



EPIDEMIOLOGY SUPPORT TO DANISH HOSPITALS IN RELATION TO AMR OUTBREAKS

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June 29th. 2022

TEN STEPS IN AN OUTBREAK INVESTIGATION (ECDC)

1. (a) Identify and confirm outbreak: (b) convene team

2. Confirm diagnosis

3. Case definition

4. Case finding

1 – 10 always in
collaboration with local
team!

5. Descriptive epidemiology (person, place, and time)

6. Hypothesis generation (interview selected cases)

7. Hypothesis testing (I) - case-control or cohort study
(analytical epidemiology)

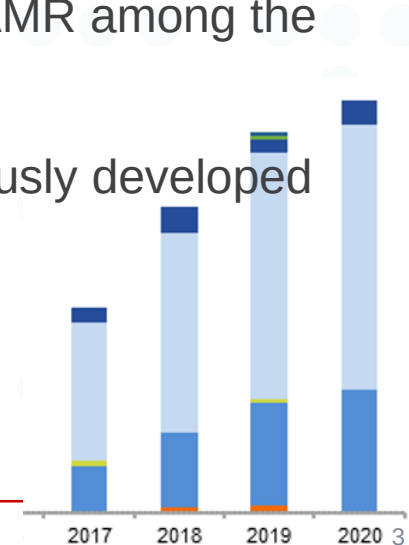
8. Hypothesis testing (II) - other studies (microbiological,
environmental, trace-back)

9. Inform risk managers, advise on control measures

10. Disseminate findings, evaluate.

The CPO/AMR outbreak database KURS

- Coordinated Outbreak Registration in the Healthcare System
- **Improve surveillance** and increase knowledge of occurrence
- **Reduce the risk** spread of outbreaks with CPO/AMR
- A registration **tool for local and central actors** that provides an **overview** of the outbreak situation in real time, both at local and central level (online in the future)
- **Increase collaboration and communication** across central and regional institutions as hospitals
- Create a greater **awareness and knowledge** about outbreaks of AMR among the various actors in Denmark
- Create secure flexible IT solutions and tools that can be continuously developed



- ❖ Outbreak database (still a pilot project)
- ❖ Overview of CPO outbreaks incl. number of patients
- ❖ Supports collaboration with the KMAs and IHEs
- ❖ Supports collaboration at SSI
- ❖ Reporting (DANMAP report, newsletters)
- ❖ Comprehend data collection regarding AMR-outbreaks
 - Future plans to include MRSA, ESBL and *C. difficile*
- ❖ Platform for an AMR database with online access for hospitals
- ❖ Understanding transmission mechanisms and risks
- ❖ Trends and research

OVERVIEW OF AN OUTBREAK

- Number of patients, hospitalisation, case definition, conclusion

Udbrud i KURS

Opret nyt udbrud

Gem udbrud

Indtast ny CPO

Indtast ny ESBL

Opdater udbrud

Gå til udbrud

Øversigt aktuelt Udbrud **Screenings information**

Anmeldelse af Udbrud:

Udbruds ID	1070
Udbrudsnavn	Cfa0001_OXA-48
Udbrydstype	CPO
Status på udbrud	Mistanke
Status på udredning	Under udredning
Anmeldelsesdato	01-03-2021
Afsluttet dato	
Anmeldt af	ssi
Anmelders arbejdsplads	
Udbrudsarkiv	\\dksund.dk\koncern\SSI\SDrev\ANMAP - AROR\Udbri
Udbrudsanalyser	
Kommentarer	

Udbruds karakteristika:

Dato for første isolat	16-04-2017	Dato for sidste isolat	03-06-2021
Species	C. farmeri		
Resistens gener	blaOXA-48		
Definition af udbruddet	Der er endnu ikke en definition på dette udbrud		
Konklusion	Sammenhæng indlæggelse og prøvedato mellem pt. 1 og 2. Patient 3 og 4 ligger langt fra i prøvedato og kan ikke umiddelbart linkes til de to første patienter.		

Patient information:

Antal konfirmerede patienter	6	Antal mistanke patienter	
Antal konfirmerede isolater	6	Antal mistanke isolater	
Antal isolater med manglende epidemiologisk link	3		
Indsendende hospitaler			
Indsendende KMA'er			
Indsendende regioner			
Hospitaler med indlæggelser			
Afdelinger med indlæggelser	and, Lunge medicinsk		
Rejseinformation			

❖ Verified outbreaks

- An epidemiological link can be established between two or more cases in the cluster, e.g. the patients have been at the same hospital ward at the same time or they live in the same geographical location such as a nursing home.

❖ Possible outbreak

- When no epidemiological link can be established between cases with the same unique genotype.
- A possible outbreak can be reclassified as a verified outbreak, if new cases or information is providing an epidemiological link between two or more of the cases.

Challenged by the long silent carrier status and the time line in detection of patients in AMR outbreaks

- ❖ Outbreak investigations of a cluster of cases is closed when no new cases has appeared within 6 months, but can be reopened, if new cases is detected in the surveillance system.

Identify and confirm outbreak and convene team

- Microbiological identification
- ❖ Convene team - CPO Outbreak Team at SSI
 - Interdisciplinary collaboration at SSI (6 members)
 - Weekly meetings to discuss findings and epidemiological investigation
 - Activities, meetings, briefing and coordination
- ❖ Local outbreak teams in hospitals (KMA and IHE)
 - where SSI can take part in investigations and meetings
- ❖ National collaboration group (approx 30 - 40 members)
 - With Clinical Microbiology Departments (KMA) and Infection Hygiene units (IHE)
 - Improve and strengthen cross regional collaboration
 - Regular online meetings (1 hour). Topics e.g. CPO in drains and toilets
 - Knowledge sharing e.g. experiences with screening of patients



We have 5 Regions in Denmark (5,8 mio inh)
The regions are responsible for a.o.:

- The hospital system, general practitioners and medical specialists
- Regional development, incl. nature and environment, employment, education and culture

Our collaborating partners

- The 10 clinical microbiology department (KMA) located at the major hospitals
- The infectious hygiene units (IHE)



- Denmark is a small country with a strong infra structure
- We all have a central personal register number (CPR-number)
 - A strong tool in data collection, combining data and research
 - Protection of personal data important (secure mail communication)
- SSI provides the cross-regional overview and share information

❖ 2. *Confirm diagnosis*

- AMR is a medical treatment issue, and without symptoms

❖ 3. **Case definition**

- Based on microbiological results
- Time, place (hospital), age, gender and residents
- Travel history and hospitalisation
- Medical history
- And other relevant characteristics



❖ 4 *Case finding*

- Is conducted at the hospitals
- Might be random (including samples from GP, unexpected hospital)
- Screening (in relation to travel, personal AMR-history, outbreaks a.o.)
- Screening requires planning, time and resources

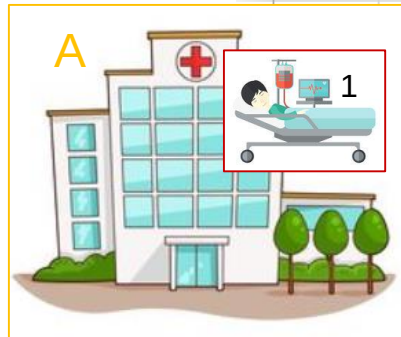
Case definition outbreak Cf0001_ST18_NDM-1 KURS ID 41

- Various agents; *C. freundii*, *E. coli*, *H. alvei*, *K. Oxytoca* and *K. Pneumoniae*
 - Defined by resistensgene blaNDM-1 including local plasmid variation
 - In total, 84 cases, primarily males, age 27 – 93 (average 64.6) (2012 – 2022)
 - Various types of medical conditions, high usage of antibiotics
 - Mainly two involved hospitals, different departments and in different regions
 - Sampling and epidemiological outbreak investigation suggest among others transmission from toilets and drains, and person-person transmission
 - Can be controlled by intensive infection control interventions
-
- SSI contributes with microbiological sampling and sampling advice
 - Epidemiological investigations, overview and support
 - Infection control advice

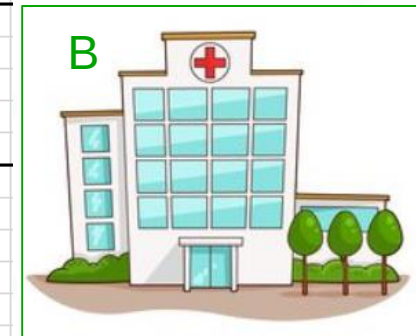
STEP 6 AND 7: HYPOTHESIS GENERATION



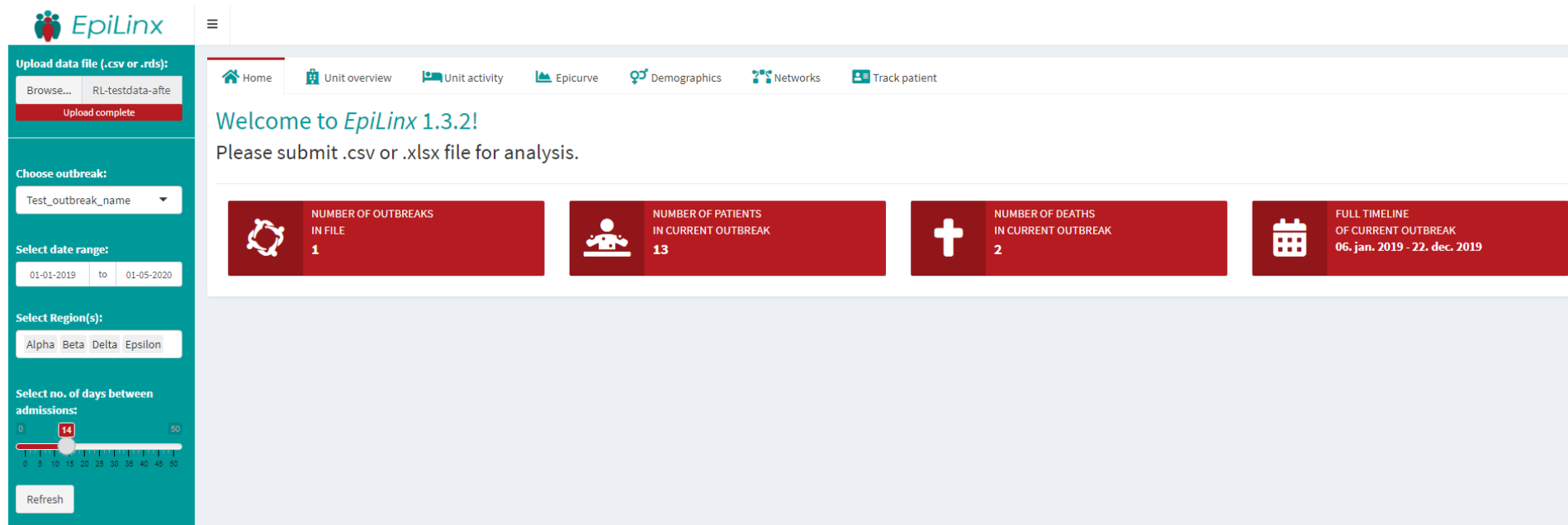
Hospitalisation data with patient transfer networks – the excel experience



	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
		0101-0101	D	D2	01-jun-18	10-jun-18	15-jan-19	18	M
		0101-0101	D	D2	01-aug-18	10-aug-18	15-jan-19	18	M
		0101-0101	D	D1	01-okt-18	10-okt-18	15-jan-19	18	M
		0101-0101	A	A1	01-jan-19	01-jan-19	15-jan-19	18	M
		0101-0101	B	B1	03-jan-19	03-jan-19	15-jan-19	18	M
		0101-0101	A	A2	06-jan-19	06-jan-19	15-jan-19	18	M
		0101-0101	A	A1	07-jan-19	08-jan-19	15-jan-19	18	M
		0101-0101	B	B1	14-jan-19	15-jan-19	15-jan-19	18	M
		0101-0101	D	D1	01-feb-19	10-feb-19	15-jan-19	18	M
		0202-0202	E	E1	02-feb-18	12-feb-18	11-jan-19	16	F
		0202-0202	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



EPILINX – A TOOL FOR MAPPING PATIENT NETWORKS



EpiLinX

Upload data file (.csv or .rds):

Browse... RL-testdata-aft'e

Upload complete

Choose outbreak:

Test_outbreak_name

Select date range:

01-01-2019 to 01-05-2020

Select Region(s):

Alpha Beta Delta Epsilon

Select no. of days between admissions:

0 14 50

Refresh

Home Unit overview Unit activity Epicurve Demographics Networks Track patient

Welcome to *EpiLinX* 1.3.2!

Please submit .csv or .xlsx file for analysis.

NUMBER OF OUTBREAKS IN FILE: 1

NUMBER OF PATIENTS IN CURRENT OUTBREAK: 13

NUMBER OF DEATHS IN CURRENT OUTBREAK: 2

FULL TIMELINE OF CURRENT OUTBREAK: 06. jan. 2019 - 22. dec. 2019

Generic “*base R*” software tool (“*Shiny*” tool package)

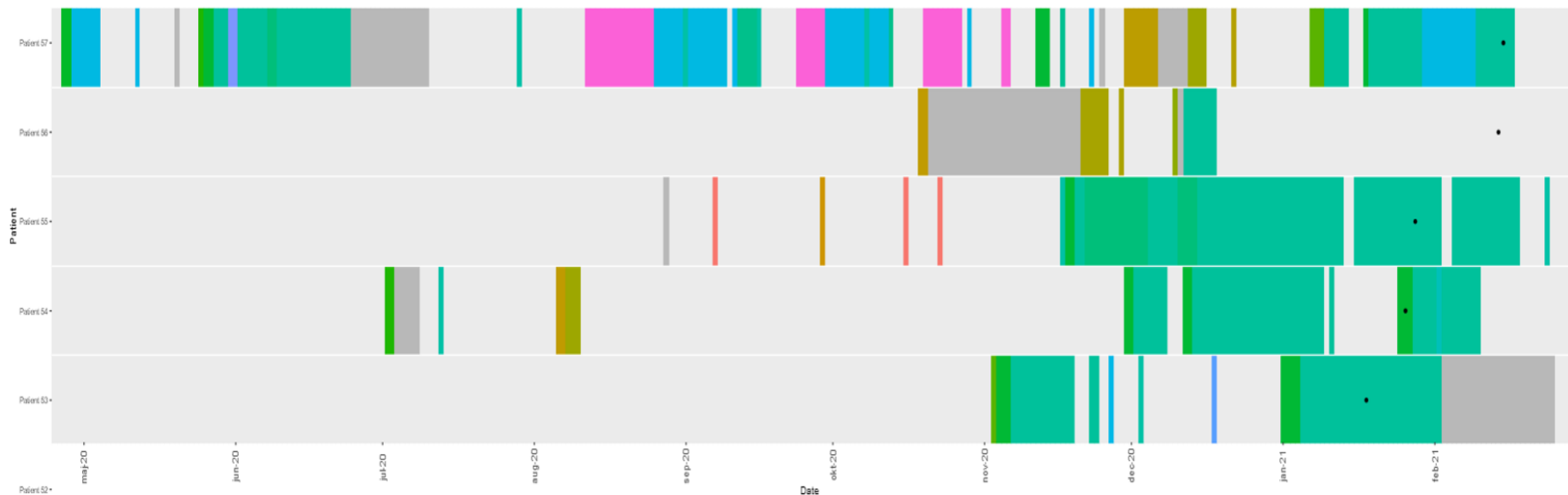
Input:

- Selected data based on typing (MLST/cgMLST)
- Patient hospitalization information (National Epi-LPR or local)
- Other epidemiological data (sample date, death ect..)



- Patient hospitalisation information (National Epi-LPR or local data)
- Other epidemiological data (sample date, date of death)
- An important and strong tool in AMR-outbreak investigation
- Communicated to KMA and IHE together with WGS-results

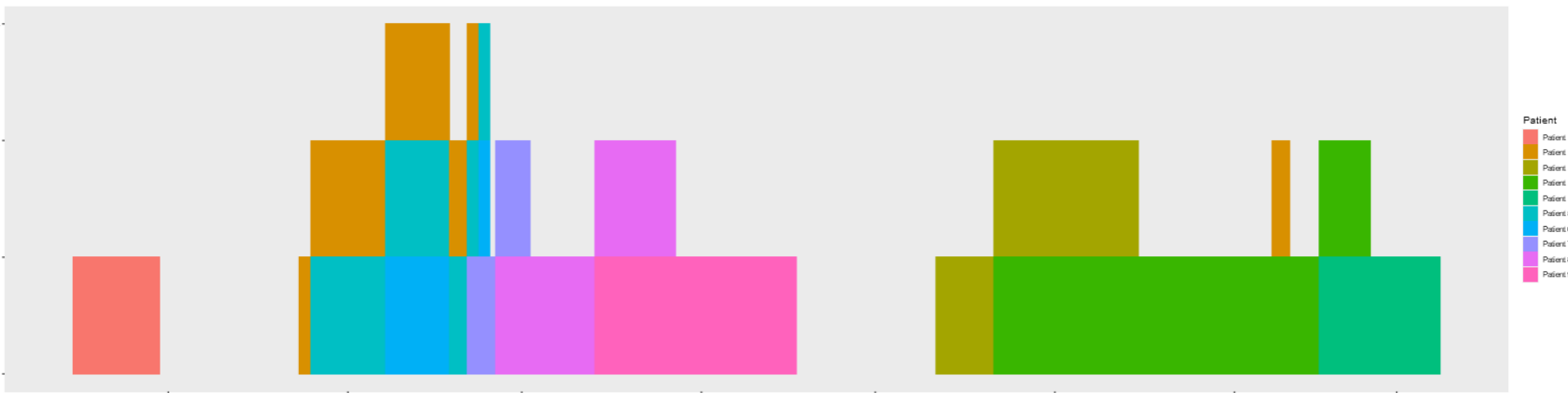
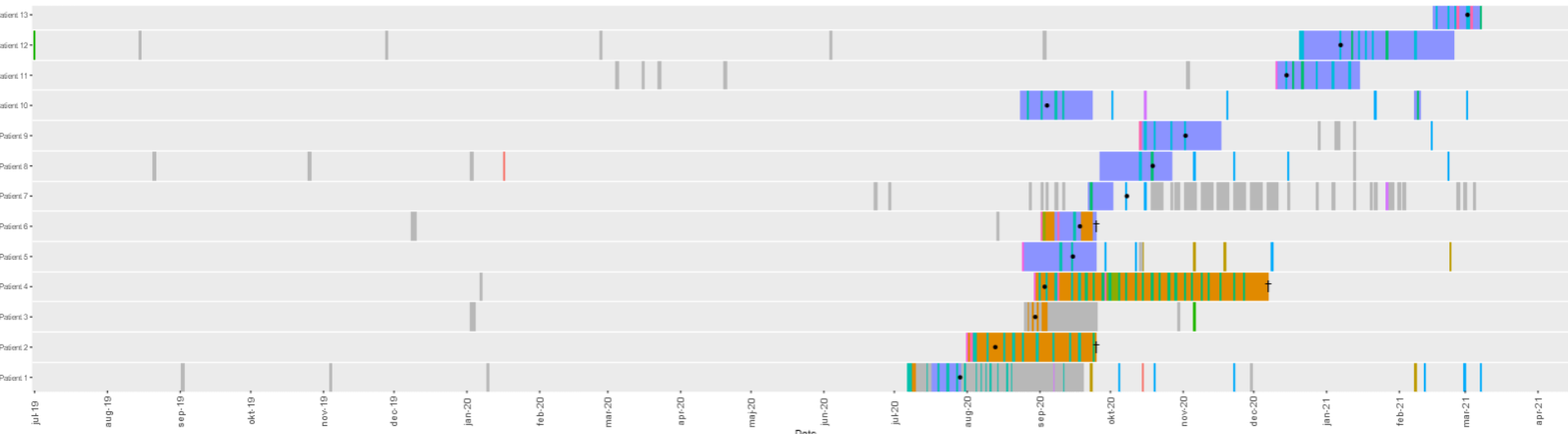
Figur 1 EpiLinX indlæggelse LPR pt. 53- 57 fra maj 2020 til 1. marts. Patient 57 øverst.



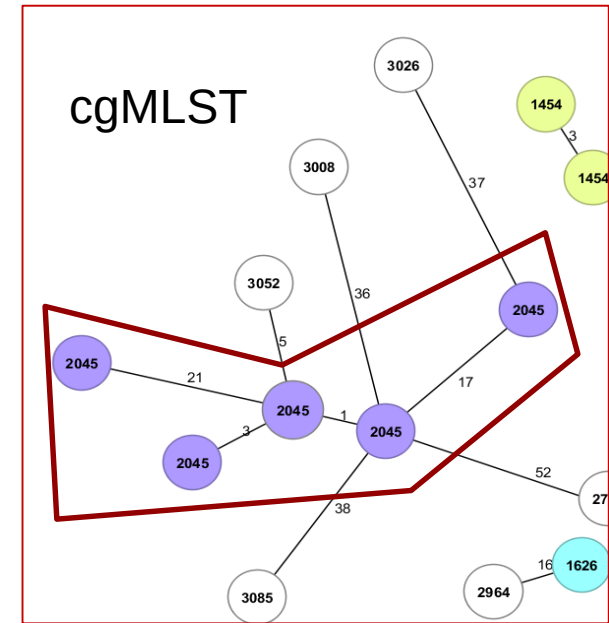
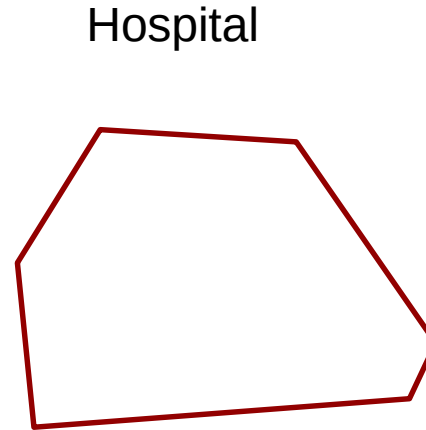
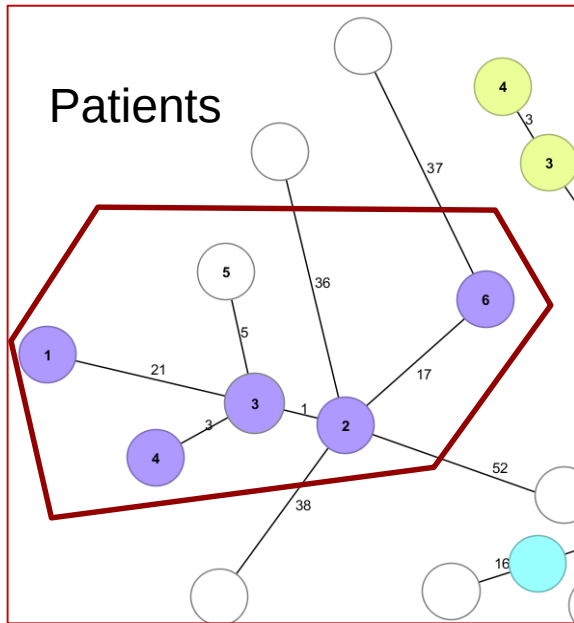
HYPOTHESIS GENERATION *A. BAUMANNII*



- Hospitalisation data (Epi-LPR) show direct contact in the same unit and very few contact to healthcare facilities in general before positive sample
- Infection control inspection pointed out critical point in treatment



A. BAUMANNII OUTBREAK - ESBJERG



Upload data file (.csv or .rds):

Browse... EpiLinx_Lpr2_Lf

Upload complete

Choose outbreak:

Ab0010_ST195_CT2045_OXA-23

Select date range:

Home Unit overview Unit activity Epicurve Demographics Networks Track patient

Patient overlaps

Direct overlaps Unit/shifted time

Select location:

☒ Unit ☐ Ward ☐ Hospital

Mouse over datapoint in plot to show values of patient ID, date and unit respectively!

- ❖ Descriptive epidemiology (person, place, and time)
- ❖ Epidemiological investigation with EpiLinx
- ❖ Local knowledge and risk handling
- ❖ One outlier case had no connection to the outbreak (travel related)



STEP 9: CPO-OUTBREAK DANMAP REPORT

Table 8.10 Outbreaks of carbapenemase-producing Enterobacterales (CPE) and carbapenemase-producing organisms (CPO) during 2020, n=20, Denmark DANMAP 2020

Outbreak ID	Year	Patients total	Patients 2020	Carbapenemase	Type of Outbreak	Species (clonal spread)	Regions	Status
Outbreaks of carbapenemase-producing Enterobacterales (CPE)								
41	2012-2020	52	13	NDM-1	Clonal/ plasmid	ST18 <i>C. freundii</i>	Capital Region/Central Denmark Region/North Denmark Region	Verified
48	2013-2020	23	4	OXA-436/OXA-48	Clonal/ plasmid	ST90 <i>E. cloacae</i> / ST22 <i>C. freundii</i>	Capital Region/South Denmark Region/Zeland Region	Verified
24	2014-2020	10	1	OXA-181	Clonal	ST410 <i>E. coli</i>	Capital Region	Verified
25	2014-2020	7	1	OXA-48	Clonal	ST38 <i>E. coli</i>	Capital Region/Zeland Region	Verified
21	2015-2020	60	19	NDM-5/OXA-181	Clonal	ST410 <i>E. coli</i>	Capital Region/Zeland Region	Verified
22	2015-2020	6	1	OXA-181	Clonal	ST440 <i>E. coli</i>	Capital Region/Central Denmark Region	Possible
42	2015-2020	9	2	OXA-48	Clonal	ST65 <i>C. freundii</i>	Capital Region/North Denmark Region/Zeland Region	Verified
33	2016-2020	23	16	OXA-232	Clonal	ST231 <i>K. pneumoniae</i>	Central Denmark Region	Verified
35	2017-2020	4	2	OXA-48	Clonal	ST15 <i>K. pneumoniae</i>	Capital Region/Zeland Region	Possible
51	2018-2020	3	1	OXA-48	Clonal	ST73 <i>E. coli</i>	Central Denmark Region	Possible
7	2019-2020	7	5	NDM-5	Clonal	ST167 <i>E. coli</i>	Capital Region	Verified
1061*	2020	3		OXA-181	Clonal	ST22 <i>C. freundii</i>	Central Denmark Region	Possible
1054*	2020	2		OXA-48	Clonal	ST16 <i>K. pneumoniae</i>	Zeland Region	Possible
1057*	2020	3		OXA-244	Clonal	ST38 <i>E. coli</i>	Capital Region, South Denmark Region	Possible
1059*	2020	2		OXA-48	Clonal	OXA-48 <i>E. hormaechei</i>	Capital Region	Possible
1060*	2020	2		NDM-1	Clonal	ST78 <i>E. hormaechei</i>	Capital Region	Verified
1062*	2020	2		NDM-5	Clonal	ST79 <i>E. hormaechei</i>	Capital Region, Central Denmark Region	Possible
1068*	2020	2		OXA-48	Clonal	ST18 <i>C. freundii</i>	Capital Region	Possible
1062*	2020	2		NDM-5	Clonal	ST79 <i>E. hormaechei</i>	Capital Region, Central Denmark Region	Possible
1068*	2020	2		OXA-48	Clonal	ST18 <i>C. freundii</i>	Capital Region	Possible
Outbreaks of carbapenemase-producing organisms (CPO)								
1058*	2020	11		OXA-23	Clonal	ST195 <i>A. baumannii</i>	Capital Region	Verified
1067*	2020	2		OXA-23	Clonal	ST195, ST1816 <i>A. baumannii</i>	South Denmark Region	Verified

* Outbreak clusters identified in 2020

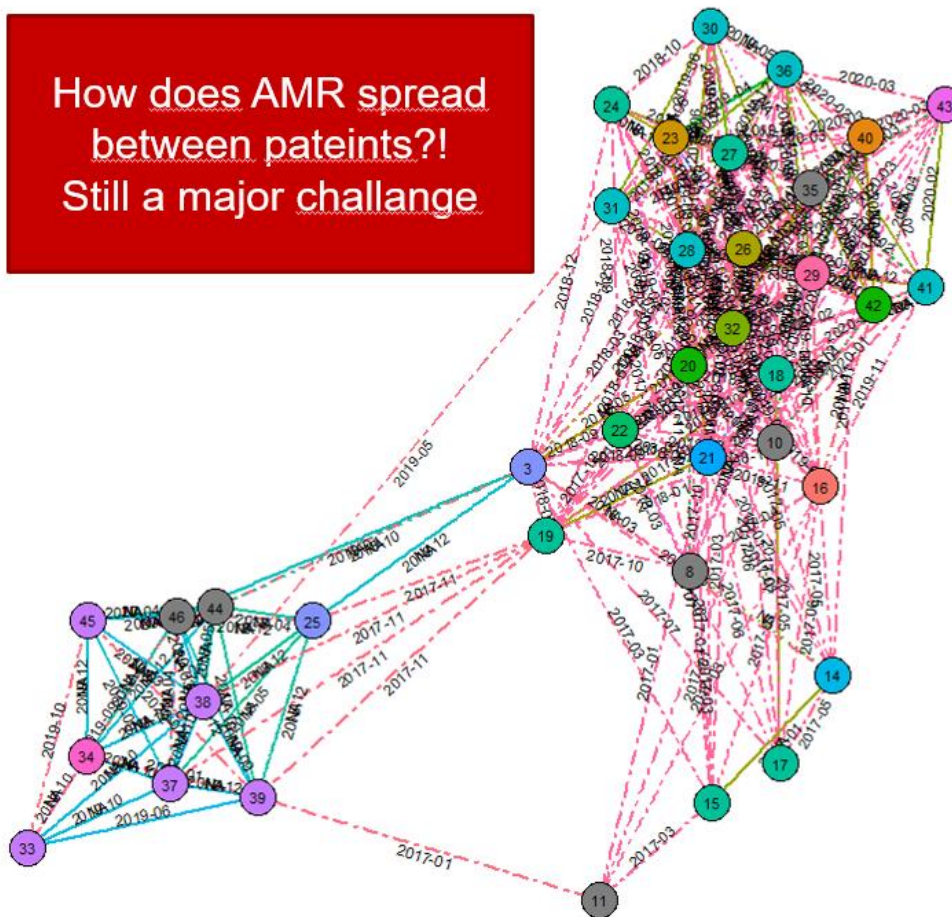


Patient network

Select linktypes:

☒ Direct unit links ☒ Indirect unit links ☒ Hospital links

How does AMR spread
between patients?!
Still a major challenge

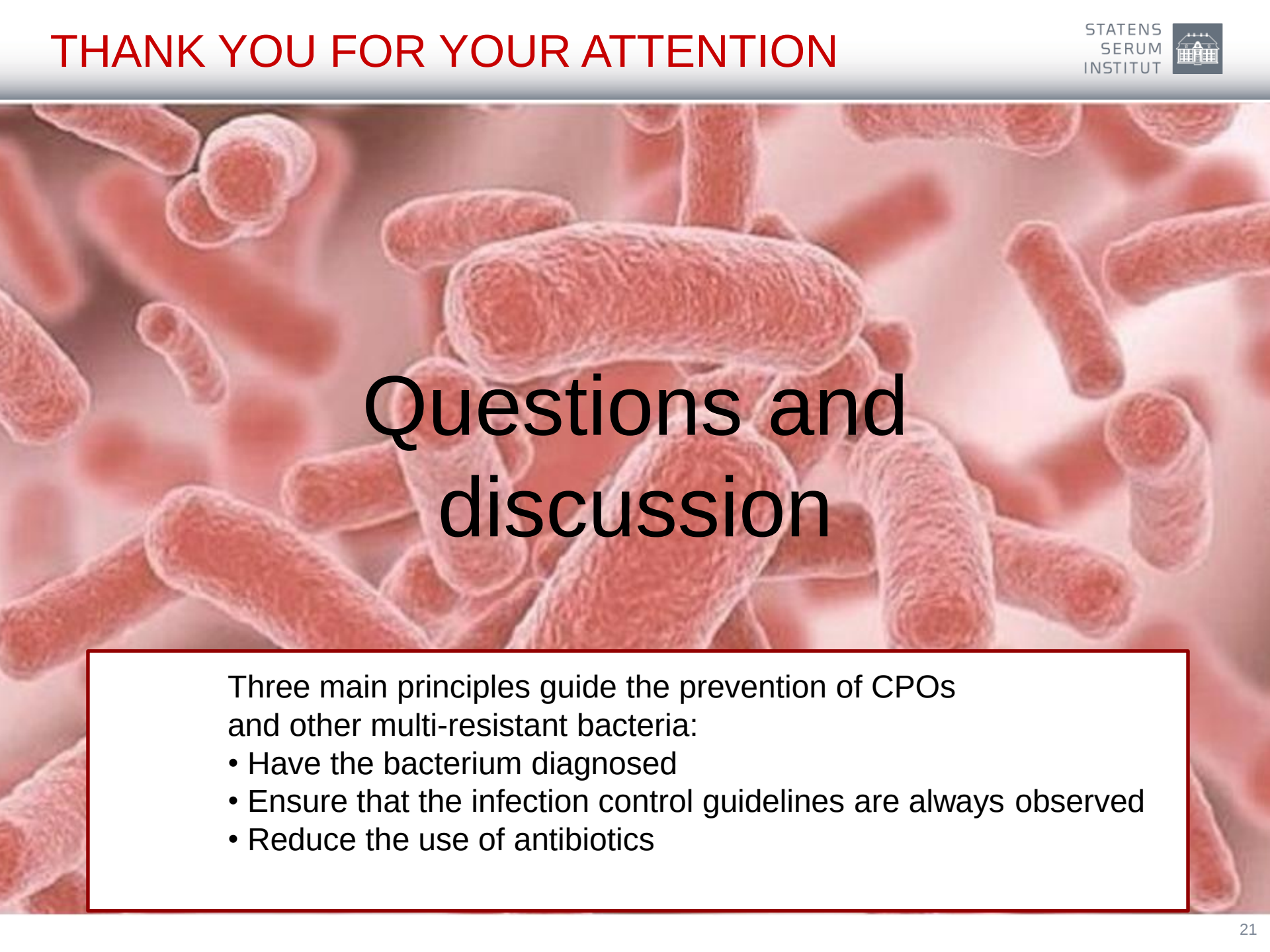


- ❖ Identification of cases
 - Often no symptoms of carrier status
 - Identified randomly
 - Patients should have been isolated
 - Patients have moved or been discharged from the hospital

- ❖ When and where did the transmission take place?
 - ❖ Who is at risk and where?
 - ❖ Where to intervene?
 - ❖ Transmission happens in another sector or hospital

Important to:

- ❖ Focus on infection hygiene prevention to prevent the spread of AMR
- ❖ Investigate outbreaks – learn transmission routes
- ❖ Collect information and knowledge on the risk of transmission of AMR
- ❖ Communicate and share information



Questions and discussion

Three main principles guide the prevention of CPOs and other multi-resistant bacteria:

- Have the bacterium diagnosed
- Ensure that the infection control guidelines are always observed
- Reduce the use of antibiotics