



National surveillance of Clostridium difficile

Outline:

- **General surveillance**
- **Genotypic antimicrobial resistance**
- **Transmission study EpiLinks / sentinel reports?**

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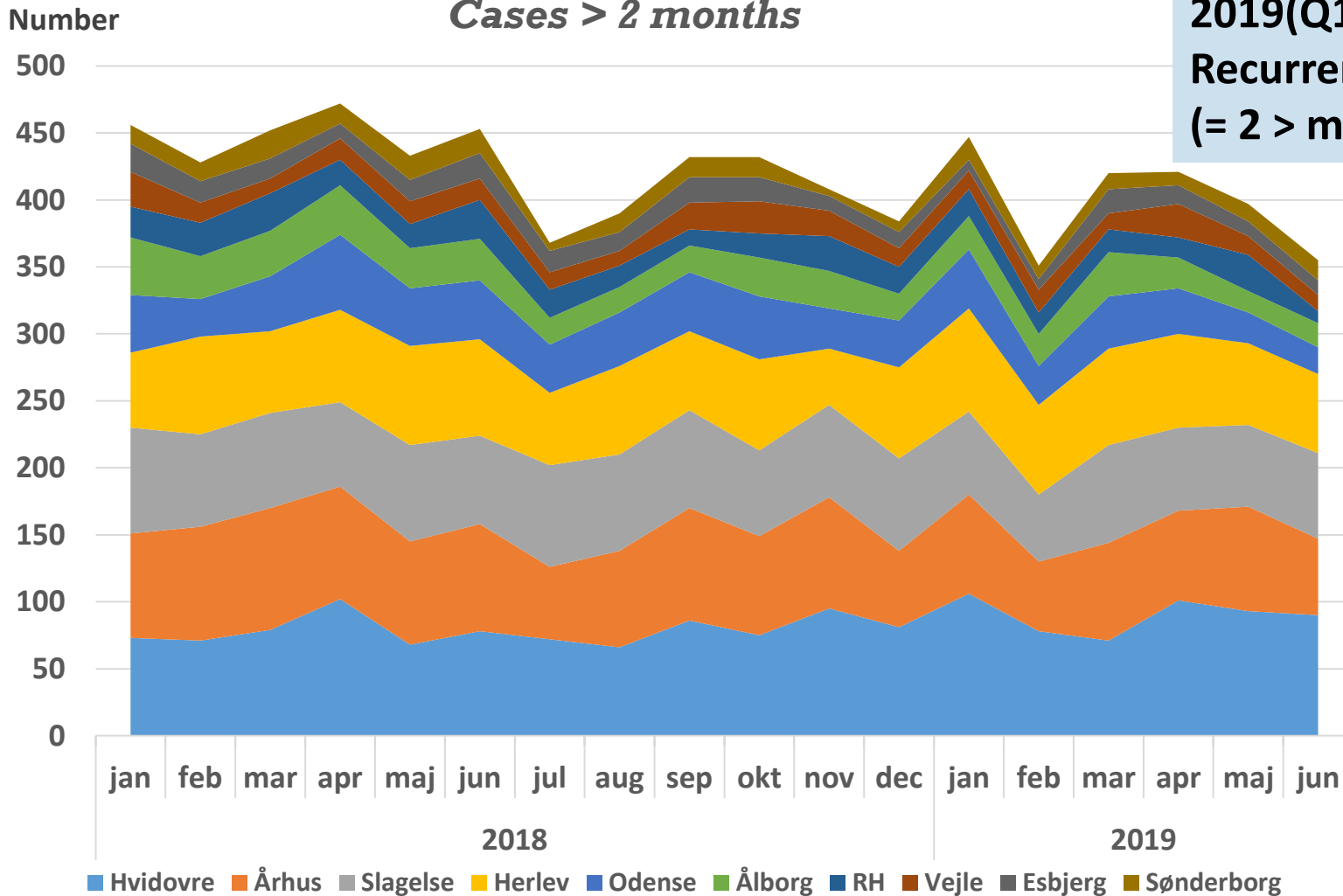
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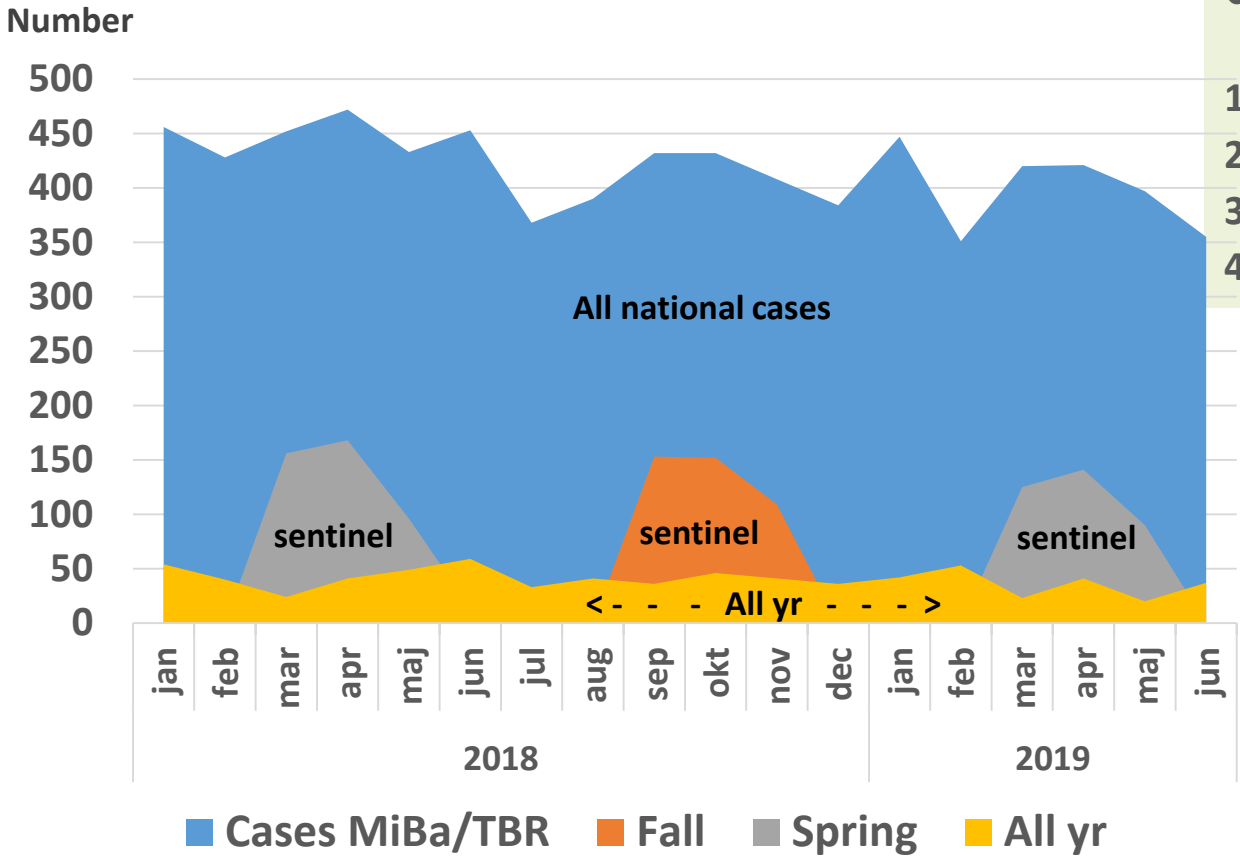
Cases 2018-19Q2 from MiBa/TBR

2018-19Q2: 7499
2018: 5108
2019(Q1+Q2): 2391
Recurrent: 2123 (28%)
(= 2 > months)

Cases > 2 months



National cases vs. cases for typing to SSI



- Danish Health Authority in 2008:
All year
- 1) Severe clinical outcome
- 2) Outbreak
- 3) Binary toxin positive
- 4) 027 (since 2012 data ok)

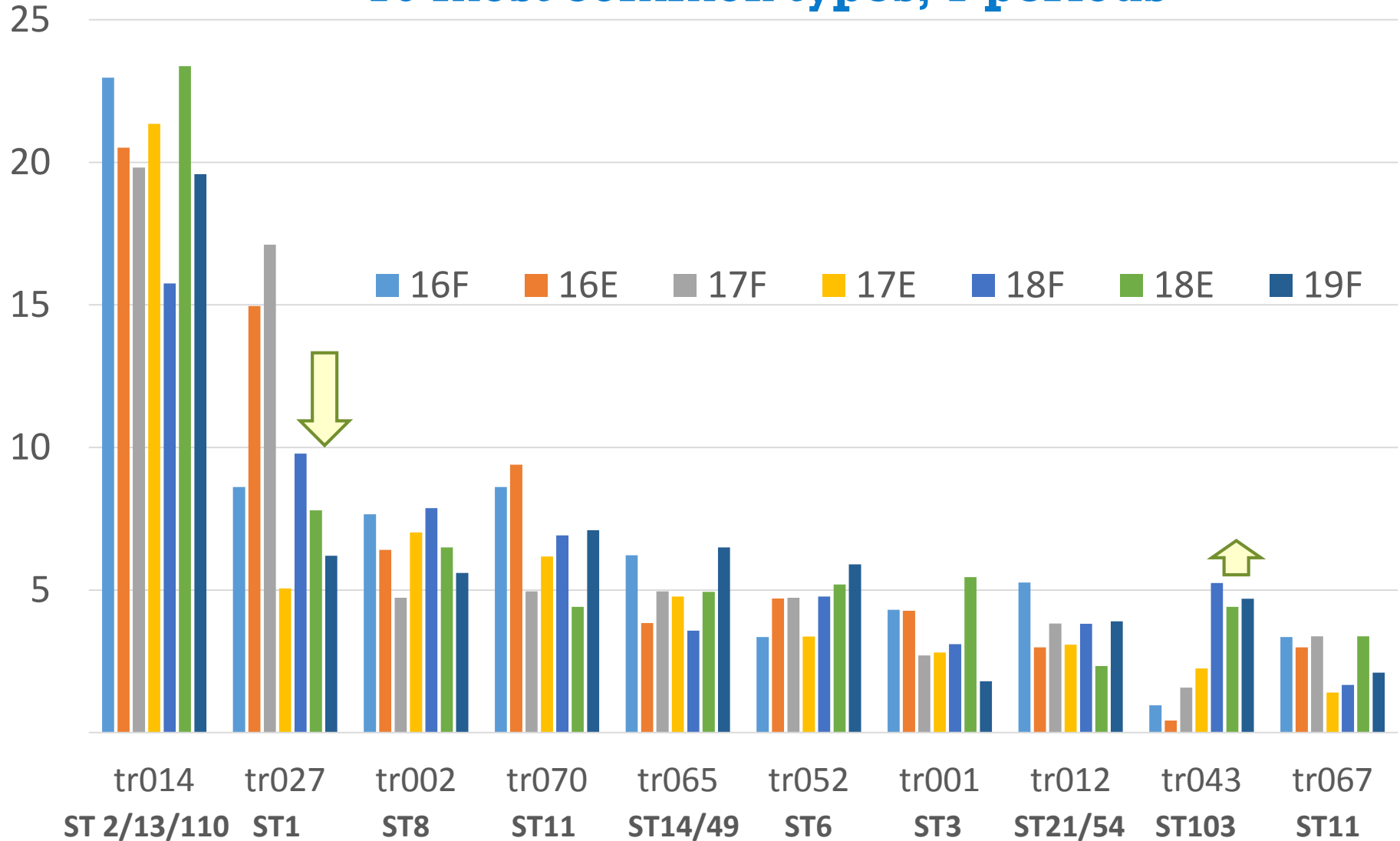
- Sentinel since 2016
All 10 DCM's, all toxigenic
1 month spring + fall
- 20108F: 495
2018E:414
2019F:295
2018-19Q2: all yr: 716
Non-cult: 198 (10%)
Total 1920

Case-definition: new type or new sample > 2 months

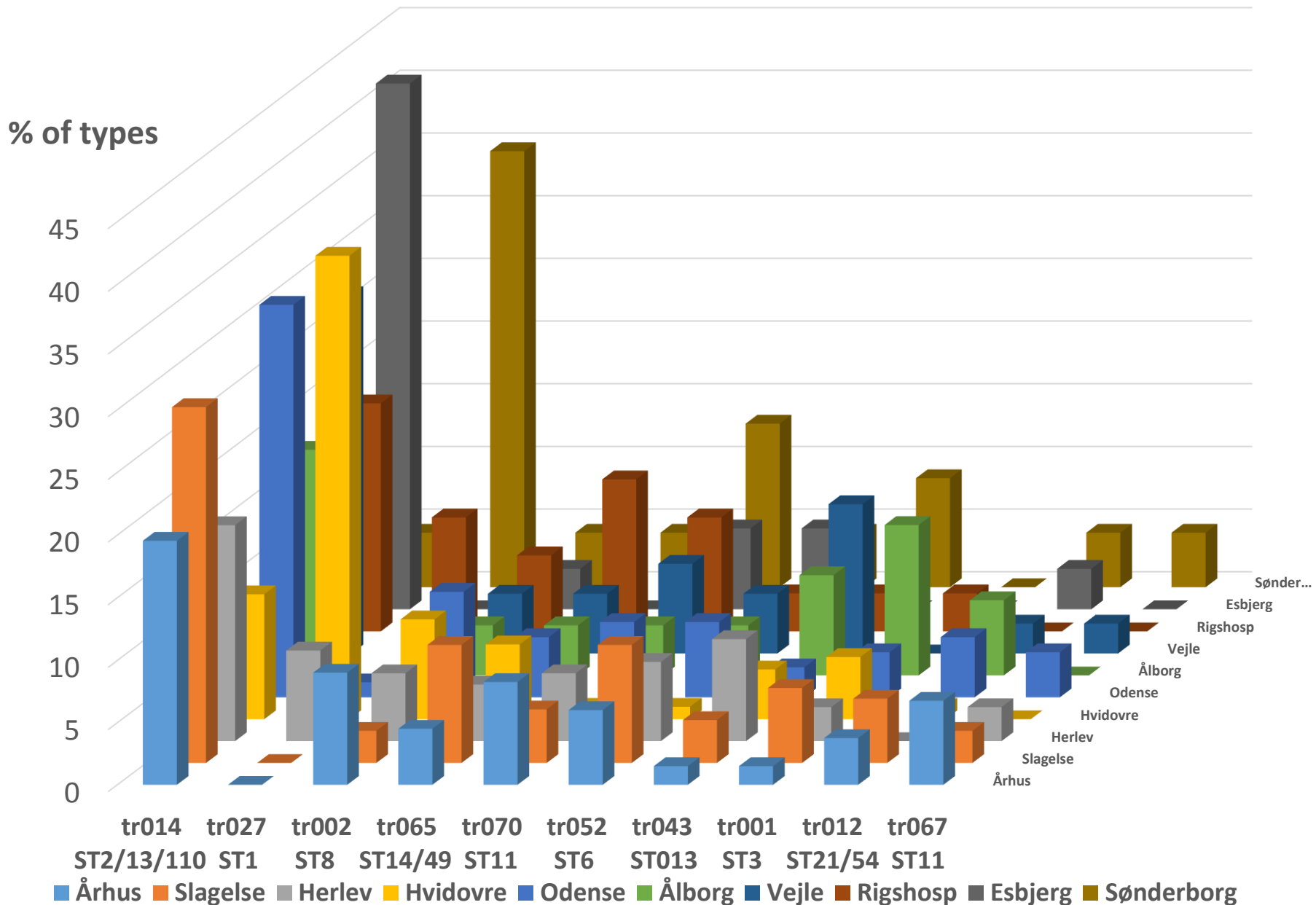
Sentinel 2016-19Q2: types vs. period

% of types in period

10 most common types, 7 periods



Sentinel 2018Q3–19Q2: Types vs. 10 DCMs



30 days mortality (crude!)

2016 sentineldata, 293 patients

ST	TRST	PCR ribotype*	Total number/ % of all	Binary toxin	Patient age Median/interval	% 30 days mortality	% 30 days mortality
2/13/110	014	RT014/RT053	93/22,5		70 (0-96)	10.7	13 → 8.9% (2016-18) 1836 pt.
8	002	RT002/RT159	27/6.5		59 (1-89)	8	
14/49	065	RT014	22/5.3		71 (1-87)	15.8	
6	052	RT117	18/4.4	negative	77 (7-92)	28.6	
21/54	012	RT012/RT053	17/4.1		79 (25-97)	30.8	
3	001	RT001	17/4.1		77 (20-96)	41.7	
9	028	RT081	10/2.4		72 (1-86)	11.1	
11	070	RT078	39/9.4		68 (31-95)	18.2	14.9 → 14.1% (2016-18) 1836 pt.
1	027	RT027	37/9.0	positive	78 (25-92)	19.4	
11	067	RT066	13/3.1		76 (28-91)	8.3	

1) Bioinfo: genes & point-mutations and 2) validate with phenotype

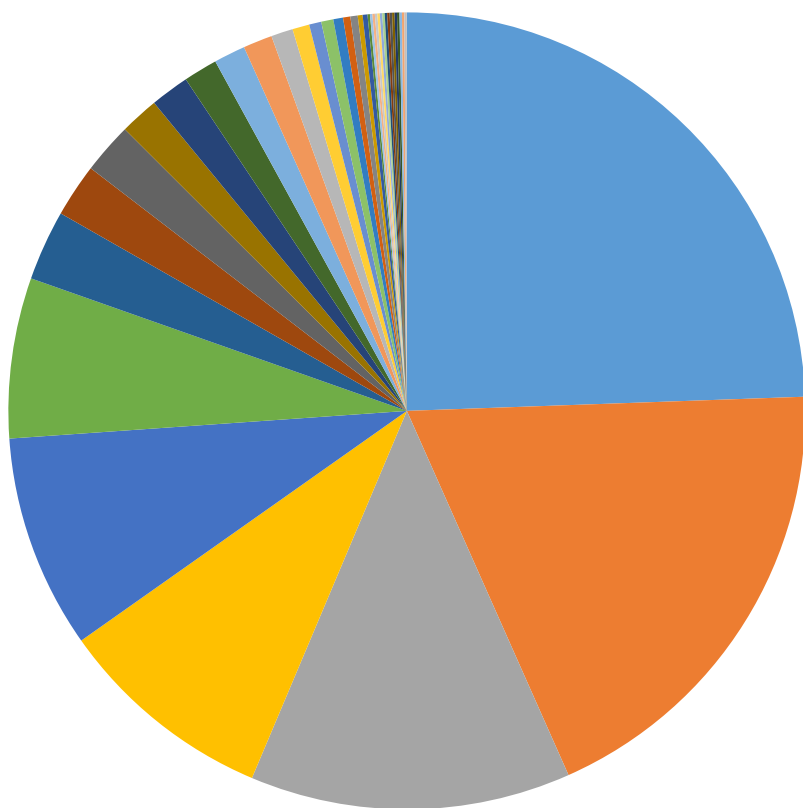
Antibiotic	Group	Target	Point-mutations
Clindamycin	Lincosamid	<i>ermB</i> (ResFinder)	NA
Erythromycin	Makrolid		
Metronidazole	Nitroimidazole	pCD-metro!	→ Germany, Spain, Czech, Poland
Moxifloxacin	Fluoroquinolone	<i>gyrA</i>	V43D, P116A D71E, D71V, D81N T82I, T82A, T82V A118S, A118T, A384D
		<i>gyrB</i>	S366A, R377G, S416A D426V, D426N, L444F R447K, E466V
Tetracyclin	Tetracyclin	<i>tetM</i> (ResFinder)	NA
Vancomycin	Glycopeptid	<i>murG</i> <i>rpoC</i>	murG: P108L rpoC: D244Y
Rifampicin	Rifamycin	<i>rpoB</i>	H502N, H502Y, H502R, H502L R505K, S488T, D492N, D492V S550F, S550Y, Q1073R

Phenotypic / genotypic AMR

	Compound	Phenotypic R/S	Genotypic R	Genotypic S	Agreement %
Validation 146 (55) isolates	Clindamycin	R=16	15	1	94
	(Lincosamide)	S=130	1	129	99
	Erythromycin	R=46	16	30 (027'ere)	35
	(macrolide)	S=100	0	100	100
	Moxifloxacin	R=38	37	1	97
	(fluorquinolone)	S=108	2	106	95
	Tetracyclin	R=3	2	1	67
	(tetracyclin)	S=52	11	41	80
	Rifampicin	R=13	13	0	100
	(rifampin)	S=133	2	131	98
"Validation" 146 isolates	Vancomycin	R=0	-	-	-
	(glycopeptide)	S=146	0	146	100
	Metronidazole	R=2	?	?	-
	(nitromidazole)	S=144	?	?	-
Only geno- typic AMR	Beta-lactam	Sulphonamide		Phenicol	
	Fosfomicin	Aminoglycoside		Quinolone	

Genotypic AMR profiles

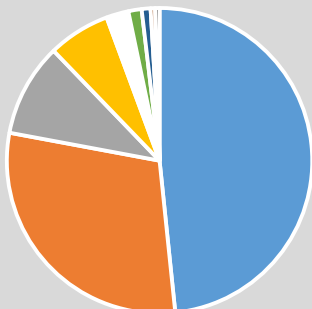
2275 isolates tested
1015 isolates genotypic resistant
for at least one compound



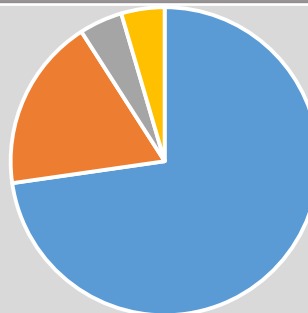
Fluoroquinolone aminoglycoside tetracycline	248
Fluoroquinolone	192
Fluoroquinolone aminoglycoside	132
Fluoroquinolone tetracycline	90
Fluoroquinolone macrolide aminoglycoside tetracycline	88
tetracycline	66
macrolide aminoglycoside tetracycline	29
macrolide	22
Fluoroquinolone Rifampicin aminoglycoside	21
macrolide aminoglycoside	16
Fluoroquinolone Rifampicin macrolide aminoglycoside tetracycline	16
Fluoroquinolone macrolide	14
macrolide tetracycline	13
Fluoroquinolone macrolide aminoglycoside	12
Rifampicin macrolide tetracycline	9
Fluoroquinolone macrolide aminoglycoside tetracycline phenicol	7
aminoglycoside tetracycline	5
aminoglycoside	5
Fluoroquinolone aminoglycoside tetracycline phenicol	4
Rifampicin	3
Fluoroquinolone Rifampicin macrolide	3
macrolide aminoglycoside phenicol	2
Fluoroquinolone macrolide tetracycline phenicol	2
macrolide aminoglycoside tetracycline phenicol	1
Fluoroquinolone macrolide tetracycline	1
Fluoroquinolone macrolide aminoglycoside phenicol	1
Fluoroquinolone aminoglycoside phenicol	1
Fluoroquinolone glycopeptide	1
Fluoroquinolone Rifampicin macrolide tetracycline phenicol	1
Fluoroquinolone macrolide aminoglycoside glycopeptide tetracycline	1
beta-lactam aminoglycoside	1
macrolide fosfomycintetracycline	1
Fluoroquinolone tetracycline phenicol	1
Rifampicin macrolide aminoglycoside tetracycline phenicol	1
glycopeptide	1
beta-lactam aminoglycoside quinolone sulphonamide tetracycline	1
Fluoroquinolone Rifampicin aminoglycoside tetracycline	1
Fluoroquinolone phenicol	1
Fluoroquinolone Rifampicin	1

Genotypic AMR in most common types

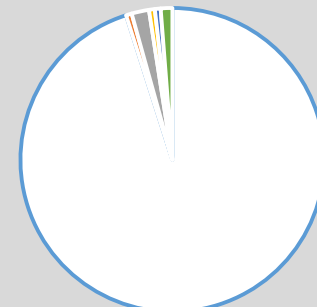
ST1/027+
215 isolates
5 sensitive



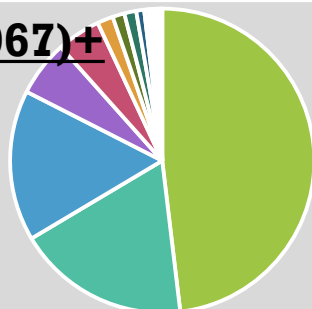
ST37 (rt017)
22 isolates
0 sensitive



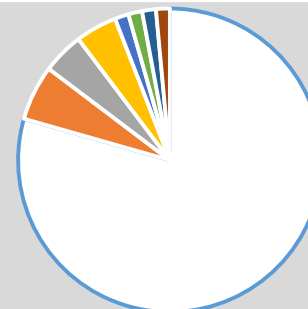
ST5 (tr016)+
164 isolates
162 sensitive



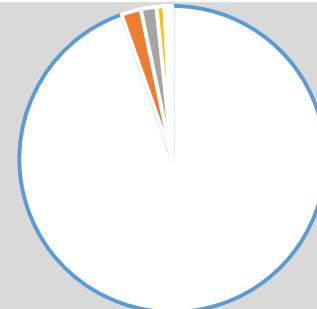
ST11(tr070/067)+
474 isolates
0 sensitive



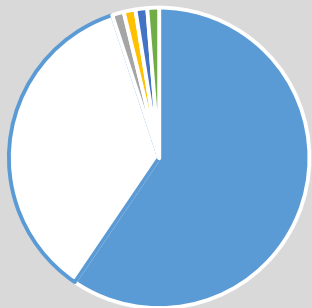
ST3 (tr001)
68 isolates
54 sensitive



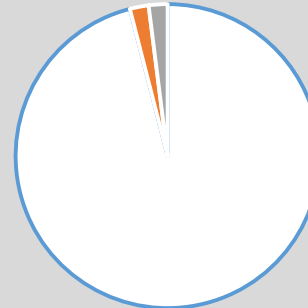
ST2 (tr014)
241 isolates
228 sensitive



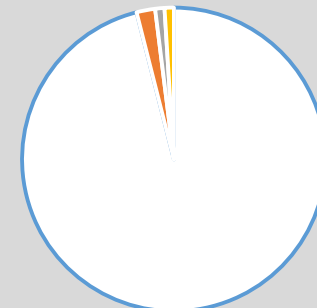
ST103(tr043)
79 isolates
28 sensitive



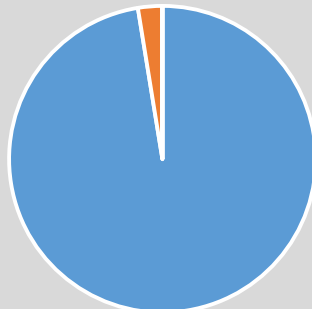
ST14 (tr065)
50 isolates
48 sensitive



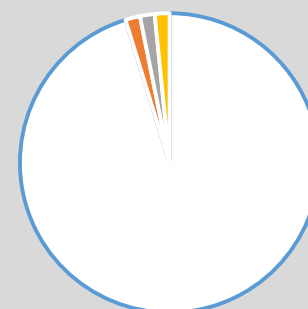
ST6(tr052)
101 isolates
97 sensitive



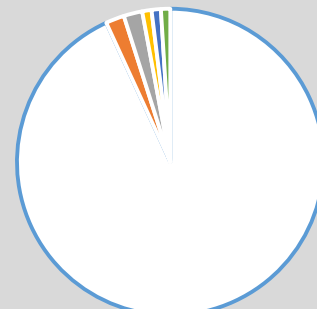
ST17 (tr005)
39 isolates
0 sensitive



ST13 (tr014)
63 isolates
60 sensitive



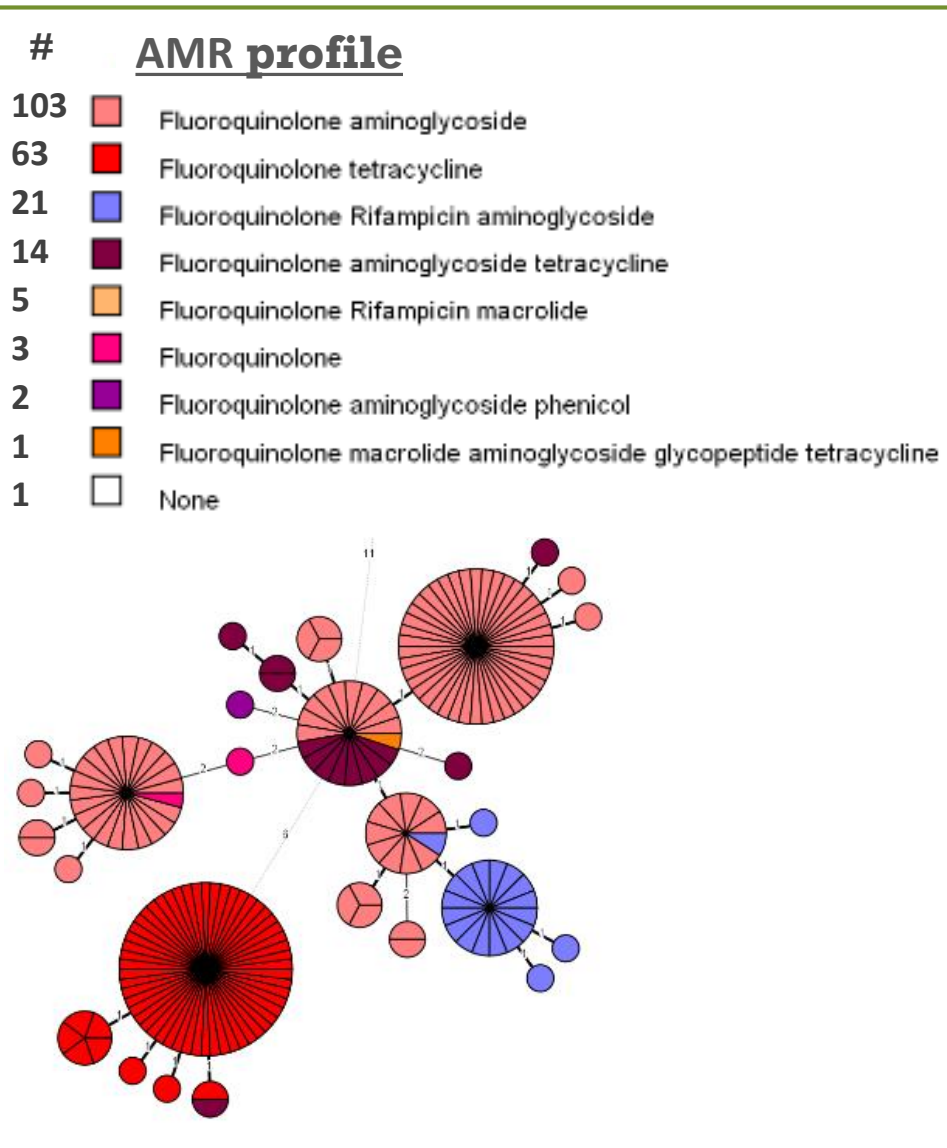
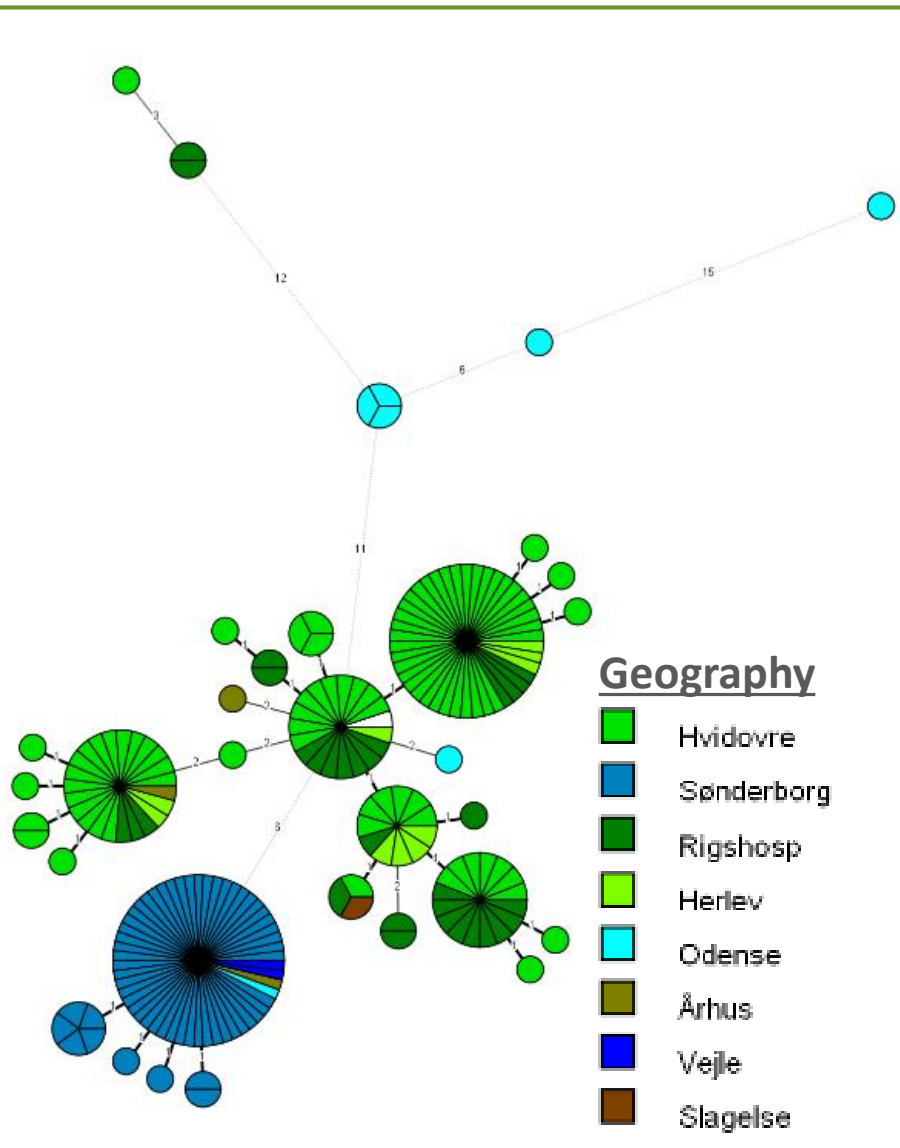
ST8 (tr002)
102 isolates
95 sensitive



ST1/027 MST: Geography and AMR profiles

2018-19Q2 (213 isolates)

OBS: ERY pheno. pos. /geno. neg

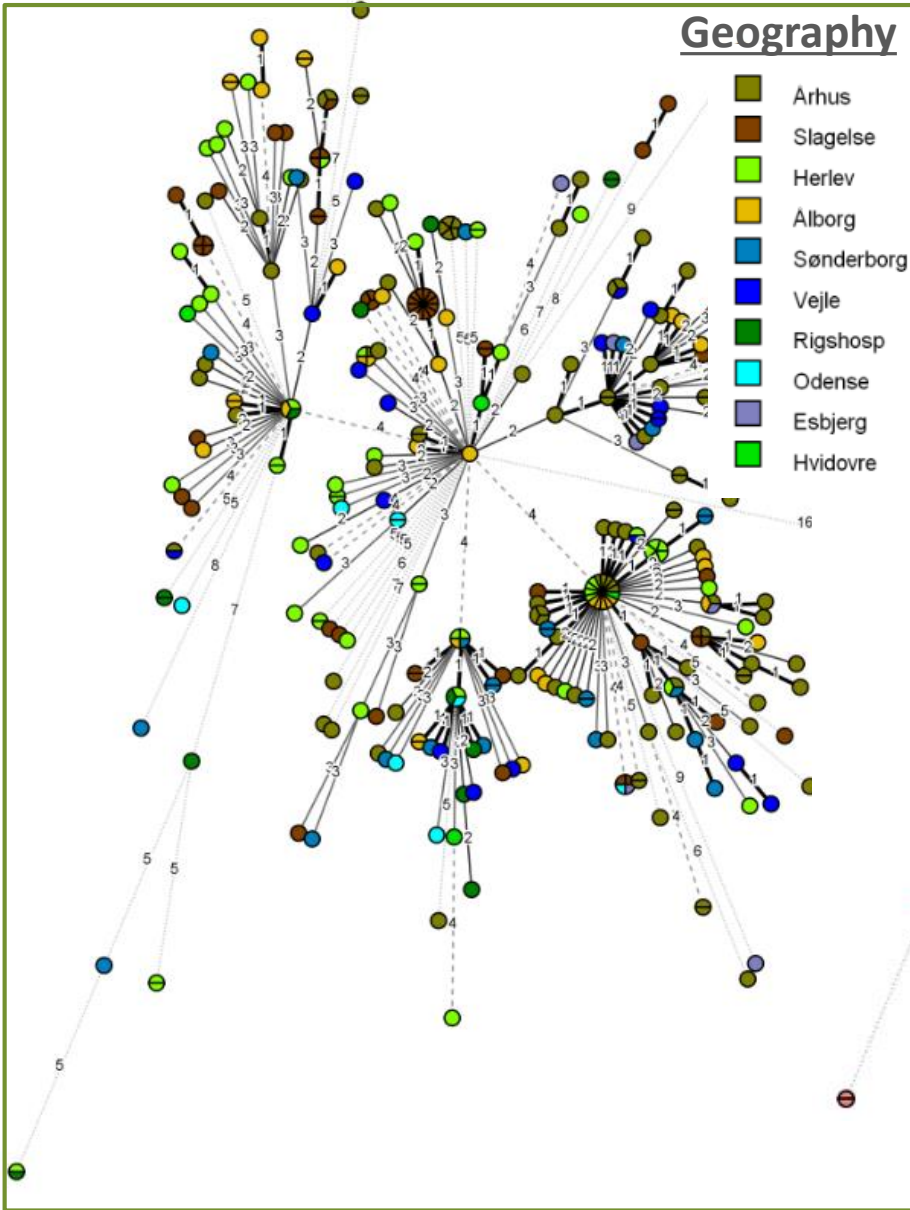


ST11(tr070) MST: geography and AMR profiles

2018-19Q2 (329 isolates)

Geography

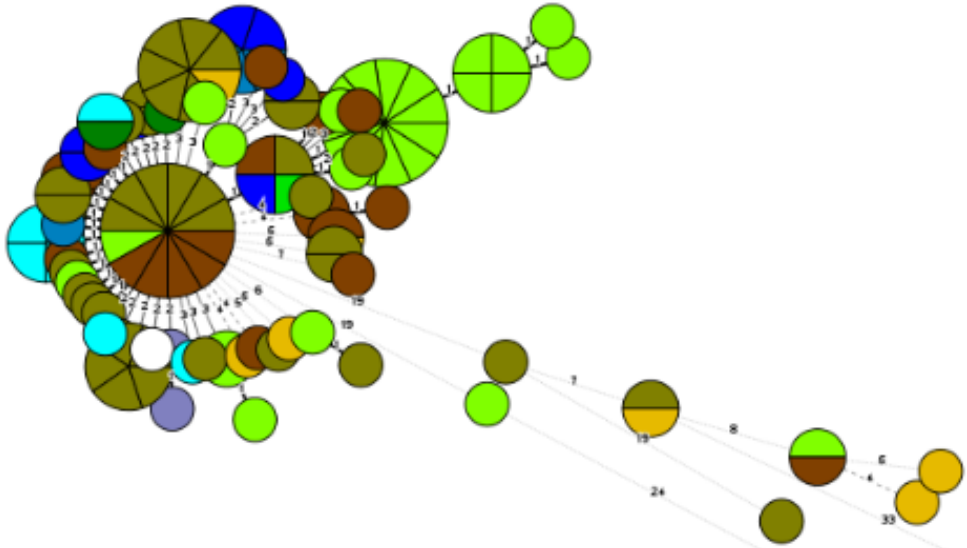
- Arhus
- Slagelse
- Herlev
- Alborg
- Sønderborg
- Vejle
- Rigshosp
- Odense
- Esbjerg
- Hvidovre



AMR profile

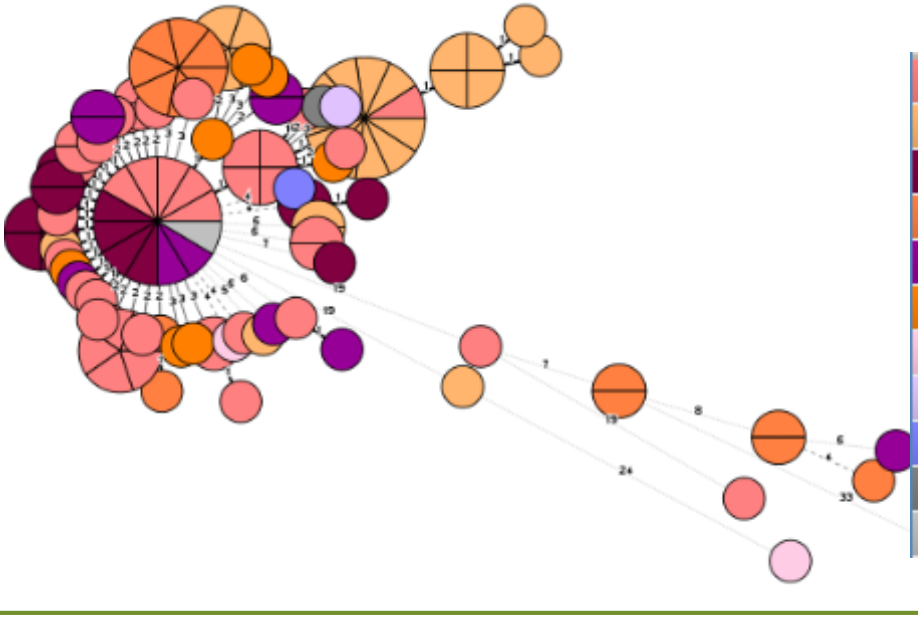
203	Fluoroquinolone aminoglycoside tetracycline
46	Fluoroquinolone macrolide aminoglycoside tetracycline
38	Fluoroquinolone
17	Fluoroquinolone aminoglycoside
6	Fluoroquinolone tetracycline
5	Fluoroquinolone macrolide aminoglycoside tetracycline phenicol
4	Fluoroquinolone aminoglycoside tetracycline phenicol
4	Fluoroquinolone macrolide
2	Fluoroquinolone macrolide tetracycline phenicol
1	Fluoroquinolone tetracycline phenicol
1	Fluoroquinolone Rifampicin aminoglycoside tetracycline
1	Fluoroquinolone glycopeptide
1	Fluoroquinolone macrolide aminoglycoside

ST11(tr067) MST: geography and AMR profiles














Geography 2018-19Q2 (124 isolates)

	42	Århus
	30	Herlev
	21	Slagelse
	7	Odense
	7	Vejle
	7	Ålborg
	4	Sønderborg
	2	Rigshosp
	2	Esbjerg
	1	Hvidovre



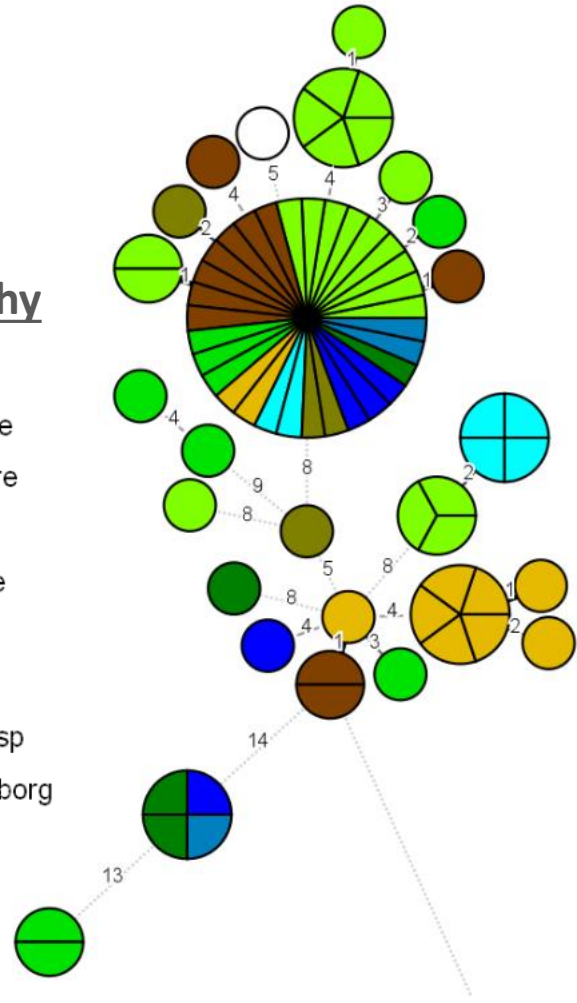
AMR profile

	44	Fluoroquinolone
	26	Fluoroquinolone macrolide aminoglycoside tetracycline
	16	Fluoroquinolone tetracycline
	14	Fluoroquinolone aminoglycoside tetracycline
	11	Fluoroquinolone aminoglycoside
	7	Fluoroquinolone macrolide aminoglycoside
	2	Fluoroquinolone macrolide
	1	Fluoroquinolone macrolide aminoglycoside phenicol
	1	Fluoroquinolone macrolide aminoglycoside tetracycline phenicol
	1	Fluoroquinolone phenicol
	1	Fluoroquinolone macrolide tetracycline

ST103(tr043) MST: geography and AMR profiles

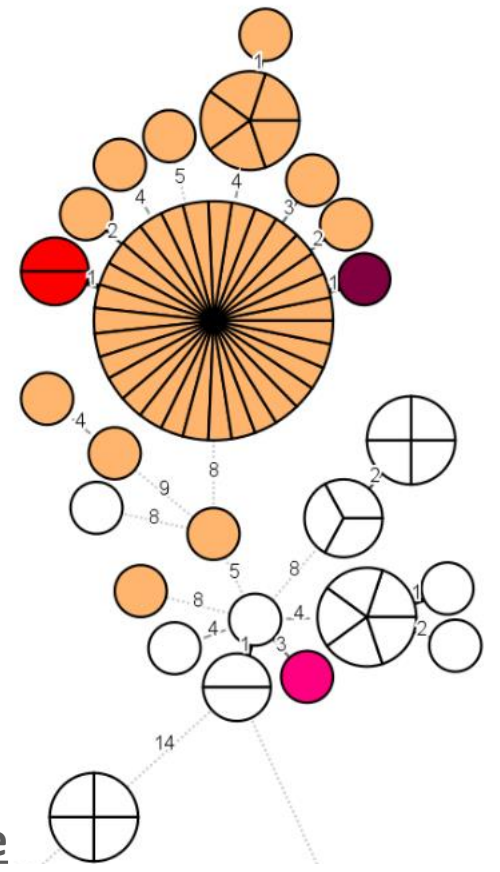
Geography

- Herlev
- Slagelse
- Hvidovre
- Ålborg
- Odense
- Århus
- Vejle
- Rigshosp
- Sønderborg



AMR profile

- 47 tetracycline
- 1 Fluoroquinolone tetracycline
- 1 macrolide aminoglycoside tetracycline
- 1 macrolide fosfomycin tetracycline
- 28 None



Generic “base R” software tool (“Shiny” tool package)
(Under development)

Input:

- Grouping with WGS-based data (MLST/cgMLST)
- patient location information (National or local, LPR2)
- Other epidemiological data (sample date, death ect..)

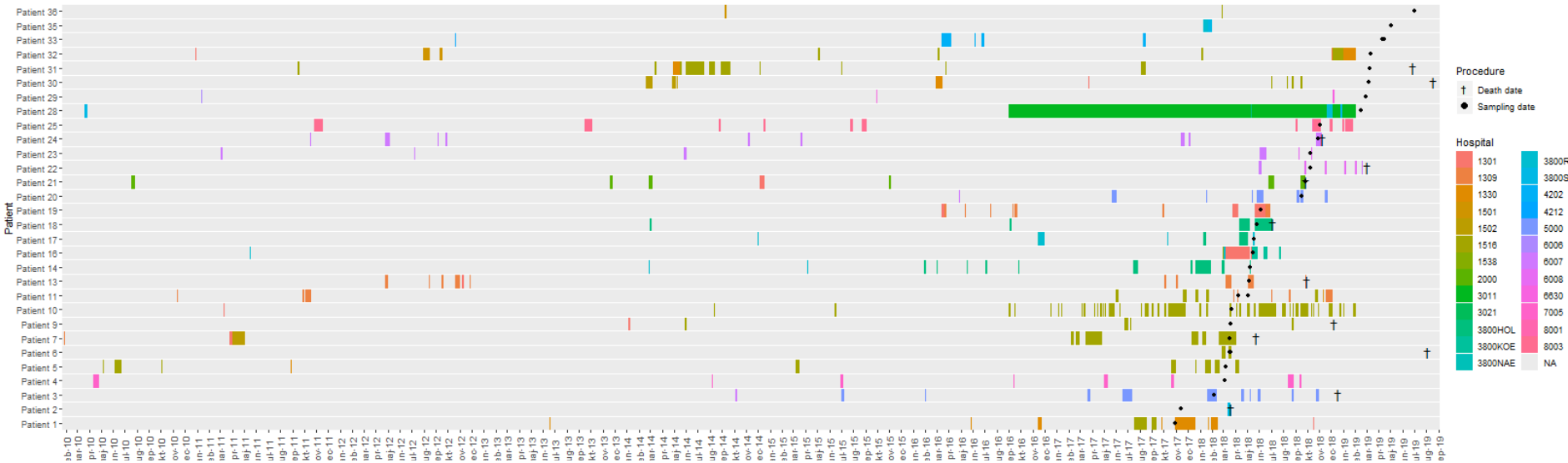
Developed by:

Anna Emilie Henius
&
Henrik Hasman
Statens Serum Institut

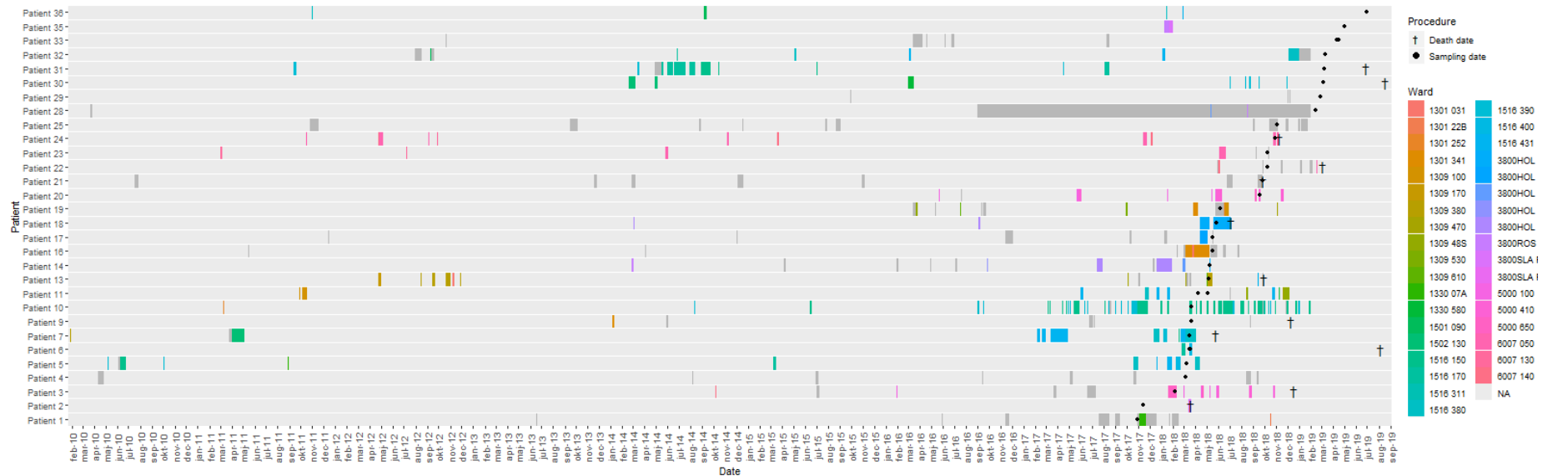
EpiLinX, ST103, tr043, 2010-2019



Overlaps at hospital level

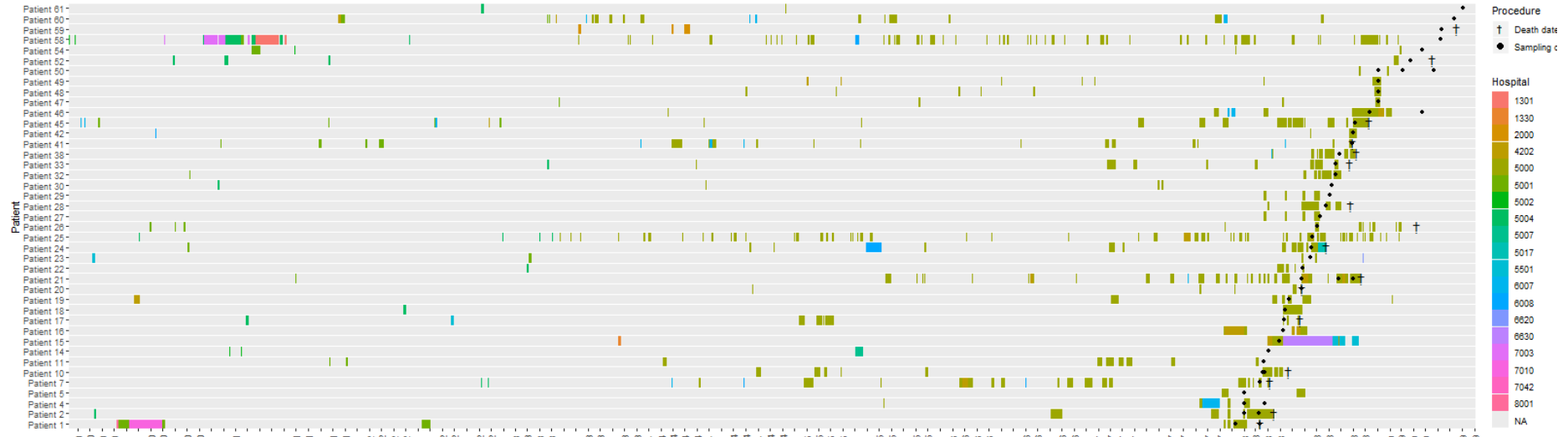


Overlaps at ward level

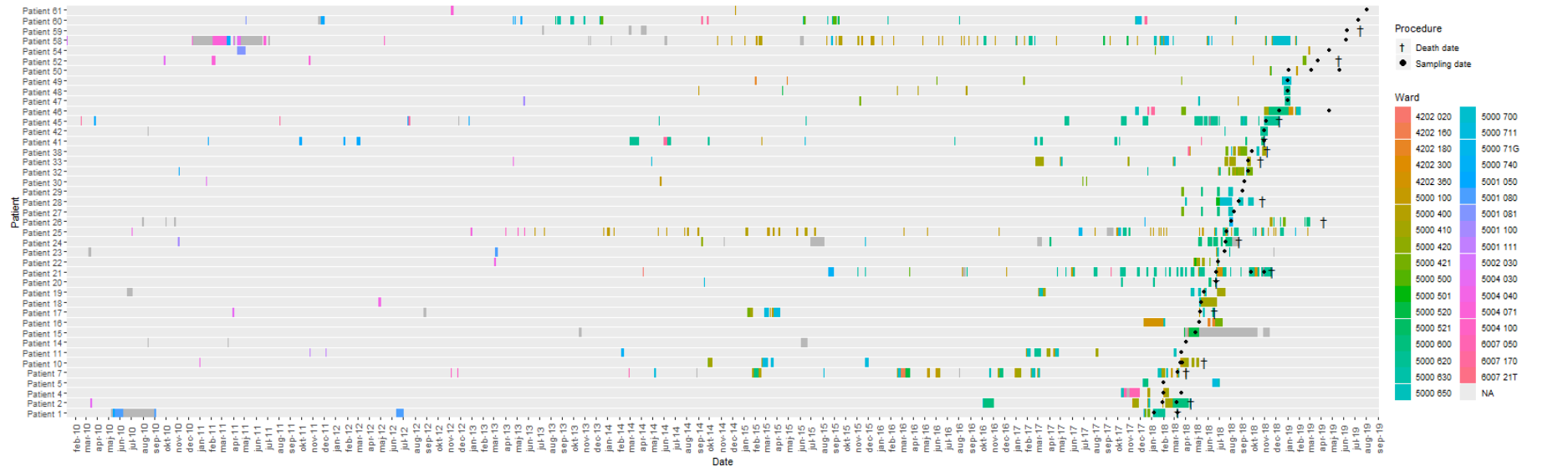


EpiLinX, 027-South, 2010-2019

Overlaps at hospital level

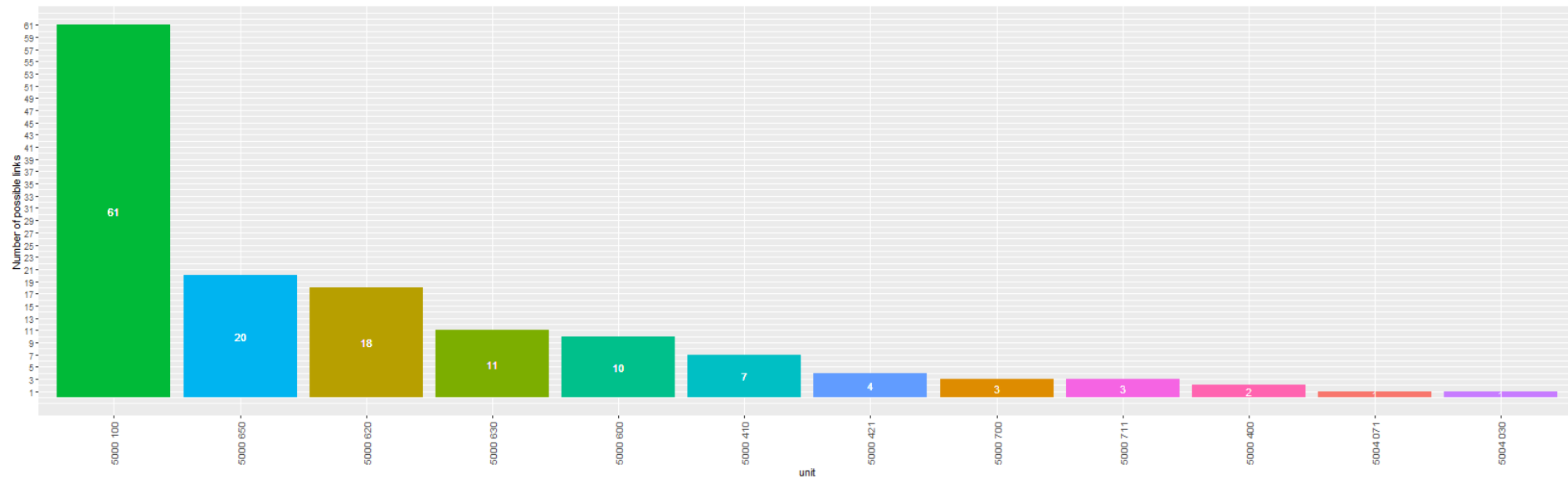


Overlaps at ward level



EpiLinX, 027-South, 2010-2019

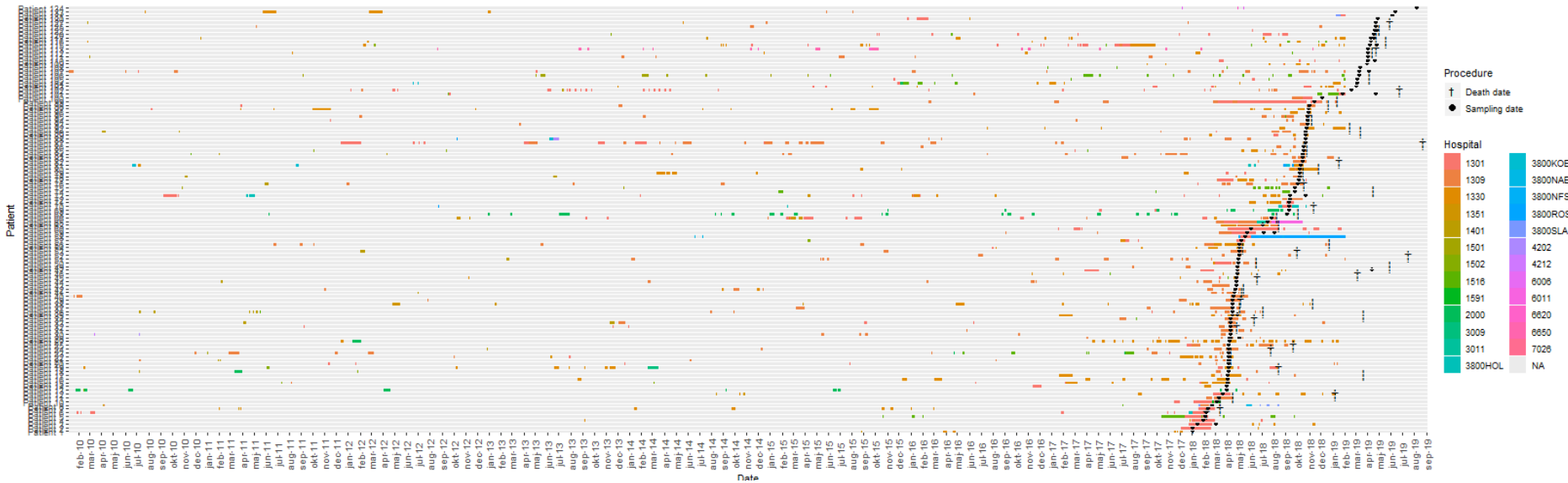
Unique patient visits per unit



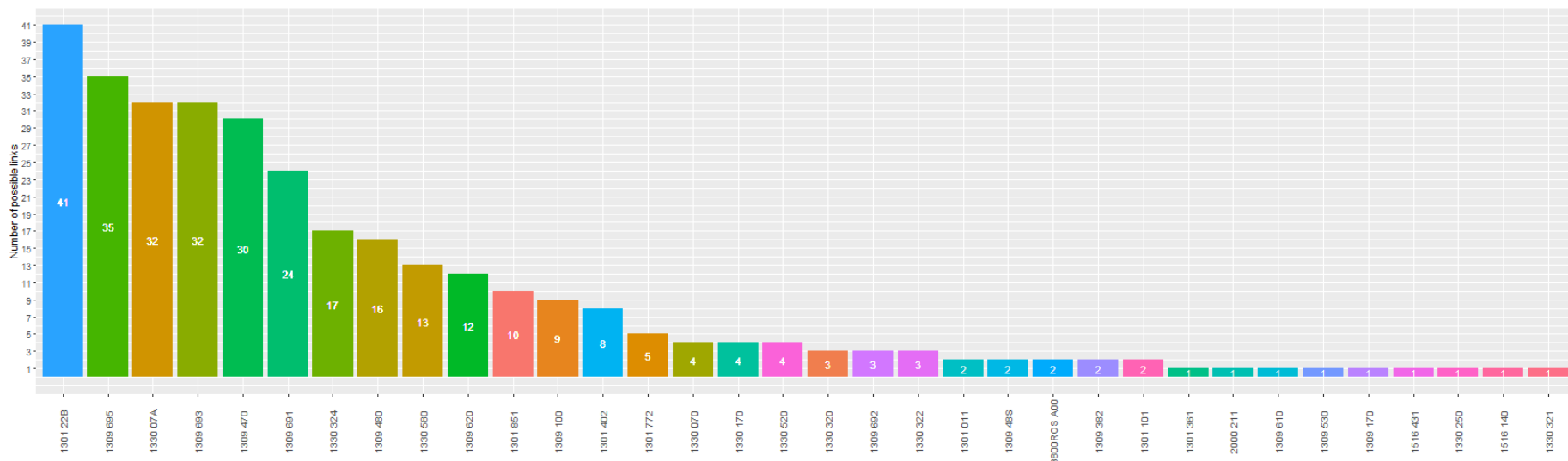
Patient overlap at hospital unit for possible transmission
Future: any hospital unit with any patient with the particular type

EpiLinX, 027-HS, 2010-2019

Overlaps at hospital level



Unique patient visits per unit



Data back to DCMs



ST	Herlev	Hvidovre	Rigshosp	Hovedtotal
Ingen vækst	15	30	3	48
11	27	1	6	34
1	4	22	5	31
103	10	4	1	15
2	6	6	3	15
5	10	1	1	12
6	5	1	1	7
8	3	4		7
17	2	4		6
14	2		2	4
3		4		4
-	3			3
19	1	2		3
42	1		2	3
13	1	2		3
37		3		3
36	1	1		2
28			2	2
16	2			2
34	2			2
512	2			2
35		2		2
26	1	1		2
431*			1	1
223	1			1
133		1		1
54			1	1
44	1			1
55		1		1
129		1		1
58	1			1
Hovedtotal	105	96	29	230

wgMLST (<All Characters>)

