

“WGS – Når tid er liv”

(“WGS – Data for action in Real-time?”)

...med fokus på *Carbapenemase Producerende Enterobakterier* (CPE)



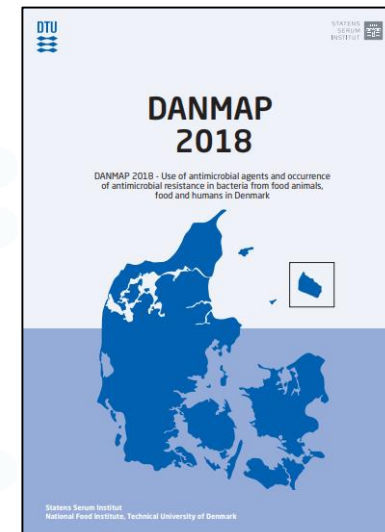
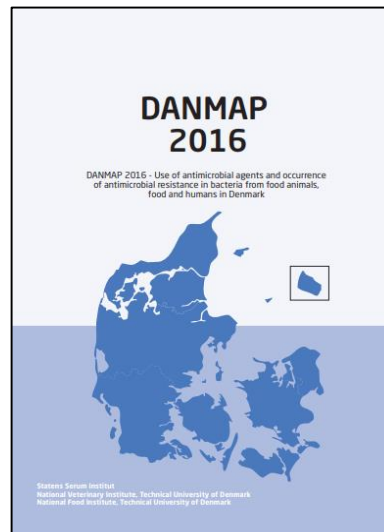
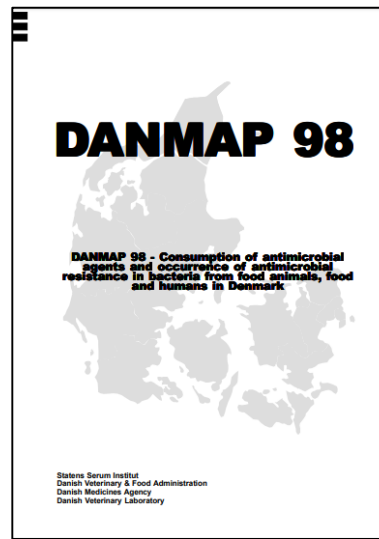
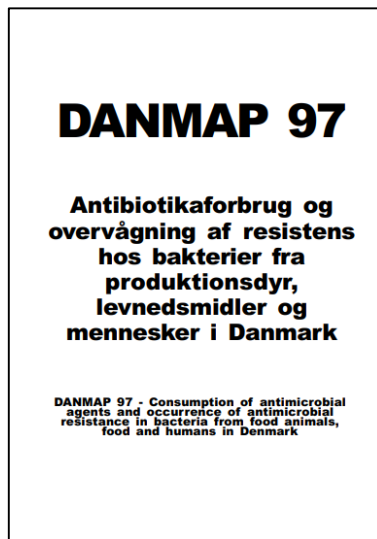
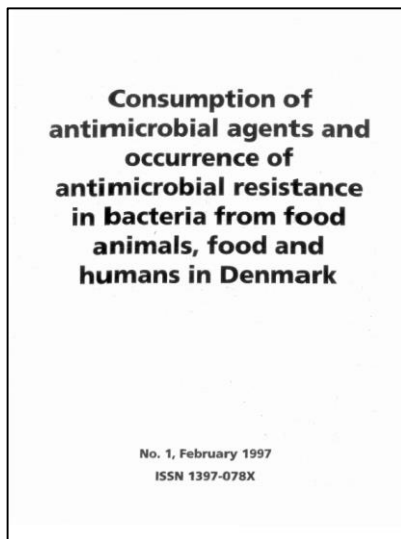
Henrik Hasman
Statens Serum Institut
København

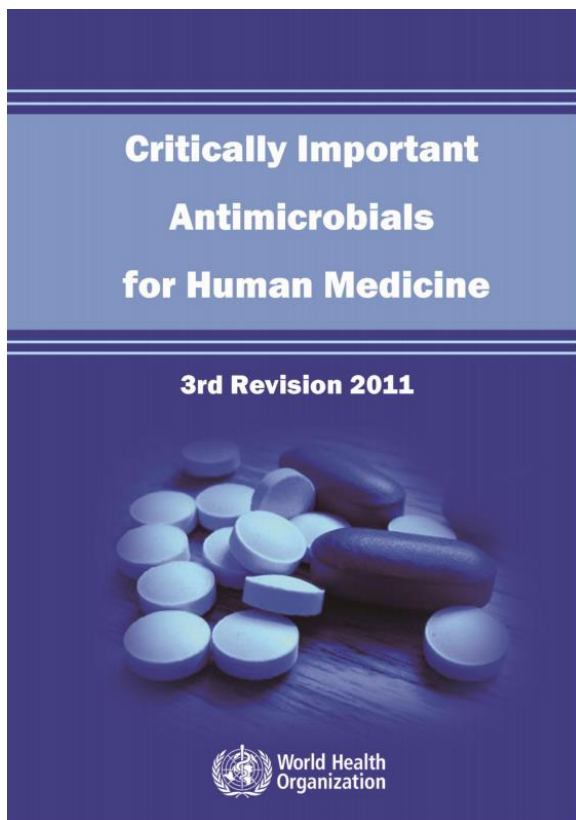


TIDSOPFATTELSE ER RELATIVT... “REAL-TID”?



OVERVÅGNING TAGER DEN TID, DEN TAGER...





Før november 2015

- Aminoglykosider (Gentamicin)
- Cephalosporiner (Cefuroxime)
- Carbapenemer (Meropenem)
- Fluoroquinoloner (Ciprofloxacin)
- Glycopeptider (Vancomycin)

Efter november 2015

+ Polimoxin E (Colistin)

- ❖ **Carbapenemer** bruges til at behandle alvorlige infektioner med multi-resistente bakterier så som:
 - ESBL producerende Enterobakterier (*Klebsiella*, *E. coli*, *Enterobacter*)
 - multi-resistente *Acinetobacter* spp. Og *Pseudomonas* spp.
- ❖ **Carbapenem-resistente bakterier** er derfor en stor udfordring for behandlingen af infektioner.
 - Dette efterlader kun få, eller ingen, behandlingsalternativer, evt. suppleret med colistin og/eller fosfomycin.
- ❖ Ofte er resistente bakterier **Carbapenem-resistent Enterobacteriaceae (CRE)**.
- ❖ **Carbapenem-resistente bakterier** er en stor udfordring for behandlingen af infektioner i Danmark.
- ❖ Man kan se et billede af **Carbapenem-resistente bakterier** (CRE) i mikroskop.
- ❖ Carbapenem-resistente bakterier er sjældne i Enterobakterier.
- ❖ Der ses især høje niveauer af CRE på hospitaler i Sydeuropa, Mellemøsten/Nordafrika og Asien.

Carbapenem-resistent Enterobacteriaceae (CRE)

Type: Bacteria

Also known as: Nightmare bacteria

About: CRE are a major concern for patients in healthcare facilities. Some Enterobacteriaceae (a family of germs) are resistant to nearly all antibiotics, leaving more toxic or less effective treatment options.

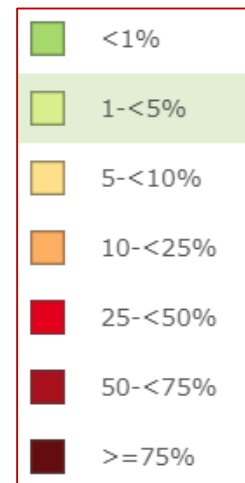
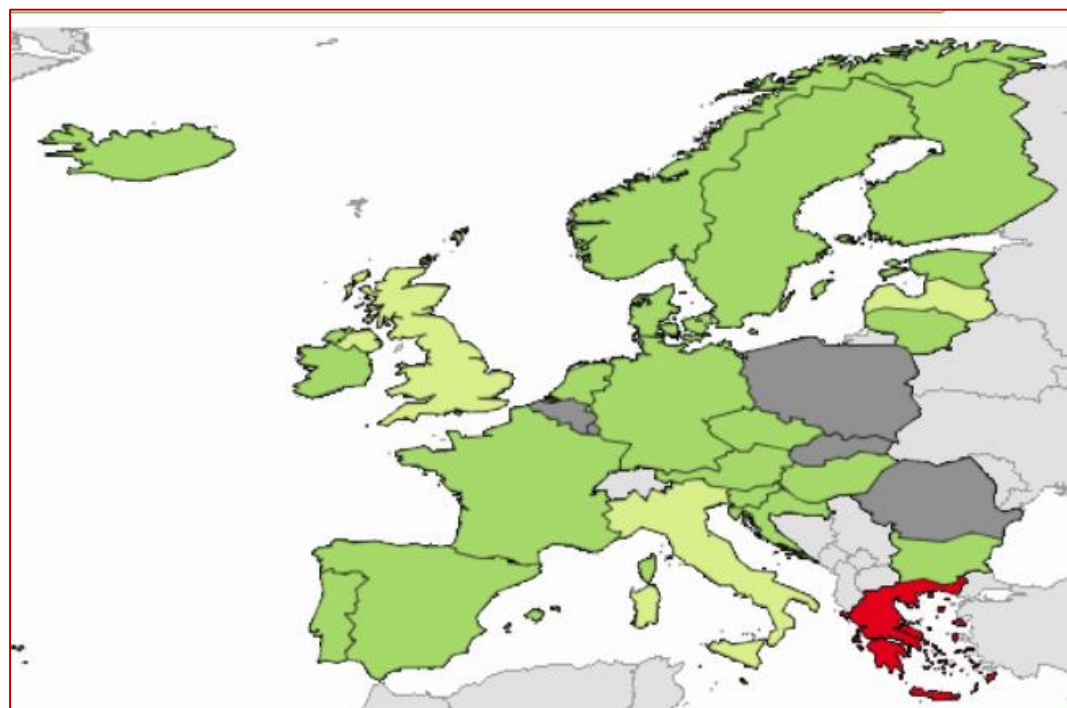
Estimated cases in hospitalized patients in 2017: 13,100

Estimated deaths in 2017: 1,100

Learn more: [CDC's CRE website](#)

Download data: [CRE Pathogen Page](#) [PDF - 2 pages]

CPE KLEBSIELLA PNEUMONIAE 2008 -2018



2018

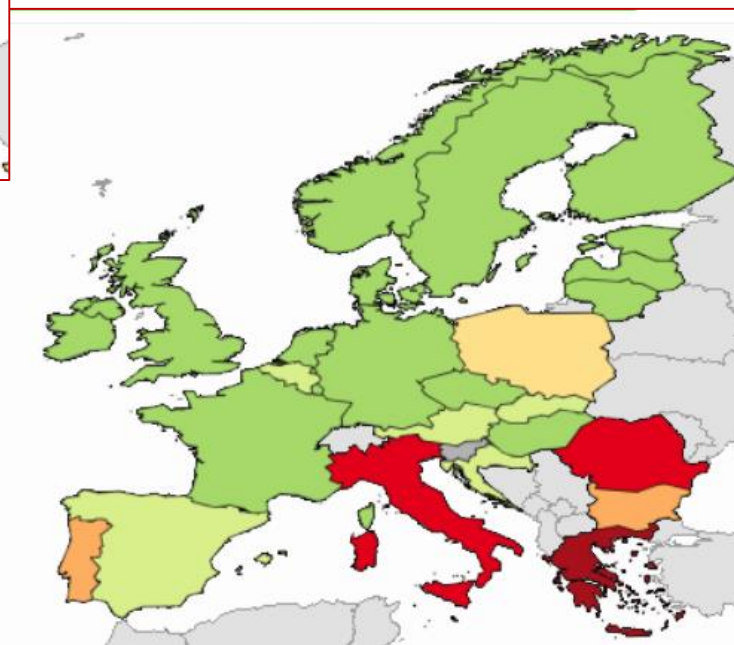
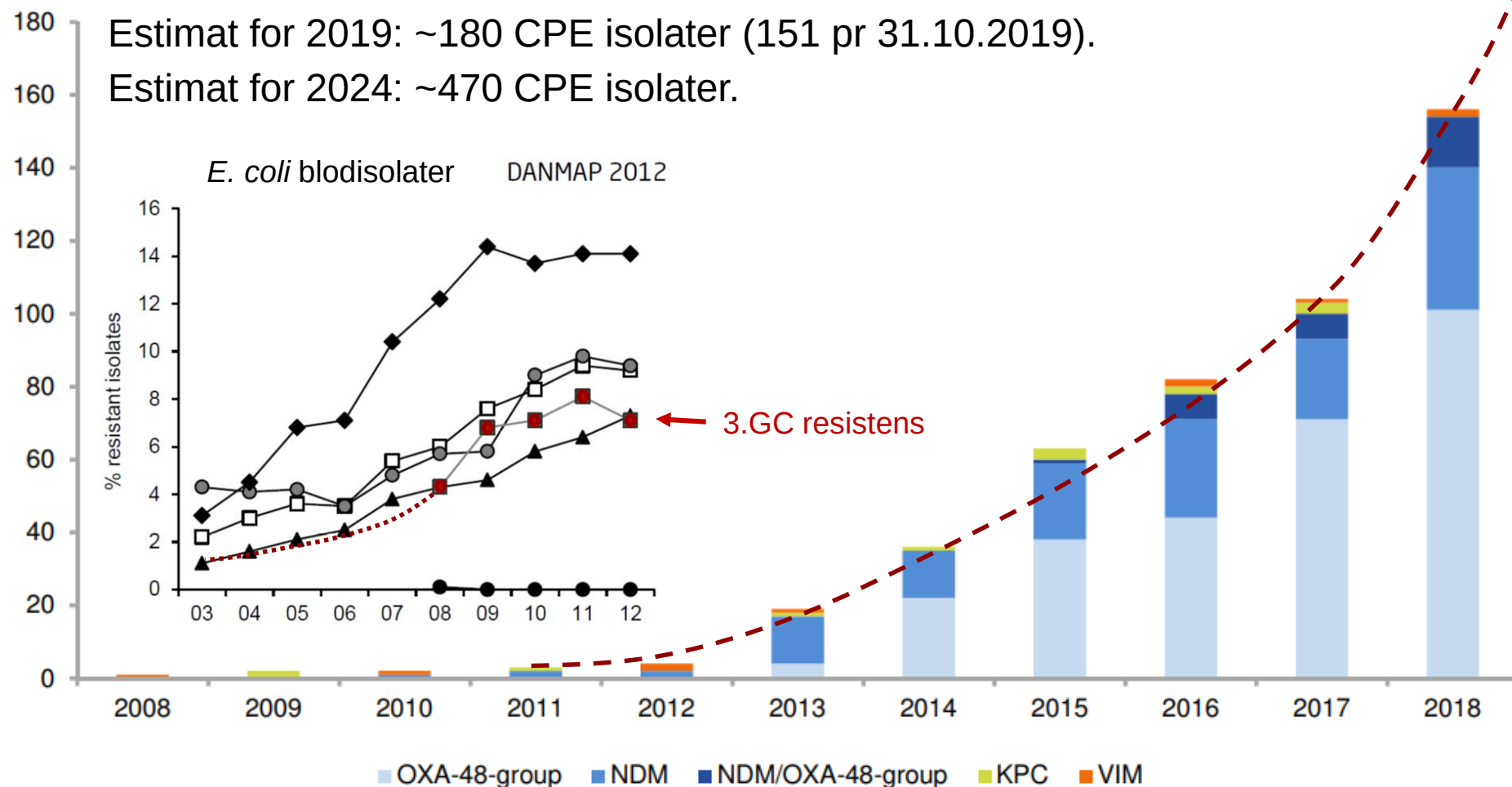
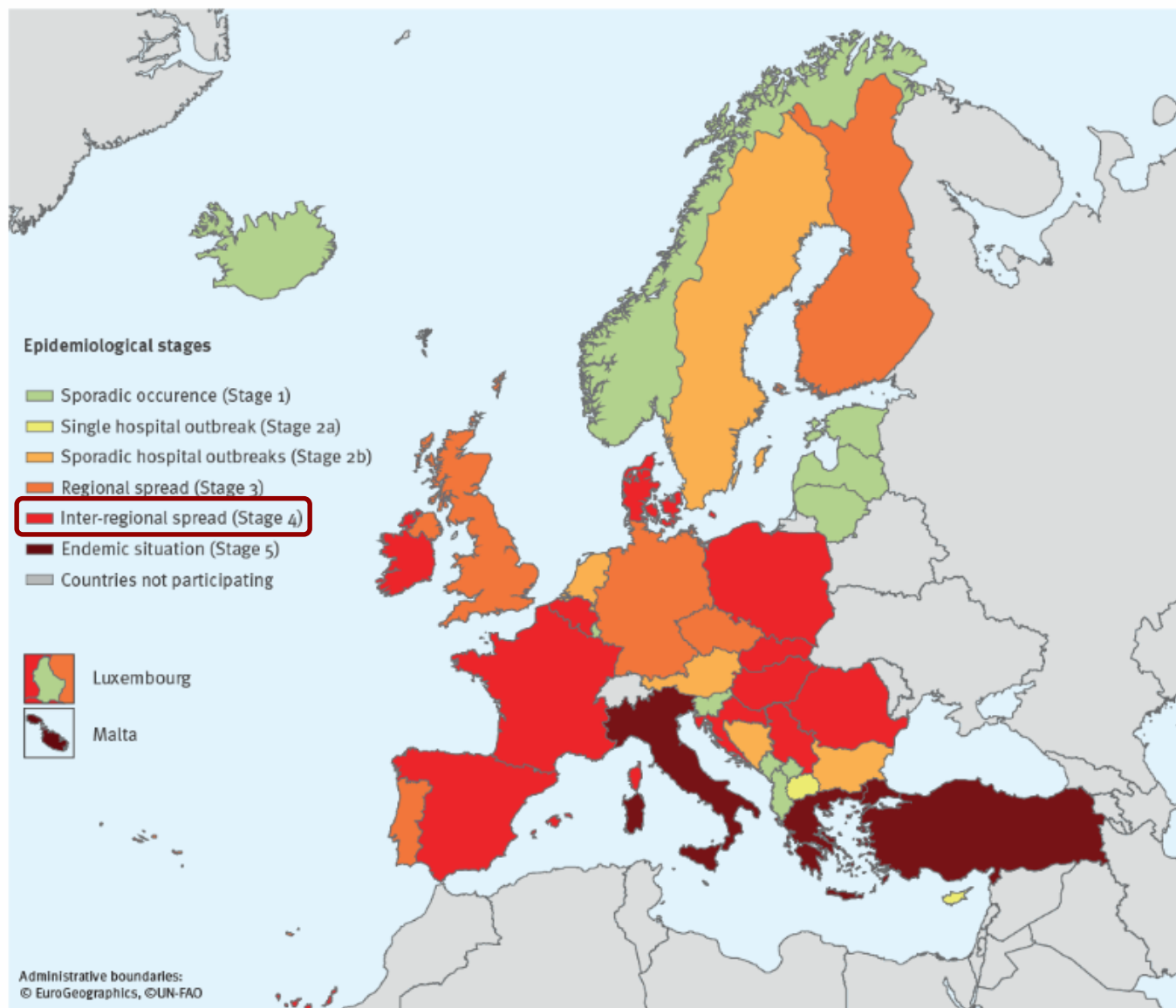


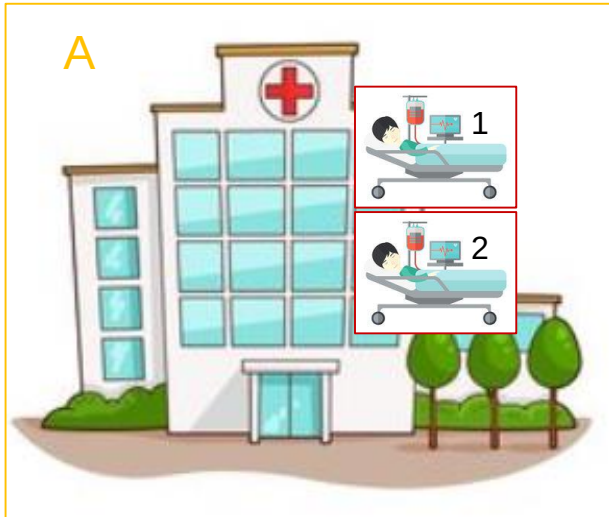
Figure 8.13 Numbers of carbapenemase-producing Enterobacterales (CPE), 2008-2018, Denmark







Hospital A Afdeling A1



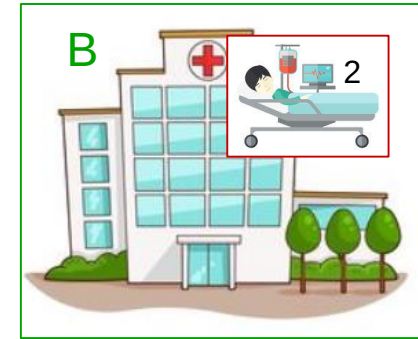
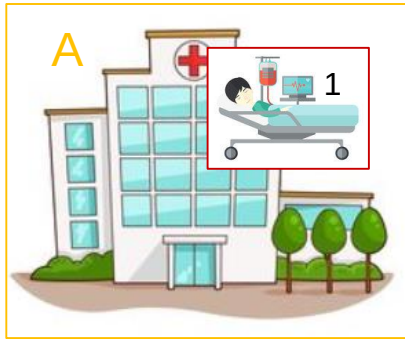
E. coli
CPE



E. coli
CPE

- Isolation CPE-positive patient(er)
- Screening af indlagte medpatienter ved 1. CPE fund
- Lokale opfølgning for at identificere mulige brud på hygieneregler
- Lokale epidemiologiske undersøgelser

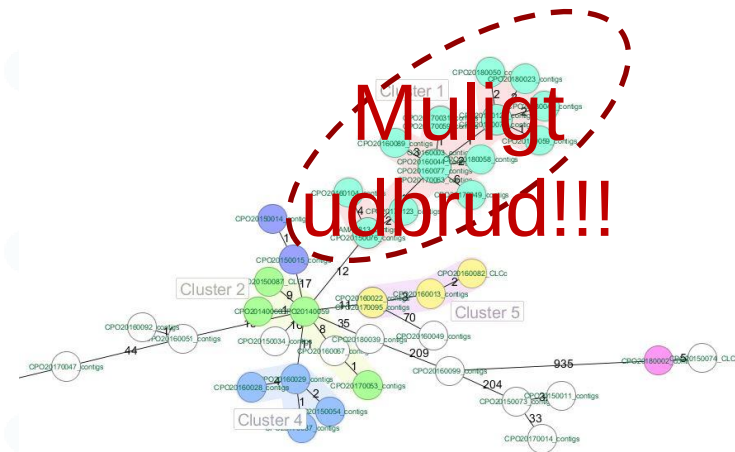
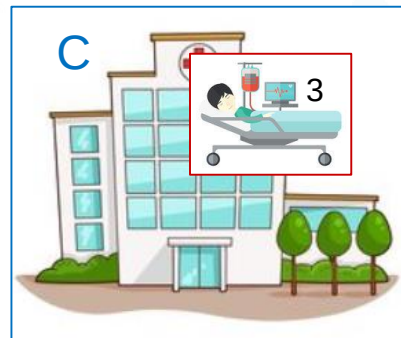
THE COMPLICATED (REGIONAL) OUTBREAK SITUATION



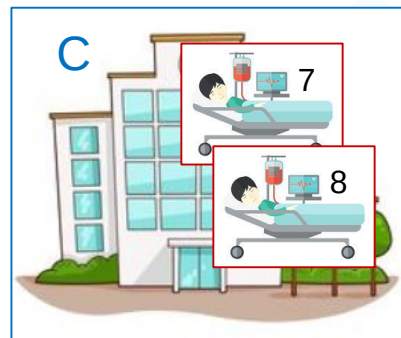
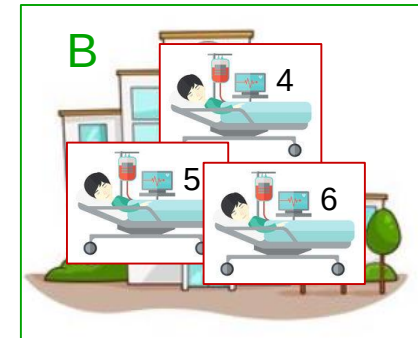
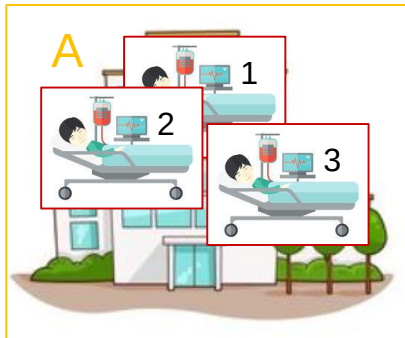
E. coli
CPE



E. coli
ST1 (CT1)
*bla*NDM-1



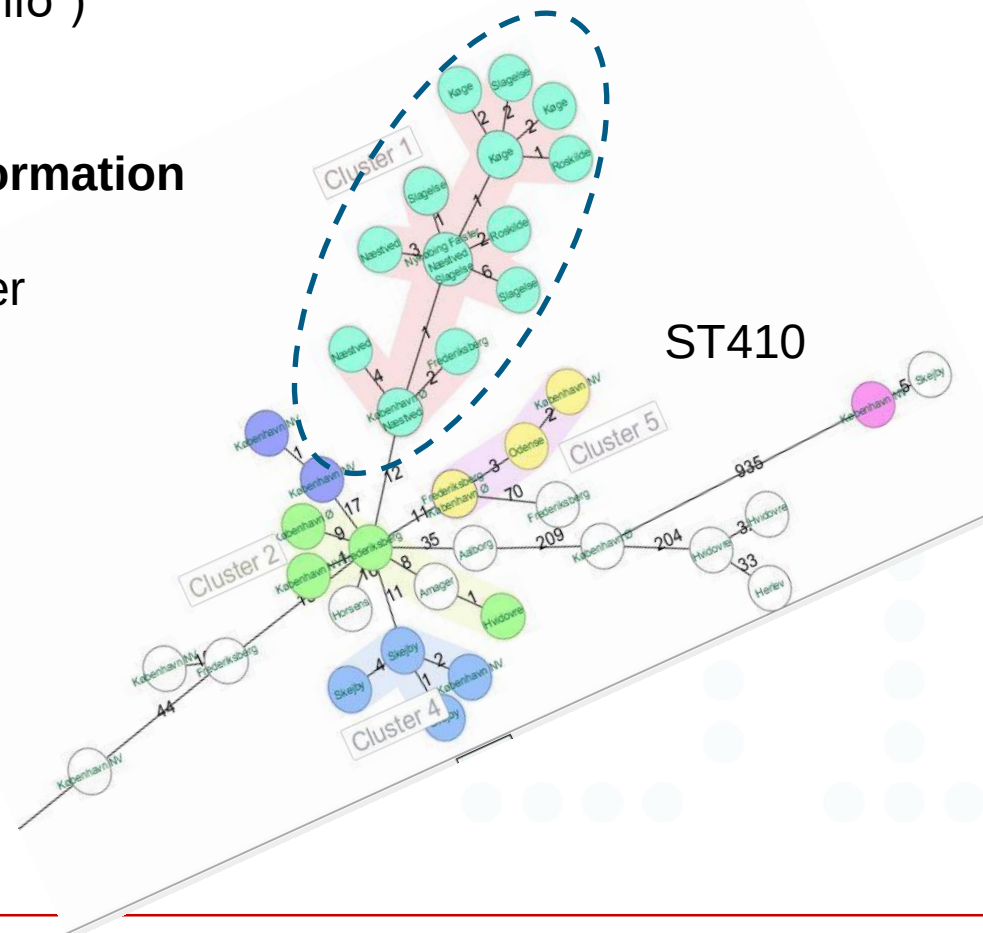
(RETTIDIG?) OPSPORING AF INTER-REGIONALE UD BRUD



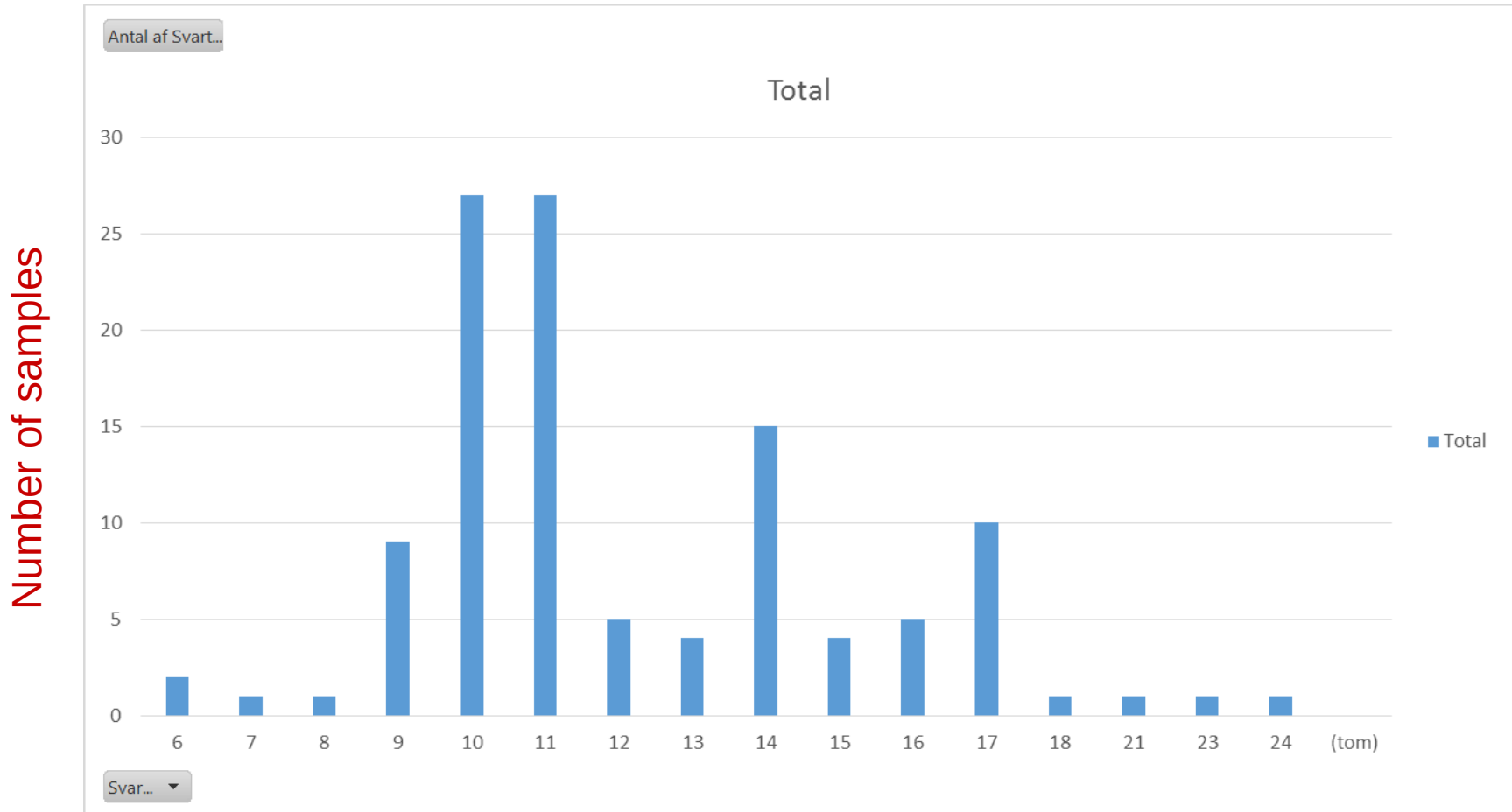


- Indsendende KMA (Regional)
- Afdeling patienten var indlagt på prøvetagningstidspunktet (Hospital)
- Rejsehistorik (Land/Ingen rejse/"ingen info")

- Hurtige udbrudsanalyser (WGS)
- Opdaterede data om patientindlæggelser
- Evnen til at håndtere disse data hurtigt
- Evnen til at kommunikere udbrud



CPO TURN-AROUND TIME AT SSI 2018



Days from registering the sample to WGS sequence is ready

HURTIG TYPNINGS INFORMATION – FAST TRACK WGS



STATENS
SERUM
INSTITUT

09.00

DNA purification

10.00

Library

14.00

MiSeq/iSeq 100

07.00

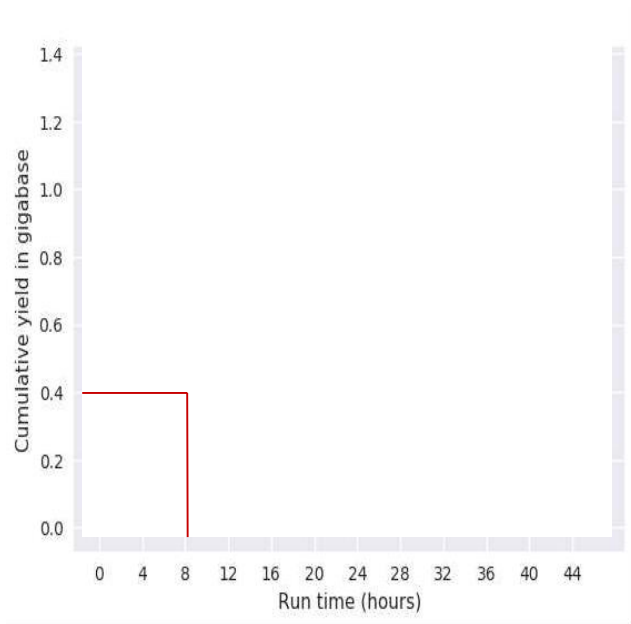
QC

07.40

cgMLST

08.00

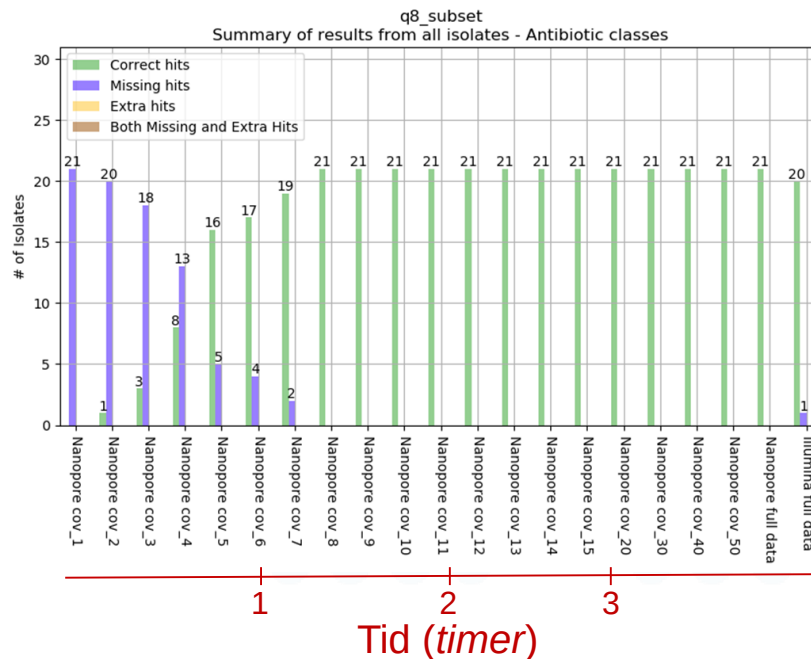




Bakteriel typning i real-tid

Genotypisk resistensbestemmelse

Korrekt genkendelse af resistens baseret på antibiotika klasser



Identity cutoff = 90.0
Coverage cutoff = 90.0
Depth cutoff (Gene-group) = 0.4
Minimum Depth = 2.0





Tilgængelig information ved prøvemodtagelsen

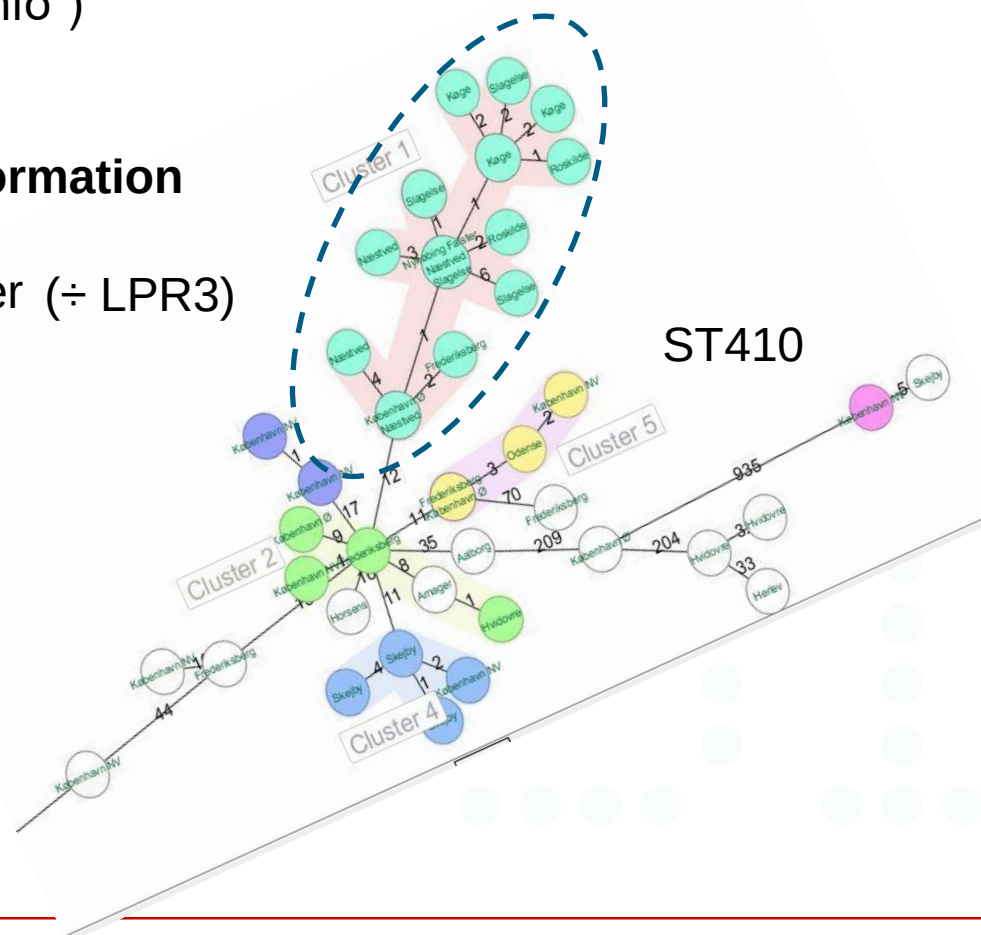
- Indsendende KMA (Regional)
- Afdeling patienten var indlagt på prøvetagningstidspunktet (Hospital)
- Rejsehistorik (Land/Ingen rejse/"ingen info")

Forudsætninger for rettidig udbrudsinformation

- Hurtige udbrudsanalyser ✓
- Opdaterede data om patientindlæggelser ($\div$ LPR3)
- Evnen til at håndtere disse data hurtigt
- Evnen til at kommunikere udbrud

LPR = LandsPatientRegisteret

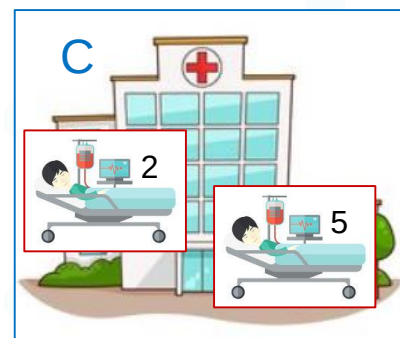
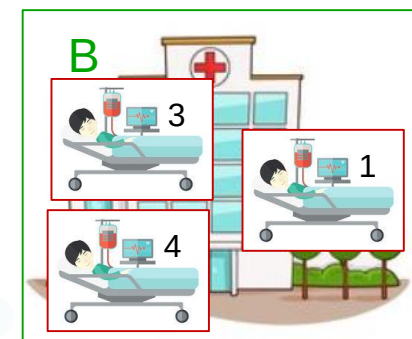
*Indeholde alle danske patienters
kontakter med hospitals-sektoren*



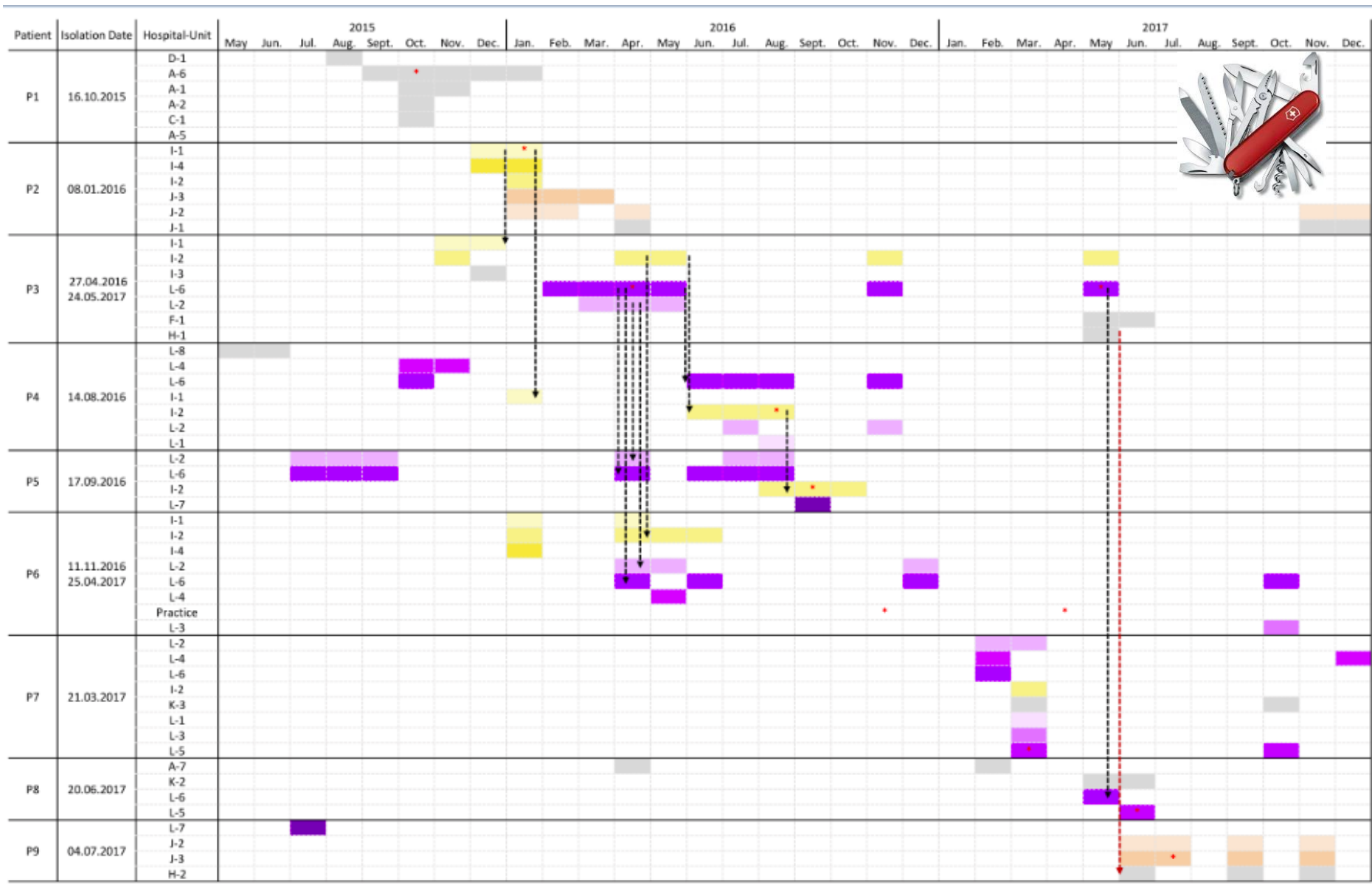
PATIENTERS INDLÆGGELSES NETVÆRK

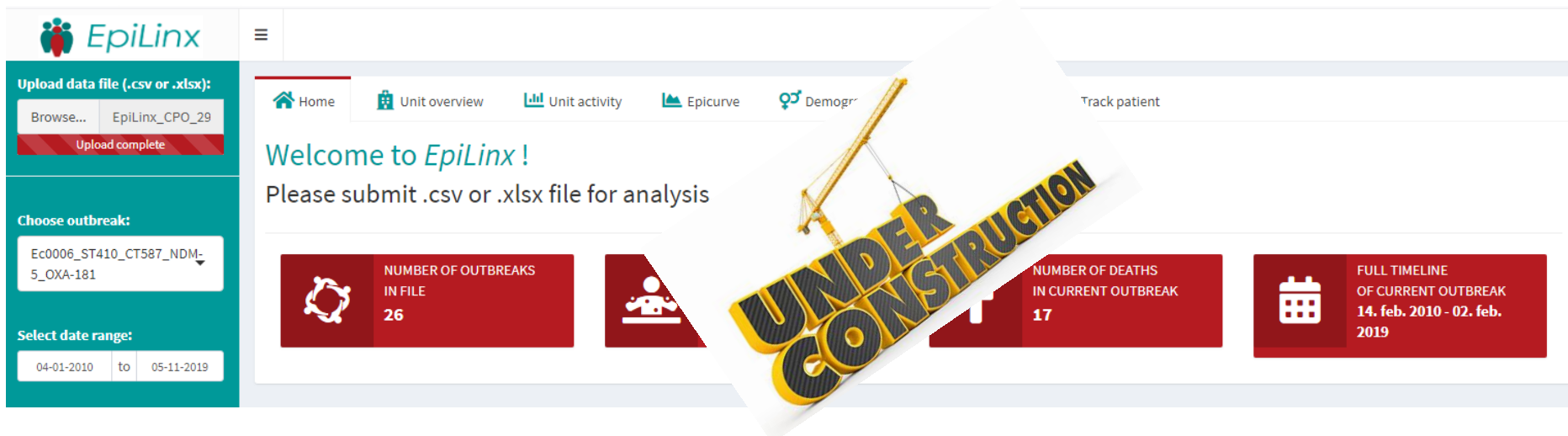


Patient	CPR	Hospital	Department	In-date	Out-date	Sample date
Patient 1	010101-0101	A	A1	01-jan-19	02-jan-19	15-jan-19
Patient 1	010101-0101	B	B1	03-jan-19	04-jan-19	15-jan-19
Patient 1	010101-0101	A	A2	05-jan-19	06-jan-19	15-jan-19
Patient 1	010101-0101	A	A1	07-jan-19	08-jan-19	15-jan-19
Patient 1	010101-0101	B	B1	14-jan-19	15-jan-19	15-jan-19
Patient 2	020202-0202	C	C1	01-jan-19	01-jan-19	11-jan-19
Patient 2	020202-0202	C	C2	02-jan-19	05-jan-19	11-jan-19
Patient 2	020202-0202	A	A1	06-jan-19	10-jan-19	11-jan-19
Patient 2	020202-0202	C	C2	10-jan-19	11-jan-19	11-jan-19
Patient 2	020202-0202	C	C1	12-jan-19	15-jan-19	11-jan-19
Patient 3	030303-0303	B	B2	02-jan-19	03-jan-19	15-jan-19
Patient 3	030303-0303	A	A1	10-jan-19	11-jan-19	15-jan-19
Patient 3	030303-0303	B	B2	15-jan-19	15-jan-19	15-jan-19
Patient 4	040404-0404	B	B1	02-jan-19	03-jan-19	12-jan-19
Patient 4	040404-0404	B	B2	04-jan-19	04-jan-19	12-jan-19
Patient 4	040404-0404	B	B3	05-jan-19	11-jan-19	12-jan-19
Patient 4	040404-0404	B	B4	12-jan-19	15-jan-19	12-jan-19
Patient 5	050505-0505	A	A1	06-jan-19	08-jan-19	08-jan-19
Patient 5	050505-0505	C	C2	13-jan-19	14-jan-19	08-jan-19



STATENS
SERUM
INSTITUT





EpiLinX

Upload data file (.csv or .xlsx):
Browse... EpiLinX_CPO_29
Upload complete

Choose outbreak:
Ec0006_ST410_CT587_NDM-5_OXA-181

Select date range:
04-01-2010 to 05-11-2019

Home Unit overview Unit activity Epicurve Demogr Track patient

Welcome to *EpiLinX* !
Please submit .csv or .xlsx file for analysis

UNDER CONSTRUCTION

NUMBER OF OUTBREAKS IN FILE: 26

NUMBER OF DEATHS IN CURRENT OUTBREAK: 17

FULL TIMELINE OF CURRENT OUTBREAK: 14. feb. 2010 - 02. feb. 2019

Generisk “R” software værktøj (“Shiny” tool package)

Input:

- Udvælgelse ud fra WGS typningen (“Mulige udbrud”)
- Indlæggelsesdata for inficerede patienter (Nationale/lokale)
- Andre epidemiological data (prøvedato, dødstidspunkt ect..)



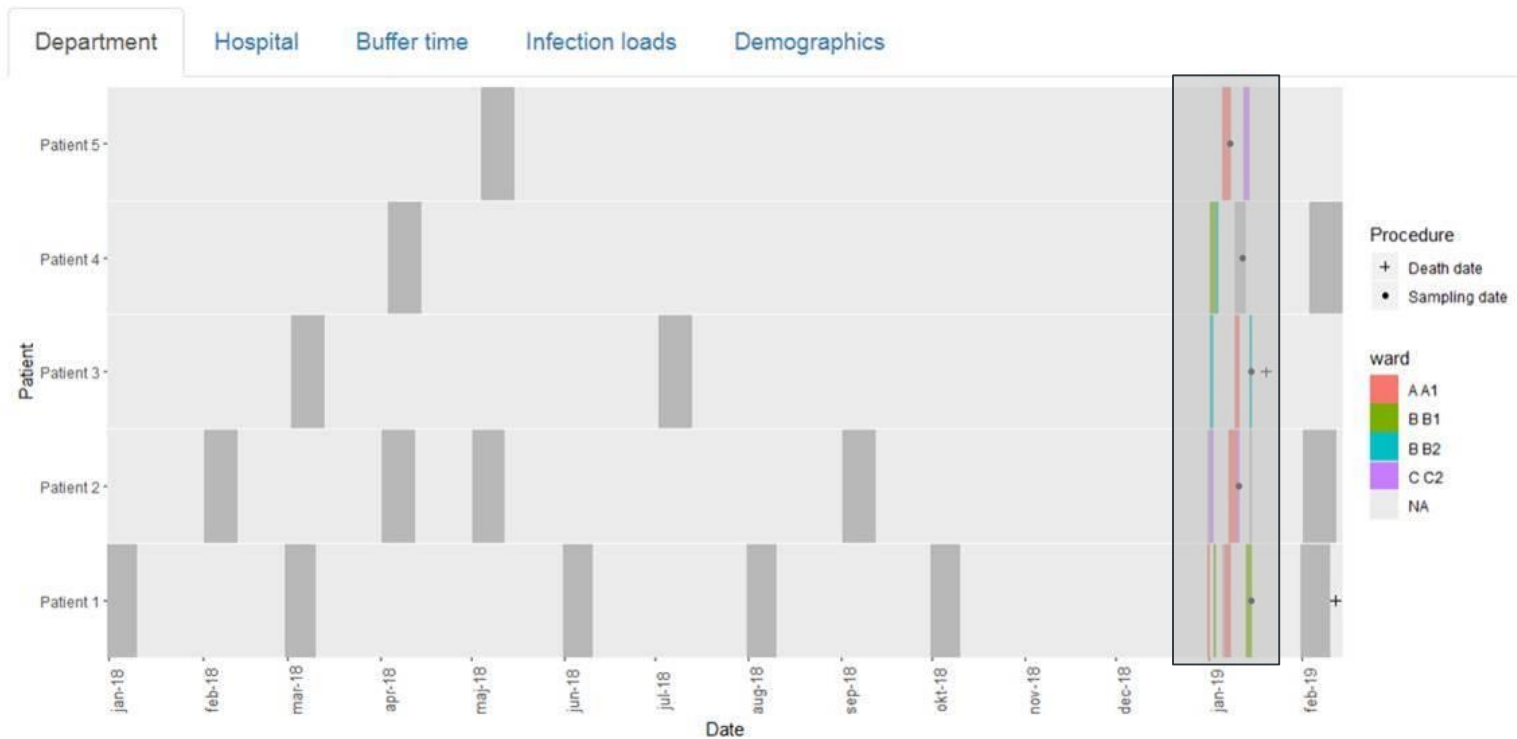
Anna Emilie Henius
Statens Serum Institut



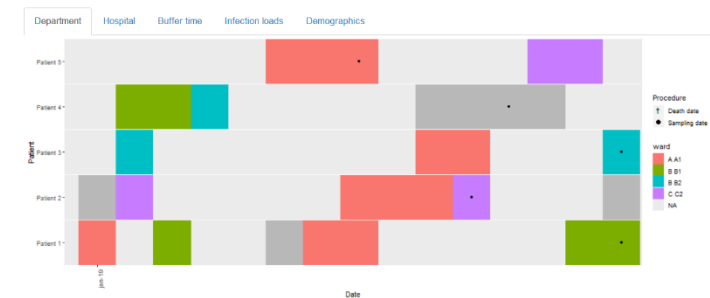
EKSEMPEL – 5 PATIENTER



	A	B	C	D	E	F	G	H	I
1	Patient	CPR	Hospital	Department	In-date	Out-date	Sample date	Age	Gender
2	1	010101-0101	D	D1	01-jan-18	10-jan-18	15-jan-19	18	M
3	1	010101-0101	D	D1	01-mar-18	10-mar-18	15-jan-19	18	M
4	1	010101-0101	D	D2	01-jun-18	10-jun-18	15-jan-19	18	M
5	1	010101-0101	D	D2	01-aug-18	10-aug-18	15-jan-19	18	M
6	1	010101-0101	D	D1	01-okt-18	10-okt-18	15-jan-19	18	M
7	1	010101-0101	A	A1	01-jan-19	01-jan-19	15-jan-19	18	M
8	1	010101-0101	B	B1	03-jan-19	03-jan-19	15-jan-19	18	M
9	1	010101-0101	A	A2	06-jan-19	06-jan-19	15-jan-19	18	M
10	1	010101-0101	A	A1	07-jan-19	08-jan-19	15-jan-19	18	M
11	1	010101-0101	B	B1	14-jan-19	15-jan-19	15-jan-19	18	M
12	1	010101-0101	D	D1	01-feb-19	10-feb-19	15-jan-19	18	M
13	2	020202-0202	E	E1	02-feb-18	12-feb-18	11-jan-19	16	F
14	2	020202-0202	E	E2	02-apr-18	12-apr-18	11-jan-19	16	F
15	2	020202-0202	E	E3	02-maj-18	12-maj-18	11-jan-19	16	F
16	2	020202-0202	E	E4	02-sep-18	12-sep-18	11-jan-19	16	F
17	2	020202-0202	C	C1	01-jan-19	01-jan-19	11-jan-19	16	F
18	2	020202-0202	C	C2	02-jan-19	02-jan-19	11-jan-19	16	F
19	2	020202-0202	A	A1	08-jan-19	10-jan-19	11-jan-19	16	F
20	2	020202-0202	C	C2	11-jan-19	11-jan-19	11-jan-19	16	F
21	2	020202-0202	C	C1	15-jan-19	15-jan-19	11-jan-19	16	F
22	2	020202-0202	E	E4	02-feb-19	12-feb-19	11-jan-19	16	F
23	3	030303-0303	F	F1	03-mar-18	13-mar-18	15-jan-19	15	M
24	3	030303-0303	F	F1	03-jul-18	13-jul-18	15-jan-19	15	M
25	3	030303-0303	B	B2	02-jan-19	02-jan-19	15-jan-19	15	M
26	3	030303-0303	A	A1	10-jan-19	11-jan-19	15-jan-19	15	M
27	3	030303-0303	B	B2	15-jan-19	15-jan-19	15-jan-19	15	M
28	4	040404-0404	G	G1	04-apr-18	14-apr-18	12-jan-19	14	F
29	4	040404-0404	B	B1	02-jan-19	03-jan-19	12-jan-19	14	F
30	4	040404-0404	B	B2	04-jan-19	04-jan-19	12-jan-19	14	F
31	4	040404-0404	B	B3	10-jan-19	11-jan-19	12-jan-19	14	F
32	4	040404-0404	B	B4	12-jan-19	13-jan-19	12-jan-19	14	F
33	4	040404-0404	G	G1	04-feb-19	14-feb-19	12-jan-19	14	F
34	5	050505-0505	H	H1	05-maj-18	15-maj-18	08-jan-19	13	M
35	5	050505-0505	A	A1	06-jan-19	08-jan-19	08-jan-19	13	M
36	5	050505-0505	C	C2	13-jan-19	14-jan-19	08-jan-19	13	M

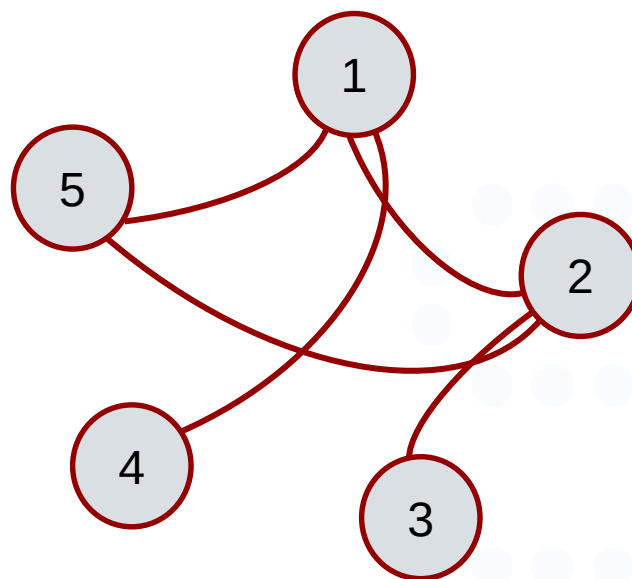


[1] Mouse over datapoint in plot to show values of patient ID, date and ward respectively

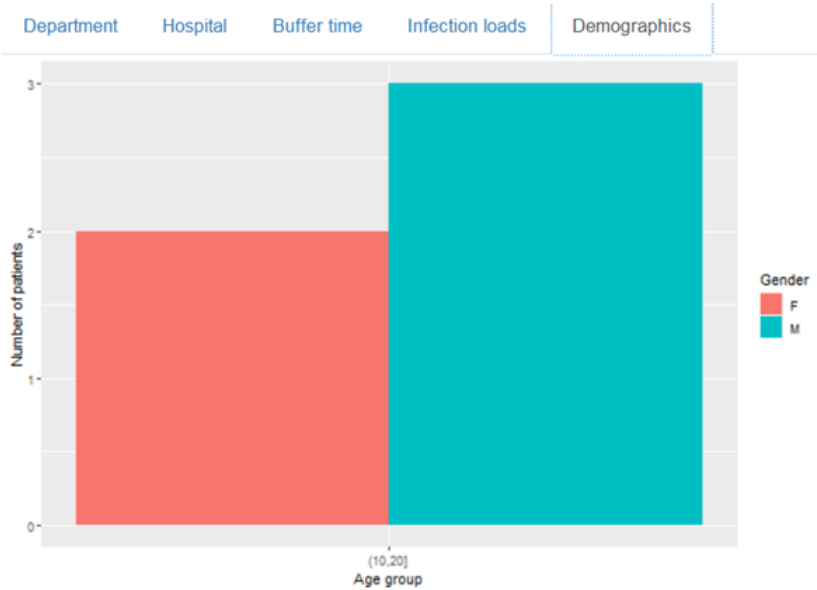
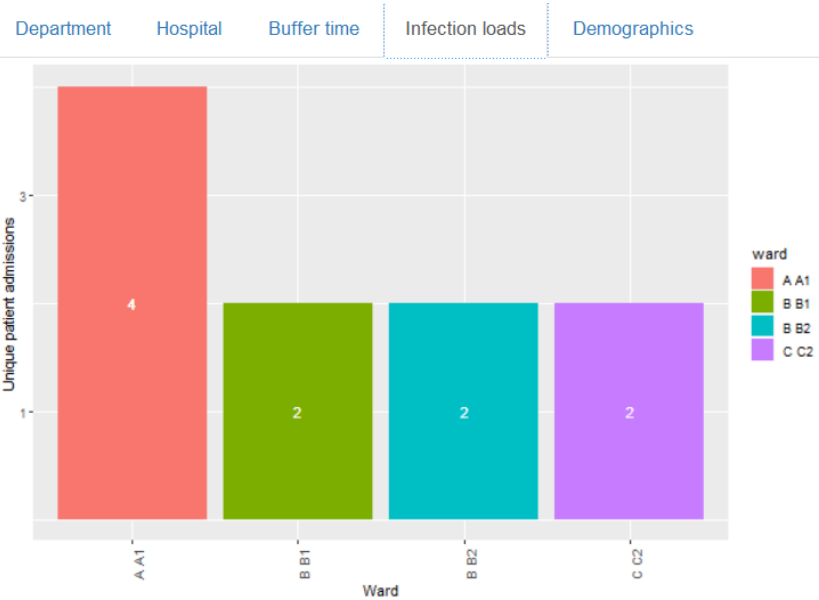




Patient.1	Patient.2	Center	Start	End	Duration_days
Patient 2	Patient 3	A A1	2019-01-10	2019-01-10	1
Patient 1	Patient 2	A A1	2019-01-08	2019-01-08	1
Patient 2	Patient 5	A A1	2019-01-08	2019-01-08	1
Patient 1	Patient 5	A A1	2019-01-07	2019-01-08	2
Patient 1	Patient 4	B B1	2019-01-03	2019-01-03	1



EPILINX – HYPPIGSTE AFDELINGER + DEMOGRAFISKE DATA



Gender	Median	Min Age	Max Age
F	15.00	14	16
M	15.00	13	17

J Antimicrob Chemother 2016; **71**: 3117–3124
doi:10.1093/jac/dkw289 Advance Access publication 1 August 2016

Journal of
Antimicrobial
Chemotherapy

Use of WGS data for investigation of a long-term outbreak of *Citrobacter freundii* producing bla_{NDM-1} associated with a cluster of *Escherichia coli*, *Klebsiella pneumoniae* and *Staphylococcus aureus* in Denmark

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Lene S. Jørgensen²

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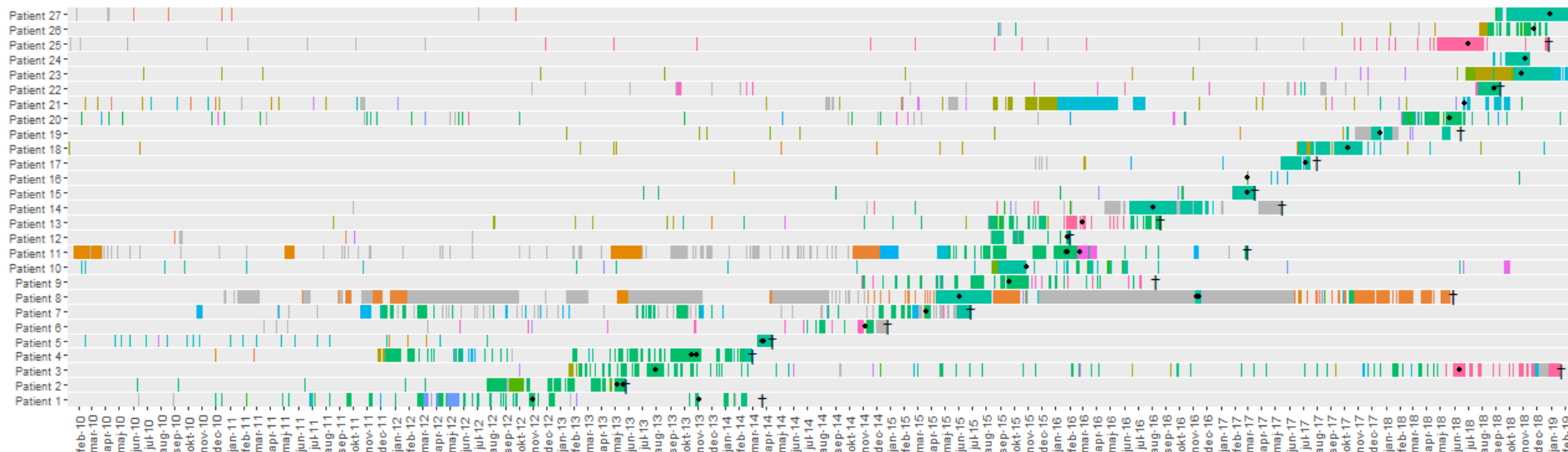
*Correspondence: Anette M. Hammerum, Department of Microbiology, Aalborg University Hospital, 9000 Aalborg, Denmark. Tel: +45-9944 1234; Fax: +45-3268-3231; E-mail: ama@ssi.dk

Received

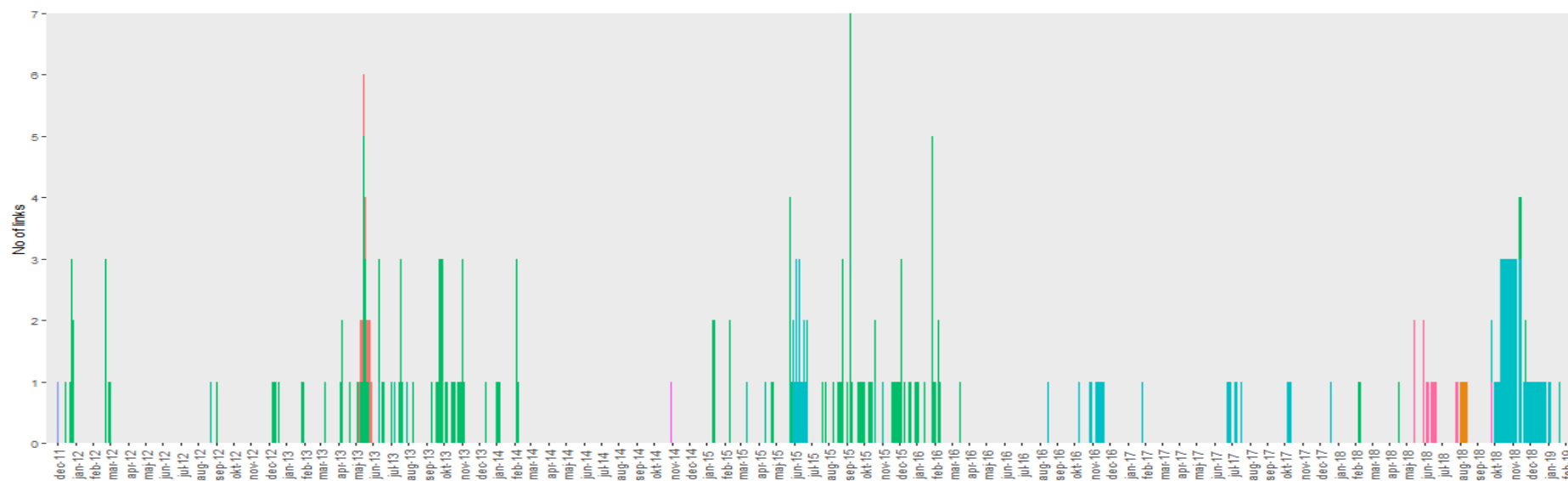
4 September 2015; revised 19 May 2016; accepted 20 June 2016

32 patienter (November 2019)
Udspringer fra Region Nord
Spredt til Region Midt
Yderligere spredning i Region Midt

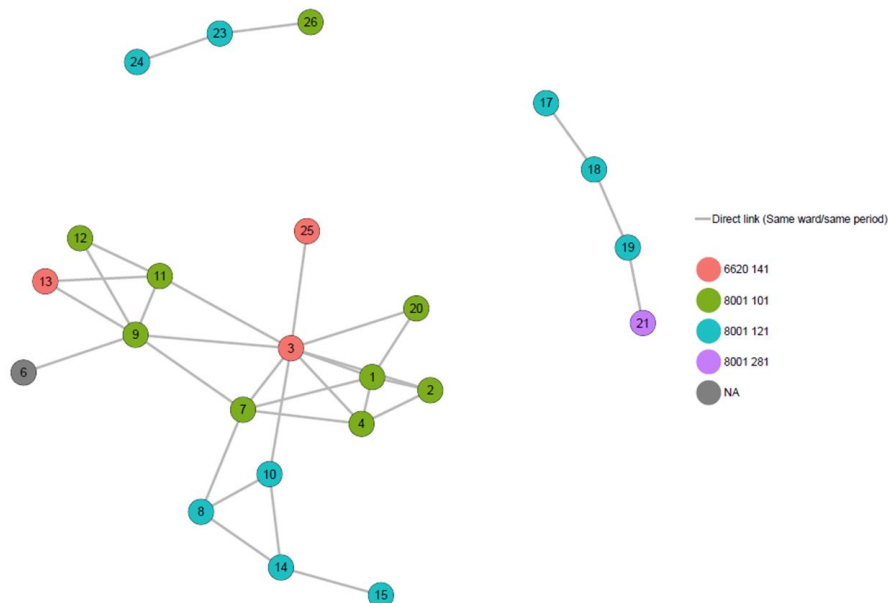
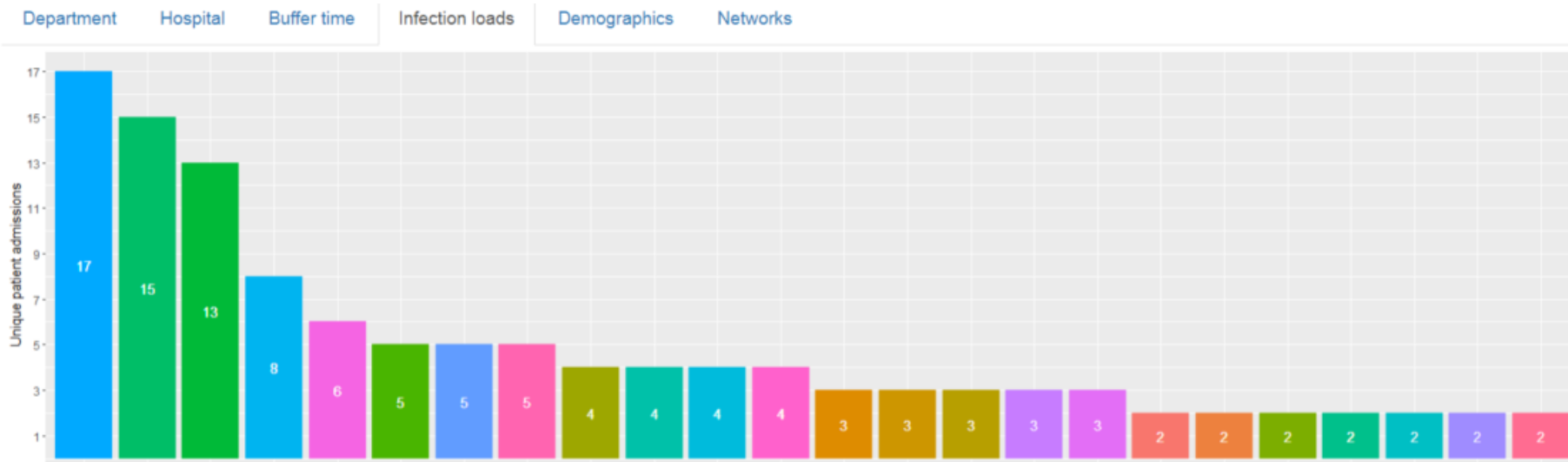
CITROBACTER FREUNDII ST18 TVÆR-REGIONALT UDBRUD



Epicurve based on direct epilinks



ST18 C. FREUNDII – HYPPIGSTE AFDELINGER + NETVÆRK



5 16 22 27

Ingen direkte Epi-link

Tilgængelig information ved prøvemodtagelsen

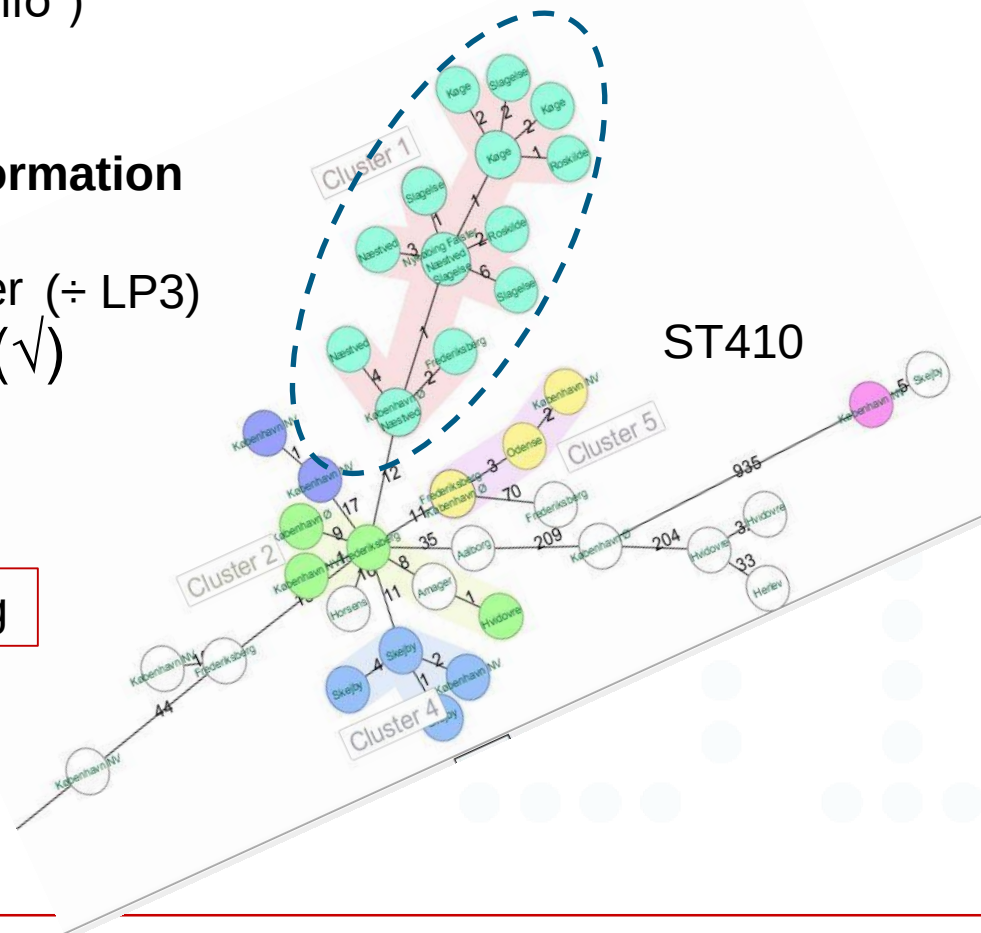
- Indsendende KMA (Regional)
- Afdeling patienten var indlagt på prøvetagningstidspunktet (Hospital)
- Rejsehistorik (Land/Ingen rejse/"ingen info")

Forudsætninger for rettidig udbrudsinformation

- Hurtige udbrudsanalyser (✓)
- Opdaterede data om patientindlæggelser (÷ LP3)
- Evnen til at håndtere disse data hurtigt (✓)
- Evnen til at kommunikere udbrud (✓)



National udbrudsgruppe under opbygning





Tak for jeres opmærksomhed

