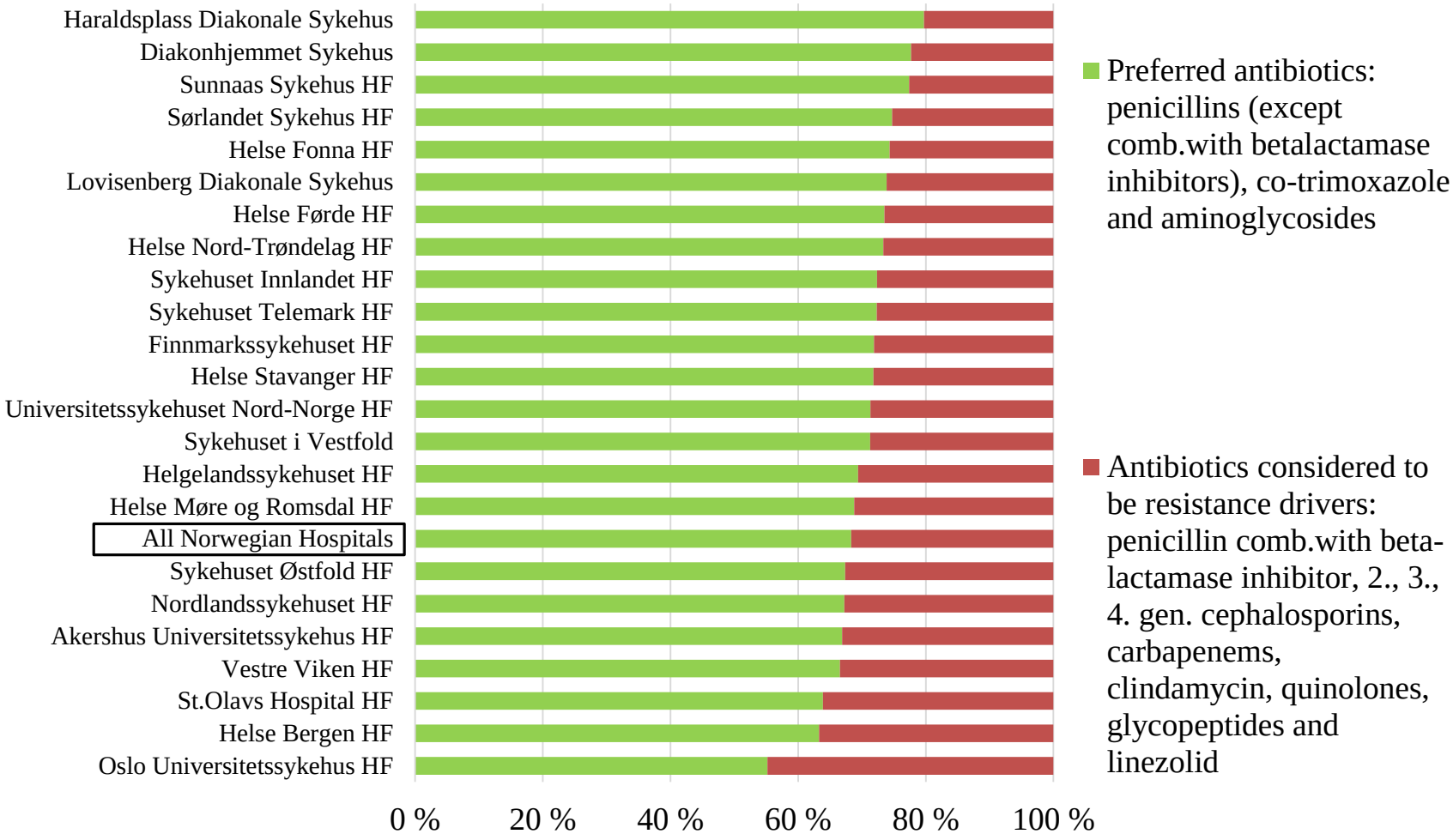
Regjeringens mål om reduksjon av antibiotikabruk



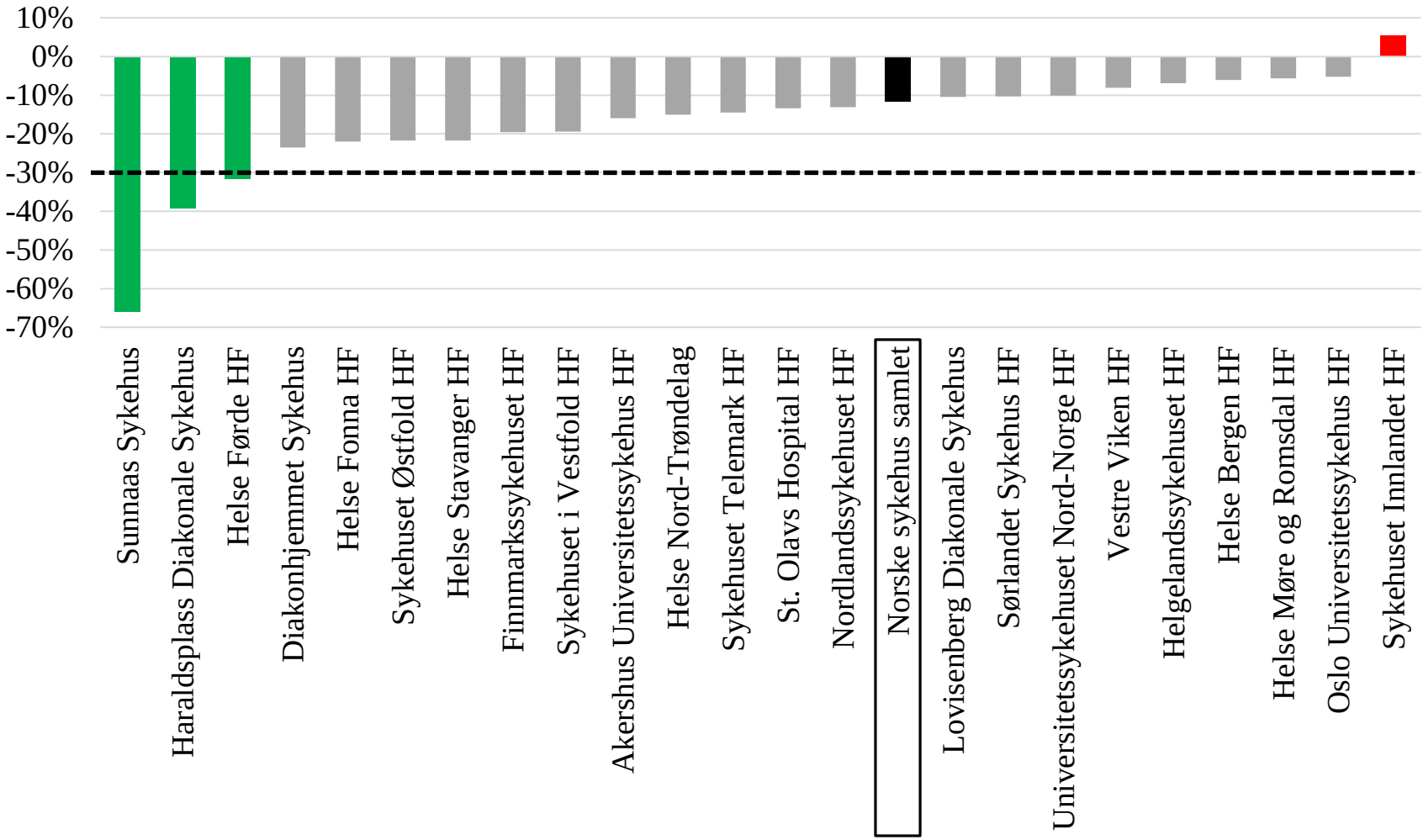
Variasjon i bruk av bredspektrede antibiotika på sykehus



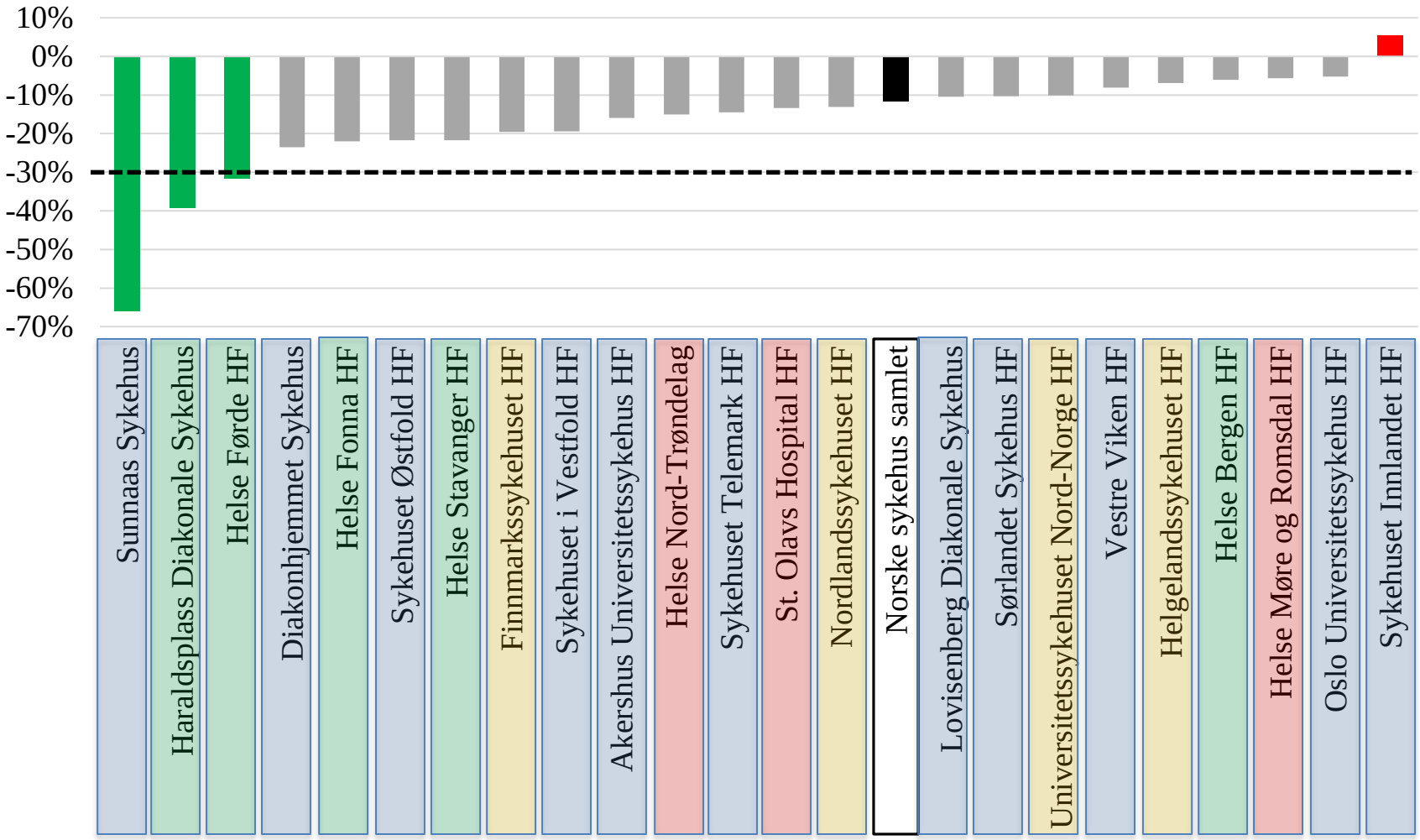
Variasjon i antibiotika forbruksprofil på sykehus



Regjeringens mål om reduksjon av antibiotikabruk

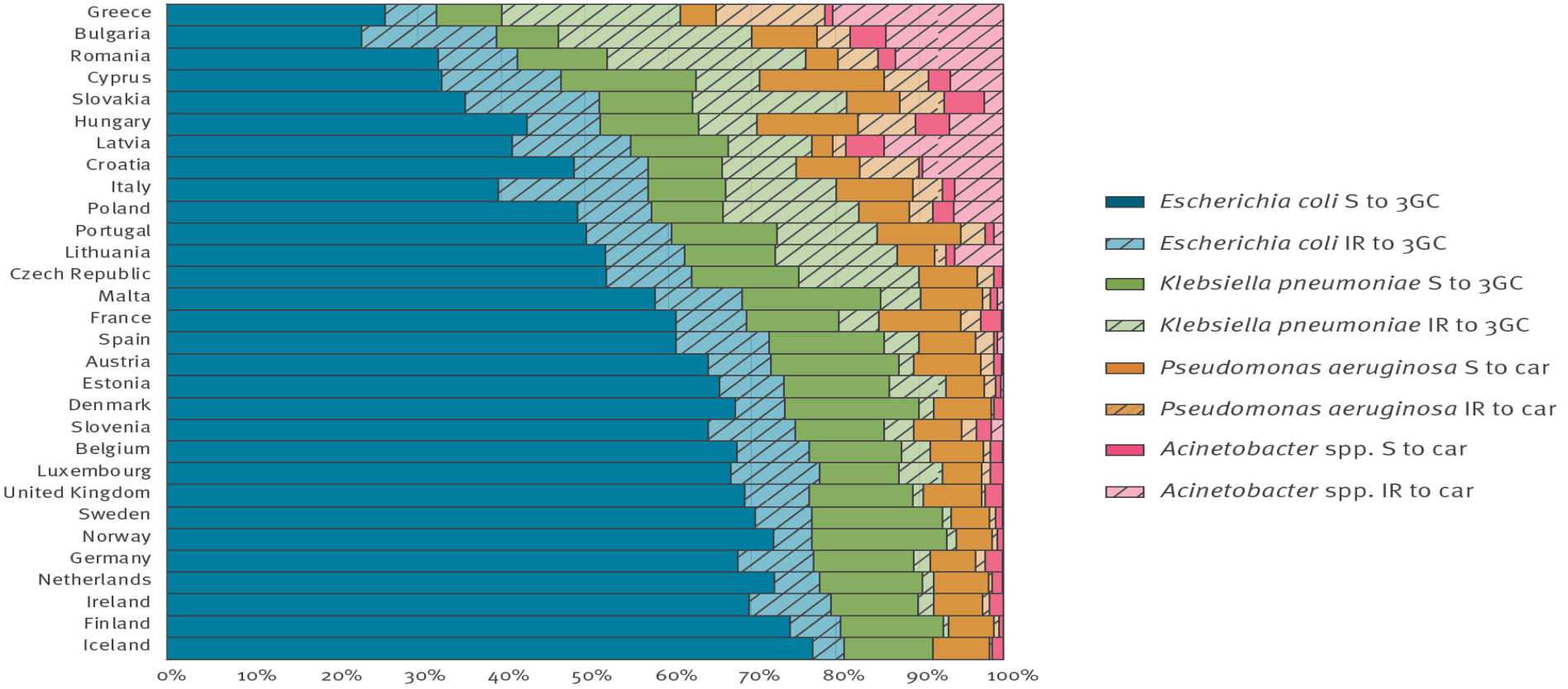


Regjeringens mål om reduksjon av antibiotikabruk



Species	No. of isolates 2018	% of all isolates					% of all isolates excluding skin flora				
		2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Staphylococcus aureus	2,040	11.0	11.1	10.5	10.1	11.1	14.2	14.4	13.6	13.1	14.2
Coagulase negative staphylococci	3,586	20.4	21.1	20.7	20.9	19.5	-	-	-	-	-
Streptococcus pneumoniae	604	3.6	3.2	3.4	2.7	3.3	4.6	4.2	4.4	3.6	4.2
Streptococcus pyogenes	215	1.1	1.3	1.1	1.2	1.2	1.4	1.7	1.4	1.5	1.5
Streptococcus agalactiae	271	1.6	1.7	1.6	1.4	1.5	2.0	2.2	2.1	1.8	1.9
Beta-haemolytic streptococci group C and G	360	1.2	1.5	1.3	1.5	2.0	1.6	2.0	1.7	2.0	2.5
Viridans- and non-haemolytic streptococci	927	4.6	4.6	5.0	5.5	5.1	5.9	6.0	6.5	7.2	6.4
Enterococcus faecalis	631	3.8	3.1	3.6	3.6	3.4	5.0	4.0	4.6	4.7	4.4
Enterococcus faecium	212	1.6	1.4	1.4	1.4	1.2	2.1	1.8	1.9	1.9	1.5
Other Gram-positive aerobic and facultative anaerobic bacteria	570	3.5	3.6	3.3	3.5	3.1	2.0	2.3	2.3	2.2	2.0
Escherichia coli	4,697	24.4	24.8	24.9	24.9	25.5	31.5	32.4	32.2	32.2	32.6
Klebsiella spp.	1,253	7.0	6.9	7.1	7.0	6.8	9.0	9.1	9.2	9.1	8.7
Enterobacter spp.	342	1.9	1.7	1.7	1.9	1.9	2.5	2.3	2.2	2.4	2.4
Proteus spp.	290	1.6	1.6	1.6	1.5	1.6	2.1	2.1	2.1	2.0	2.0
Other *Enterobacteriaceae*	625	2.2	1.8	1.8	2.3	3.4	2.9	2.3	2.3	3.0	4.3
Pseudomonas spp.	304	1.8	1.7	1.6	1.4	1.7	2.3	2.2	2.0	1.8	2.1
Other Gram-negative aerobic and facultative anaerobic bacteria	185	2.0	2.1	2.4	2.0	1.0	2.6	2.7	3.0	2.6	1.3
Bacteroides spp.	352	2.2	2.2	1.9	2.3	1.9	2.9	2.8	2.4	2.9	2.4
Other anaerobic bacteria	679	3.1	3.2	3.8	3.7	3.7	3.6	3.7	4.4	4.4	4.2
Yeasts	200	1.4	1.4	1.3	1.2	1.1	1.8	1.8	1.7	1.6	1.4
Total	**18,343**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**	**100.0**

Økologiske endringer ved økt forekomst av ervervet resistens



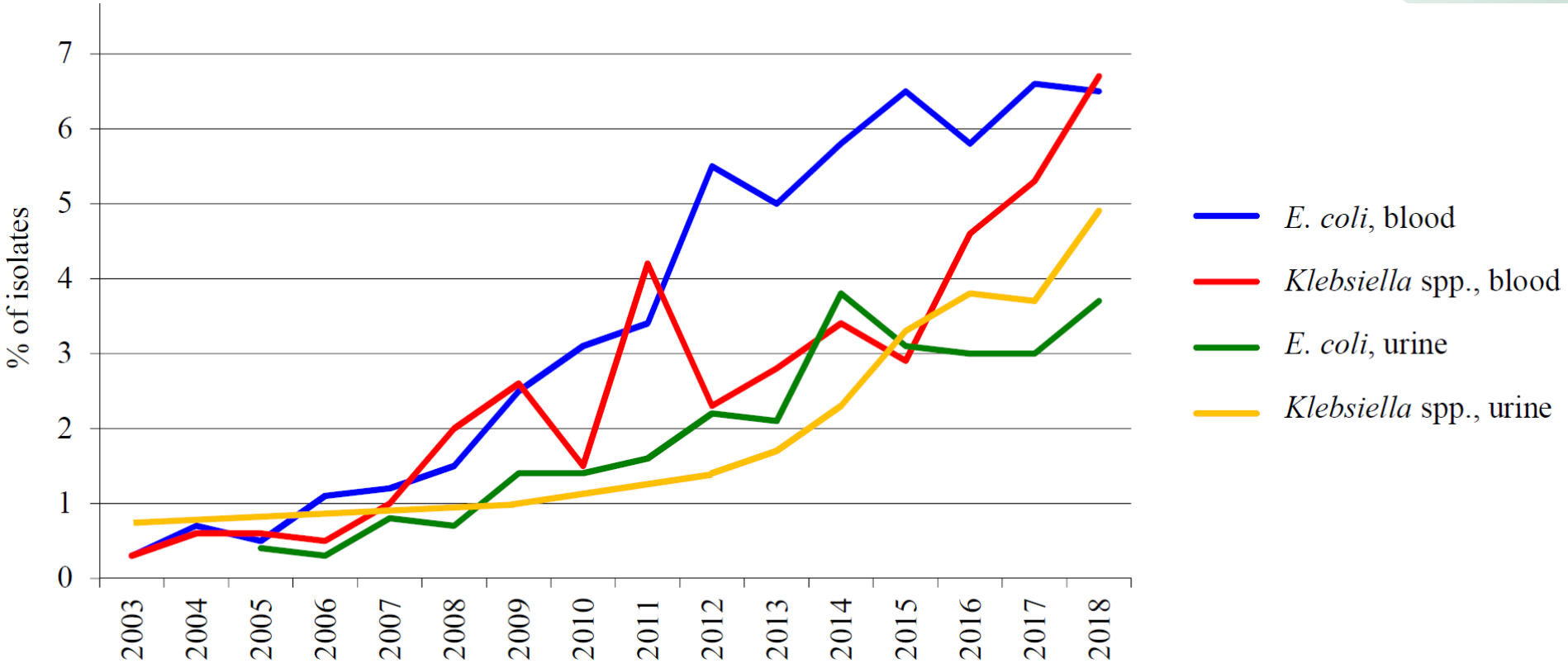
Jarlier *et al.* Eurosurveillance 2019

Tidsskriftet
DEN NORSKE LEGEFORENING

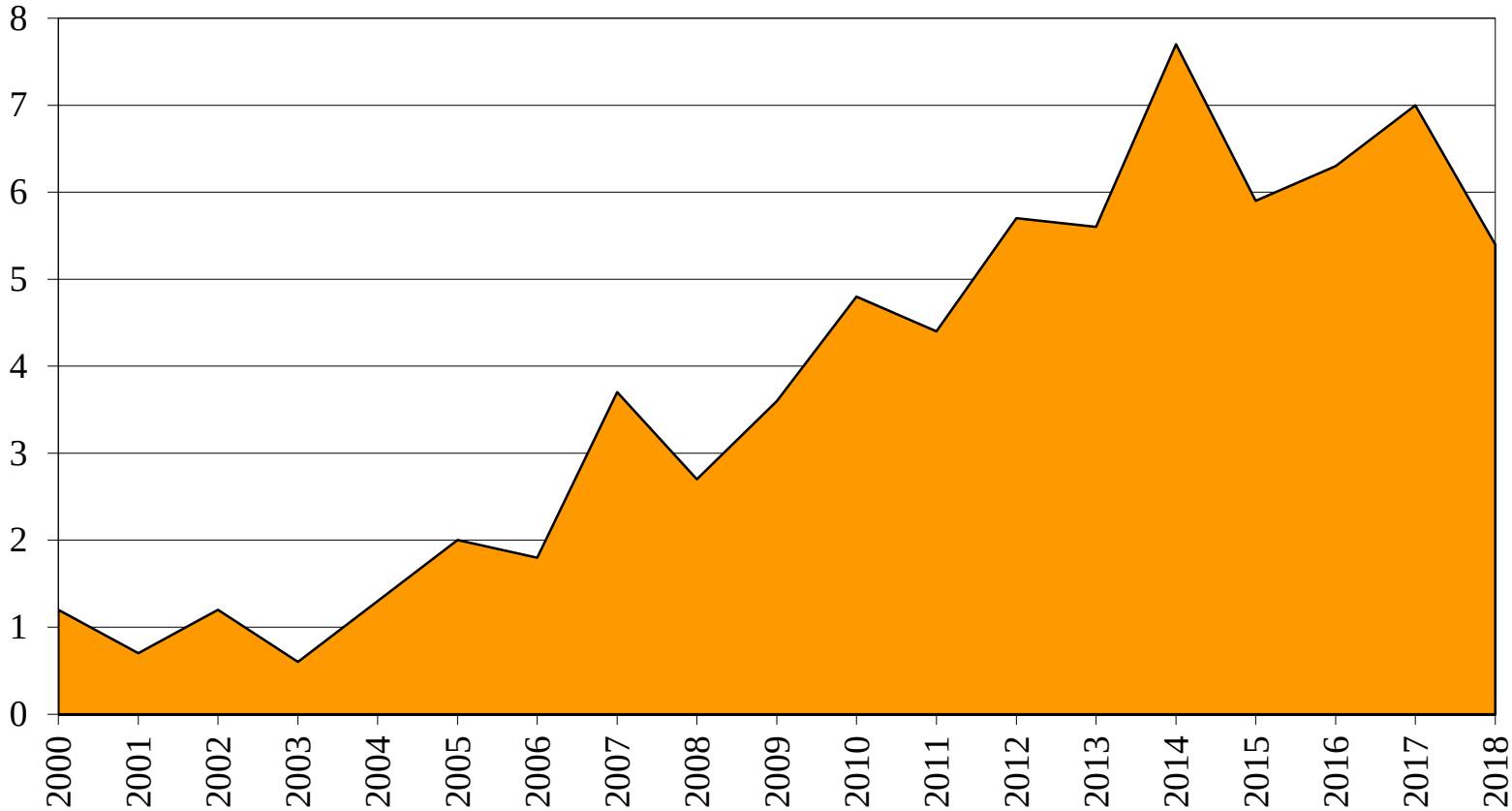
Valg av antibiotika – viktig endring i prøvesvar fra mikrobiologen

Lindemann PC, Gammelsrud KW, Löhr IH, Akselsen PE, Lindbæk M, Sundsfjord A. Tidsskr Nor Legeforen Sept 2019

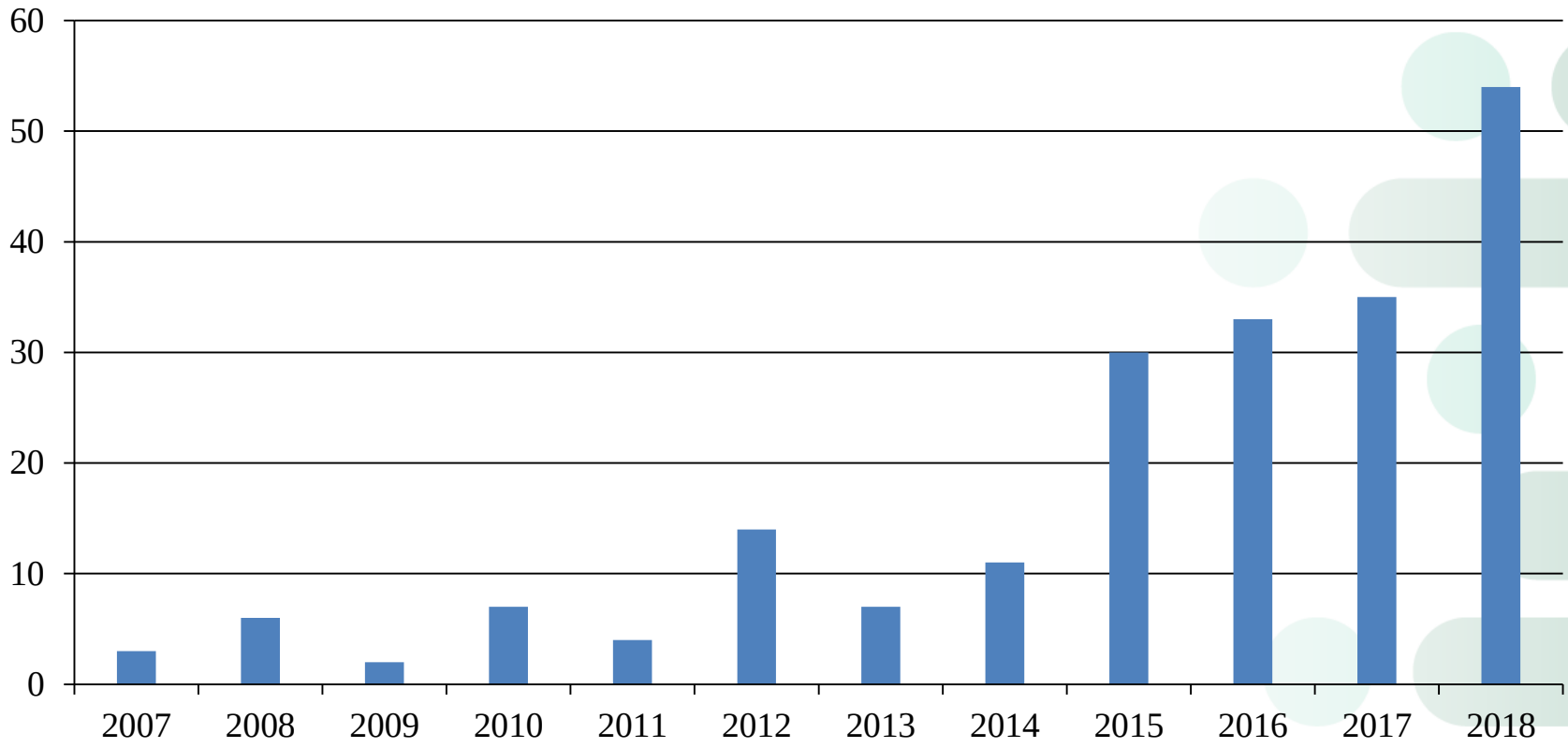
E. coli og *K. pneumoniae* ESBL i blodkultur og urin



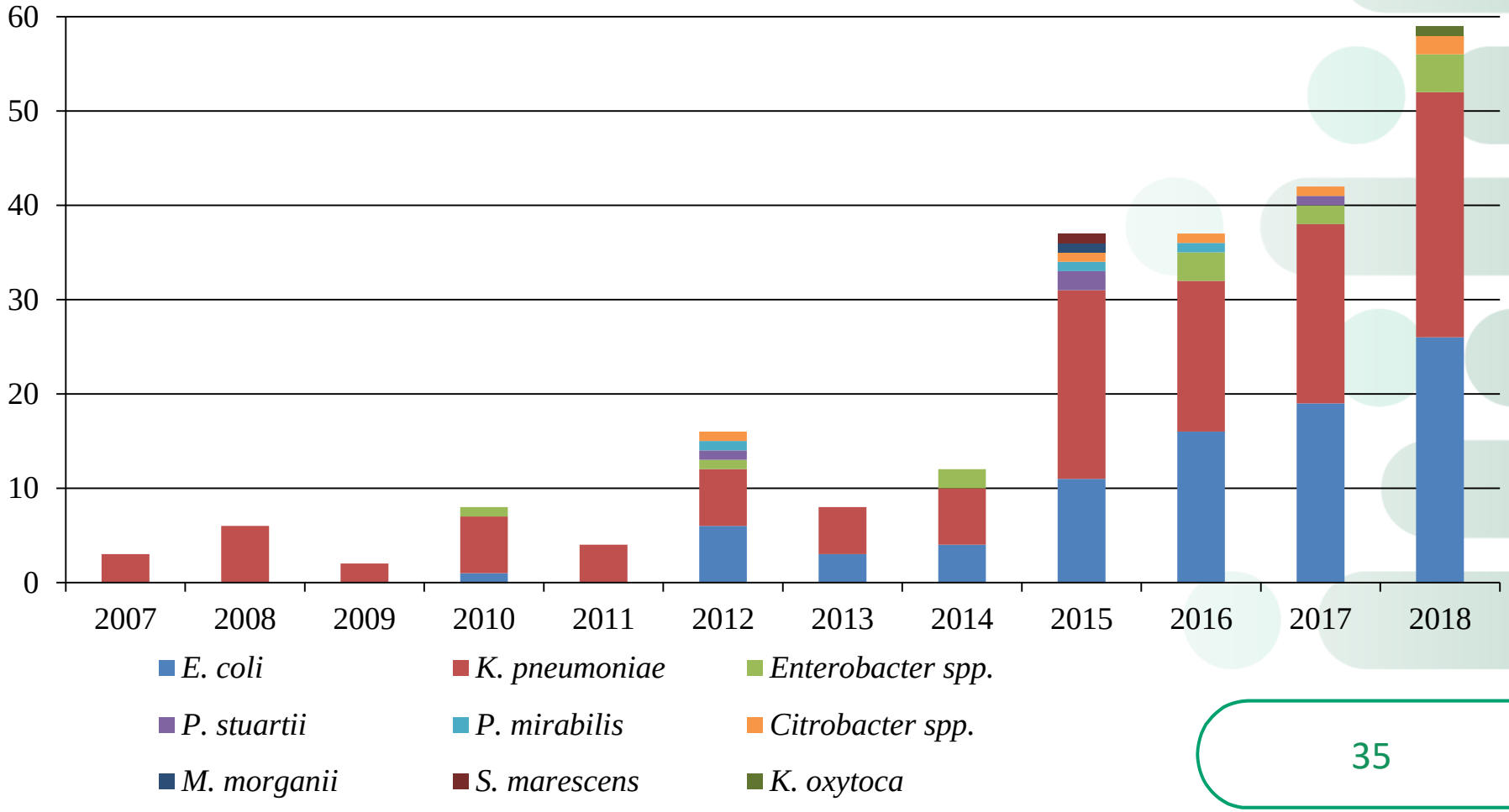
E. coli i blod, resistens mot gentamicin



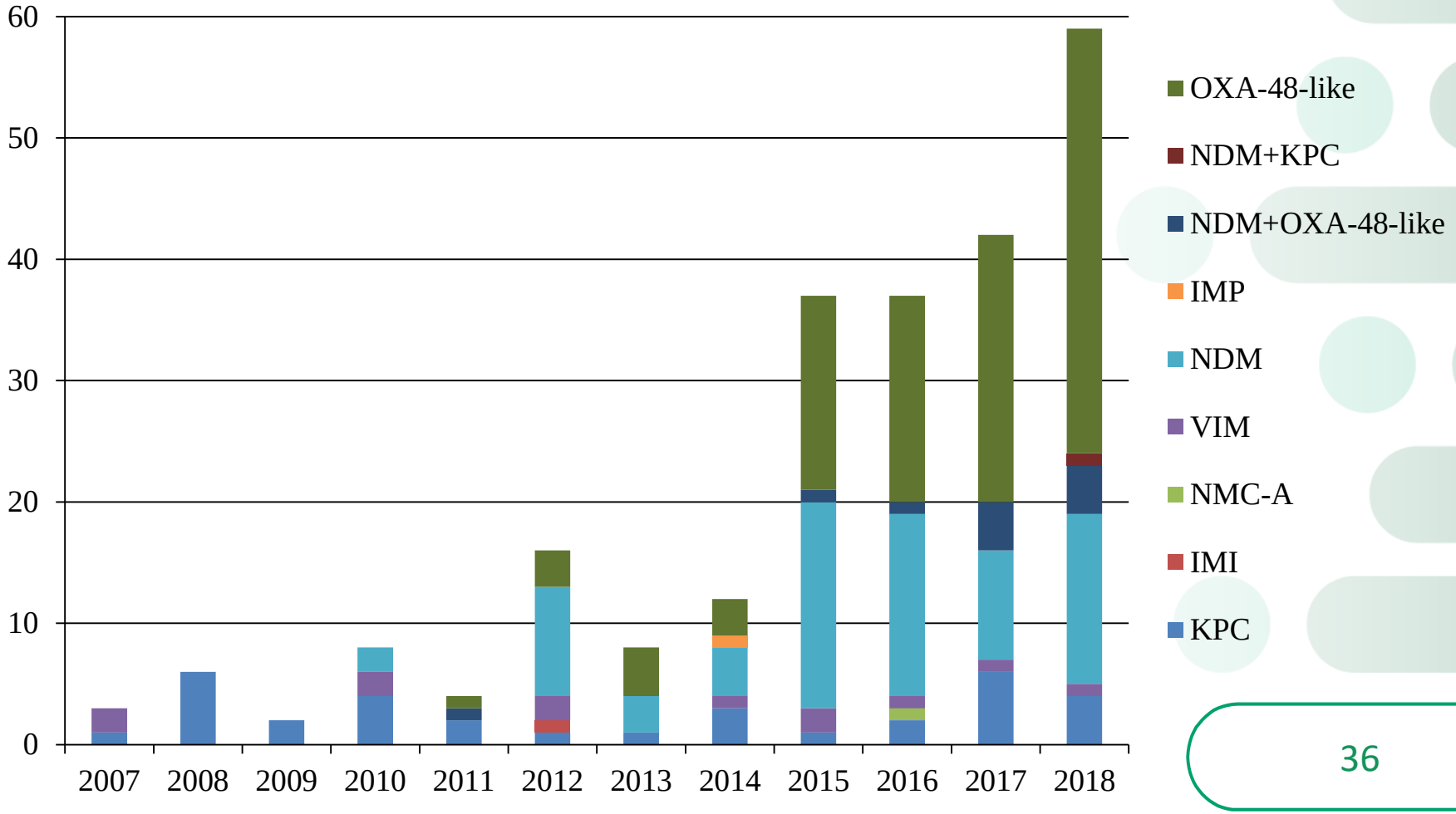
Karbapenemaseproduserende *Enterobacteriaceae* – Antall pasienter



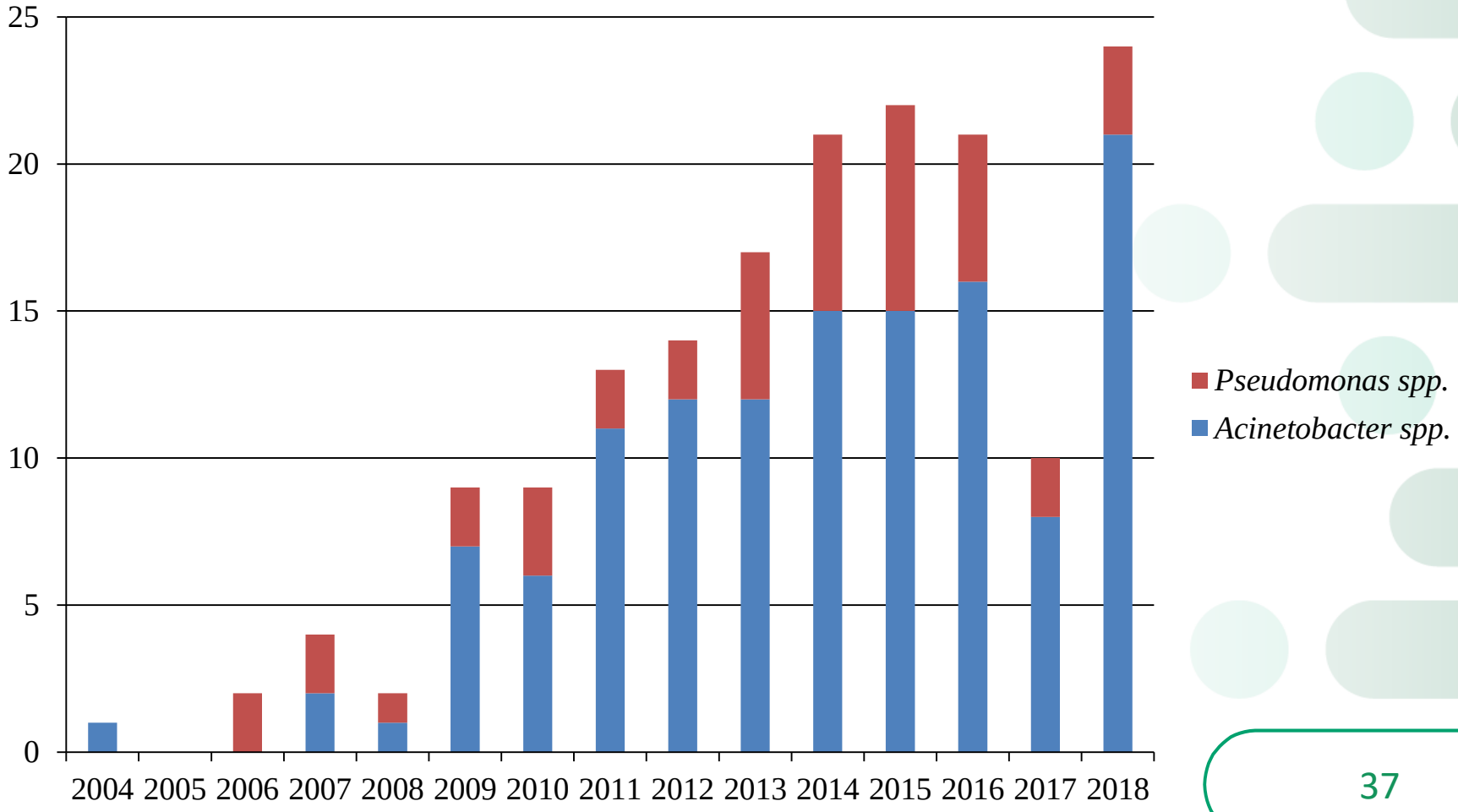
Karbapenemaseproduserende *Enterobacteriaceae* - Speciesfordeling



Karbapenemaseproduserende *Enterobacteriaceae* - Genotyper



Karbapenemaseproduserende *P. aeruginosa* og *A. baumannii*



Haemophilus influenzae fra blod og spinalvæske

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 1	> 1	85.7	-	14.3
Amoxicillin-clavulanic acid	≤ 2	> 2	92.9	-	7.1
Cefuroxime	≤ 1	> 2	85.8	7.1	7.1
Cefotaxime	≤ 0.125	> 0.125	100.0	-	0.0
Ceftriaxone	≤ 0.125	> 0.125	92.9	-	7.1
Meropenem*	≤ 2	> 2	100.0	-	0.0
Ciprofloxacin	≤ 0.06	> 0.06	100.0	-	0.0
Chloramphenicol	≤ 2	> 2	100.0	-	0.0
Tetracycline	≤ 1	> 2	100.0	0.0	0.0
Trimethoprim-sulfamethoxazole*	≤ 0.5	> 1	78.6	7.1	14.3
Beta-lactamase	Negative	Positive	85.7	-	14.3

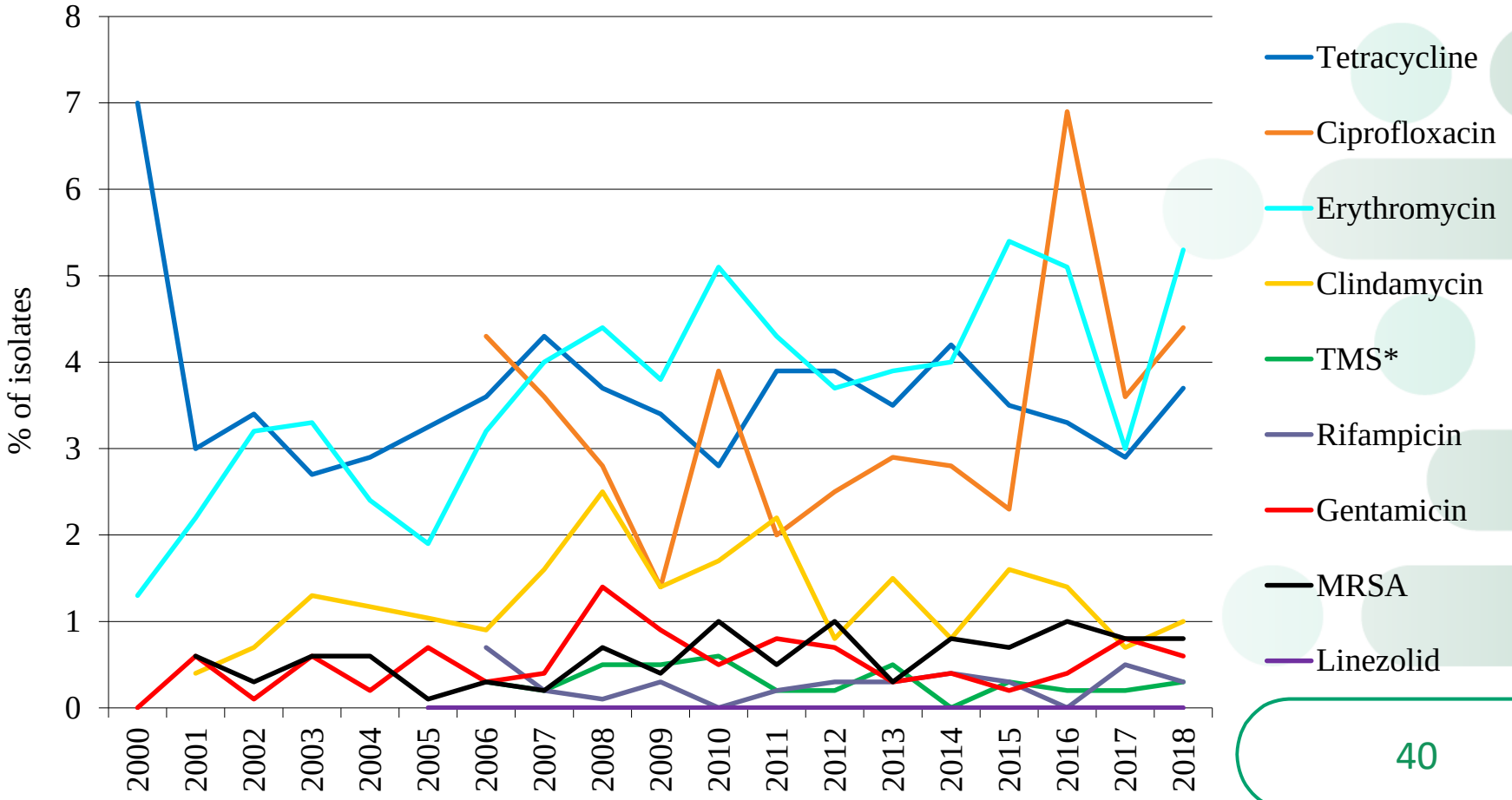
S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for indications other than meningitis. **Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

Neisseria gonorrhoeae fra alle materialer

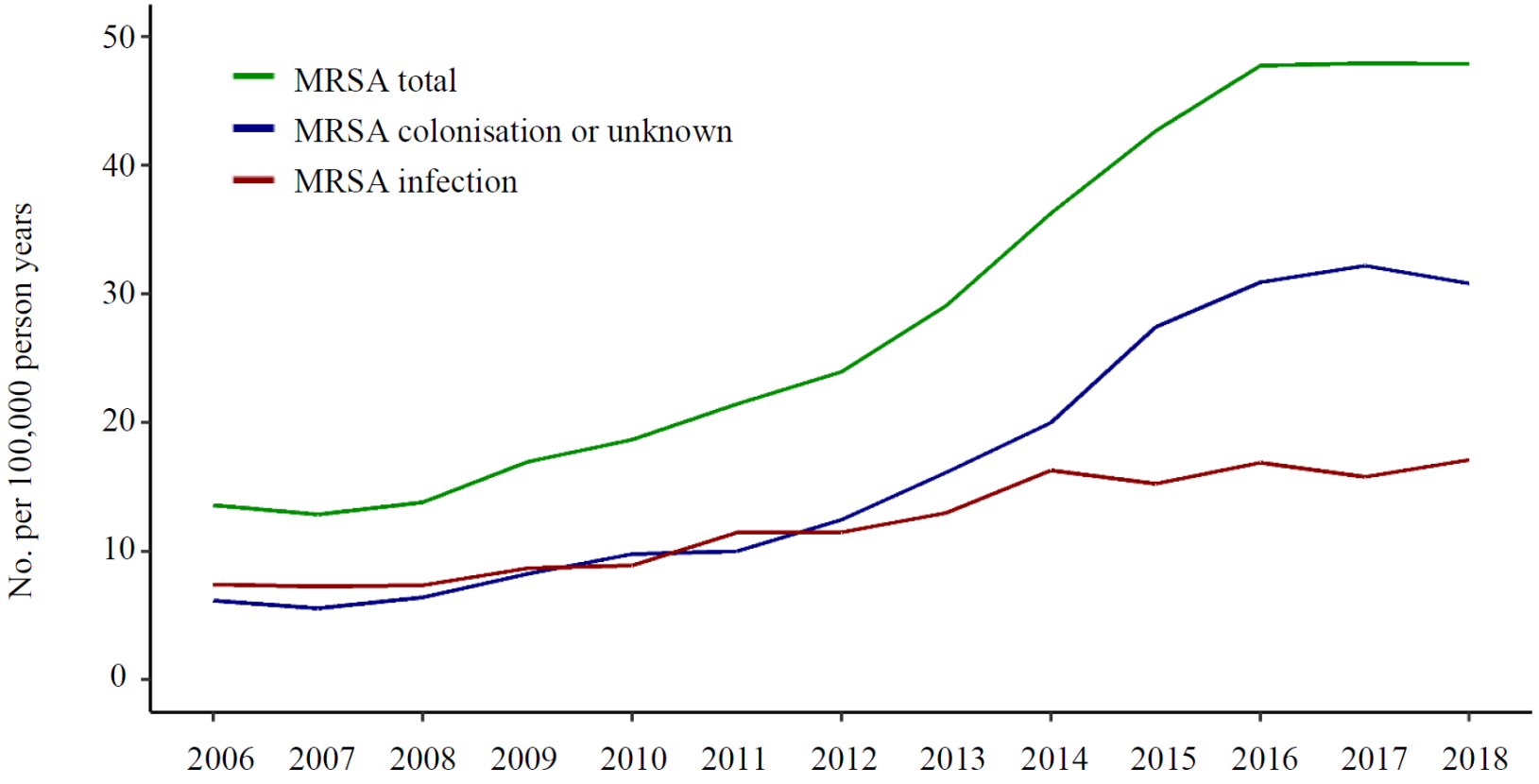
	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.06	> 1	1.0	88.3	10.7
Ceftriaxone	≤ 0.125	> 0.125	100.0	-	0.0
Cefixime	≤ 0.125	> 0.125	98.7	-	1.3
Ciprofloxacin	≤ 0.03	> 0.06	31.1	0.0	68.9
Tetracycline	≤ 0.5	> 1	44.4	35.9	19.7
Spectinomycin	≤ 64	> 64	100.0	-	0.0
Beta-lactamase	Negative	Positive	91.4	-	8.6

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

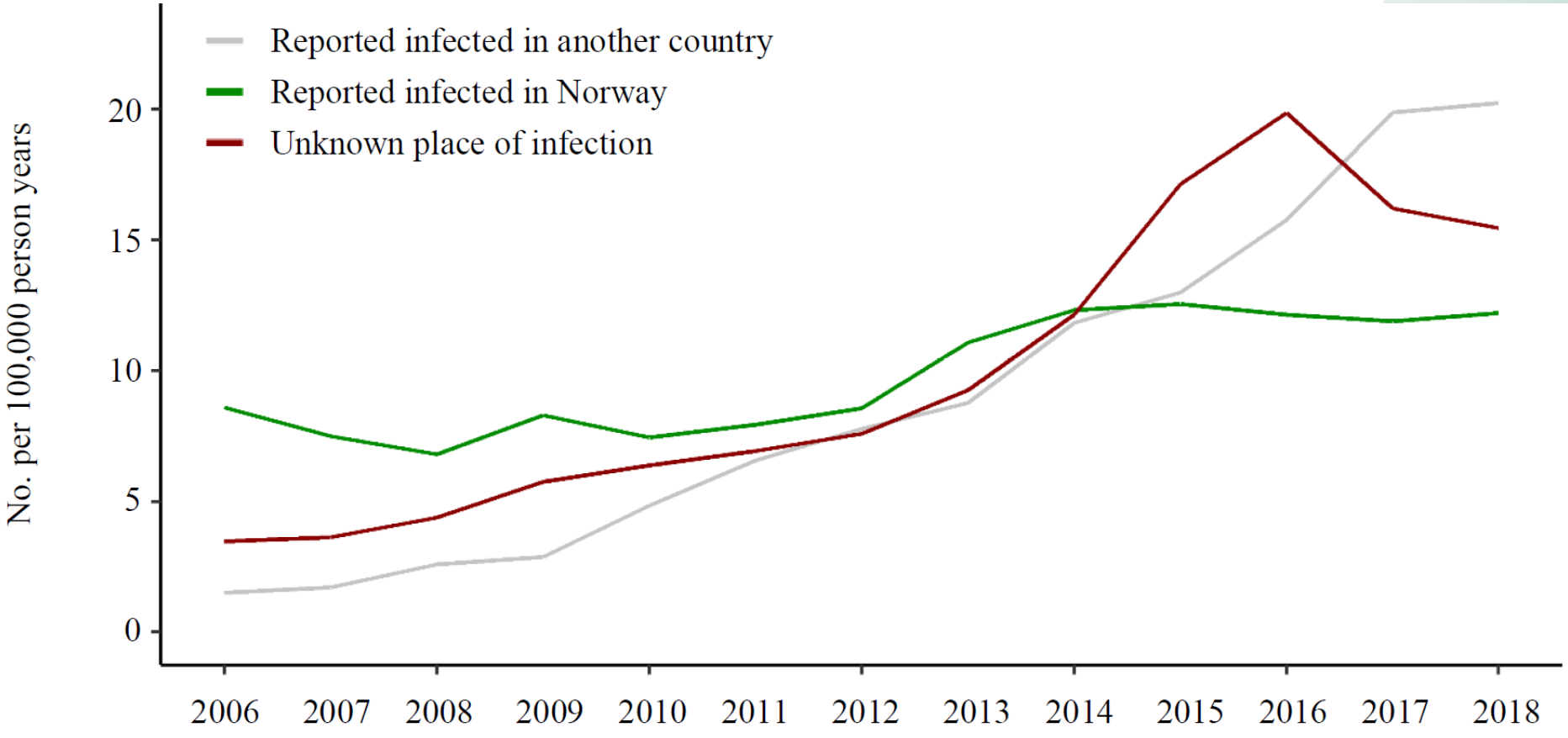
Staphylococcus aureus i blodkultur



MRSA – Infeksjon / kolonisering per 100 000



MRSA – Smittested per 100 000

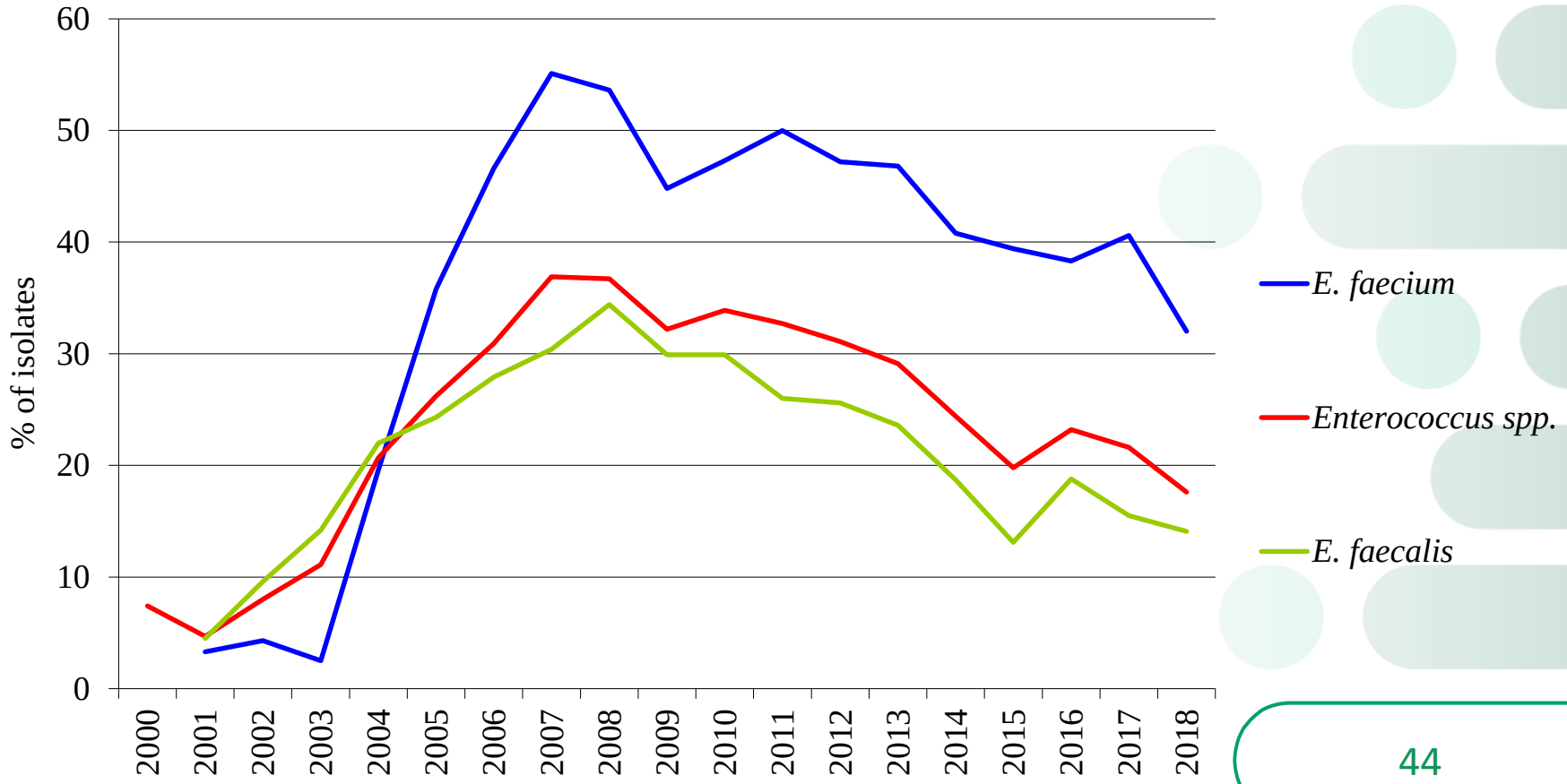


MRSA – Følsomhet for øvrige antibiotika

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Erythromycin	≤ 1	> 2	67.5	0.2	32.3
Clindamycin	≤ 0.25	> 0.5	89.9	2.0	8.1*
Fusidic acid	≤ 1	> 1	88.9	-	11.1
Ciprofloxacin	≤ 1	> 1	78.5	-	21.5
Gentamicin	≤ 1	> 1	88.8	-	11.2
Linezolid	≤ 4	> 4	100.0	-	0.0
Rifampicin	≤ 0.06	> 0.5	99.0	0.5	0.5
Tetracycline	≤ 1	> 2	75.2	0.3	24.5
Trimethoprim-sulfamethoxazole**	≤ 2	> 4	97.4	1.3	1.3
Mupirocin	≤ 1	> 256	96.8	2.5	0.7
Vancomycin	≤ 4	> 4	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Due to an error, the proportion of clindamycin resistant strains was reported to be 21.9% in 2017. The correct number should have been 9.6%. **Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

Gentamicinresistente enterokokker i blodkultur

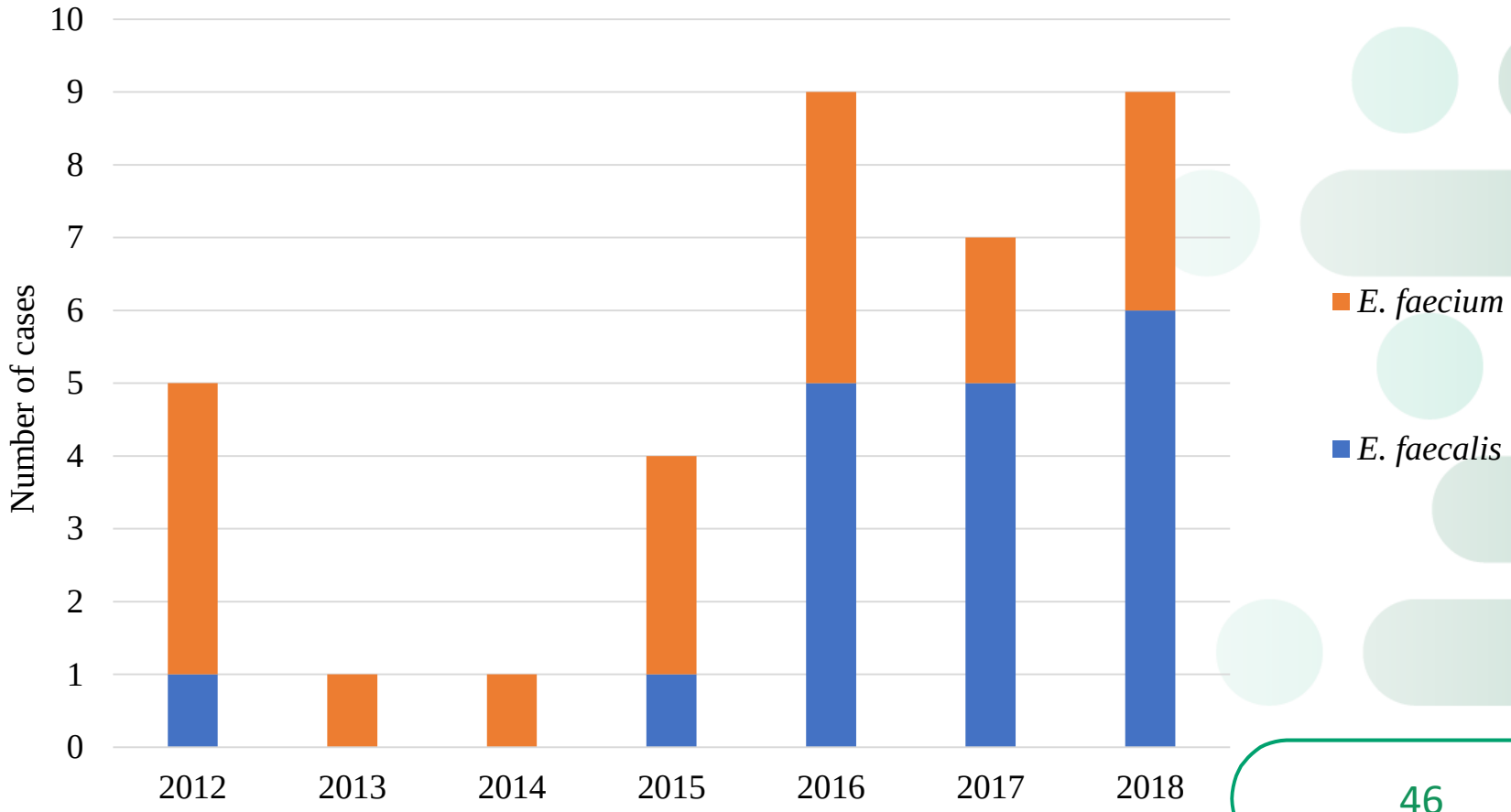


Enterokokker i urin

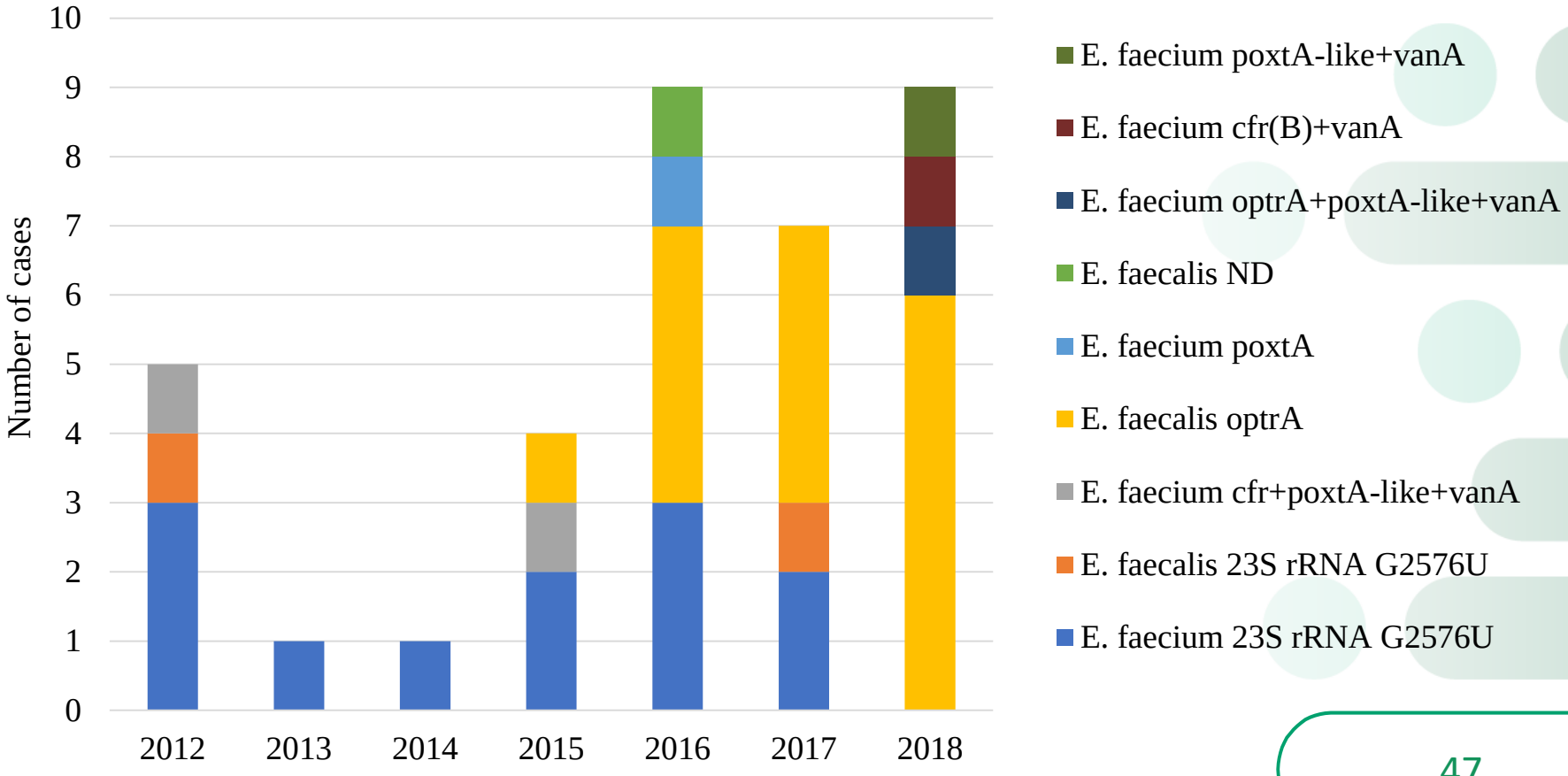
	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Ampicillin	≤ 4	> 8	95.9	0.0	4.1
Gentamicin HLR*	≤ 128	> 128	86.3	-	13.7
Ciprofloxacin	≤ 4	> 4	88.5	-	11.5
Trimethoprim	≤ 1	> 1	78.5	-	21.5
Linezolid	≤ 4	> 4	100.0	-	0.0
Vancomycin (any genotype)	≤ 4	> 4	99.9	-	0.1
Vancomycin (*vanA* or *vanB*)	Negative	Positive	99.9	-	0.1

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *HLR=High Level Resistance.

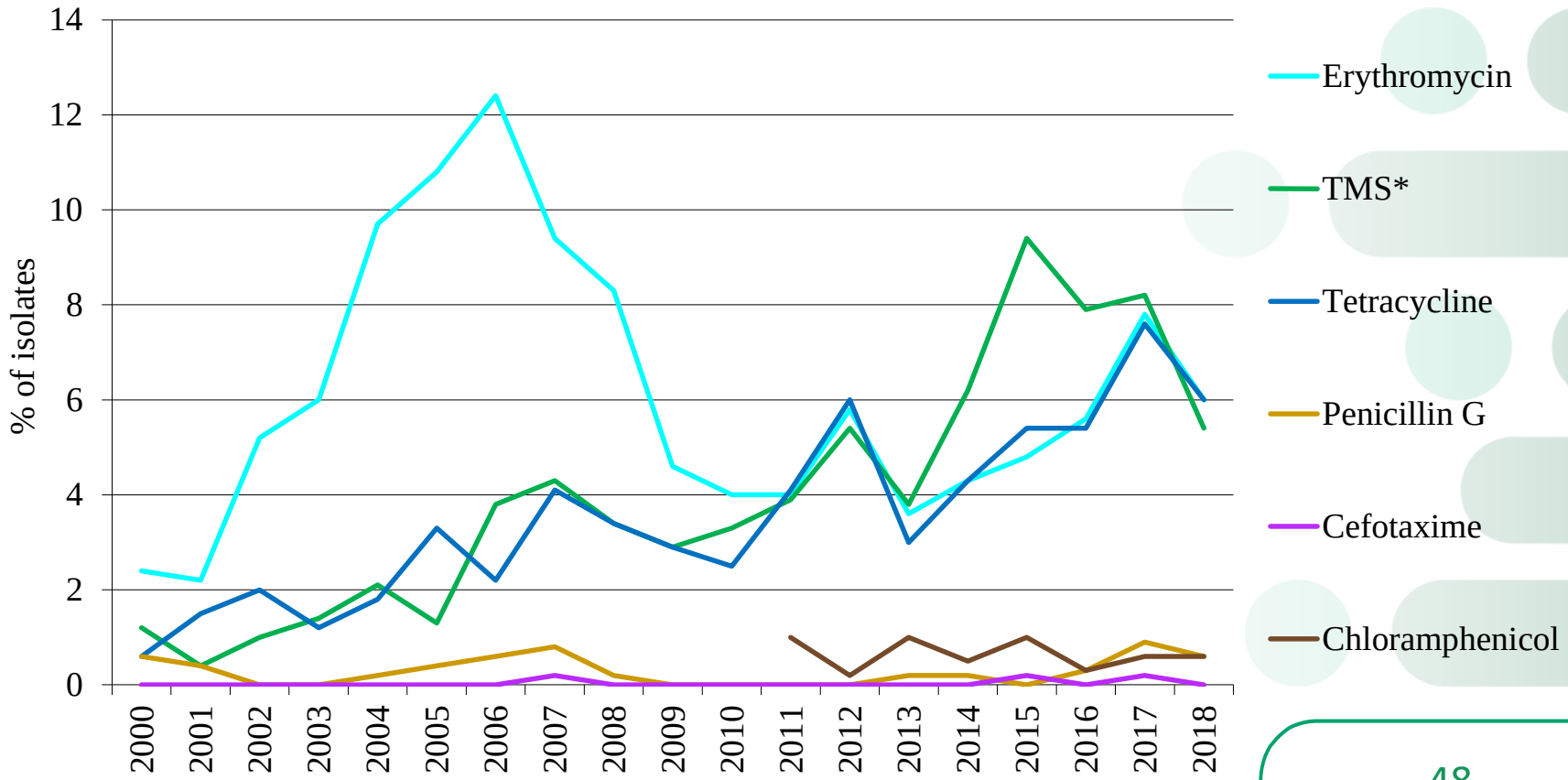
Linezolidresistente enterokokker



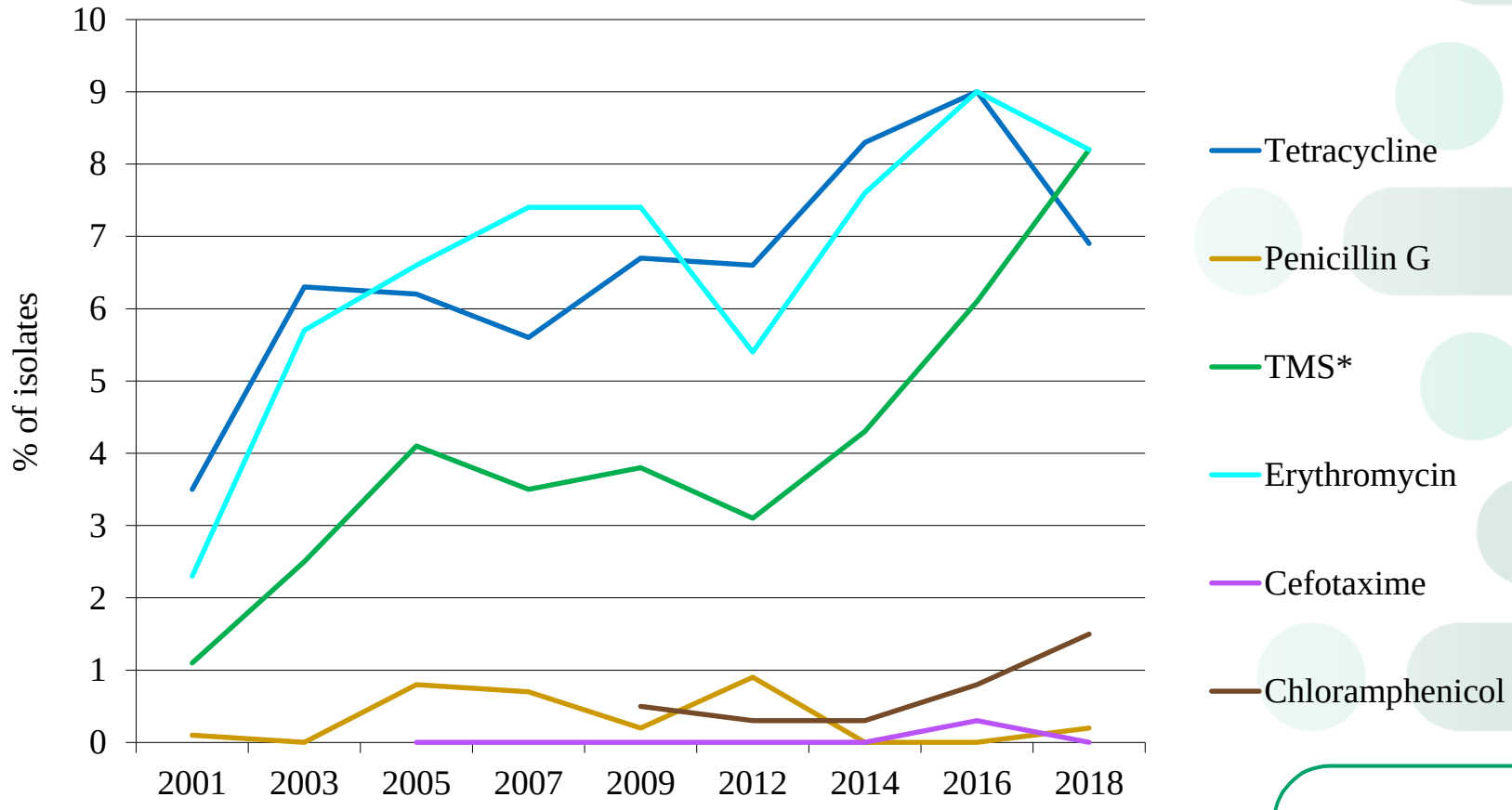
Linezolidresistente enterokokker



Streptococcus pneumoniae i blodkultur



Streptococcus pneumoniae i luftvegsprøver



Streptococcus agalactiae (GBS) i blodkultur og spinalvæske

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.25	> 0.25	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.5	77.4	0.0	22.6
Clindamycin	≤ 0.5	> 0.5	87.5	-	12.5
Tetracycline	≤ 1	> 2	24.2	0.4	75.4
Vancomycin	≤ 2	> 2	100.0	-	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant.

Streptococcus dysgalactiae (GCS/GGS) i blodkultur og sår

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Penicillin G	≤ 0.25	> 0.25	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.5	89.1	0.7	10.2
Clindamycin	≤ 0.5	> 0.5	96.7	-	3.3
Tetracycline	≤ 1	> 2	65.7	12.4	21.9
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	100.0	0.0	0.0
Penicillin G	≤ 0.25	> 0.25	100.0	-	0.0
Erythromycin	≤ 0.25	> 0.5	91.4	0.9	7.7
Clindamycin	≤ 0.5	> 0.5	97.9	-	2.1
Tetracycline	≤ 1	> 2	73.1	6.0	20.9
Trimethoprim-sulfamethoxazole*	≤ 1	> 2	100.0	0.0	0.0

S=Susceptible with standard exposure, I=Susceptible with increased exposure, R=Resistant. *Breakpoints for the trimethoprim-sulfamethoxazole combination are given for the trimethoprim component only.

Mycobacterium tuberculosis

Origin of birth	No. of cases	No. of isolates	Resistance to antimicrobial agents (No. of isolates)				
			Isoniazid	Rifampicin	Ethambutol	Pyrazinamid	MDR-TB
Norway	29 (30)	21 (20)	2 (1)	0 (1)	0 (1)	1 (1)	0 (1)
Europe excl. Norway	25 (24)	22 (20)	3 (3)	3 (2)	2 (1)	2 (3)	2 (2)
Asia	79 (97)	69 (80)	5 (4)	2 (1)	1 (0)	3 (0)	2 (1)
Africa	76 (109)	55 (93)	5 (12)	1 (5)	0 (2)	0 (8)	0 (5)
America	0 (1)	0 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Oseania	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Unknown	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	209 (261)	167 (214)	15 (20)	6 (9)	3 (4)	6 (12*)	4 (9)
Proportion resistant isolates (%)			9.0 (9.3)	3.6 (4.2)	1.8 (1.9)	3.6 (5.6)	2.4 (4.2)

Candida albicans fra blodkultur

	Breakpoints (mg/L)		Proportion of isolates (%)		
	S	R	S	I	R
Amphotericin B*	≤ 1	> 1	100.0	-	0.0
Fluconazole*	≤ 2	> 4	100.0	0.0	0.0
Voriconazole*	≤ 0.064	> 0.25	100.0	0.0	0.0
Anidulafungin*/**	≤ 0.032	> 0.032	99.1	-	0.9
Micafungin*/**	≤ 0.016	> 0.016	99.1	-	0.9

S=Susceptible, I=Intermediately susceptible, R=Resistant. *Recommended breakpoints by the European Committee on Antimicrobial Susceptibility Testing – EUCAST 2018. The EUCAST AFST subcommittee is currently reviewing breakpoint tables to introduce necessary changes to match the new EUCAST definitions of S, I and R. **There are no European breakpoints for caspofungin. Strains susceptible to anidulafungin and micafungin are considered susceptible.

…..og i tillegg artikler om:

- ✓ Urinvegsinfeksjoner hos menn
- ✓ Behandling av Lyme borreliose
- ✓ Antibiotikaresistens hos Legionella
- ✓ Behandlingslengde for antibiotika i sykehus og primærhelsetjeneste
- ✓ Én helse – Metagenombasert resistensovervåking

pluss mye mer!

Hovedfunn fra overvåkingen i 2018 - Antibiotikabruk

- ✓ Totalforbruket redusert med 3 % fra 2017 til 2018, 24 % reduksjon fra 2012 til 2018, 30% reduksjon til 2020 fullt mulig
- ✓ 84 % forskrives i primærhelsetjenesten utenfor helseinstitusjoner
- ✓ Store geografiske forskjeller, en viss utjevning med RAK og RASK
- ✓ Totalforbruk i sykehus opp 10% per liggedøgn fra 2012 til 2018
- ✓ Bredspektrede midler redusert med 12 % fra 2012 til 2018
- ✓ Store forskjeller i bruk og endring mellom sykehus

Hovedfunn fra overvåkingen i 2018 - Antibiotikaresistens

- ✓ Vedvarende økning av ESBL *E. coli* og *Klebsiella pneumoniae*
- ✓ Økt antall pasienter med karbapenemresistens, ofte importsmitte
- ✓ Stabil situasjon mht MRSA
- ✓ Langsomt økende resistens mot penicillin i luftveisbakterier
- ✓ Store resistensproblemer ved gonorré uansett smittekilde
- ✓ Behov for økt fokus på smittevern

Stor takk til alle……

- ✓ …som har vært med på å skrive rapporten
- ✓ …som har levert data som er med i rapporten
- ✓ …som driver fornuftig forskrivning av antibiotika og godt smittevern

…og til alle de som har hørt på!

THAT'S A GOOD QUESTION!