3rd EURGen-RefLabCap Network Meeting:

Dates: September 18, 2024, from 13:00 to 17:45 CET
September 19, 2024, from 9:30 to 14:00 CET

Location: DTU, Kgs. Lyngby, Denmark

PRESENTATIONS

The meeting will cover the following three themes:

- Impact of EURGen-RefLabCap project activities at national levels
- Epidemiological situation of the 4 EURGen-RefLabCap pathogens in Europe, including cross-border collaboration discussions
- Usefulness of External Quality Assessments (EQAs)

EURGen-RefLabCap Network Meeting 2024

Overview of activities and outcomes during the project

18-19 September 2024

Birgitte Helwigh

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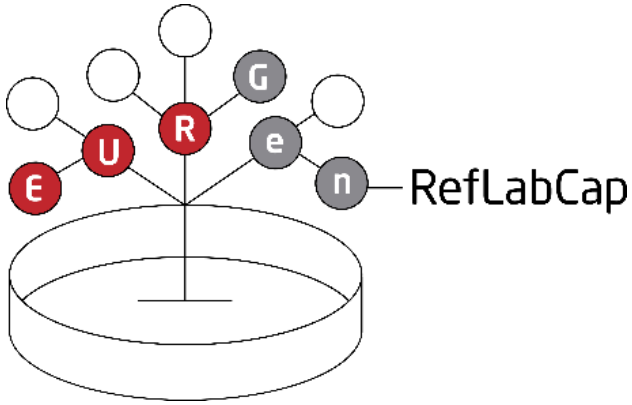

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Deliverables

- Established reference laboratory network for the target pathogens and create a website to host resources

- Identified capacity gaps for national surveillance and integrated outbreak investigations of the target pathogens
  – identification of priority countries

- Develop work plans for technical support activities to meet the identified gaps and needs
  – Action plans for each of the priority countries

- Reports strengths/ weaknesses and gaps/ needs to develop national capacity building activities for regional and local labs

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Deliverables cont.

- Identify existing initiatives in WGS and validate/ propose a common WGS-based genome analysis methods and standard protocols for national surveillance and integrated outbreak investigations
- Provide tailored operation support/ training to priority countries addressing the identified gaps for WGS
- Develop a guidance document on internal quality control schemes for phenotypic antimicrobial susceptibility testing and propose *in vitro* and *in silico* quality assurance scheme(s) to be executed annual for years 2, 3 and 4
- Provide surveys, reports, supporting documents and analysis related to all activities

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Overview of the country's participation in the EURGen-RefLabCap project

Albania
Austria
Belgium
Bosnia-Herzegovina
Bulgaria
Croatia
Cyprus
Czechia
Denmark
Estonia
Finland
France
Germany
Greece
Hungary
Iceland
Ireland
Italy
Kosovo

Latvia
Lithuania
Luxembourg
Malta
Moldova
Montenegro
Netherlands
North Macedonia
Norway
Poland
Portugal
Romania
Serbia
Slovakia
Slovenia
Spain
Sweden
Turkey

Funded by the European Union

Survey on capacity and selection of priority countries

- Establishment of the network
- Kick-off meeting

- Survey on
  - Existing NRL capacity for CCRE
  - Gaps in WGS capacity
- Scoring system for selection of priority countries
  - Invitation to priority countries
- Workplan for technical support for all countries

- Survey on
  - Existing NRL capacity for C/CRAb and C/CRPa

Activity	Participants	Date	No. countries participate
1 Survey on NRL capacity and gaps in WGS for CCRE	All	Jul-21	37
2 Survey on NRL capacity for C/CRAb and C/CRPa	All	Nov-22	22

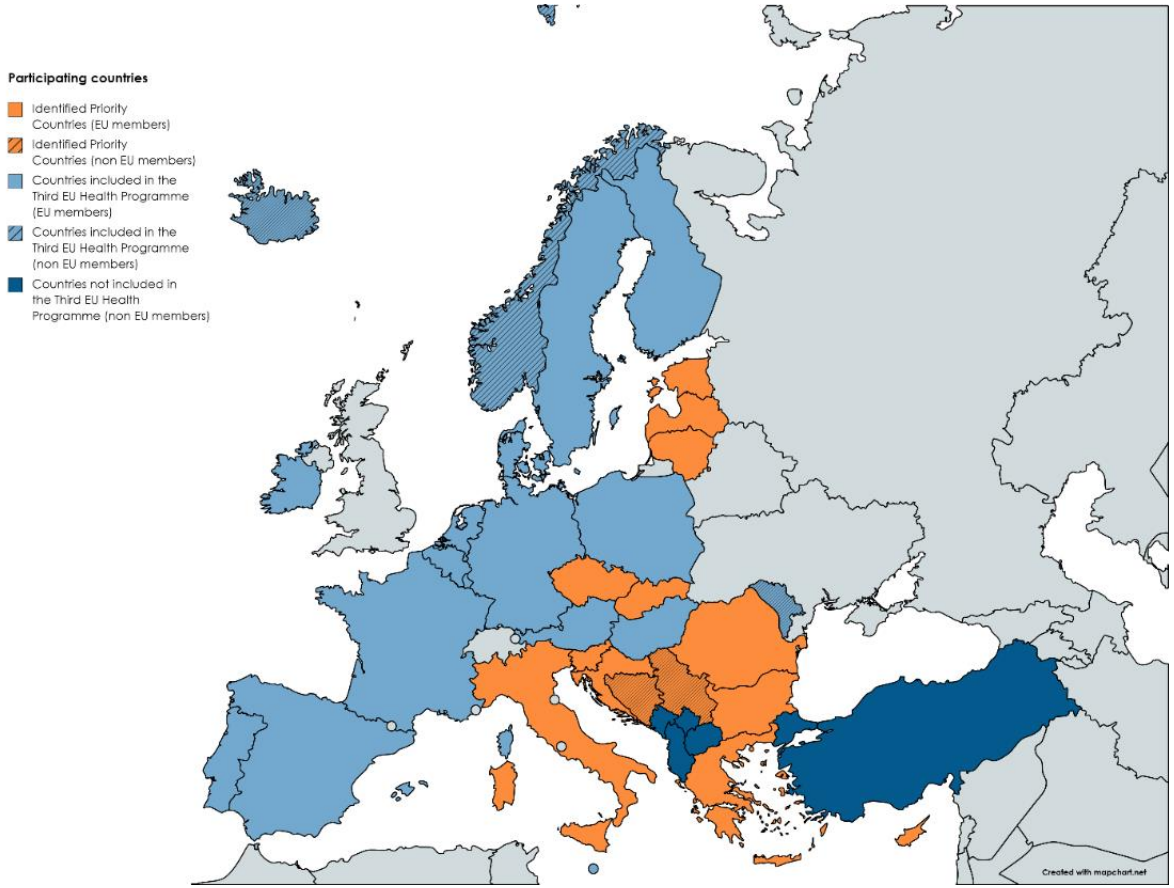
Overview of the country's participation in the EURGen-RefLabCap project

15 countries
Austria
Belgium
Denmark
Finland
France
Germany
Hungary
Iceland
Luxembourg
Malta
Norway
Ireland
Slovakia
Sweden
Netherlands

13 priority countries
Bosnia-Herzegovina
Bulgaria
Croatia
Cyprus
Czechia
Estonia
Greece
Italy
Latvia*
Lithuania
Romania*
Serbia*
Slovenia

4 additional countries
Moldova
Poland
Portugal
Spain

5 CESEAR countries supported by WHO Europe
Albania
Kosovo
Montenegro*
North Macedonia
Turkey

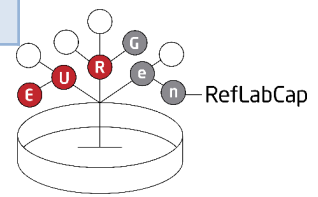


* Latvia, Romania, Serbia and Montenegro ECDC national focal points for AMR did not assign a contact for C/CRAb and C/CRPa (WS2)

Network meetings

Activity	Participants	Date	Total countries participate
1 network meeting (virtual)	All	Dec-21	35
2 network meeting (SSI)	All	Jun-23	32
3 network meeting (DTU)	All	Sep-24	29

Support activities	Priority countries	Additional countries	Non-priority countries
2 Network meeting -overall rating	4.6	4.5	4



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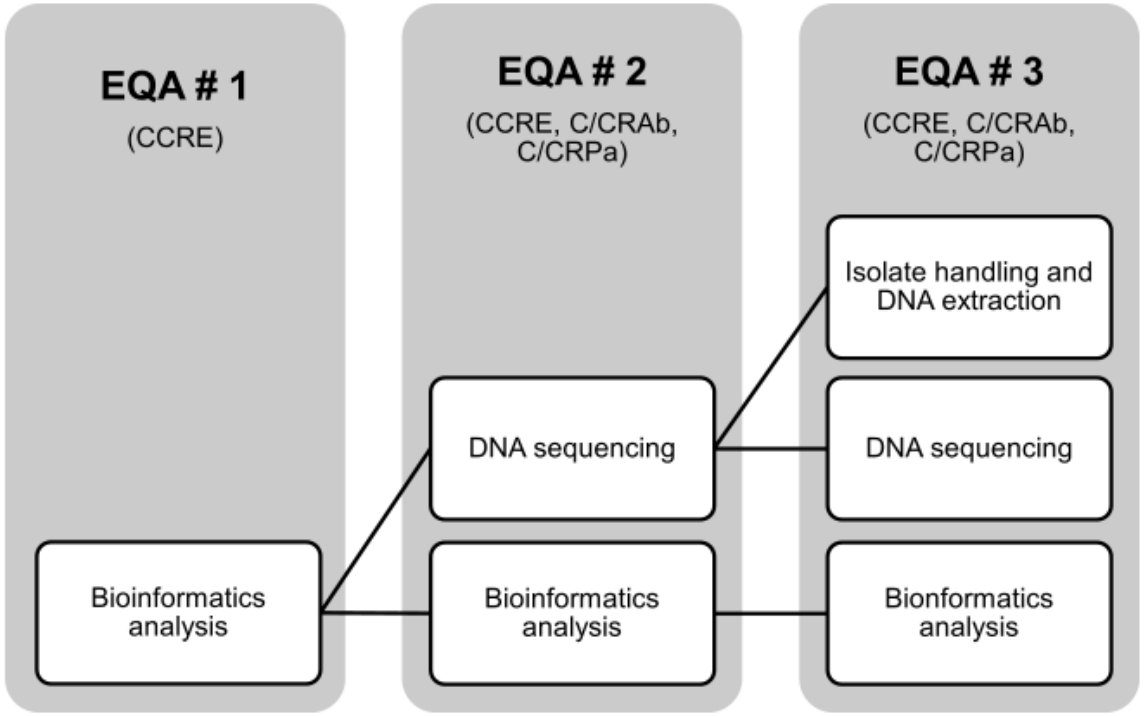
EQAs



Support activities	Priority countries	Additional countries	Non-priority countries
EQA 2023: Protocol	4.6	4.8	4.2
EQA 2023: Webtool for results	4.3	4.2	3.9
EQA 2023: Individual participants' reports	5	4.6	4.3
EQA 2023: Learning	4.9	4.4	4.4

Activity	Participants	Date	Total countries participate
1 EQA WS1	All	2022	29
2 EQA WS1+WS2	All	2023	30
3 EQA WS1+WS2	All	2024	31

Multidisciplinary simulated outbreak exercises

- 5 exercises in total
- Each exercise
  - Two online sessions
  - 4-5 times data sharing between the two online sessions

Priority countries	Additional countries	Non-priority countries
4.6	4.7	4.2

- Outbreak of carbapenemase-producing *Escherichia coli*
- Outbreak of carbapenem-resistant (CRE) *Klebsiella pneumoniae*
- Outbreak of carbapenem-resistant *Pseudomonas aeruginosa* (CRPa)
- Outbreak of carbapenem-resistant and/or colistin-resistant *Acinetobacter baumannii* (CRAb)
- 1 CCRE outbreak simulation in October 2024

Activity	Participants	Date	No. countries participate
1 simulated excercise WS1	All	Sep-22	26
2 simulated excercise WS1	All	May-23	28
3 simulated excercise WS1	All	Oct-24	
1 simulated excercise WS2	All	Sep-23	19
2 simulated excercise WS2	All	Jan-24	21

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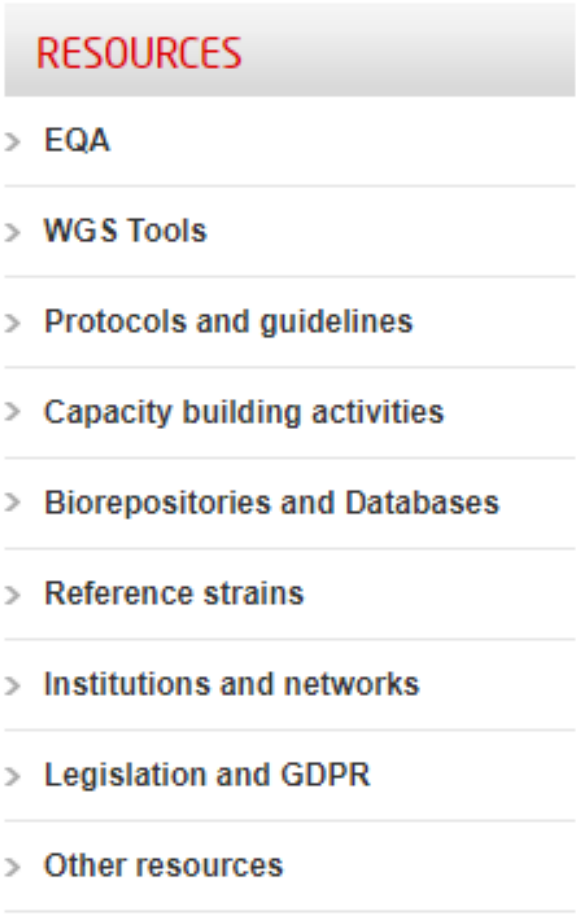
Ressources

Support activities	Priority countries	Additional countries	Non-priority countries
Standard WGS protocol C/CRPa and C/CRAb	4.4	4.8	4.6
Report on national mapping surveys	4.2	4.2	3.6

- Agreed protocols for
  - CCRE surveillance
  - *Pseudomonas aeruginosa* and *Acinetobacter baumannii* surveillance
- Guidance documents on ‘Internal QC schemes
- Reports on national mapping surveys on country specific strengths, weaknesses and further needs
- List of reference strains (https://www.eurgen-reflabcap.eu/resources/reference-strains)



In-person workshops

Activity	Participants	Date	Total countries participate
Train-the-trainer workshop (DTU) (expanded to all) on capacity building activities	All	Jun-22	33
Laboratory workshop (DTU) (WS1) (expanded to all) on WGS and bioinformatics analysis applied to CCRE	All	Dec-22	27
Train-the-trainer workshop (DTU) on organisation of physical and virtual training courses and exercises	PC+Add	Jun-23	13
Laboratory workshop on Nanopore sequencing (MinION) (WS1+WS2)	PC+Add	Dec-23	17
Technical training workshop (DTU) (WS2) (expanded to all) on DATA-for ACTION	All	Sep-24	27

Questions on additional activities for priority and additional countries	Priority countries	Additional countries
Train-the-trainer workshop on organisation of physical and virtual training courses and exercises	4.4	4.5
Laboratory workshop on WGS and bioinformatics analysis applied to CCRE	4.6	4.5
Laboratory workshop on Nanopore sequencing	4.6	4.8

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Activities for priority countries (and additional countries)

- Project management course
- Development of national action plans
- Ongoing bespoke consultancy
- 2 country visits
- Mapping exercise (extended to all)

Activity	Participants	Date	Total countries participate
1 country visit	PC	2022	12
2 country visit	PC	2023/2024	12

- Financial support for
  - Mapping exercise (12 PC and Add)
  - MinION consumables (15 PC and Add)
  - Pilot study (PC and Add)

Activity	Participants	Date	Total countries participate
Nat. mapping survey NRL survey to map local and regional clinical laboratory capacity (expanded to all)	All	2022/2023	26
Pilot study	PC+Add	2023/2024	15 (13)

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Rating of activities

Support activities	Priority countries	Additional countries	Non-priority countries
Conducting mapping exercise of national networks of clinical laboratories	4.7	4.4	3.4

Questions on additional activities for priority and additional countries	Priority countries	Additional countries
National action plan	4.3	-
Bespoke consultancy (regular meetings)	4.5	-
Engagement with clinical laboratories as a result of conducting the survey	4.2	-
WGS pilot study	4.8	4.5
Purchase of Nanopore equipment	4.6	5
Average rating	4.5	4.7

Webinars

Webinars and surveys	participants	date	number of participants
1st virtual workshop/webinar (out of 6) on capacity building (sustainability plans and exit strategies).	PC	May-22	13 countries
2nd virtual workshop/webinar (out of 6) on capacity building (business cases and stakeholders). Course materials are available on the we	PC	Sep-22	8 countries
3rd virtual workshop/webinar (out of 6) on how to plan an EQA	All	Jan-23	28
4th virtual workshop/webinar (out of 6) on ISO principles	All	Apr-24	32
5th virtual workshop/webinar (out of 6) on EU Structure for EU funding by the Commission	All	May-24	49
6th virtual workshop/webinar (out of 6) – topic TBD	**All**	**Nov-24**	
1st webinar (out of 3) about "Demystifying genomics, how do we get started"	All	Sep-22	-
2nd webinar (out of 3) on bioinformatics approaches for plasmid analysis	All	May-23	-
3rd webinar (out of 3) on IPSN	All	Jun-24	35
1st webinar (out of 2) presenting the Guidance document on QC schemes – WS1	All	Nov-22	-
1st webinar (out of 2) presenting the Guidance document on QC schemes – WS2	All	Apr-23	-
2nd webinar (out of 2) – participants experience with IQC	**All**	**Oct-24**	

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Webinars cont.

Webinars and surveys	participants	date	number of participants
1st EQA - webinar presenting results	All	Jun-23	32
2nd EQA - webinar presenting results	All	Nov-23	51
3rd EQA - webinar presenting results	All	Sep-24	48
Webinar presenting WS1 protocol	All	Dec-21	35
Webinar presenting WS2 protocol	All	Jun-23	32
Webinar presenting the Survey on NRL capacity for WS1 pathogens	All	Dec-21	35
Webinar presenting the highlights of existing WGS initiatives regarding CRE/CCRE - WS1	All	Dec-21	35
Webinar presenting the survey on NRL capacity for phenotypic, molecular and WGS-based characterization of CRE/CCRE - WS1	All	Apr-22	22
Webinar presenting the results of the survey on genotypic methods used at the NRLs for WS2 pathogen typing	All	Mar-23	35
1st webinar (out of 3) introducing the WS2 by ECDC	All	Mar-23	35
2nd webinar (out of 3) Data sharing for European surveillance	All	Apr-24	32
3rd webinar (out of 3) Sum-up, next steps for the NRLs, goodbye	**All**	**Nov-24**	

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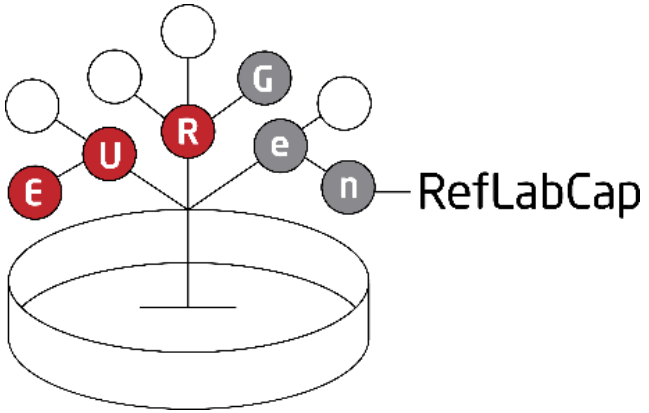

Thank you on behalf of the EURGen-RefLabCap team

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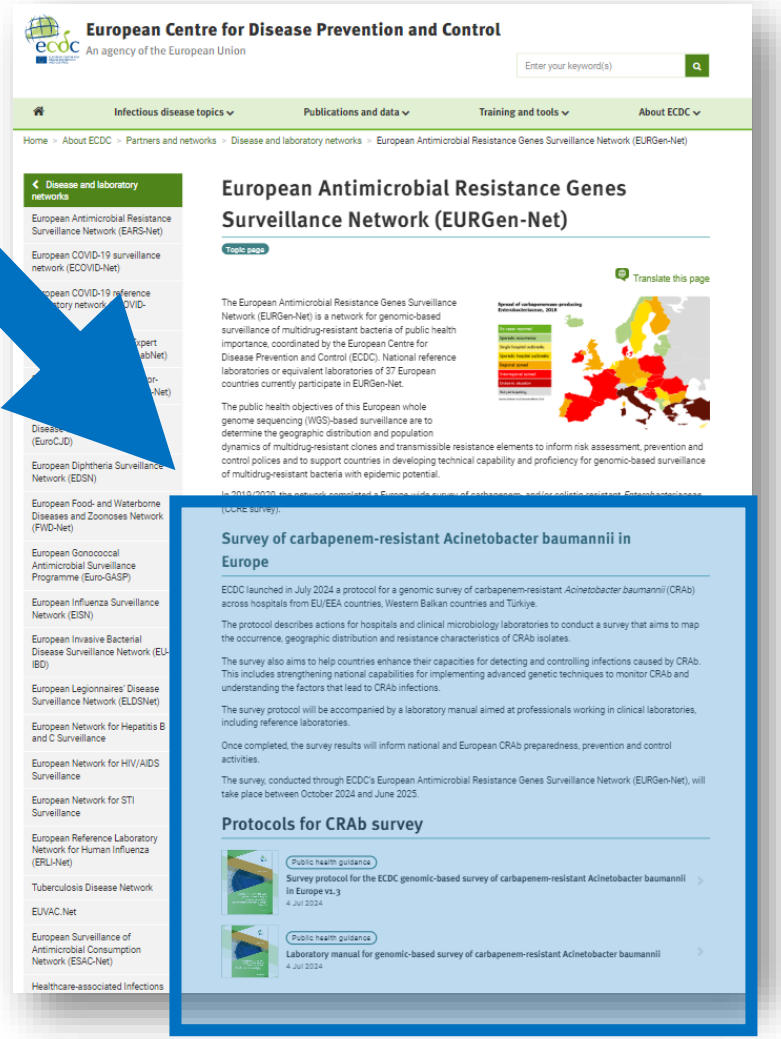
European Centre for Disease Prevention and Control

ECDC genomic-based survey of carbapenem-resistant *Acinetobacter baumannii* in Europe, 2024–2025

Pete Kinross, Principal Expert Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI); ARHAI Section, ECDC; **3rd EURGen-RefLabCap Network Meeting; 18 September 2024**

Rapid overview of ECDC CRAb survey

Full description and survey materials:	See the ECDC EURGen-Net webpage
Isolate collection:	10 consecutive *Acinetobacter `baumannii'* in hospitals **from 1 October 2024** – 30 June 2025
Metadata collection:	Isolate, patient & hospital levels
Why?	**Snapshot of (CR)Ab strains,** and/or transmissible resistance/genetic elements of critical public health importance across <36 European countries, **to inform (CR)Ab IPC and prevention.**



www.ecdc.europa.eu/en/about-us/who-we-work/disease-and-laboratory-networks/EURGen-net

Acknowledgements

ECDC	ARHAI	**Dominique Monnet**, **Holger Hastén**
	Microbiology & Molecular Surveillance Group	**Andreas Hoefer**, **Daniel Palm** Karin Johanson, Marius Linkevicius, Maximillian Reiss
	EARS-Net	**Hanna Merk**, Carlo Gagliotti (contractor), Liselotte Diaz Högberg
	ESAC-Net	**Vivian Leung**, Liselotte Diaz Högberg
	HAI-Net	**Carl Suetens**, Tommi Kärki, Diamantis Plachouras
	EURGen-Net	**Anke Kohlenberg**
	International Relations	Agne Bajoriniene, Georgeta Mureanu
Expert Group	Silva Tafaj, Anette Hammerum, Sotirios Tsiodras, Antoni Hendrickx, Ørjan Samuelsen, Dorota Żabicka, Vera Manageiro, Ana Rita Rebelo **(EARS-Net EQA** and **EURGen-RefLabCap),** Thierry Naas **(ESGARS),** Emine Alp Mese **(ESGCIP** and **EUCIC),** Christian Giske **(EUCAST)**	
EUCAST	**Christian Giske**	
Institut Pasteur (CRBIP)	**Fay Betsou; Mariana Ferrari**, Olivier Chesneau, Dominique Clermont	
EURGen-RefLabCap	**Ana Rita Bastos Rebelo**, Birgitte Helwigh, Rene Hendriksen (DTU FOOD) **Valeria Bortolaia**, Lina Maria Cavaco (SSI, DK)	

Participants in EURGen-Net, EURGen-RefLabCap, and the EuSCAPE projects

(Observer) National Focal Points for AMR; Operational Contact Points/Contact Points for Operations for AMRISO

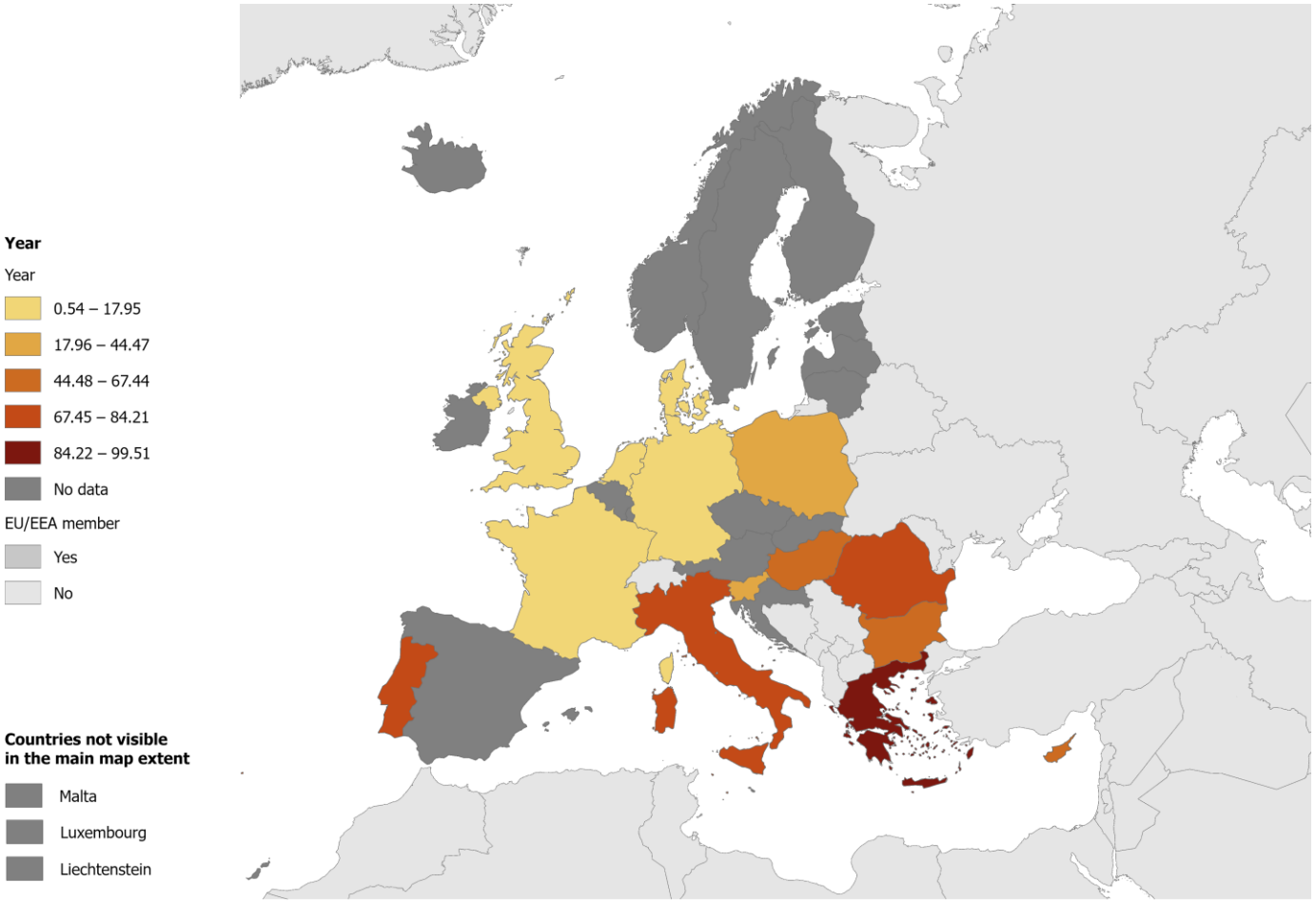
Trends in % phenotypic resistance to carbapenems, among invasive isolates of *Acinetobacter* spp.

EARS-Net, 2012–2023

% resistance to carbapenems, among invasive isolates of *Acinetobacter* spp. reported to ECDC

EARS-Net, 2012–2022

2012

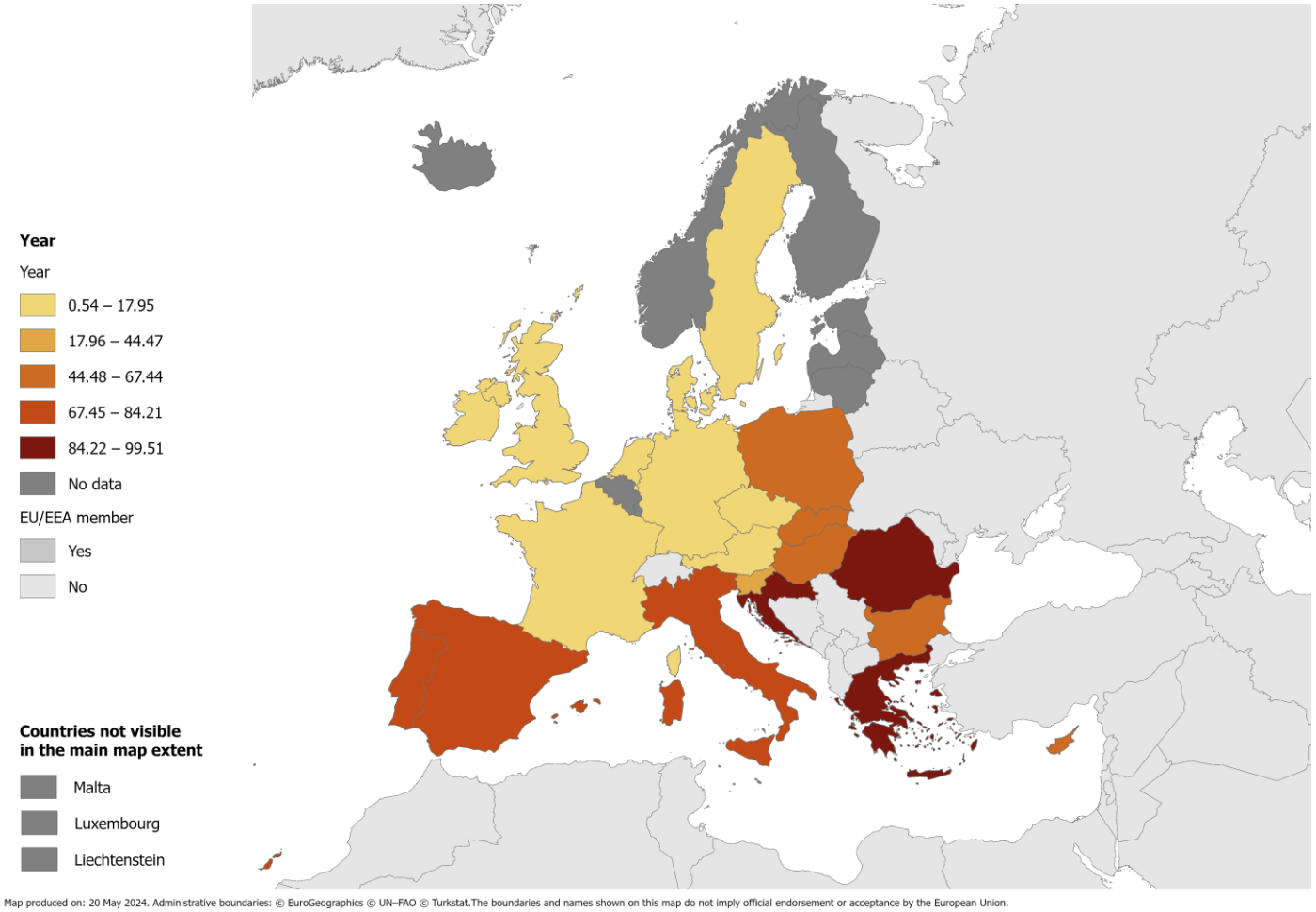


Source: Surveillance Atlas of Infectious Diseases (europa.eu) / https://geoportal.ecdc.europa.eu/

% resistance to carbapenems, among invasive isolates of *Acinetobacter* spp. reported to ECDC

EARS-Net, 2012–2022

2013



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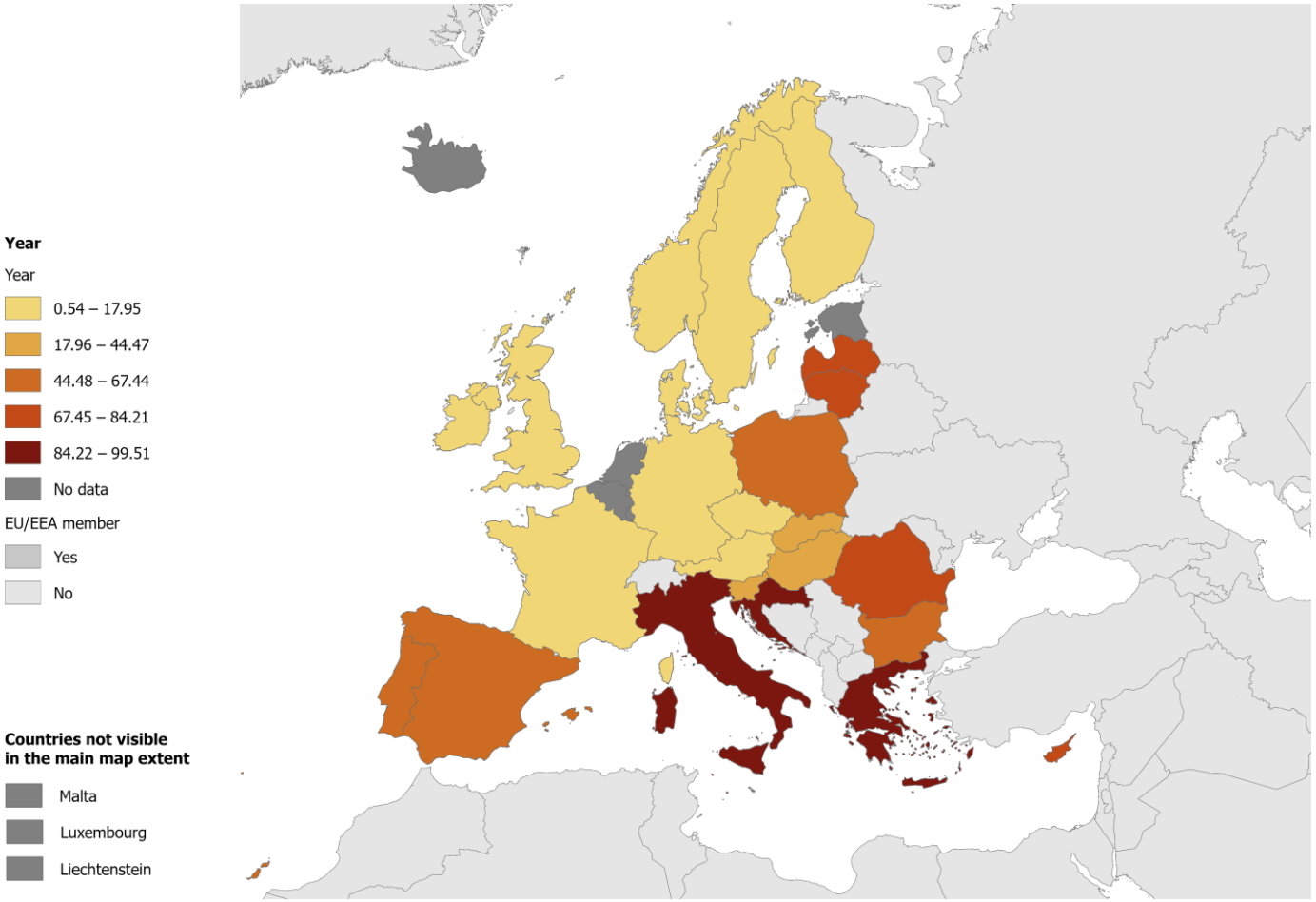
EARS-Net, 2012–2022

2014



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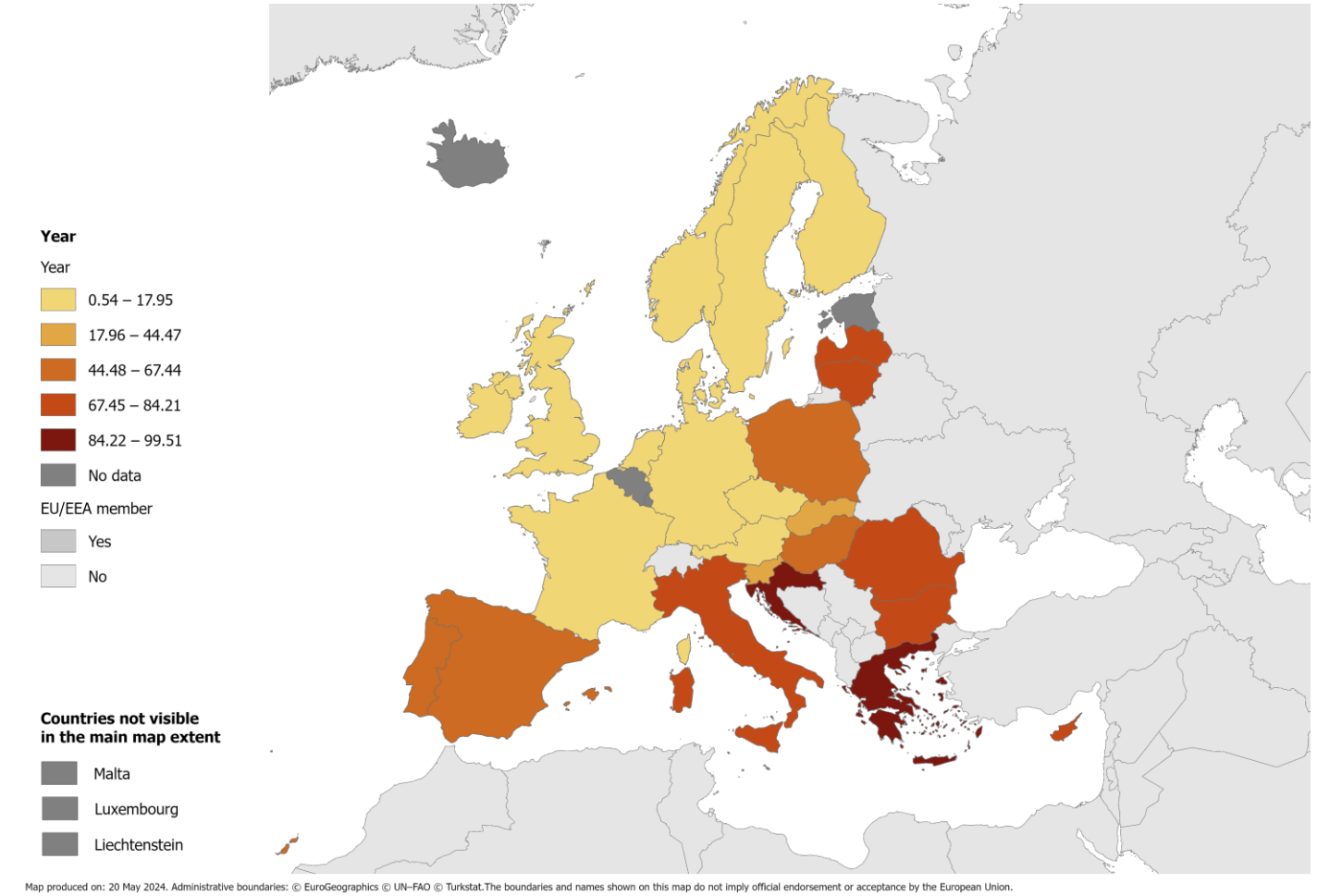
EARS-Net, 2012–2022

2015



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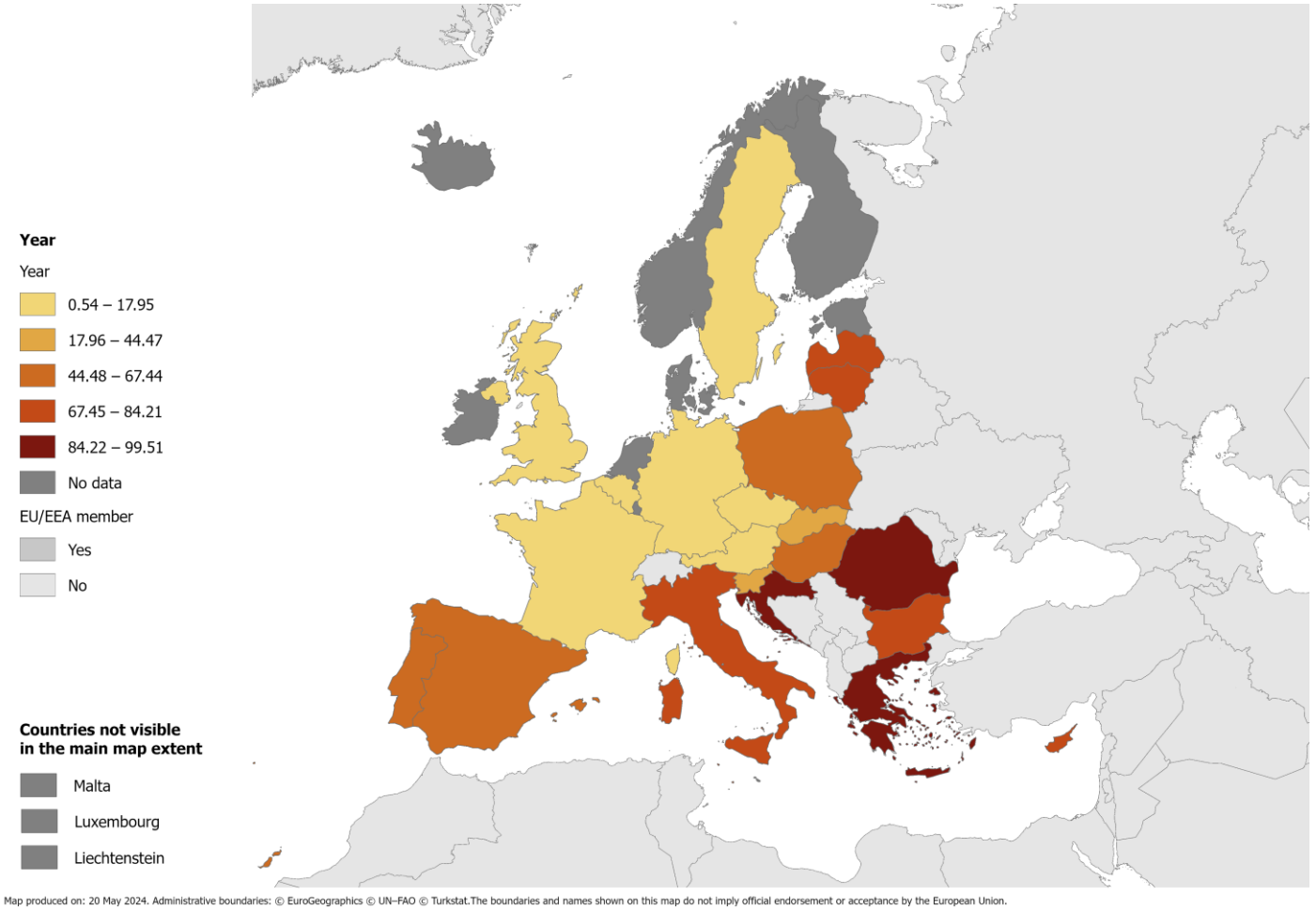
EARS-Net, 2012–2022

2016



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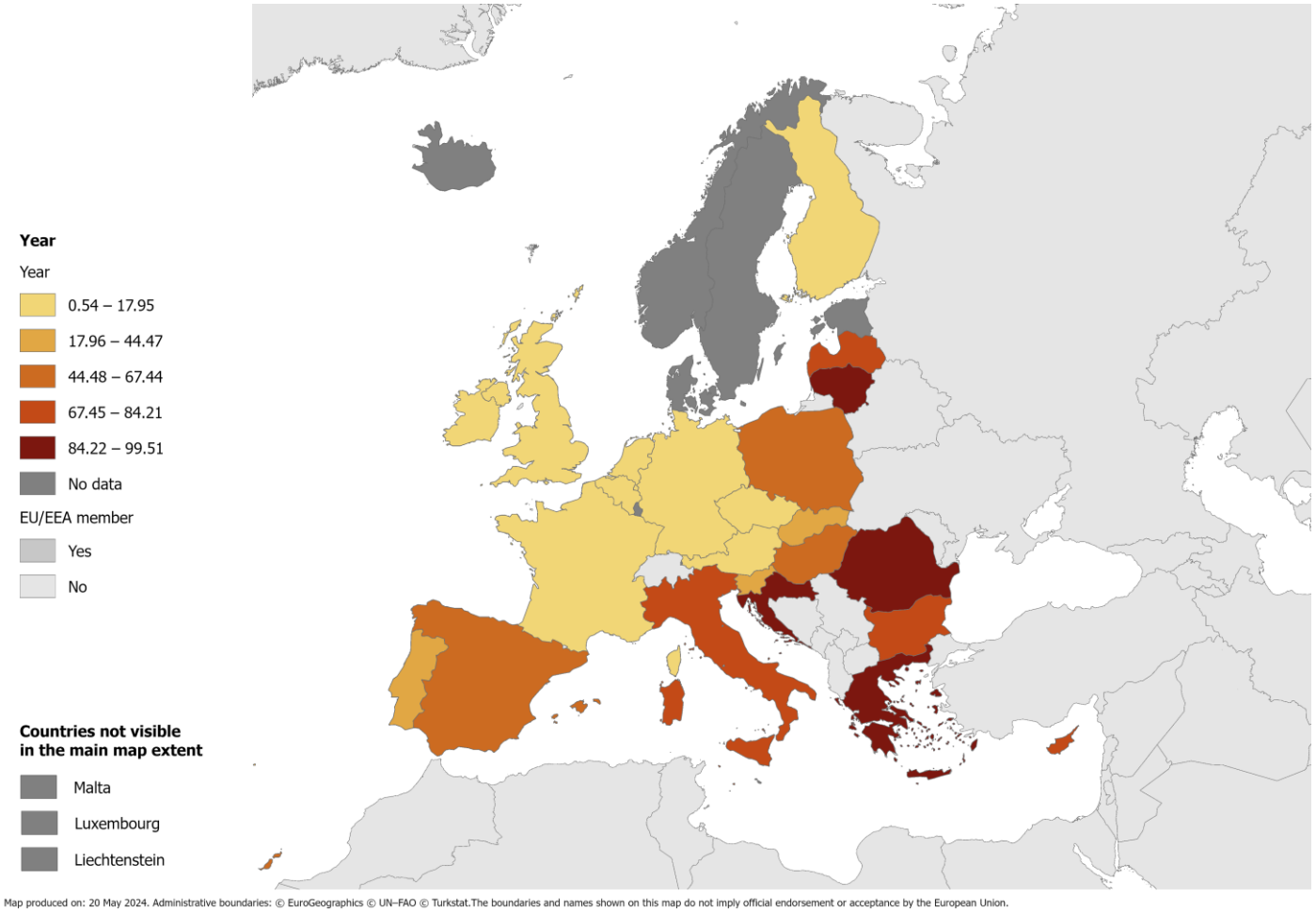
EARS-Net, 2012–2022

2017



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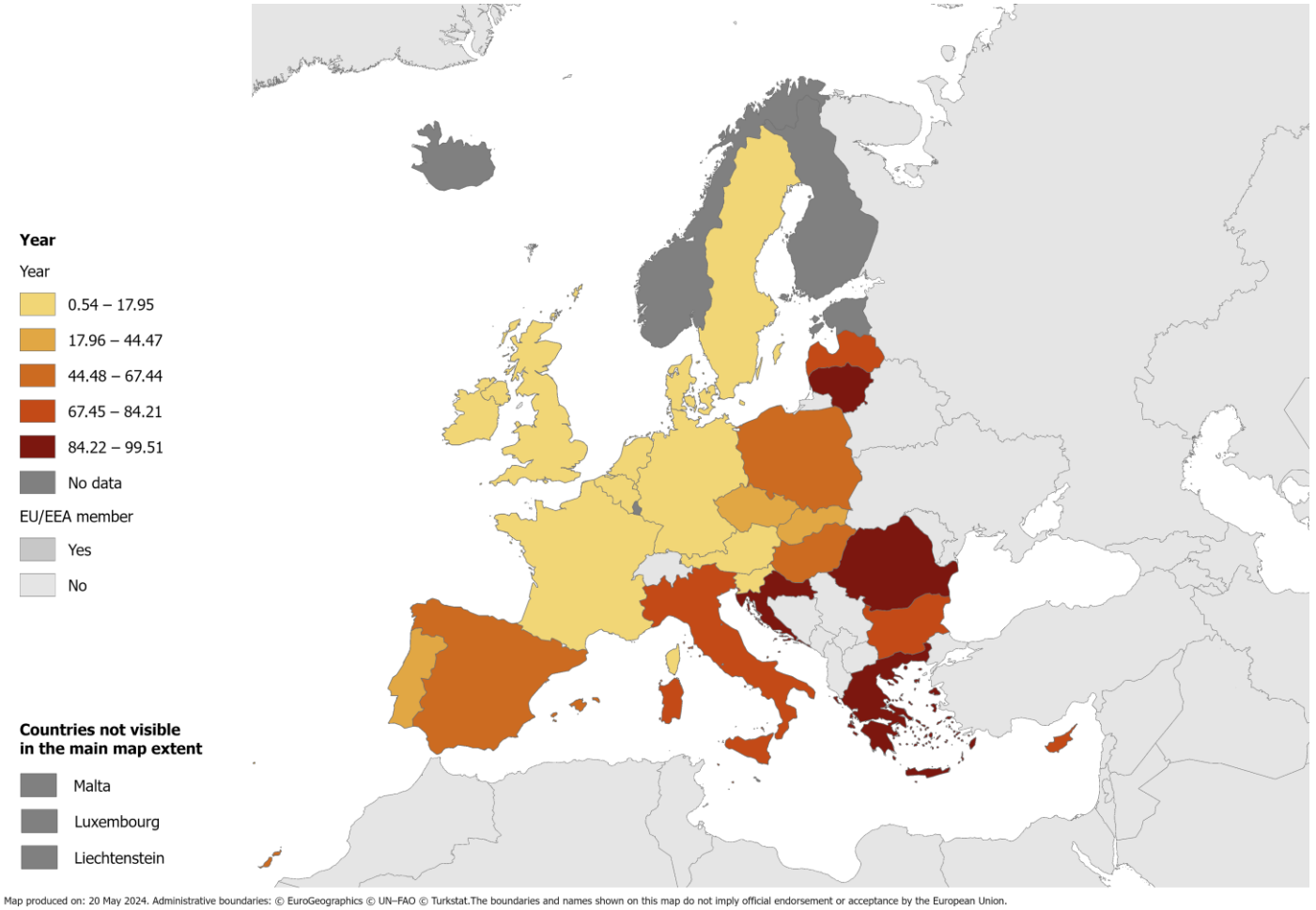
EARS-Net, 2012–2022

2018



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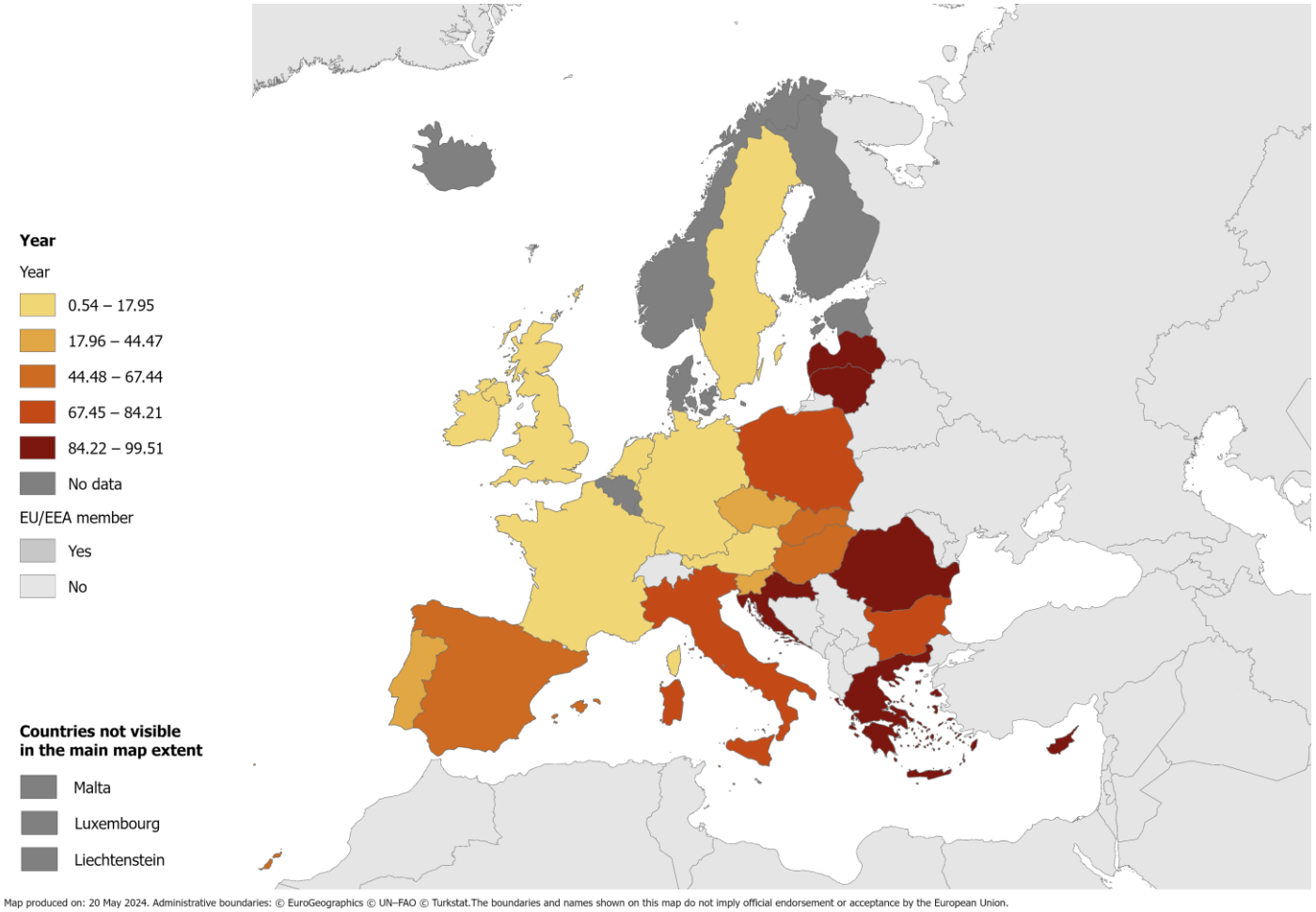
2019



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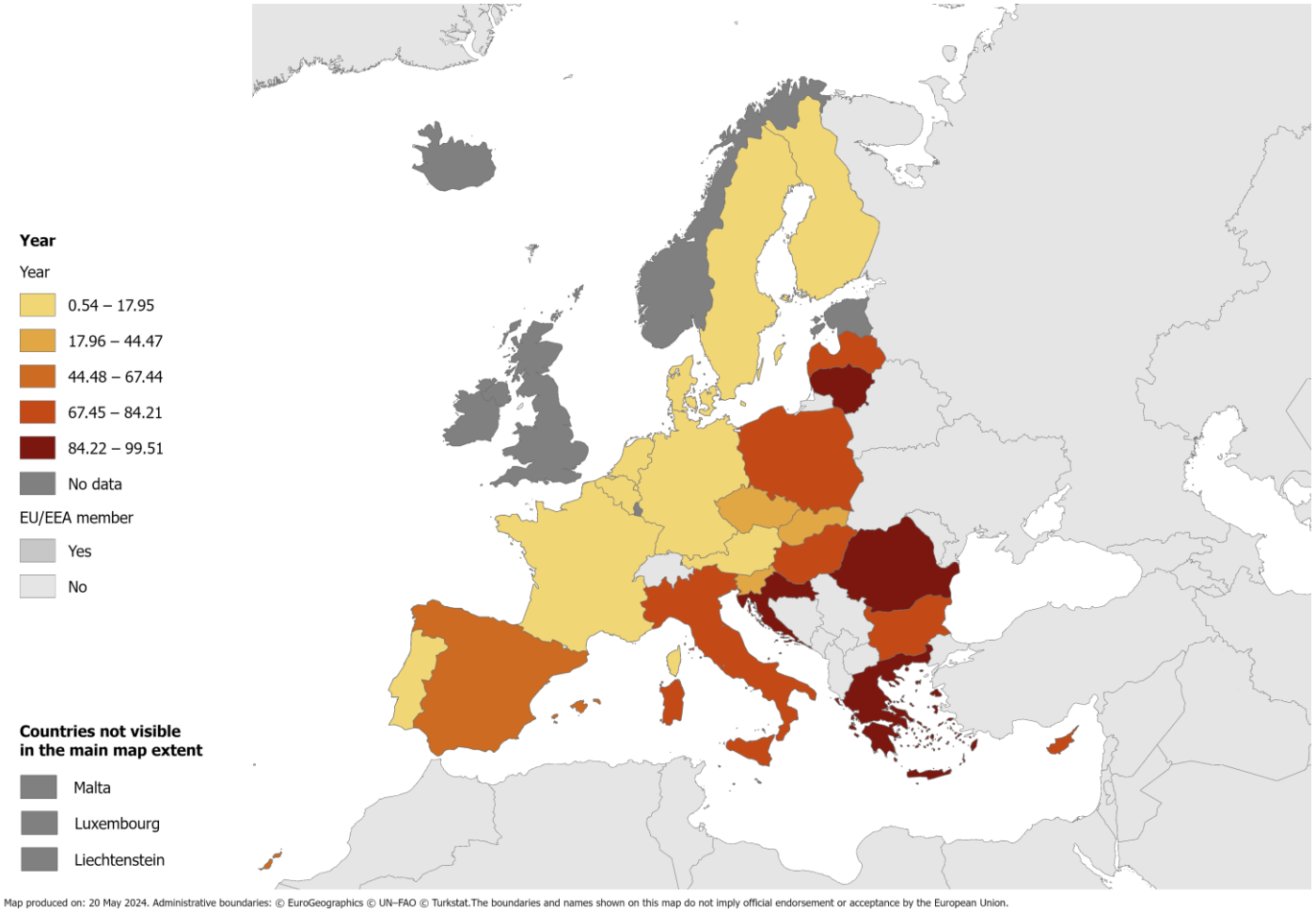
2020



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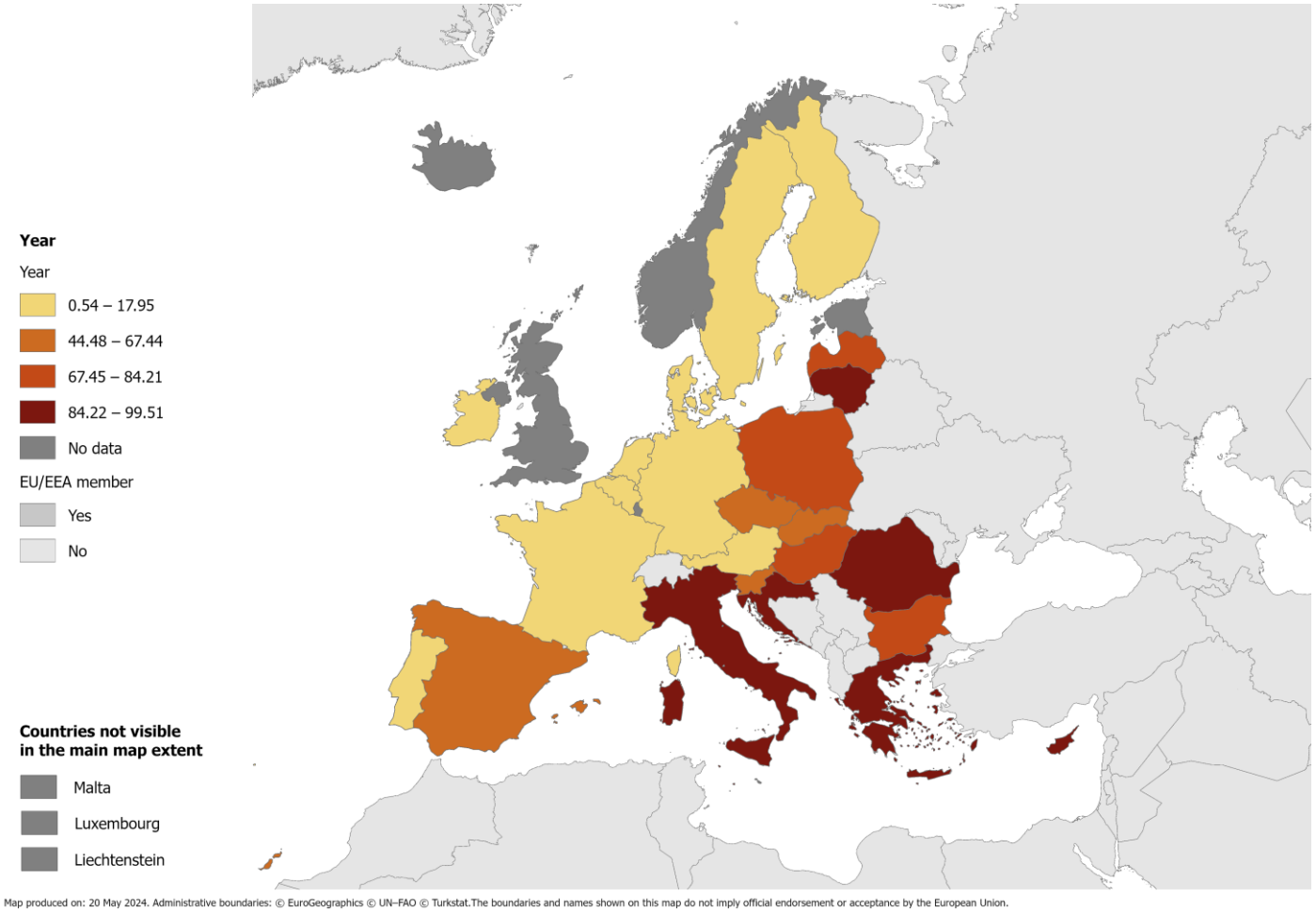
2021



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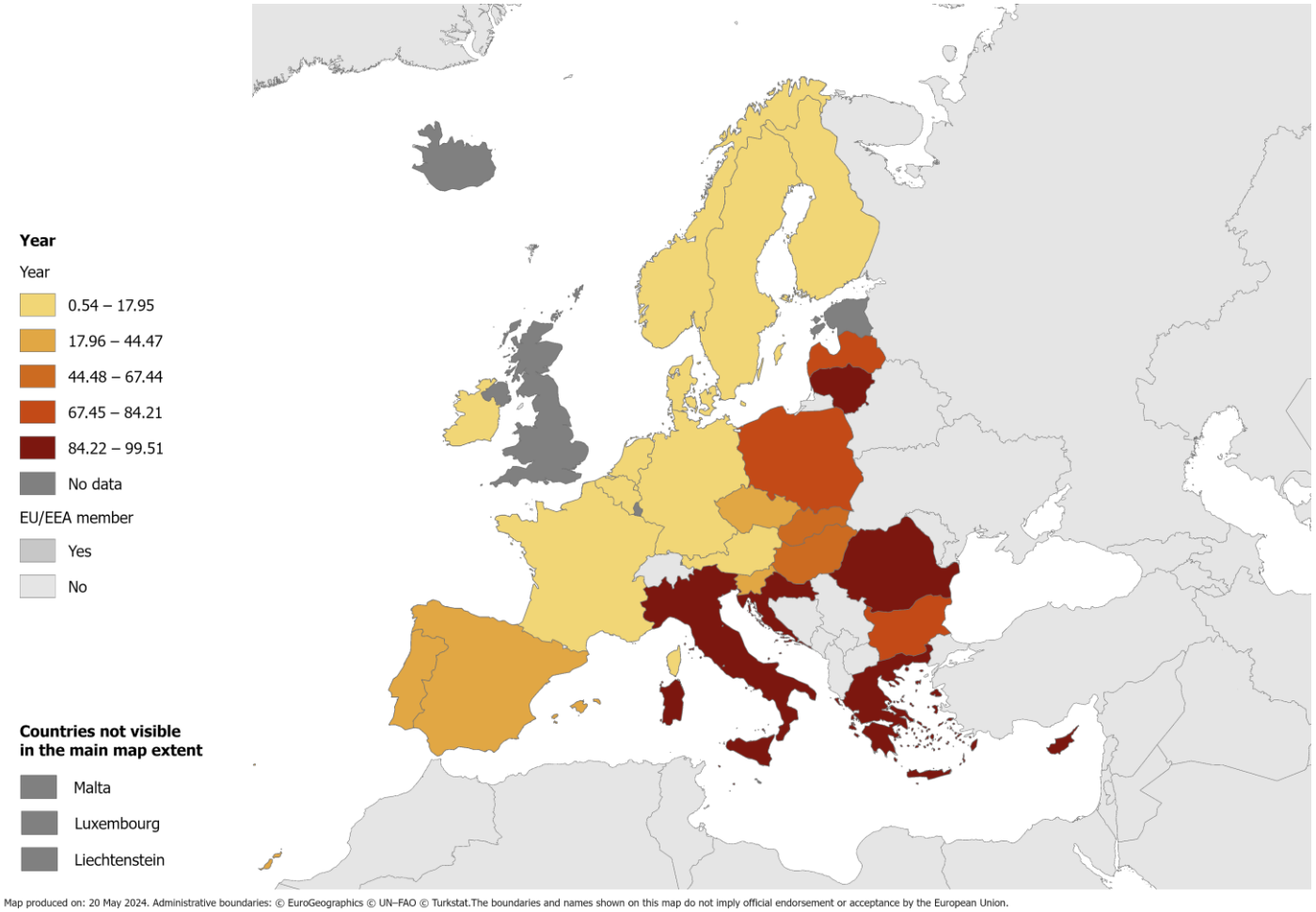
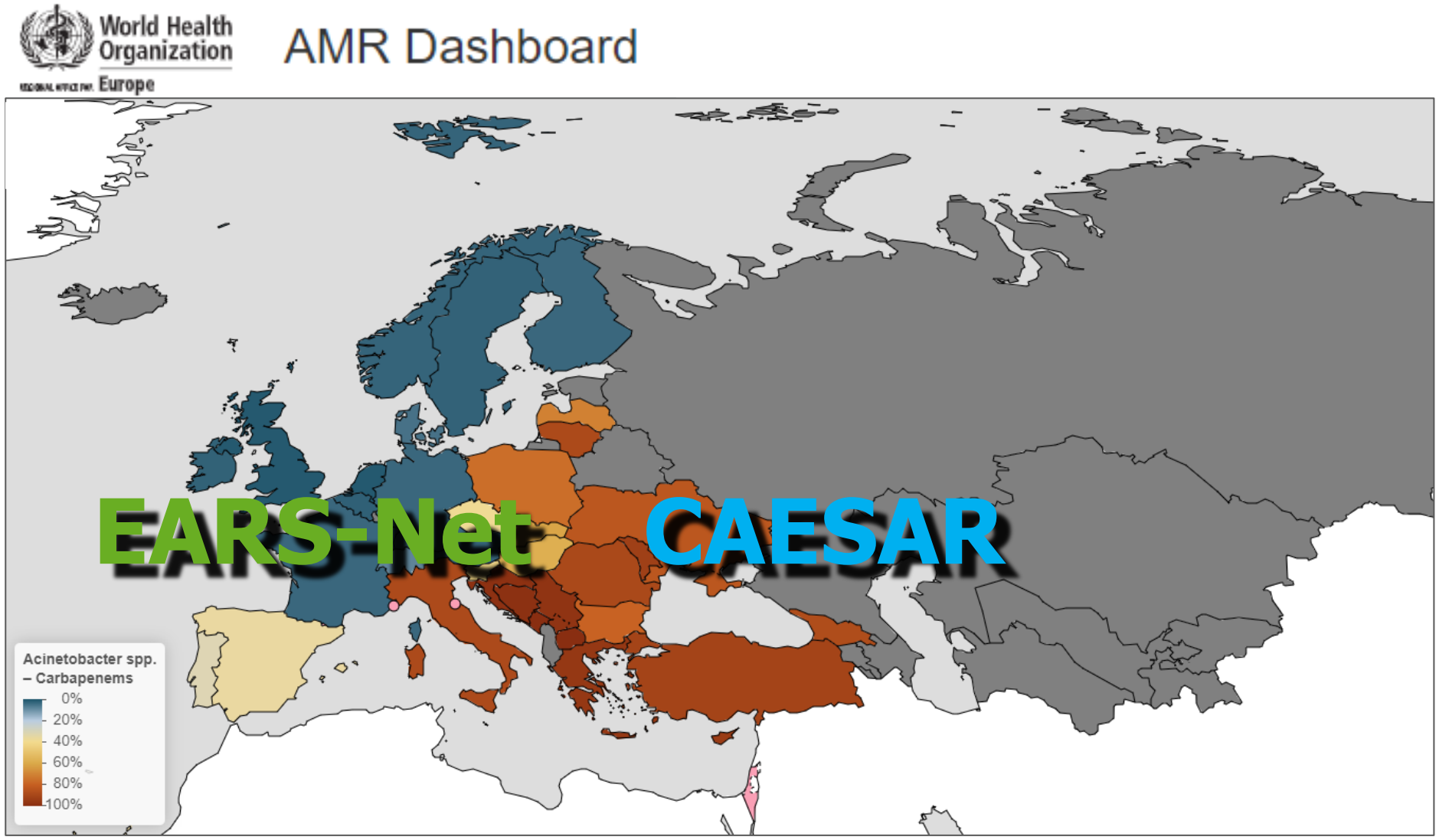
2022



Source: Surveillance Atlas of Infectious Diseases (europa.eu) / https://geoportal.ecdc.europa.eu/

% of invasive isolates of *Acinetobacter* species with resistance to carbapenems, by country, 2022



Source: Antimicrobial resistance dashboard. Copenhagen: WHO Regional Office for Europe; 2023 (https://worldhealthorg.shinyapps.io/WHO-AMR-Dashboard-main/, accessed 24-11-2023).

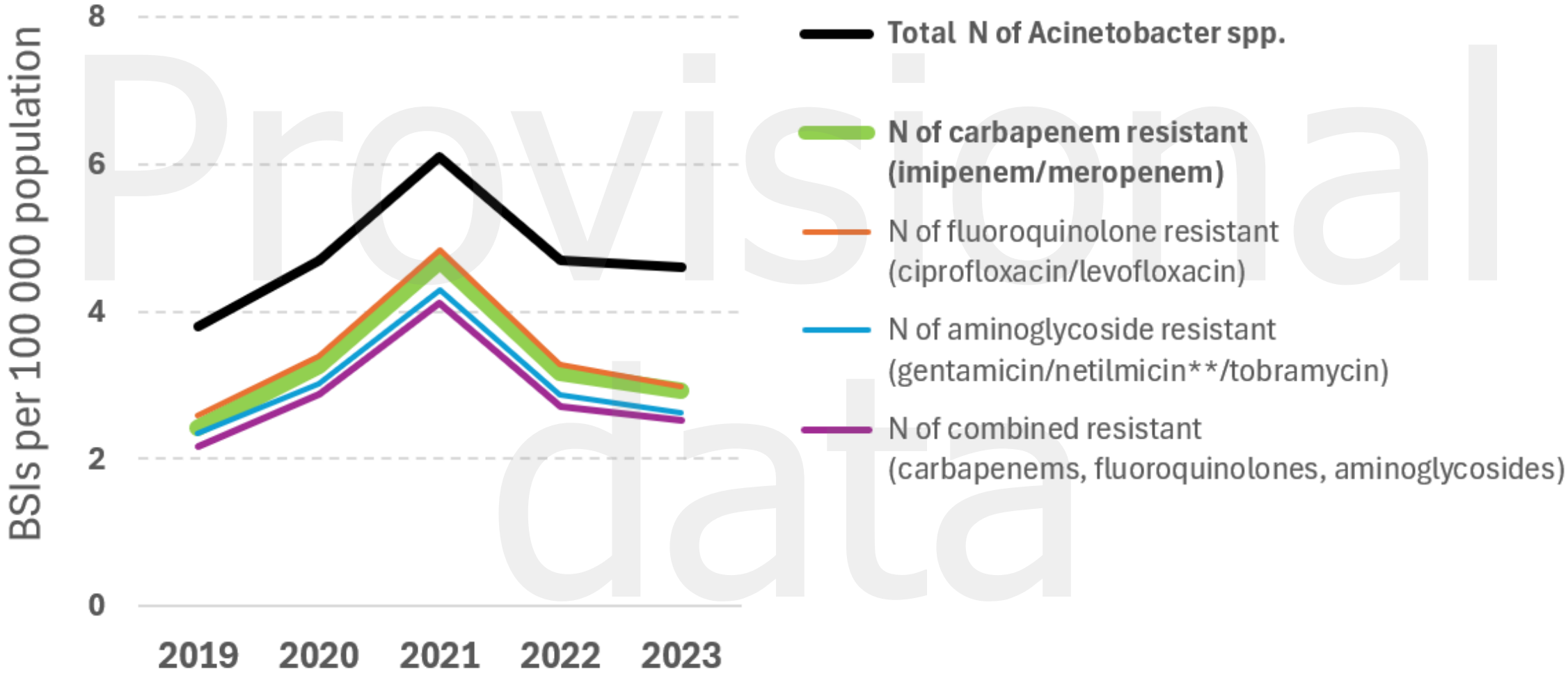
New surveillance data: EARS-Net **2023**

Estimated incidence of bloodstream infections (BSIs) with *Acinetobacter* species, EU/EEA*

Provisional data

* excluding the United Kingdom; excluding France for results other than *Streptococcus pneumoniae*;
** aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.

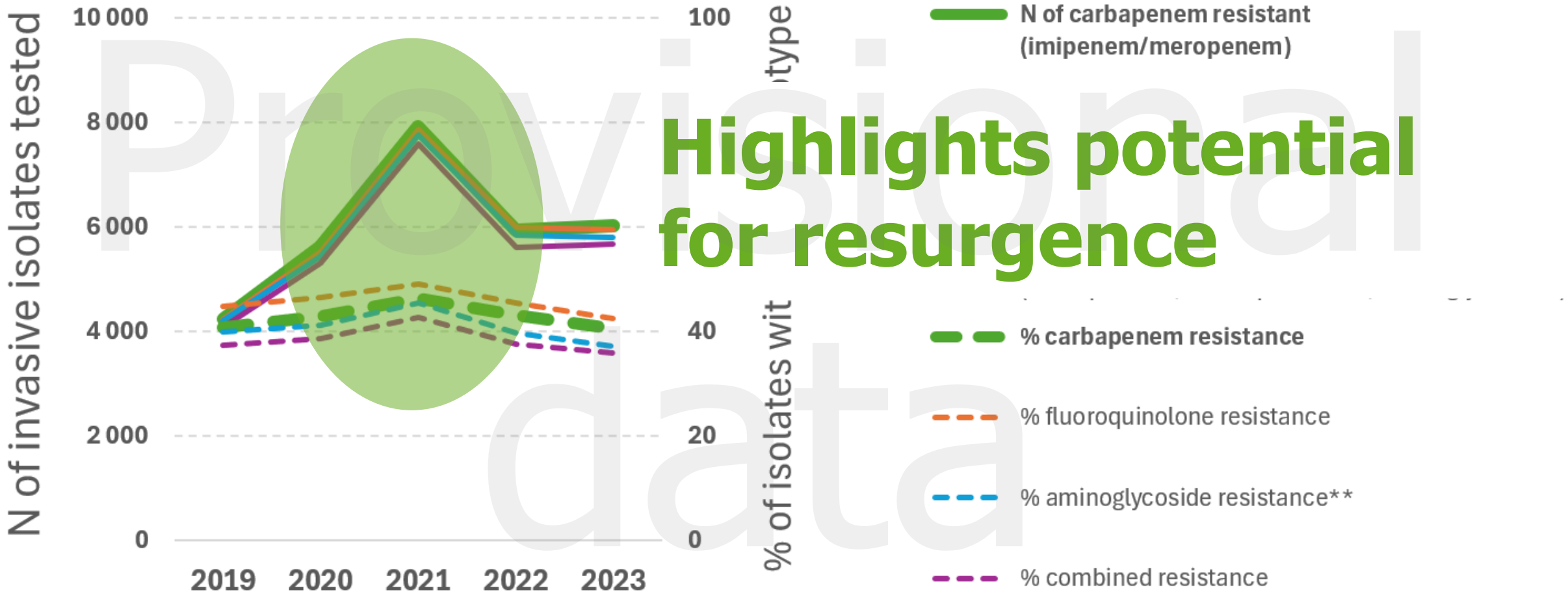
Estimated incidence of bloodstream infections (BSIs) with *Acinetobacter* species, EU/EEA*



* excluding the United Kingdom; excluding France for results other than *Streptococcus pneumoniae*;

** aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.

Total N of invasive isolates (BSI and CSF samples) tested and % of isolates with AMR phenotype in EU/EEA*, 2019–2023 among labs reporting consistently over the 5-years period



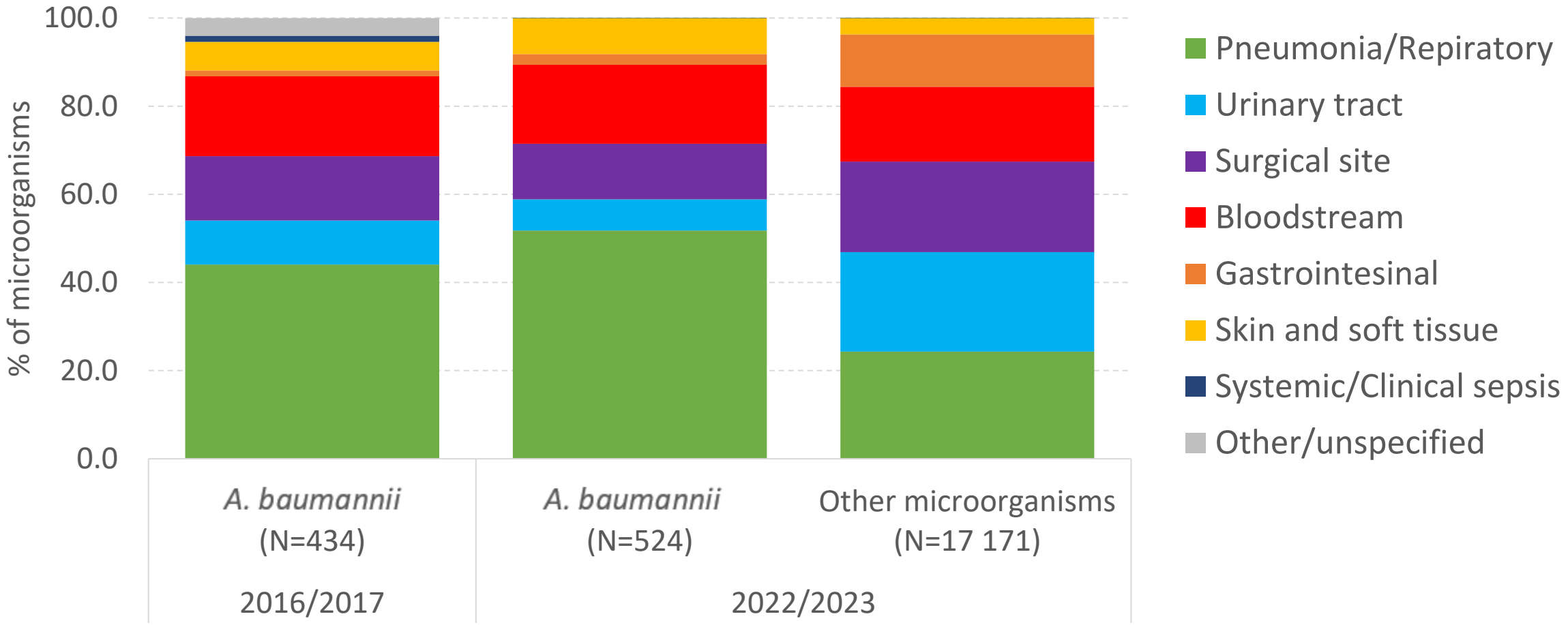
Highlights potential for resurgence

* excluding the United Kingdom; excluding France for results other than *Streptococcus pneumoniae*;

** aminoglycoside group includes only gentamicin and tobramycin from 2020 onwards.

Infection type of healthcare-associated infections, by reported microorganism

ECDC point prevalence surveys of European acute care hospitals, 2016/2017 and 2022/2022



Sources: adapted from 'ECDC PPS of HAIs and antimicrobial use in European acute care hospitals, 2016/2017' and 'ECDC PPS of HAIs and antimicrobial use in European acute care hospitals, 2022/2023'

ECDC CRAb survey

1 October 2024 – 30 June 2025

General approach for the ECDC CRAb survey,

2024/2025

Avoid/minimise	Promote/incorporate
× Duplication of parallel activities (e.g. capacity building, genomic proficiency testing, …).	☑ **Acquire a comparable sample of isolates from the post-pandemic period from across Europe *before resurgence?!?***
× Submission of national WGS data for this study.	☑ **Acquire a standardised, centrally-produced WGS (FASTA) dataset.**
× National/regional/local genomic screening/analyses.	☑ Standard reporting to ECDC (EpiPulse Cases*).
× **Non-routine laboratory procedures for local/regional laboratories.**	☑ Minimise laboratory procedures at local/ regional/national levels. ☑ **Utilise & support national pathways for CRAb isolates**.

* EpiPulse Cases is the successor to TESSy, the ECDC public health surveillance database.

Aim

to conduct a survey of

carbapenem-resistant *Acinetobacter baumannii** (CRAb)

in **European clinical laboratories**,

in order to acquire

a snapshot of circulating strains,

for the purposes of genomic surveillance,

and

to support national activities to collect a representative sample of CRAb isolates, for national CRAb infection prevention and control efforts.

Primary objective

to describe
the **occurrence and geographic distribution** of

CRAb strains, and/or

transmissible resistance/genetic elements of critical public health importance within CRAb strains,

among **patients**

in acute care hospitals in Europe,

in order to inform prevention and control activities.

* See specific session regarding species identification, i.e.
'gold standard' *Acinetobacter baumannii* species = NCBI taxonomy code NCBI:txid470 (Bouvet and Grimont, 1986)

Secondary objectives

- To **estimate the cumulative incidence of CRAb** in participating acute care hospitals during the survey period.

- To **identify epidemiological factors for infection (or colonisation)** with CRAb at clonal and sub-genomic level.

- To **support EU/EEA countries** in developing technical capabilities and proficiency in genomic-based surveillance and risk assessments of CRAb, **to facilitate their identification of transmission chains, to enable targeted infection control interventions**.

Timeline

Activities for 'National Survey Coordinators' (NSCs)

Survey protocol & lab manual

Finalisation | Publication

ECDC CRAb survey:
6-month survey period
within 1 Oct 2024 – 30 Jun 2025

Designation as **NSC**

ECDC technical meeting for NTCs

ECDC kick-off meeting for NTCs

EURL for AMR:
TBC: (EARS-Net) EQA of phenotypic AST

Mar Apr May Jun Jul Aug Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

2024 23/5 26/9 **2025**

- **Recruit hospitals & labs;** Support hospitals & labs in execution of survey
- Material Transfer Agreements (MTA) (1 per country, based on CCRE MTA) with strain collection contractor

Receive & collate hospital & lab metadata

Upload AMRISO metadata to ECDC*

Liaise with ECDC re uploaded AMRISO data
e.g. correcting implausible/missing data

* i.e. report to EpiPulse Cases (the ECDC surveillance database) e.g. in collaboration with OCP colleagues.

Activities for National Reference/Expert Laboratories

Survey protocol & lab manual

Finalisation | Publication

ECDC CRAb survey:
6-month survey period
within 1 Oct 2024 – 30 Jun 2025

Designation as **NRL**

ECDC technical meeting for NTCs

ECDC kick-off meeting for NTCs

EURL for AMR:
TBC: (EARS-Net) EQA of phenotypic AST

Mar Apr May Jun Jul Aug Sept Oct Nov Dec Jan Feb Mar Apr May Jun Jul Aug Sep Oct Nov Dec

2024 23/5 26/9 **2025**

Receive isolates from regional/local labs;
perform confirmatory carbapenem susc. testing

Prepare bacterial cultures/pellets/agar plates
& send to ECDC contractor (Institut Pasteur, Paris)

If insufficient sample quality, re-send

Optionally: report additional phenotypic AST results to NSC

Reviewed survey protocol & lab manual

Virtual meeting: Expert Group for microbiological aspects

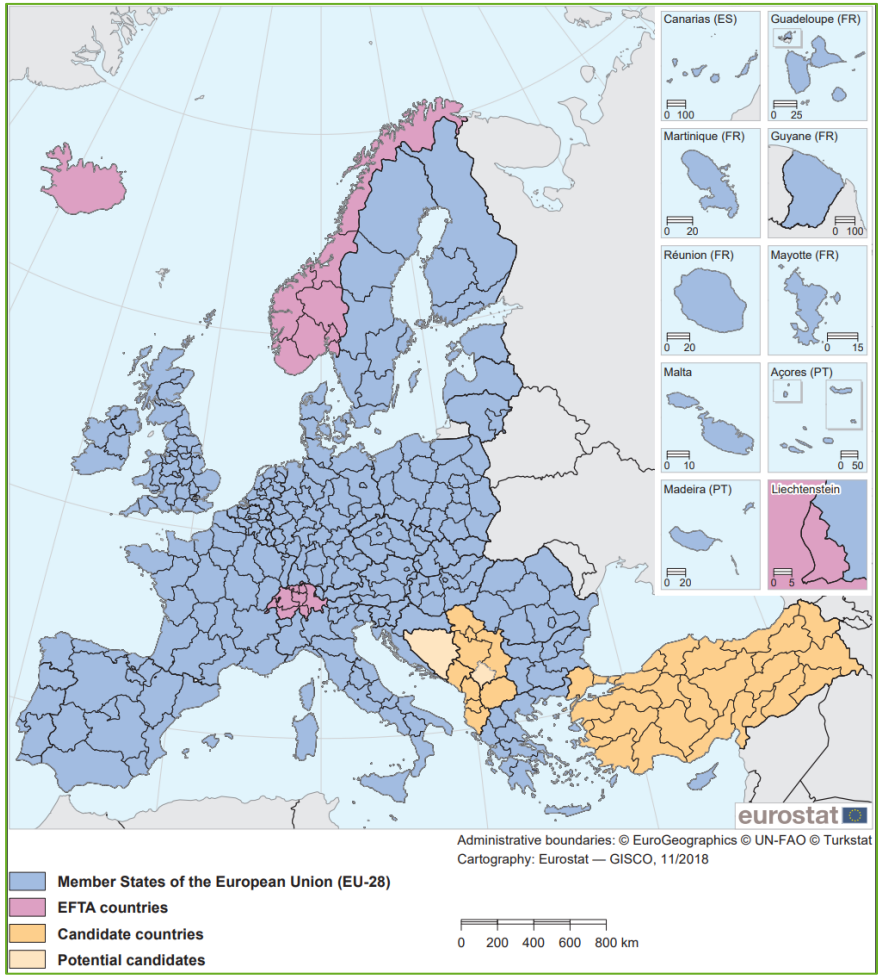
* including NFPs for AMR & OCPs for AMRISO

Study design

Proposed sampling frame: 1 acute care hospital per NUTS 2 region, in EU/EEA countries, Western Balkan countries, and Türkiye

These geographical criteria are flexible

NUTS 2 regions (N~290 †)



NUTS 2 populations

Mean: **1.84 M**
EU/EEA

Smallest: 86 487
Melilla, ES

Largest: 12.2 M
Île-de-France, FR

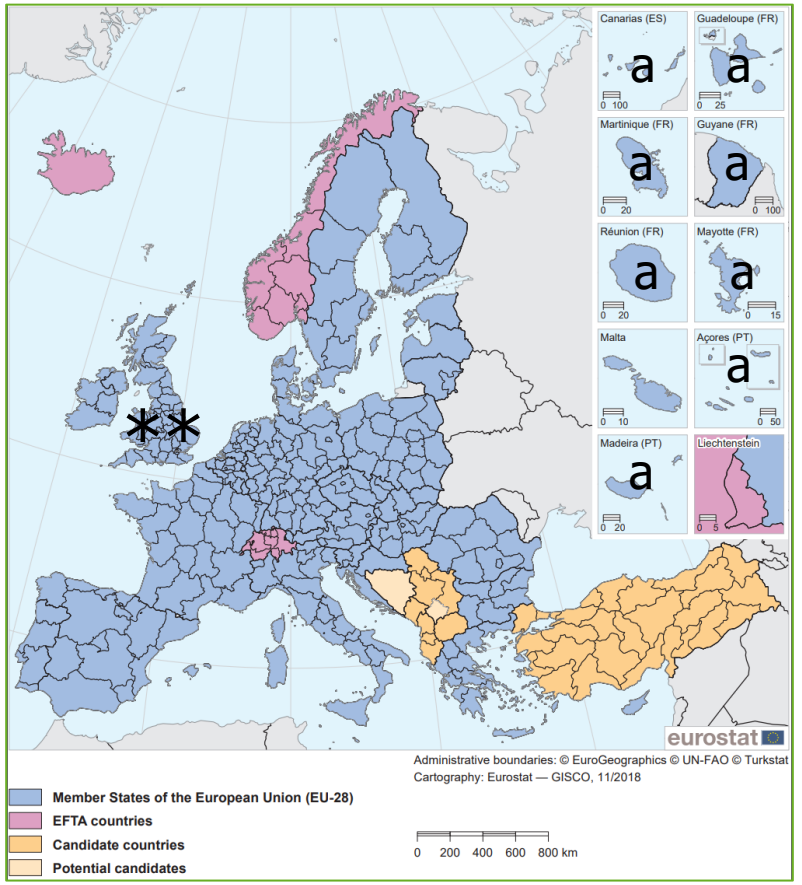
*Eurostat, 2024. †– excludes 'extra-territorial regions'

Number and location of NUTS 1 and NUTS 2 regions in countries eligible to participate in the ECDC CRAb survey 2024/2025

These geographical criteria are flexible; the table is a guide

	NUTS 1	NUTS 2		NUTS 1	NUTS 2		NUTS 1	NUTS 2
Austria	3	**9**	Italy	5	**21**	Iceland	1	**1**
Belgium	3	**11**	Latvia	1	**1**	Liechtenstein	1	**1**
Bulgaria	2	**6**	Lithuania	1	**2**	Norway	1	**7**
Croatia	1	**4**	Luxembourg	1	**1**	**Total EEA**	**3**	**9**
Cyprus	1	**1**	Malta	1	**1**	Albania	1	**3**
Czechia	1	**8**	The Netherlands	4	**12**	Bosnia and Herzegovina	1[b]	**2**[b]
Denmark	1	**5**	Poland	7	**17**	Kosovo*	1	**1**
Estonia	1	**1**	Portugal	3	**9**	Montenegro	1	**1**
Finland	2	**5**	Romania	4	**8**	North Macedonia	1	**1**
France	14	**27**	Slovenia	1	**4**	Serbia	2	**4**
Germany	16	**38**	Slovenia	1	**2**	Türkiye	12	**26**
Greece	4	**13**	Spain	7	**19**	**Total EU candidate /potential candidate**	18[b]	**26**[b]
Hungary	3	**8**	Sweden	3	**8**			
Ireland	1	**3**	**Total EU**	92	**244**			
						All EU/EEA and non-EU/EEA	114[b]	**290**[b]

NUTS 2 regions (N~290 †)



**UK not eligible to participate, as it is not a EU candidate country; [a] – table excludes extra-territorial regions; [b] estimate, based on population size (no Eurostat data available)
* This designation is without prejudice to positions on status, and is in line with UNSCR 1244 and the ICJ Opinion on the Kosovo declaration of independence
Source: Eurostat, 2024 update; In non-EU/EEA countries, NUTS='Statistical regions'

Estimated N of CRAb & CSAb detections in each participating hospital, ECDC CRAb survey 2024/2025

Prioritisation of strain collection for the ECDC CRAb survey, 2024/2025: CRAb infections > CRAb colonisations > CSAb infections > CSAb colonisations

	A. baumannii* infections detected in each participating hospital
Country percentile of est. incidence of invasive *Acinetobacter* spp. (EARS-Net)	
10th percentile	
25th percentile	
50th percentile	
75th percentile	
90th percentile	

* Assumes a catchment area of 1.8 million population, and population coverage of 70% and 30% in countries with CR-Acinetobacter incidence >25th percentile and ≤25th percentile, respectively. Methodology to estimate total CRAb follows: ECDC BCoDe (Cassini, LID, 2019) / ECDC technical report 'Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020', 2022. Est. incidence = estimated cases per 100 000 population per year (average of 2019 and 2022).

Estimated N of CRAb & CSAb detections in each participating hospital, ECDC CRAb survey 2024/2025

Prioritisation of strain collection for the ECDC CRAb survey, 2024/2025: CRAb infections > CRAb colonisations > CSAb infections > CSAb colonisations

	A. baumannii* infections detected in each participating hospital	
	CRAb isolates	
Country percentile of est. incidence of invasive *Acinetobacter* spp. (EARS-Net)	**N of weeks to collect 10 isolates**	**N of isolates in 6 months**
10th percentile	662	1
25th percentile	163	1
50th percentile	54	5
75th percentile	5	57
90th percentile	2	120

* Assumes a catchment area of 1.8 million population, and population coverage of 70% and 30% in countries with CR-Acinetobacter incidence >25th percentile and ≤25th percentile, respectively. Methodology to estimate total CRAb follows: ECDC BCoDe (Cassini, LID, 2019) / ECDC technical report 'Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020', 2022. Est. incidence = estimated cases per 100 000 population per year (average of 2019 and 2022).

Estimated N of CRAb & CSAb detections in each participating hospital, ECDC CRAb survey 2024/2025

Prioritisation of strain collection for the ECDC CRAb survey, 2024/2025: CRAb infections > CRAb colonisations > CSAb infections > CSAb colonisations

	A. baumannii infections detected in each participating hospital*			
	CRAb isolates		CSAb isolates	
Country percentile of est. incidence of invasive *Acinetobacter* spp. (EARS-Net)	N of weeks to collect 10 isolates	N of isolates in 6 months	N of weeks to collect 10 isolates	N of isolates in 6 months
10th percentile	662	1	5	49
25th percentile	163	1	4	61
50th percentile	54	5	22	12
75th percentile	5	57	15	18
90th percentile	2	120	20	13

* Assumes a catchment area of 1.8 million population, and population coverage of 70% and 30% in countries with CR-Acinetobacter incidence >25th percentile and ≤25th percentile, respectively. Methodology to estimate total CRAb follows: ECDC BCoDe (Cassini, LID, 2019) / ECDC technical report 'Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020', 2022. Est. incidence = estimated cases per 100 000 population per year (average of 2019 and 2022).

Estimated N of CRAb & CSAb detections in each participating hospital, ECDC CRAb survey 2024/2025

Prioritisation of strain collection for the ECDC CRAb survey, 2024/2025: CRAb infections > CRAb colonisations > CSAb infections > CSAb colonisations

	A. baumannii infections detected in each participating hospital*				N isolates reported by each participating hospital in 6 months (MAX=10)	
	CRAb isolates		CSAb isolates			
Country percentile of est. incidence of invasive *Acinetobacter* spp. (EARS-Net)	N of weeks to collect 10 isolates	N of isolates in 6 months	N of weeks to collect 10 isolates	N of isolates in 6 months	N of isolates from CRAb infections	N of isolates from CSAb infections
10th percentile	662	1	5	49	**1**	**9**
25th percentile	163	1	4	61	**1**	**9**
50th percentile	54	5	22	12	**5**	**5**
75th percentile	5	57	15	18	**10**	**0**
90th percentile	2	120	20	13	**10**	**0**

* Assumes a catchment area of 1.8 million population, and population coverage of 70% and 30% in countries with CR-Acinetobacter incidence >25th percentile and ≤25th percentile, respectively. Methodology to estimate total CRAb follows: ECDC BCoDe (Cassini, LID, 2019) / ECDC technical report 'Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020', 2022. Est. incidence = estimated cases per 100 000 population per year (average of 2019 and 2022).

Estimated N of CRAb & CSAb detections in each participating hospital,
ECDC CRAb survey 2024/2025

Prioritisation of strain collection for the ECDC CRAb survey, 2024/2025:
CRAb infections > CRAb colonisations > CSAb infections > CSAb colonisations

	A. baumannii infections detected in each participating hospital*				N isolates reported by each participating hospital in 6 months (MAX=10)	
	CRAb isolates		CSAb isolates			
Country percentile of est. incidence of invasive *Acinetobacter* spp (EARS-Net)	N of	N of	N of	N of	N of isolates from CRAb infections	N of isolates from CSAb infections
10th percentile					1	9
25th percentile	163	1	4	61	1	9
50th					5	5
75th					10	0
90th					10	0

Importations?

In later years become established?

Explore relatedness.

Compare to surveys in later years

Representative of endemic strains +/- outbreaks

Context for future CRAb outbreak investigations

* Assumes a catchment area of 1.8 million population, and population coverage of 70% and 30% in countries with CR-Acinetobacter incidence >25th percentile and ≤25th percentile, respectively. Methodology to estimate total CRAb follows: ECDC BCoDe (Cassini, LID, 2019) / ECDC technical report 'Assessing the health burden of infections with antibiotic-resistant bacteria in the EU/EEA, 2016-2020', 2022. Est. incidence = estimated cases per 100 000 population per year (average of 2019 and 2022).

Planned analyses and outputs

National WGS data:

- **National Survey Coordinators receive WGS data for hospitals/laboratories in their country**.
- National WGS are not under embargo. If publish, please acknowledge ECDC*.

Planned data analyses of centrally-produced FASTQ files by ECDC:

- Phylogenetic analysis, species identification, characterisation of the baseline genomic population structure, and cgMLST-based cluster analysis; and resistome/virulence profiling for antimicrobial resistance genes and chromosomal point mutations.

Planned ECDC outputs

- **Report:** ECDC Technical Report, with country reports, for each country, as Annex(es).
  Produced in parallel to a manuscript for peer-review.
- **ECDC Molecular Typing Tool:** Bioinformatic analyses + subset of the isolate-level data**
  Visualisation tool for genomic data in EpiPulse, for e.g. OCPs for AMRISO and NFPs for AMR
- **Publicly accessible article(s) :**
  Named co-authors: include National Survey Coordinator.
  Co-author group, identifiable on PubMed: 1–3 people/country who meet ICJME criteria.
  Acknowledgements group: Chosen by each National Survey Coordinator and/or NFP for AMR.

*e.g. 'Whole-genome sequencing was (partly) performed using funding from the European Centre for Disease Prevention and Control (ECDC)'; ** e.g. derived sequence type, phenotypic carbapenem susceptibility testing result (SIR), a subset of the epidemiological data (e.g. country), an isolate date (e.g. *DateOfReceiptSourceLab*), and/or infection/colonisation (*SpecimenSource*).

Thank you for listening!

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Acknowledgements

ECDC	ARHAI	**Dominique Monnet**, **Holger Hastén**
	Microbiology & Molecular Surveillance Group	**Andreas Hoefer**, **Daniel Palm** Karin Johanson, Marius Linkevicius, Maximillian Reiss
	EARS-Net	**Hanna Merk**, Carlo Gagliotti (contractor), Liselotte Diaz Högberg
	ESAC-Net	**Vivian Leung**, Liselotte Diaz Högberg
	HAI-Net	**Carl Suetens**, Tommi Kärki, Diamantis Plachouras
	EURGen-Net	**Anke Kohlenberg**
	International Relations	Agne Bajoriniene, Georgeta Mureanu
Expert Group		Silva Tafaj, Anette Hammerum, Sotirios Tsiodras, Antoni Hendrickx, Ørjan Samuelsen, Dorota Żabicka, Vera Manageiro, Ana Rita Rebelo **(EARS-Net EQA** and **EURGen-RefLabCap),** Thierry Naas **(ESGARS),** Emine Alp Mese **(ESGCIP** and **EUCIC),** Christian Giske **(EUCAST)**
EUCAST		**Christian Giske**
Institut Pasteur (CRBIP)		**Fay Betsou; Mariana Ferrari**, Olivier Chesneau, Dominique Clermont
EURGen-RefLabCap		**Ana Rita Bastos Rebelo**, Birgitte Helwigh, Rene Hendriksen (DTU FOOD) **Valeria Bortolaia**, Lina Maria Cavaco (SSI, DK)

Participants in EURGen-Net, EURGen-RefLabCap, and the EuSCAPE projects

(Observer) National Focal Points for AMR; Operational Contact Points/Contact Points for Operations for AMRISO

Thank you for listening!

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Spare slides

How to submit samples

Submitting isolates for this survey

Storage of original isolates

Ideally, bacterial samples should be stored for up to two years, following national best practices.

Submitting bacterial sample

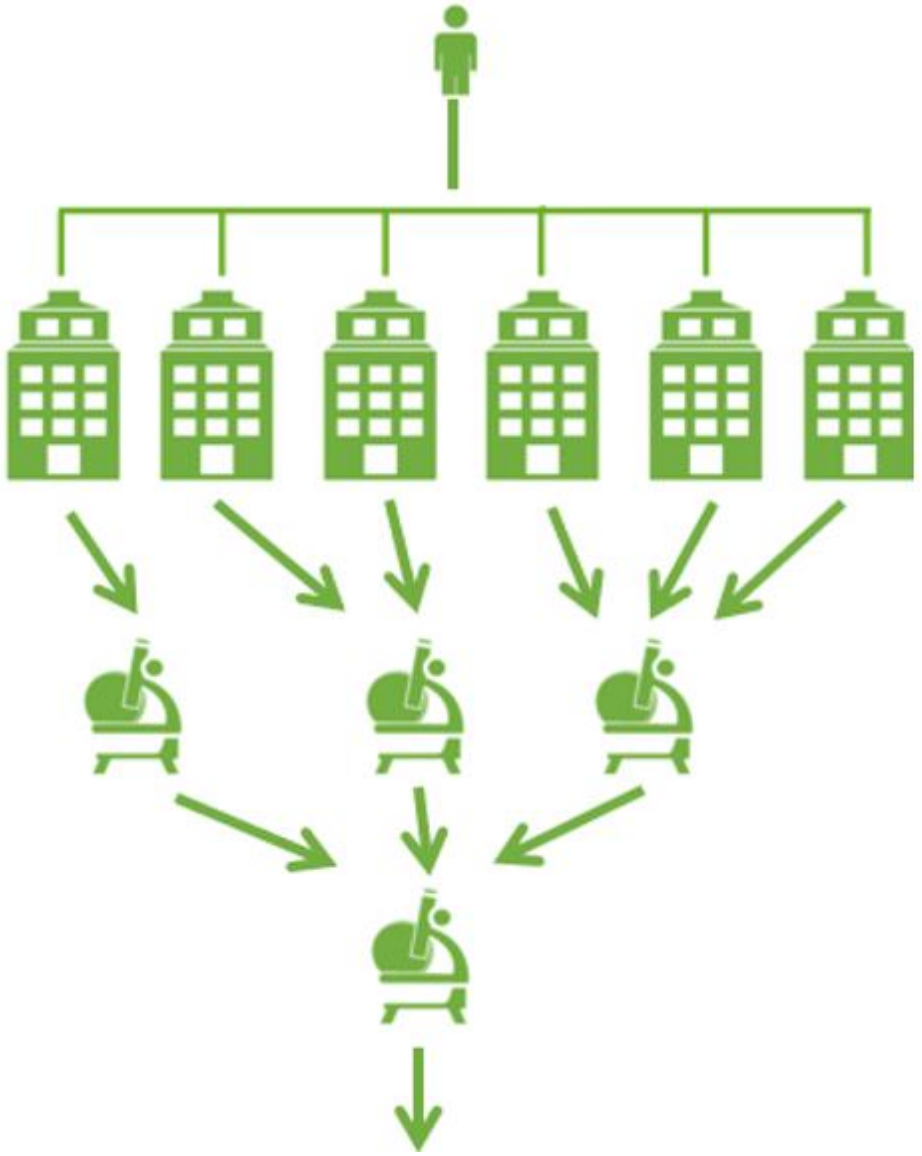
The bacterial sample may be supplied as 2×1 ml overnight cultures (optical density ≥1 at 600 nm), expecting each culture to contain 8×10^8 cells on average) OR a pellet from equivalent cultures in 2 ml screw cap tubes; OR plated colonies on agar plates (≥10 colonies with a diameter ≥0.8 mm).

Shipment of materials

The packaging and shipment of isolates should comply with national and international shipment regulations for biohazardous material (packaging instructions P650, UN3373[7]).

Source: https://www.ecdc.europa.eu/en/publications-data/laboratory-manual-genomic-based-survey-carbapenem-resistant-acinetobacter

National workflow for ECDC CRAb survey, 2024/2025



National Survey Coordinator

- Recruits hospitals and laboratories.
- Collates and reports all metadata.
- Technical contact point for technical/logistic questions regarding the national survey and its metadata.

Hospitals

- Collects samples during normal clinical practice and sends them to regional/local laboratories for this survey.
- Collects hospital level metadata (Form C)
- On request from regional/local laboratories, collects patient level metadata (Form B) for eligible patients.

Regional/local laboratories

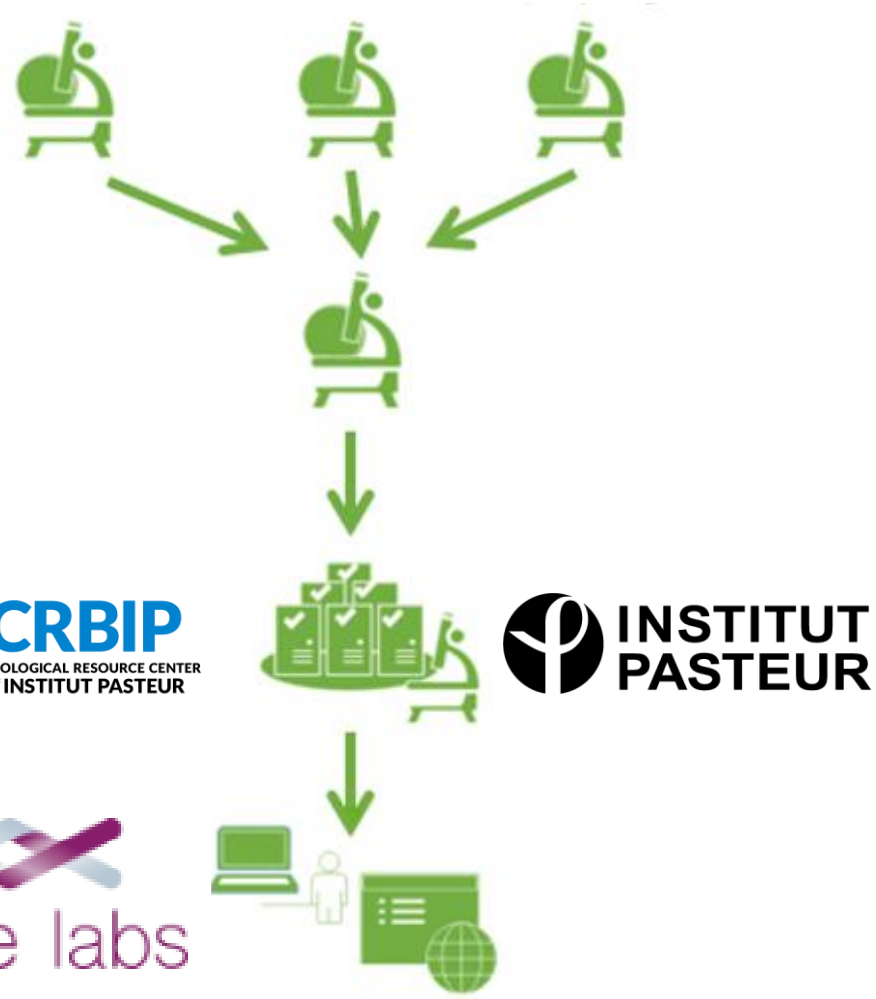
- Isolates *Acinetobacter baumannii**.
- Performs phenotypic carbapenem susceptibility testing.
- Collects metadata at isolate (specimen) level (Form A).
- Asks hospital to collect patient-level metadata (Form B) from each patient that supplied the eligible sample. produced an eligible isolate.
- Stores all eligible isolates (N=10/hospital).
- Sends sample to national reference/expert laboratory.

National reference/expert laboratory

- Confirmatory AST for carbapenem susceptibility.
- (Optional) AST for NRL-selected antimicrobial agents.
- Prepares and stores isolates; and sends bacterial sample to 'central strain collection laboratory'.

AST – antimicrobial susceptibility testing; NRL – national reference laboratory; * – see 'Criteria for bacterial species'

National workflow for ECDC CRAb survey, 2024/2025



Regional/local laboratories

- Isolates *Acinetobacter baumannii*.*
- Performs phenotypic carbapenem susceptibility testing.
- Collects metadata at isolate (specimen) level (Form A).
- Asks hospital to collect patient-level metadata (Form B) from each patient that supplied the eligible sample. produced an eligible isolate.
- Stores all eligible isolates (N=10/hospital).
- Sends sample to national reference/expert laboratory.

National reference/expert laboratory

- Confirmatory AST for carbapenem susceptibility.
- (Optional) AST for NRL-selected antimicrobial agents.
- Prepares and stores isolates; and sends bacterial sample to 'central strain collection laboratory'.

Central strain collection laboratory (ECDC contractor)

- Confirms quality of submitted samples (bacterial sample).
- Liaises with National Survey Coordinator(s), if applicable, to identify samples that should be resubmitted, due to insufficient quality of the bacterial sample.
- Sends bacterial sample to central sequencing laboratory.

Central sequencing laboratory (2x ECDC contractors)

- Performs DNA extraction (DANTE) and WGS (T.B.A.), generating raw reads.
- Sends raw read data to each national reference/expert laboratory (national data) and to ECDC (all data).

AST – antimicrobial susceptibility testing; NRL – national reference laboratory; * – see 'Criteria for bacterial species'

ECDC production of survey documents/pipeline, 2024/2025

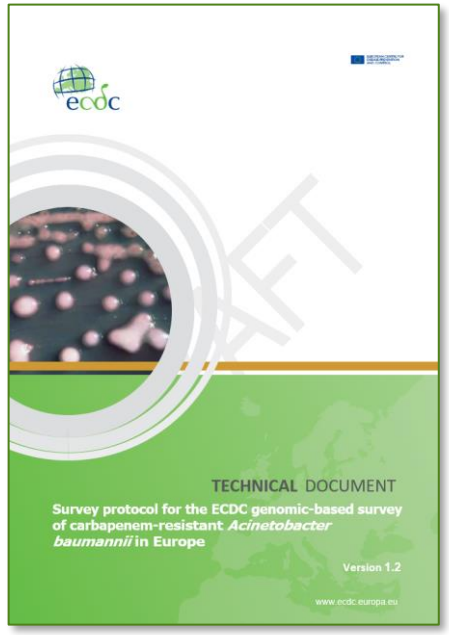
Survey protocol		Laboratory manual		Bioinformatics pipeline

For all participants

Describes every aspect; refers to lab manual

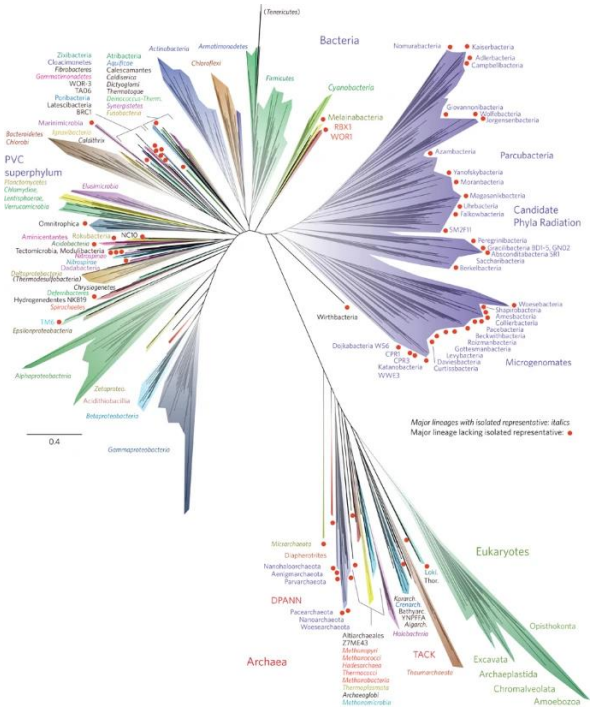
For clinical labs & NRLs

Provides details not in the survey protocol



For primary objective

'To describe occurrence & distribution of strains.'



Images: 'A new tree of life' (Hug, LA; Nature Microb. 2016) https://www.nature.com/articles/nmicrobiol201648 & https://pixabay.com/vectors/europe-map-dots-halftone-geography-6752857/

ECDC production of survey documents/pipeline, 2024/2025

Month

MM	YYYY	Survey protocol	Laboratory manual	Bioinformatics pipeline
11	2023	**EURGen-Net Network meeting:** - Hear and discuss draft protocol aims, objectives, design, & sampling frame; - Brief overview of laboratory manual		
12	2023	Finalise draft protocol		
01	2024	**Send draft survey protocol for country comments** (To: NFPs for AMR, Cc: OCPs for AMRISO)	**- Establish an 'Expert Group' to finalise the lab manual;** **- 'Expert Group' receives draft lab manual for comments**	Located Accession numbers from published outbreaks;
02	2024	Incorporate national comments		Conversation with N=1 country to share unpublished WGS+analyses
03	2024	**NFPs for AMR (cc OCPs for AMRISO):** **- receive updated survey protocol;** **- designate 'national technical coordinators'**	- Incorporate comments. - Specify 'material transfer agreement' (MTA) for incorporation into lab manual*	
04	2024		**- Virtual expert meeting of the Expert Group for the lab manual;** **- Send draft lab manual for country comments** (To: NFPs for AMR, Cc: OCPs for AMRISO)	Develop ECDC analysis pipeline, and compare to output from national analysis . TBC: ECDC tc with selected countries regarding their analysis pipelines for published investigations.
05	2024	**Technical meeting for 'national technical coordinators'** (A) train in use of the survey protocol and laboratory manual; 23 May (B) finalise outstanding items		
06	2024	**Publish survey protocol**	**Publish lab manual protocol**	
07	2024			
08	2024			
09	2024	**'Kick-off technical virtual meeting' with 'national technical coordinators'** 26 September		
10	2024	**1 Oct 2024 – 30 June 2025: survey period.**		
11	2024			
12	2024			
Q1-Q2	2025			Implement ECDC analysis pipeline in EpiPulse.
Q3	2025			**First analysis of ECDC CRAb survey FASTA files**

* analogous to CCRE survey 'Privacy statement'

Formulating the Expert Group

"…based on the relevance of their expertise to the scope of the Expert Group specified above…"

"…we will specifically seek to identify experts from a diverse group of countries and expert stakeholder groups, such as EUCAST…"

…until we have 8–15 Expert Group members."

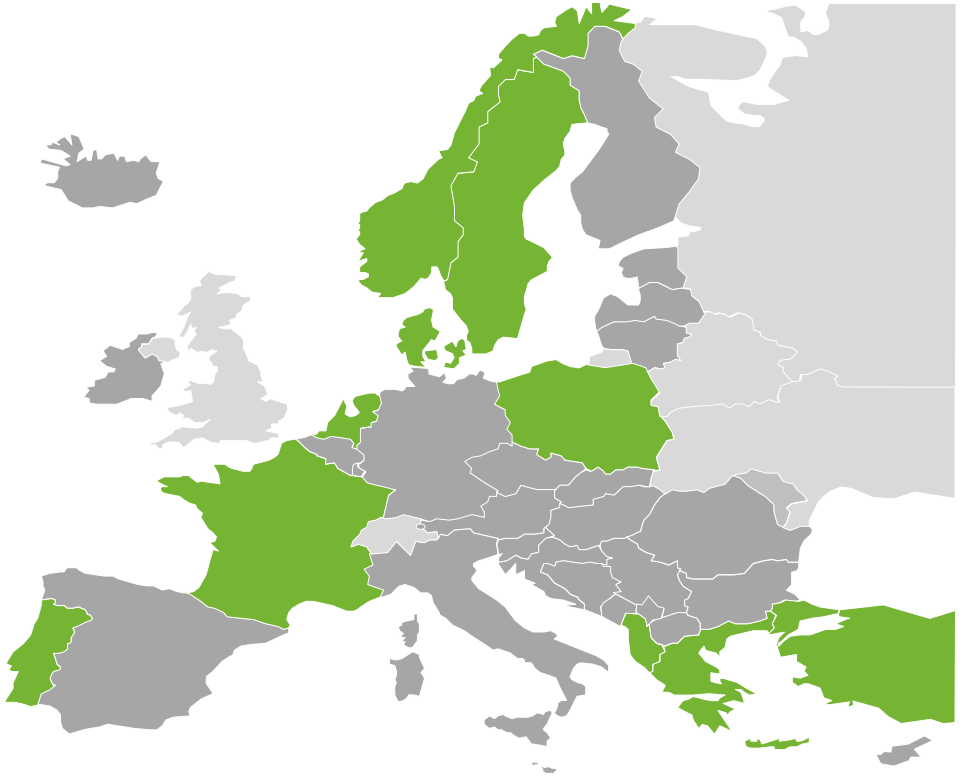
Members of the Expert Group for Microbiological Support to the ECDC CRAb Survey, 2024-2025 (N=11)

Silva Tafaj	Univ. Hosp. 'Shefqet Ndroqi', Tirana, Albania
Anette Hammerum	NRL for AMR, Statens Serum Institut, Copenhagen, Denmark
Sotirios Tsiodras	Attikon Univ. Hosp., Athens, Greece
Antoni Hendrickx	Center for Infectious Disease Control, Diagnostics & Lab. Surveillance (IDS), RIVM, the Netherlands
Ørjan Samuelsen	Norwegian National Advisory Unit on Detection of AMR, Tromsø, Norway
Dorota Żabicka	National Reference Centre for Susceptibility Testing, Warsaw, Poland
Vera Manageiro	NRL of AMR and HAIs, NIH Doctor Ricardo Jorge, Lisbon, Portugal
Ana Rita Rebelo	**EARS-Net EQA** (ECDC contractor) and **EURGen-RefLabCap**
Thierry Naas	**ESGARS**
Alp Elmine	**ESGCIP** and **EUCIC**
Christian Giske	**EUCAST**

Members of the Expert Group for Microbiological Support to the ECDC CRAb Survey, 2024-2025 (N=11)

Pre-specified criteria

"a diverse group of countries"



Post-evaluation statistics.

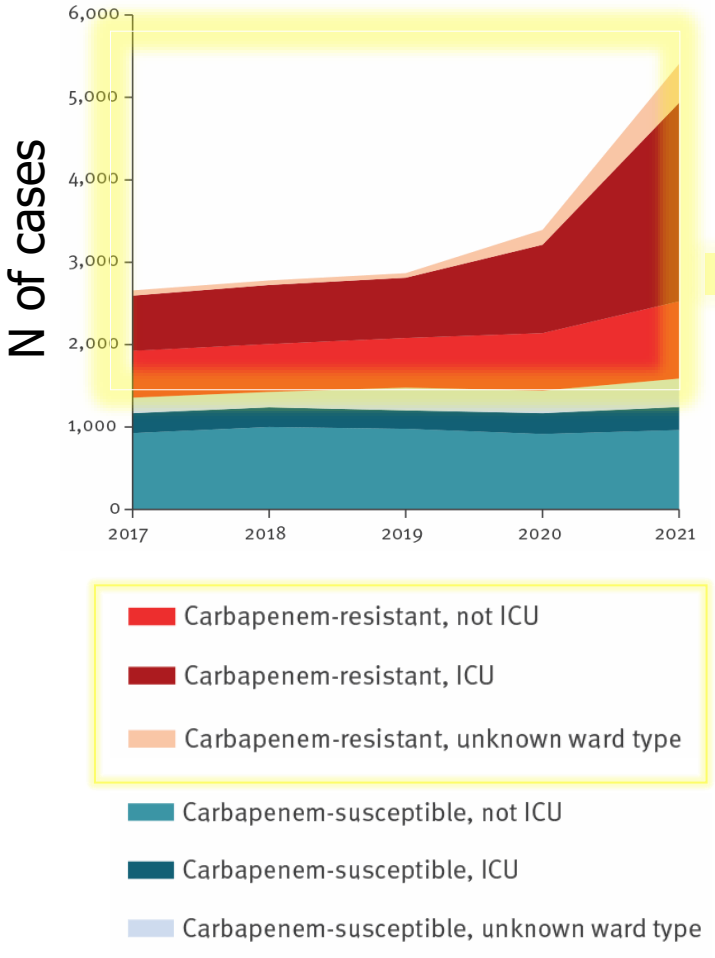
Not used for selection

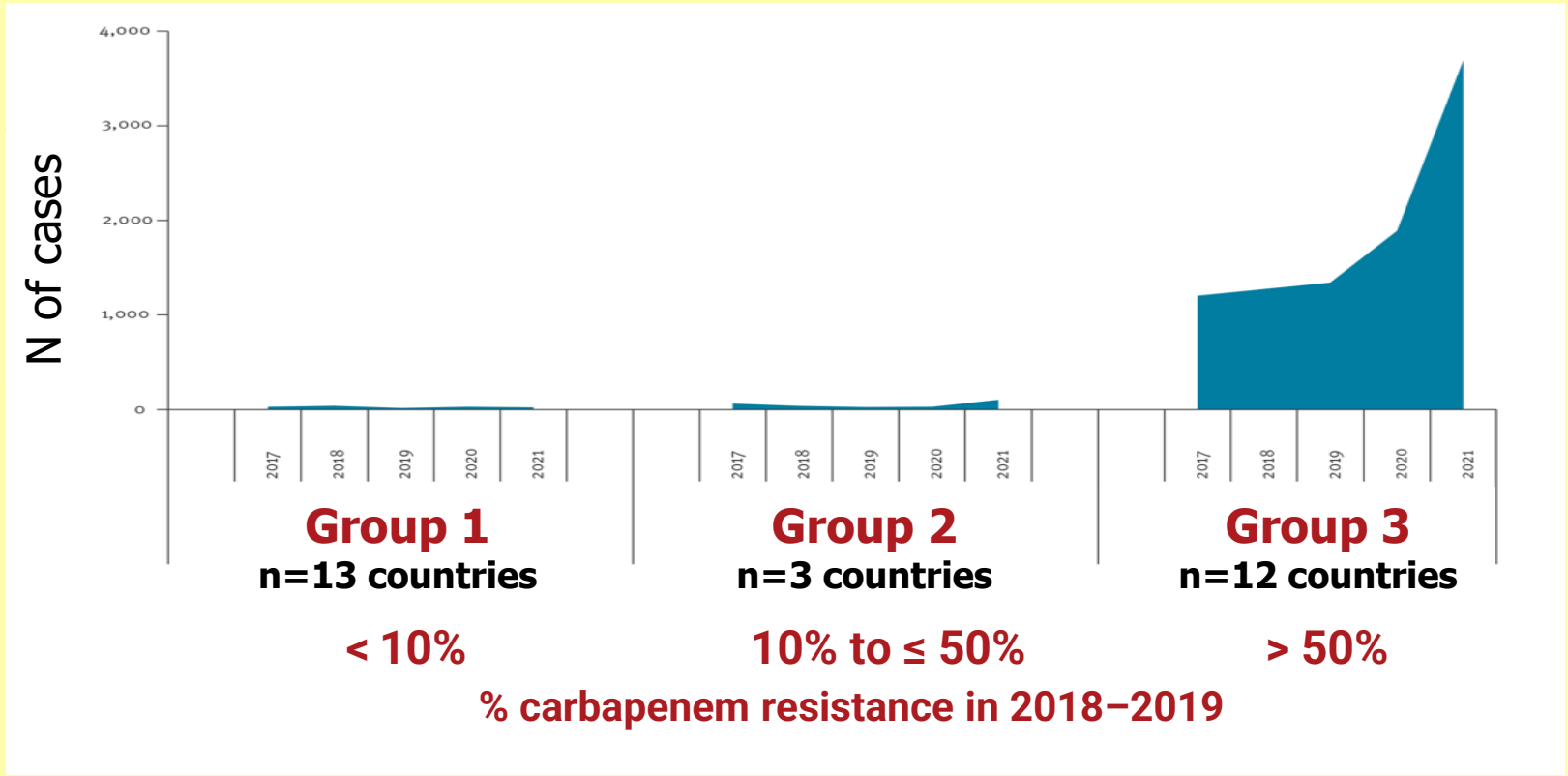
% Professors	45%
% Clinical doctors (MD)	36%
% Stakeholder groups	36%
% DNCC/AF (Member/Observer)	36%
% NFP	27%
% EU candidate countries	18%
Mean h-score	42
Proportion male	0.5

AF – Advisory Forum; DNCC – Disease Network Coordination Committee; NFP – National Focal Point; h-score – calculated from Scopus (Feb 2024)

Large increase in bloodstream infections with carbapenem-resistant *Acinetobacter* spp. during the first 2 years of the COVID-19 pandemic, EU/EEA, 2020 and 2021

Laboratories that continuously reported *Acinetobacter* spp. data to EARS-Net in 2017–2021

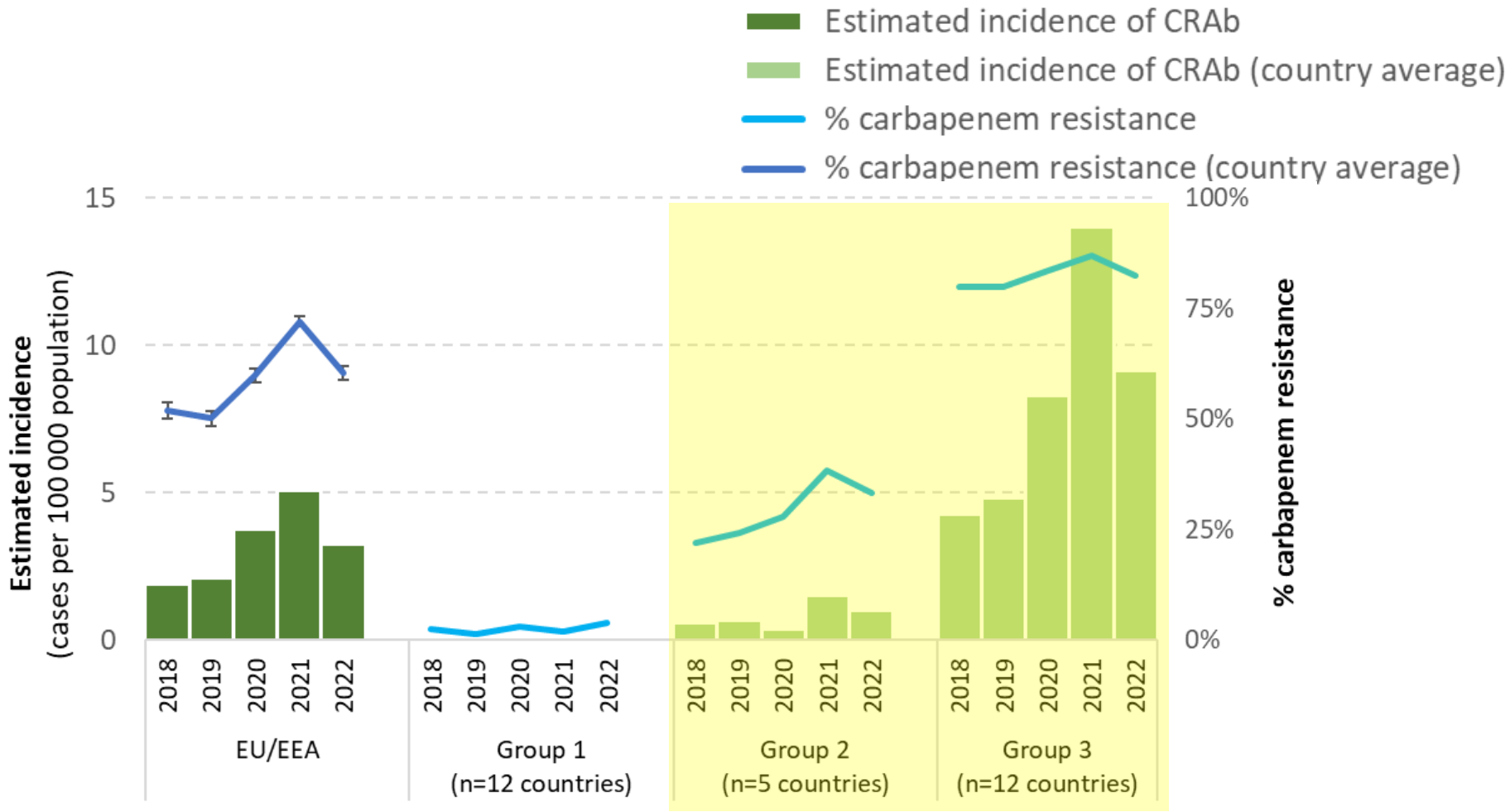




Eurosurveillance Volume 27, Issue 46, 17/Nov/2022

Data: ECDC EARS-Net. **Group 1:** Austria, Belgium, Denmark, Estonia, Finland, Germany, Iceland, Ireland, Luxembourg, Malta, the Netherlands, Norway and Sweden; **Group 2:** Czechia, Portugal, and Slovenia; **Group 3:** Bulgaria, Croatia, Cyprus, Greece, Hungary, Italy, Latvia, Lithuania, Poland, Romania, Slovakia and Spain.

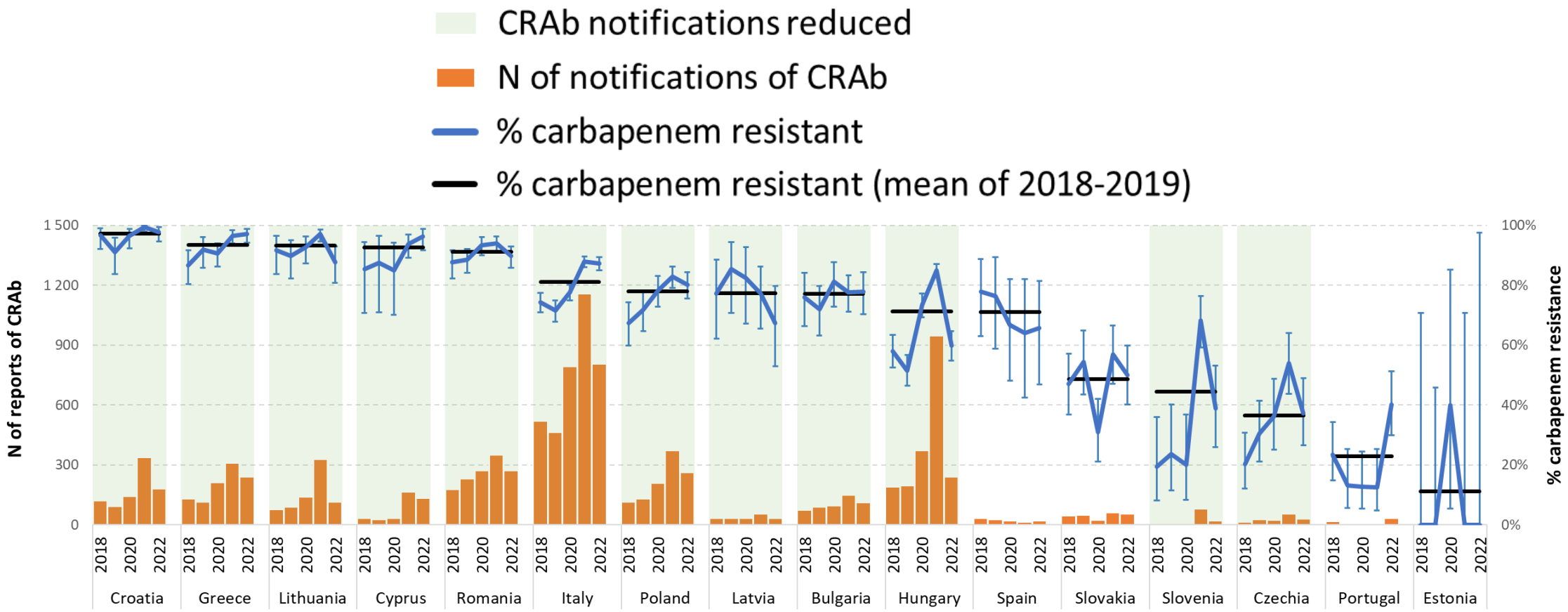
Estimated incidence of carbapenem-resistant *Acinetobacter* spp. and % carbapenem resistance* among *Acinetobacter* spp., by country group**, EARS-Net, 2018–2022



* Among laboratories that reported *Acinetobacter* spp. data every year

** **Group 1 (< 10% carbapenem resistance in 2018–2019):** AT, BE, DE, DK, EE, FI, IE, IS, LU, MT, NL, NO and SE;
Group 2 (10% to < 50% carbapenem resistance in 2018–2019): CZ, PT, and SI;
Group 3 (≥ 50% carbapenem resistance in 2018–2019): BG, CY, EL, ES, HR, HU, IT, LV, LT, PL, RO and SK.
See Kinross P et al, Eurosurveillance, 2022

N of reported carbapenem-resistant *Acinetobacter* spp. isolates* and % carbapenem resistance* among *Acinetobacter* spp., in 'Group 2' and 'Group 3' countries**, EARS-Net, 2018–2022



* among laboratories that reported *Acinetobacter* spp. data every year

** Group 2 – 10% to < 50% carbapenem resistance in 2018–2019; Group 3 – ≥ 50% carbapenem resistance in 2018–2019.

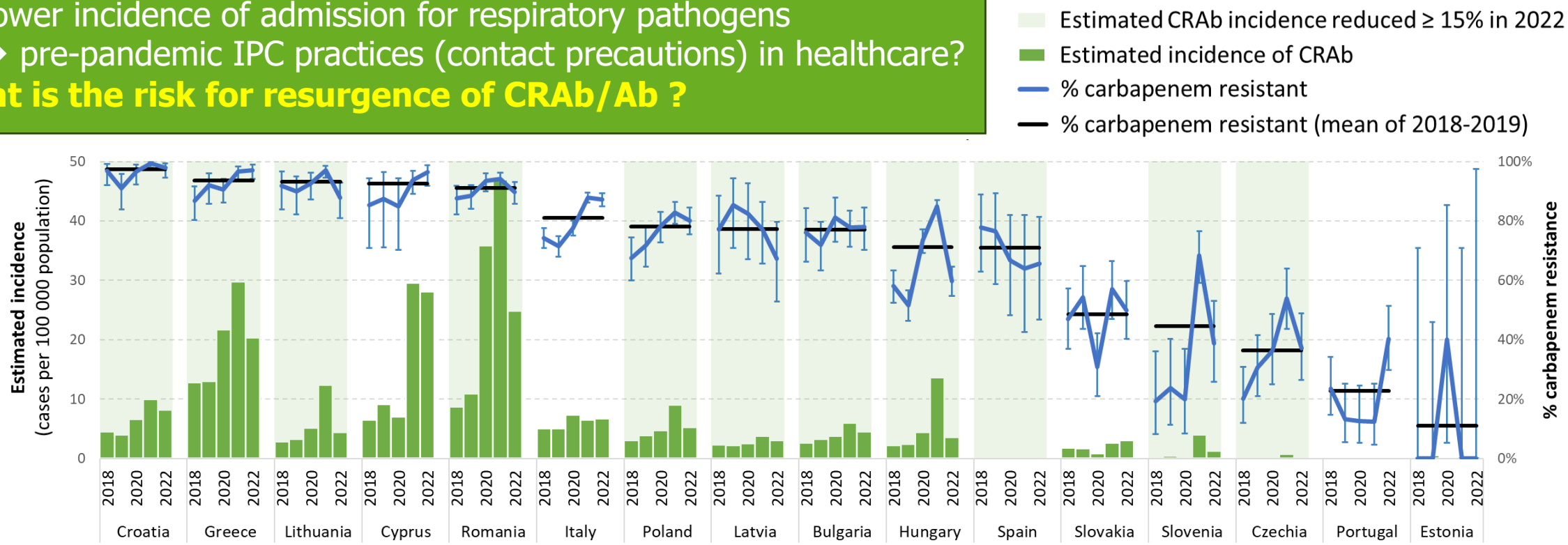
Source: EARS-Net 2023; Kinross P *et al*, Eurosurveillance, 2022

Estimated incidence of carbapenem-resistant *Acinetobacter* spp. and % carbapenem resistance* among *Acinetobacter* spp., in 'Group 2' and 'Group 3' countries**, EARS-Net, 2018–2022

Reasons for 2022 move towards baseline?

- Lower incidence of admission for respiratory pathogens
  ➔ pre-pandemic IPC practices (contact precautions) in healthcare?

What is the risk for resurgence of CRAb/Ab ?



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** Group 2 – 10% to < 50% carbapenem resistance in 2018–2019; Group 3 – ≥ 50% carbapenem resistance in 2018–2019.

Source: EARS-Net 2023; Kinross P *et al*, Eurosurveillance, 2022

Selected recommendations from ECDC Rapid Risk Assessment (RRA) 'Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings' Dec 2016

RAPID RISK ASSESSMENT

Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings

8 December 2016

Main conclusions and options for response

Carbapenem-resistant *A. baumannii* poses a significant threat to patients and healthcare systems in all EU/EEA countries. *A. baumannii* is the cause of serious infections in healthcare settings, and carbapenem resistance limits treatment options and increases the risk for adverse outcomes for patients. The epidemiological situation in Europe has worsened in the past years, with a higher number of countries reporting interregional spread or endemicity of carbapenem-resistant *A. baumannii*.

A. baumannii is adapted to persistence in healthcare settings and is difficult to eradicate once it has become endemic. Increased efforts are therefore needed for the detection of cases and the control of outbreaks in order to prevent carbapenem-resistant *A. baumannii* from becoming endemic in further European regions and health facilities.

Options for actions to reduce identified risks

Clinical management

Timely and appropriate laboratory investigation and reporting are essential to avoid delays in appropriate treatment, which are associated with increased morbidity and mortality. Patients with carbapenem-resistant *A. baumannii* infections are likely to benefit from consultations with experts in infectious diseases or clinical microbiology to ensure the best possible outcome considering the limited treatment options.

Prevention of transmission of carbapenem-resistant *A. baumannii* in hospitals and other healthcare settings

Good standard infection control, including environmental cleaning, adequate reprocessing of medical devices, adequate capacity of microbiological laboratories as well as sufficient capacity of healthcare facilities for contact isolation, are the basis for prevention of transmission of highly resistant bacteria, such as carbapenem-resistant *A. baumannii*. Prompt notification of the clinical team and of the infection prevention

Erratum, 10 February 2017: The caption for Figure 2 on p. 8 now reads 'Percentage (%) of invasive *Acinetobacter* spp. isolates with resistance to carbapenems, by country, EU/EEA countries, 2015 (A) and 2014 (B)'.

Suggested citation: European Centre for Disease Prevention and Control. Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings – 8 December 2016. Stockholm: ECDC; 2016.

Source: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-outbreak-vim-producing-carbapenem-resistant-pseudomonas

Selected recommendations from ECDC Rapid Risk Assessment (RRA) 'Carbapenem-resistant *Acinetobacter baumannii* in healthcare settings'

December 2016

Prevention of transmission in healthcare	Consider targeted screening of patients at risk for CRAb carriage. **≥ 2 detections ➔ initiate epi investigation (outbreak control)** • **Active screening** (i.e. delineate the outbreak & monitor IPC effectiveness) • **Molecular typing** (i.e. delineate the outbreak) • **IPC, environmental cleaning** • **Environmental sampling** (e.g. verification of enhanced cleaning) • **Antimicrobial stewardship**
Prevention of cross-border transmission	**Inter-national:** Exchange information via electronic early warning platforms* **Local:** Consider CRAb/XDR-Ab admission screening, based on foreign healthcare contact.
Improve preparedness	**EU/EEA:** Periodic pan-EU surveys for CRAb/XDR-Ab to monitor spread/prevalence. **National:** Prospective prevalence surveys; typing (distinguish epidemic/new clones). **(Sub-)national:** Improve lab capacities for CRAb characterisation. **Local:** (see above)

* EpiPulse Events/EWRS/IHR

Source: https://www.ecdc.europa.eu/en/publications-data/rapid-risk-assessment-outbreak-vim-producing-carbapenem-resistant-pseudomonas

DTU

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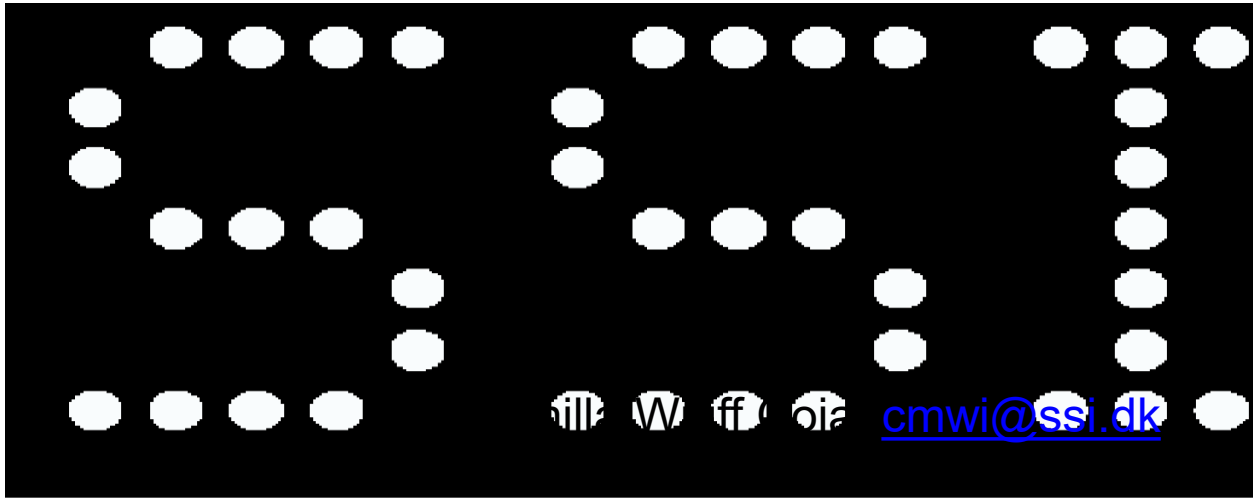
USER SURVEYS – A TOOL IN CAPACITY BUILDING PROJECTS

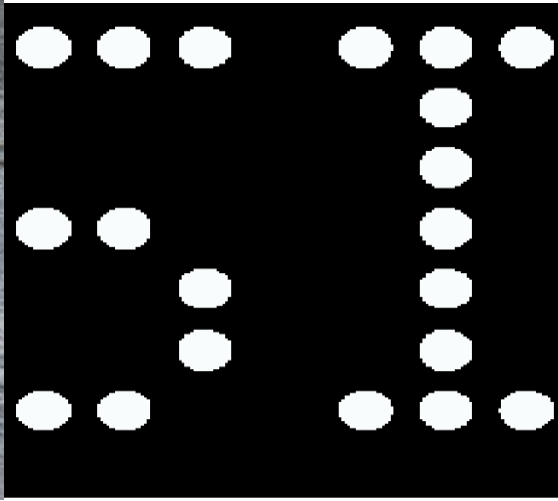
RefLabCap

3rd EURGen-RefLabCap Network Meeting
18 September 2024 (14.40-15-20)
DTU



cmwi@ssi.dk

THE SITUATION AT THE START OF THE PROJECT IN EARLY 2021



FIRST STEPS IN EURGEN-REFLABCAP

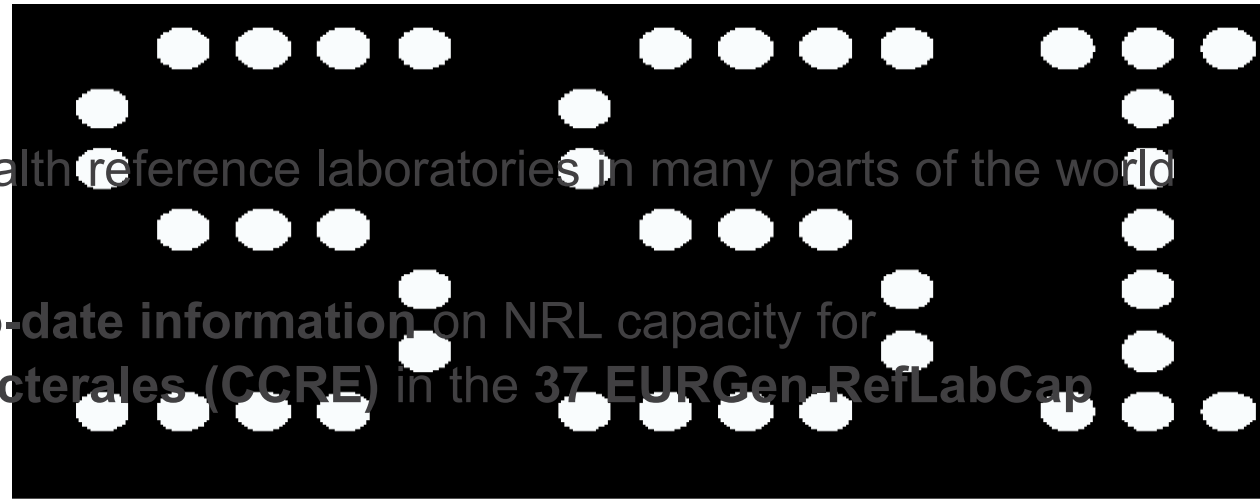
- At the start of the project (May 2021), we reviewed publicly available reports (“grey literature”) on capacity for national reference laboratories functions, Sources of information included reports from:
  - ECDC, WHO, EC, National Institutes/Organisations

- For many indicators of NRL capacity there was little (or no) up-to-date information publicly available at country-level

- AMR awareness was rising globally and new national and regional strategies and policies had been developed in recent years

- Implementation of WGS was underway in public health reference laboratories in many parts of the world

- There was a need to obtain **comparable and up-to-date information** on NRL capacity for **carbapenem- and/or colistin- resistant Enterobacterales (CCRE)** in the **37 EURGen-RefLabCap countries**



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EURGEN-REFLABCAP CRE/CCRE QUESTIONNAIRE

- The questionnaire was completed by the coordinators in all 37 countries in July-September 2021
- It addressed the **5 National Reference Laboratory** (NRL) **core functions** as defined by ECDC:

1. **Reference diagnostics***
2. **Reference material resources**
3. **Scientific advice**
4. **Collaboration and research**
5. **Monitoring, alert and response***

- Additional information was collected on: the NRL setup, epidemiological stage and rating of training activities
- Answers were analysed for each country. Particular importance was given to **i) availability of WGS for CRE/CCRE reference diagnostic functions** and ii) **CRE/CCRE monitoring, alert and response set-up in the countries**.

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CATEGORIES OF QUESTIONS

REFERENCE DIAGNOSTICS

REFERENCE MATERIAL RESOURCES

SCIENTIFIC ADVICE

COLLABORATION AND RESEARCH

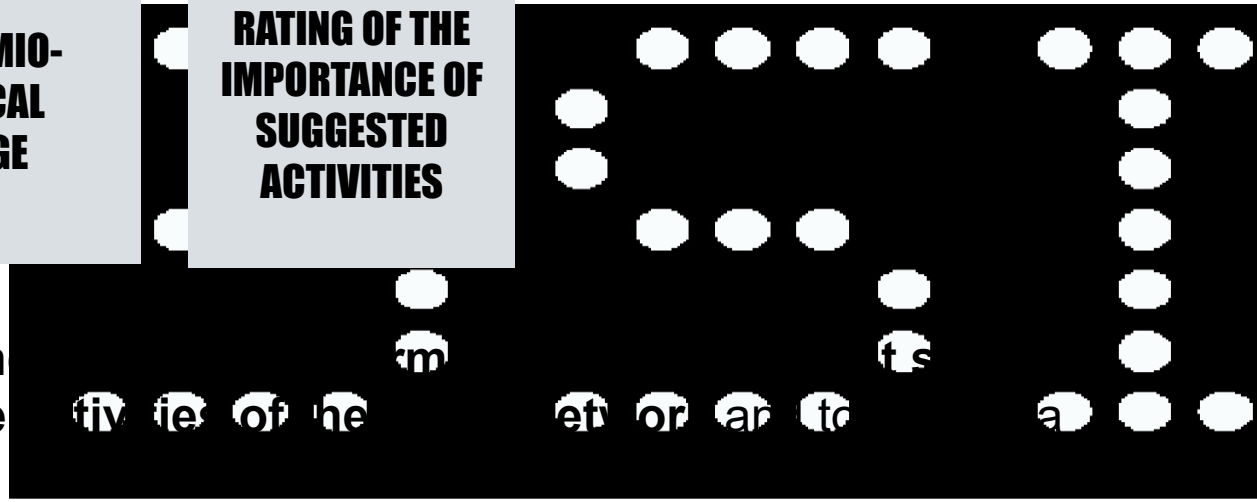
MONITORING, ALERT AND RESPONSE

NRL PROVISION

EPIDEMIO-LOGICAL STAGE

RATING OF THE IMPORTANCE OF SUGGESTED ACTIVITIES

The questions were aimed at **gaining more detailed an**
in each of the participating countries in order to **plan the**
number of priority countries



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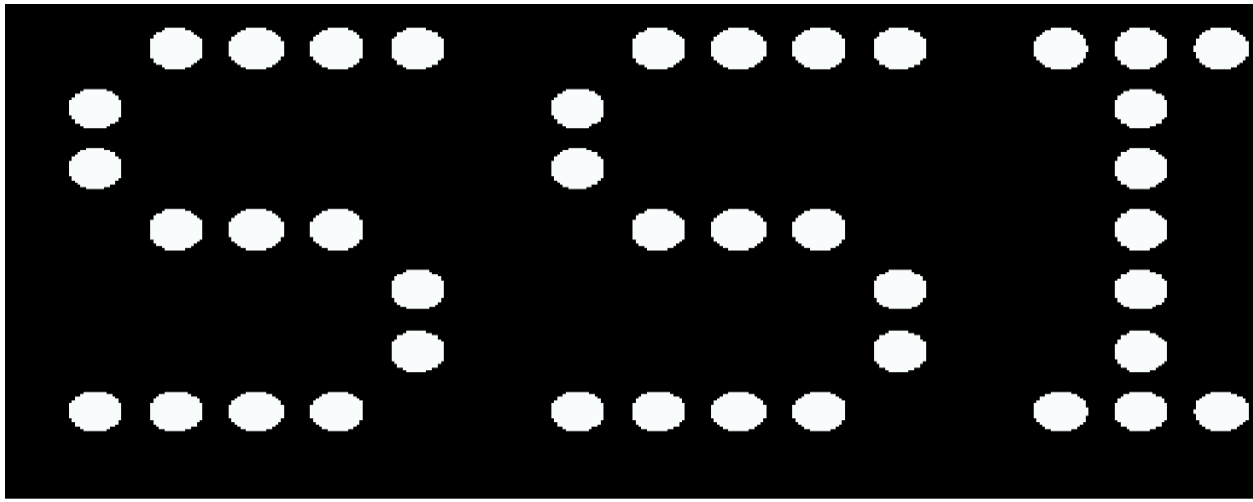
NRL FUNCTIONS, EQUIPMENT AND ROLES

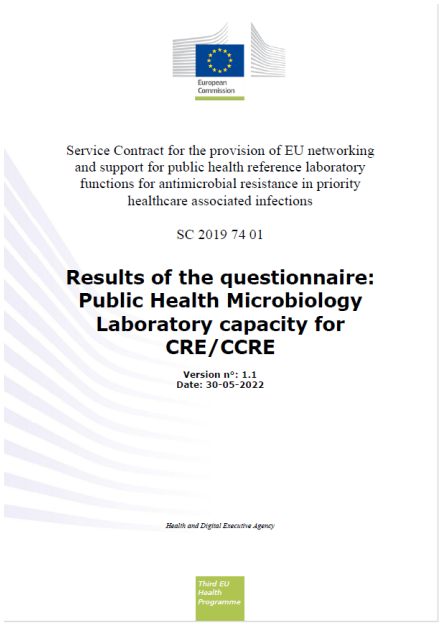
- NRL designation and placement in public health/health systems
- Referral of samples to the NRL
- Testing services provided; phenotypic and genotypic
- Methods used
- Equipment used
- Quality control setup
- Compliance with testing guidance
- Whole Genome Sequencing (WGS)
- Bioinformatics skills
- Reporting of results
- Surveillance and alert functions
- IT setup (NRL and wider in country)
- Advisory functions
- Research collaborations

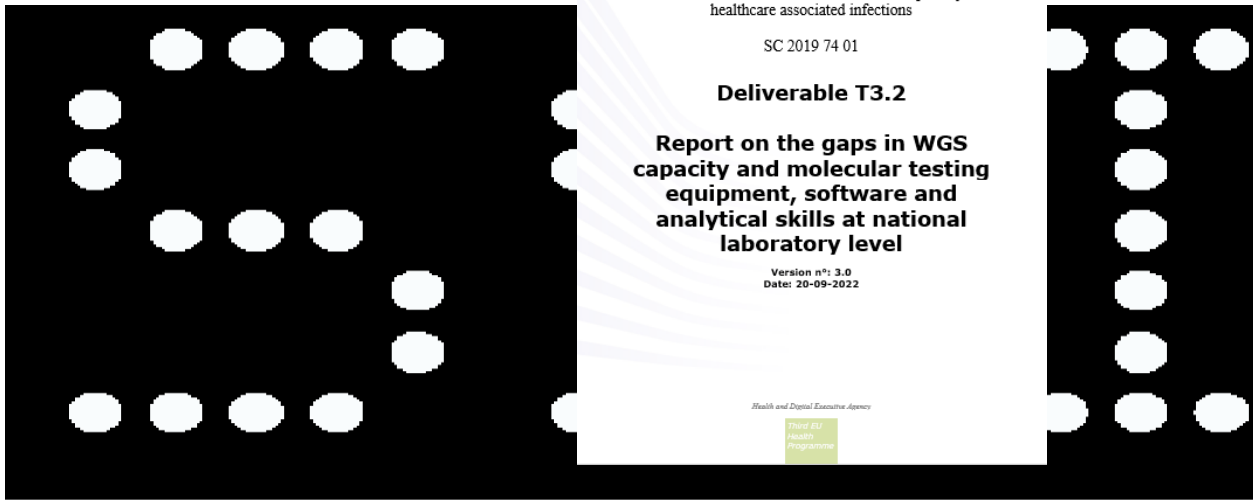


REPORTS ON CRE/CCRE SURVEY RESULTS

- Results of the questionnaire: Public Health Microbiology Laboratory capacity for CRE/CCRE **Deliverable T1.4** (June 2022).

- Report on the gaps in WGS capacity and molecular testing equipment, software and analytical skills at national laboratory level': **Deliverable T3.2** (October 2022).
  - This was an in-depth analysis of selected questions from the CRE/CCRE survey





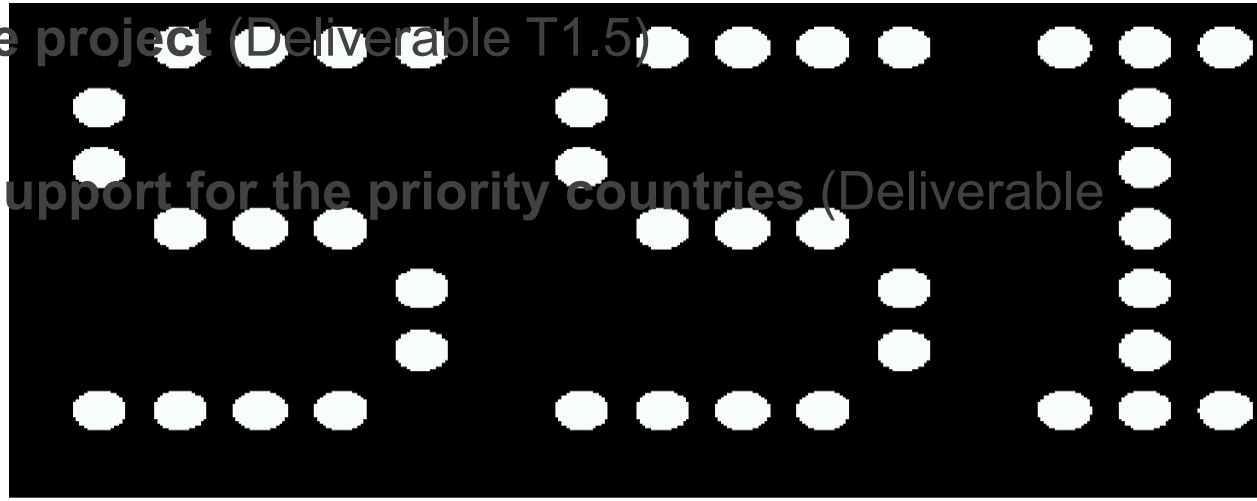
HOW DID WE USE THE RESULTS OF THE SURVEYS?

- **We identified countries with a need for further support** – 13 (out of 14) countries accepted the invitation to participate in EURGen-RefLabcap as a priority country

- **We identified key areas for the first network meeting in December 2021**
  - Aims and benefits of using WGS at your NRL
  - Barriers to implementing WGS at your NRL
  - NRL preparedness and outbreak response
  - Providing scientific advice

- **We designed an overall work plan for the entire project** (Deliverable T1.5)

- **We designed a plan for training and bespoke support for the priority countries** (Deliverable T2.2)



KEY AREAS AMONG THE NRL CORE FUNCTIONS

REFERENCE DIAGNOSTICS

REFERENCE MATERIAL RESOURCES

SCIENTIFIC ADVICE

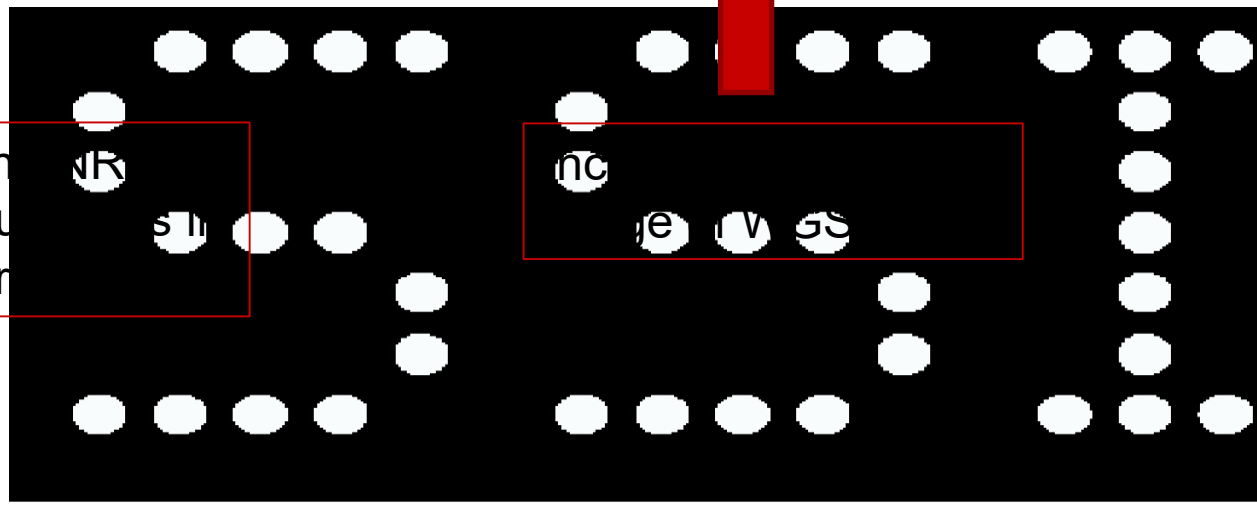
COLLABORATION AND RESEARCH

MONITORING, ALERT AND RESPONSE

Including WGS implementation

Including th NR roles and fu s in their countr

nc ge in WGS



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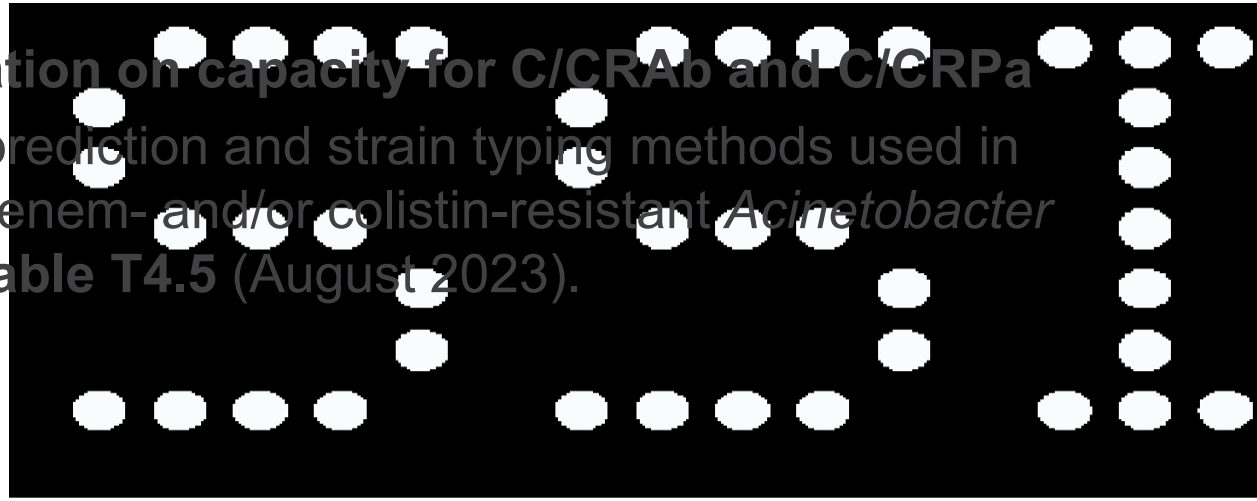
IDENTIFICATION OF ADDITIONAL PATHOGENS FOR WORSKSTREAM 2 (WS2)

- Questionnaire to select two additional priority antimicrobial resistant pathogens for capacity building in the EURGen-RefLabCap project and molecular surveillance in EURGen-Net (addendum to **Deliverable T1.4**)
  - Members of EURGen-Net and participants of EURGen-RefLabCap completed this questionnaire

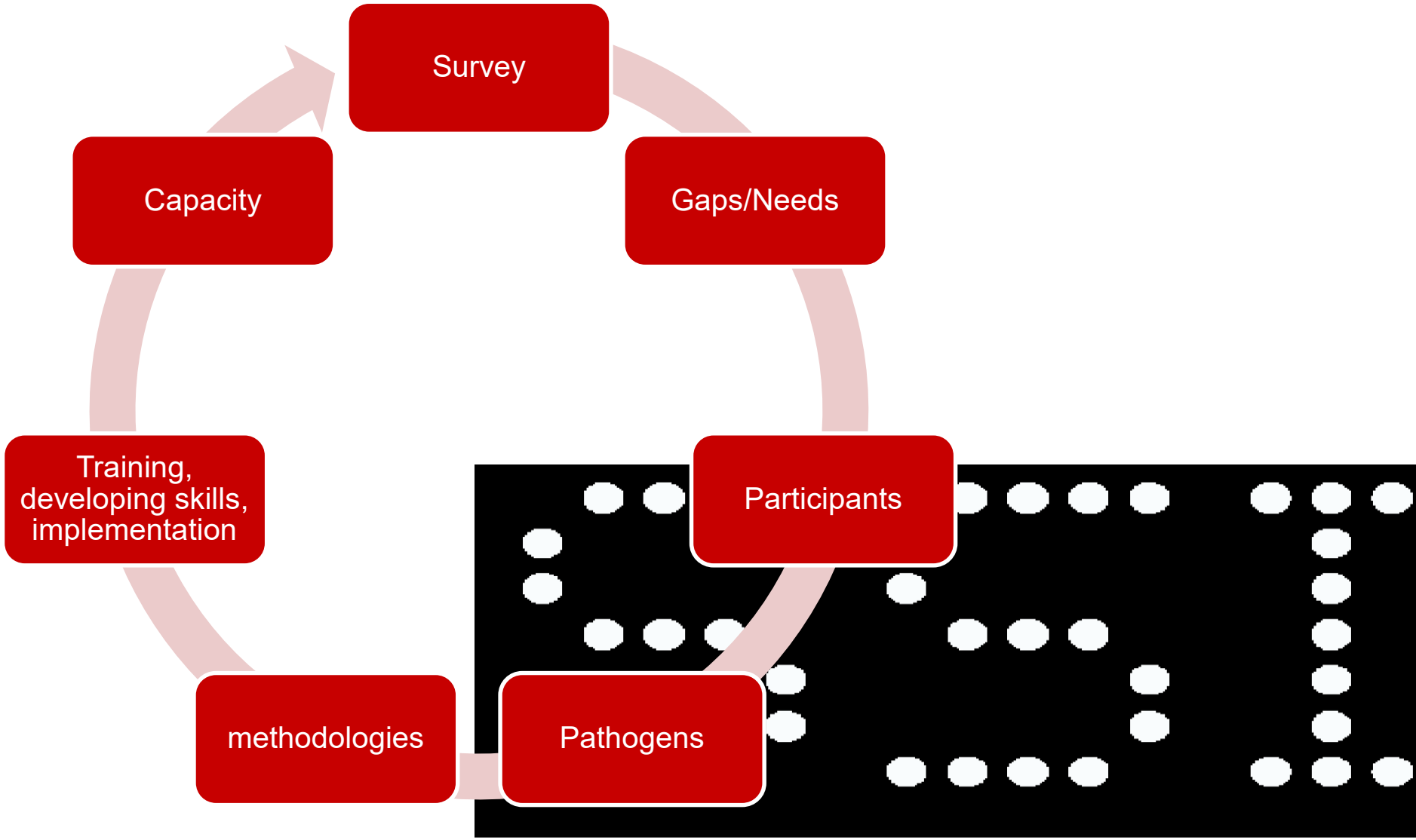
- 23 countries nominated NRLs for participation in WS2

- **A new survey was launched to collect information on capacity for C/CRAb and C/CRPa**

'Survey of the current molecular or genomic AMR prediction and strain typing methods used in NRLs for public health with competence for carbapenem- and/or colistin-resistant *Acinetobacter baumannii* and *Pseudomonas aeruginosa*' **Deliverable T4.5** (August 2023).



USER SURVEYS IN CAPACITY BUILDING PROJECTS

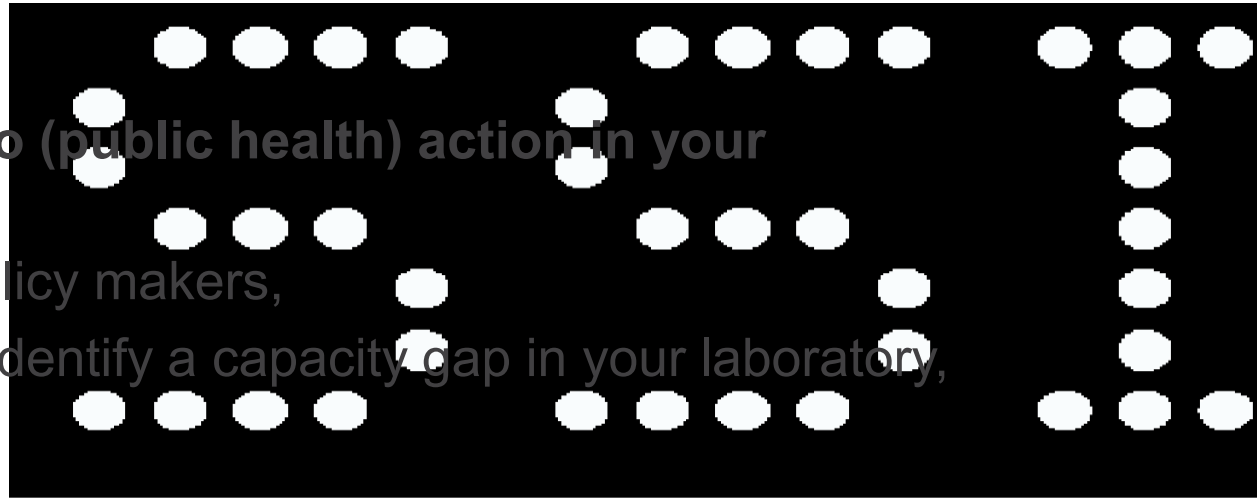


IMPROVEMENTS OF USER SURVEYS

- **The presentation of data/findings**
  - The large dataset be easy/easier to use and communicate
  - Histograms, tables, geographical maps
  - Infographics, illustrations

- **The availability of data – publication in the public domain (reports, websites etc.)**
  - Is this a good idea?
  - How is validation done efficiently?
  - How is sign-off organised?

- **How could survey data be used and turned into (public health) action in your laboratory/organisation/country?**
  - Sharing data survey in your organisation, to policy makers,
  - Who do you communicate with when you see/identify a capacity gap in your laboratory, organisation or country?



BREAK-OUT SESSION:

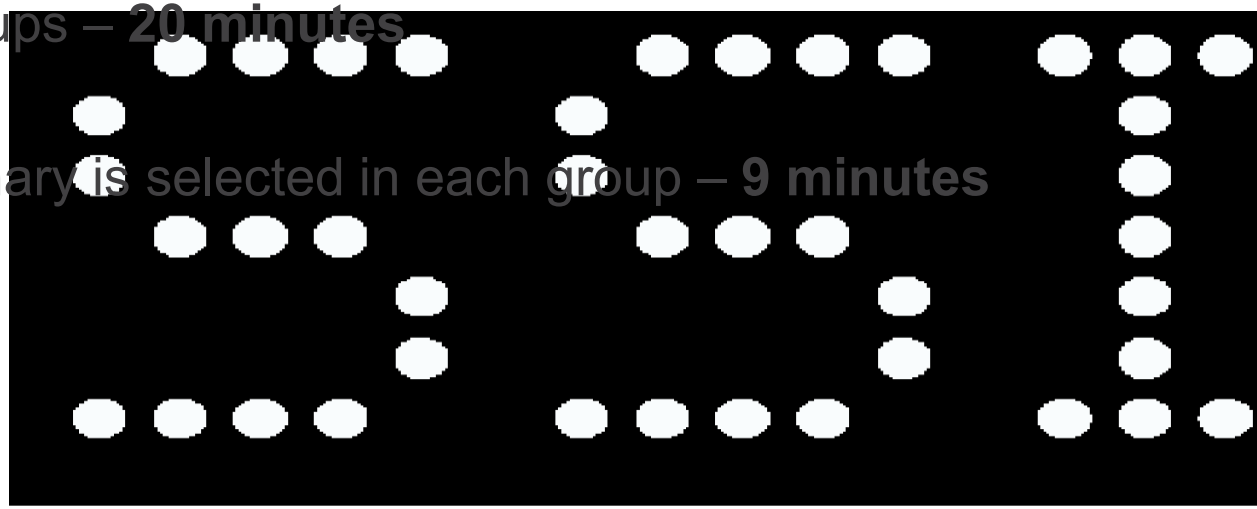
NEW WAYS OF PRESENTING AND COMMUNICATING USER SURVEY RESULTS

- The purpose of this group work is to generate new ideas on how to compile, communicate and use the valuable information collected in the user surveys

- Participants are randomly grouped in 9 groups (by picking numbers from a “hat”).

- Each of the 3 topics are discussed in 3 groups – **20 minutes**

- A spokesperson that will report back in plenary is selected in each group – **9 minutes**
  (3 minutes for each question, all 3 groups)

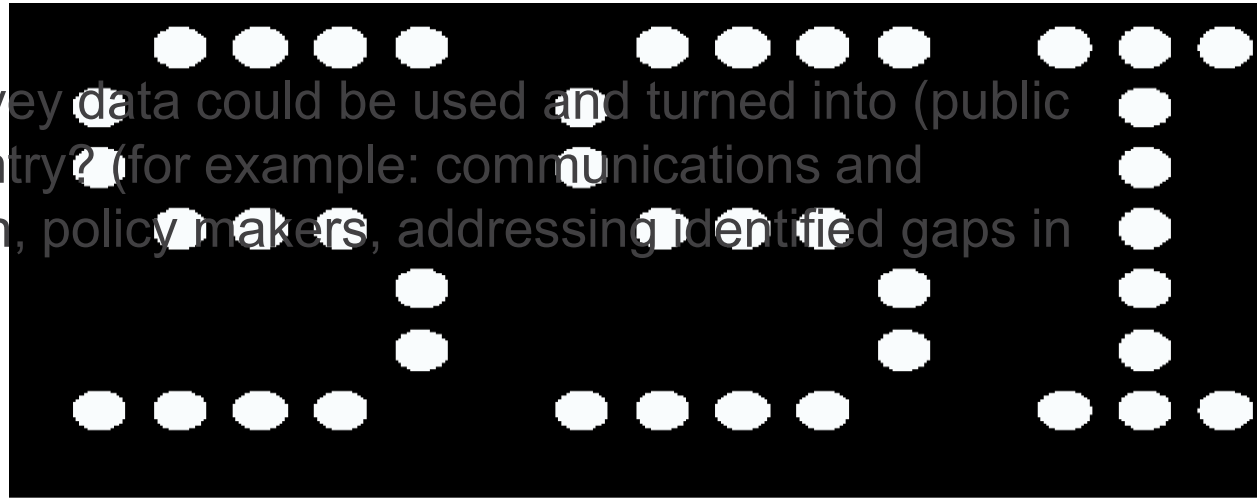


QUESTIONS FOR BREAK-OUT SESSION

- **Groups 1-3 (3 groups):** Please produce suggestions for new ways of presenting (for example: visualization of results, infographics etc.) and communicating results from user surveys that could improve the accessibility, communication and utility of the survey results.

- **Groups 4-6 (3 groups):** Would publication of capacity survey results in the public domain be beneficial to your NRL/institute (please describe why/why not)?

- **Groups 7-9 (3 groups):** Please suggest how survey data could be used and turned into (public health) action in your laboratory/organisation/country? (for example: communications and presentations to management of your organisation, policy makers, addressing identified gaps in local action plans etc.)




DTU

Multidisciplinary workshops: Simulated exercises on outbreak investigations

EURGen-RefLabCap
Network meeting 18/09/2024

Faisal Ahmad Khan
(fakh@food.dtu.dk)

Purpose of the simulation exercises in EURGen-RefLabCap

- To train participants in genomic analyses i.e.,
  - Genotypic characterization of AMR
  - MLST and cgMLST
  - Using phylogenetic analysis for detecting and investigating outbreaks in clinical settings

- Multidisciplinary simulated exercises
  - Microbiologists, epidemiologists and bioinformaticians with little to no knowledge of bacterial genomics were encouraged to join
  - Web-based bioinformatics tools were used to get started on bacterial phylogenetics and outbreak detection

Simulated exercises in EURGen-RefLabCap

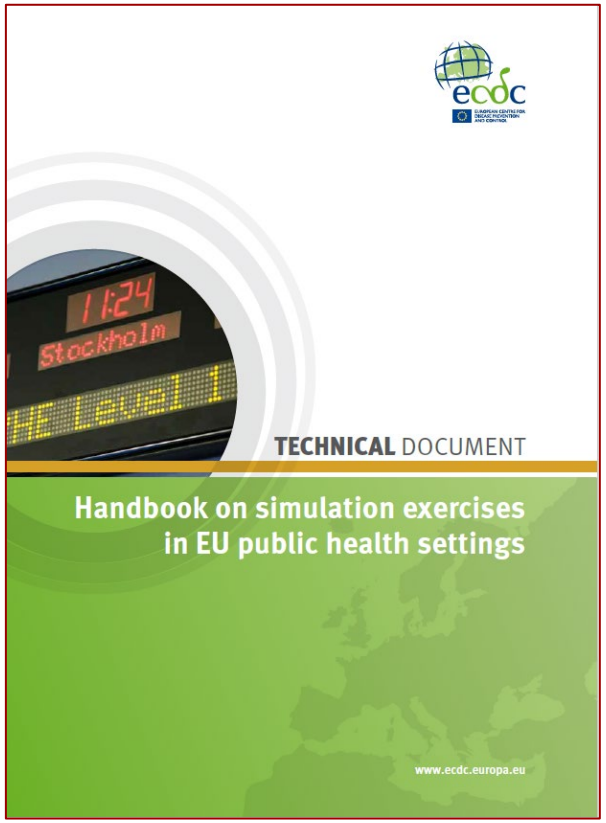
- Series of multidisciplinary training workshops

1. Sept/Oct 2022 – Introduction to SNP analysis and cgMLST for cluster analysis
2. May 2023 – Simulated exercise on outbreak analysis (*Klebsiella pneumoniae*; WS1)
3. Sept 2023 – Simulated exercise on outbreak analysis (*Pseudomonas aeruginosa*; WS2)
4. Jan 2024 – Simulated exercise on outbreak analysis (*Acinetobacter baumannii*; WS2)
5. Oct 2024 – Simulated exercise on outbreak analysis (WS1 pathogens)

WS1: CCRE/ *E. coli* and *K. pneumoniae*
WS2: CPO/ *P. aeruginosa* and *A. baumannii*

Overview of Simulation exercises in EURGen-RefLabCap

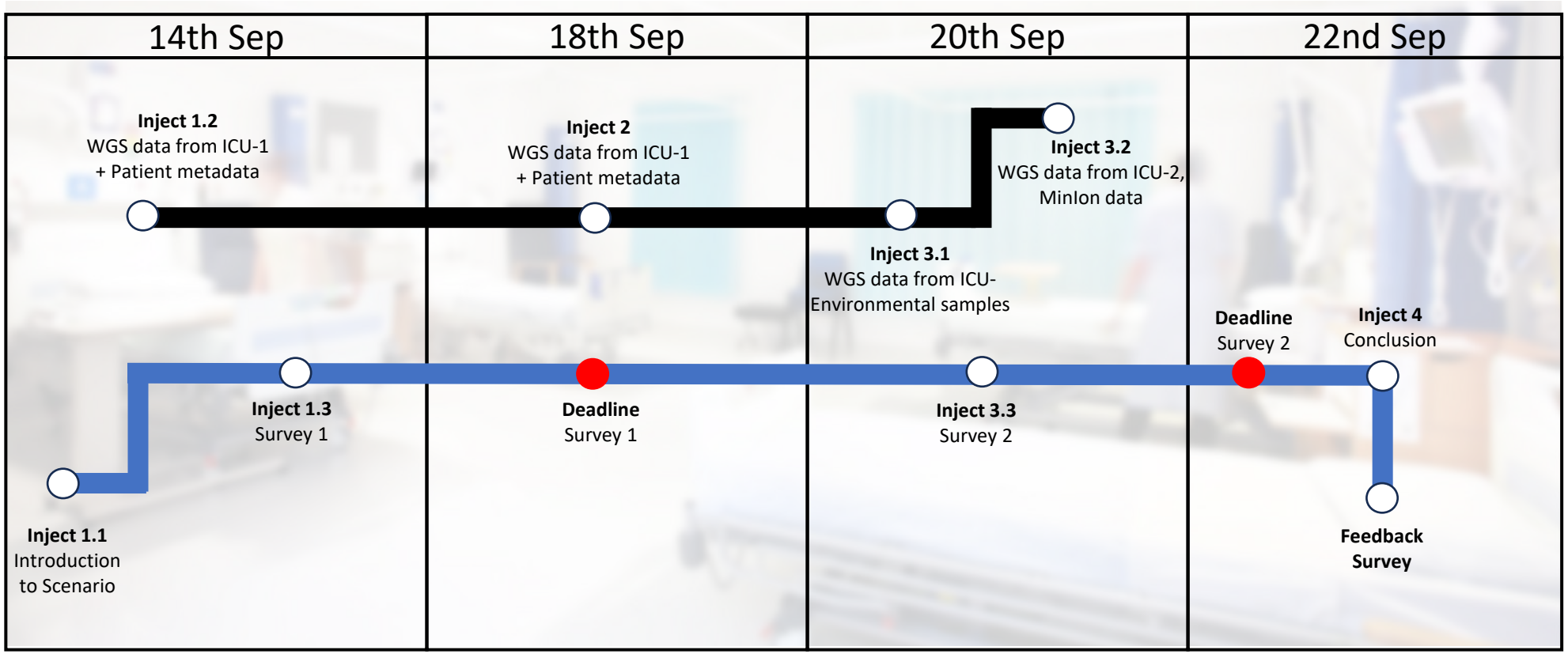
- Multidisciplinary workshop 1
- Multidisciplinary workshop 2
- Multidisciplinary workshop 3
- Multidisciplinary workshop 4
- Multidisciplinary workshop 5
  - Investigation of multispecies outbreak from strains in an hospital archive
    - Cluster Analysis (Illumina and ONT data)
    - A refresher of tools used in previous exercises



ECDC Handbook for Simulation exercises

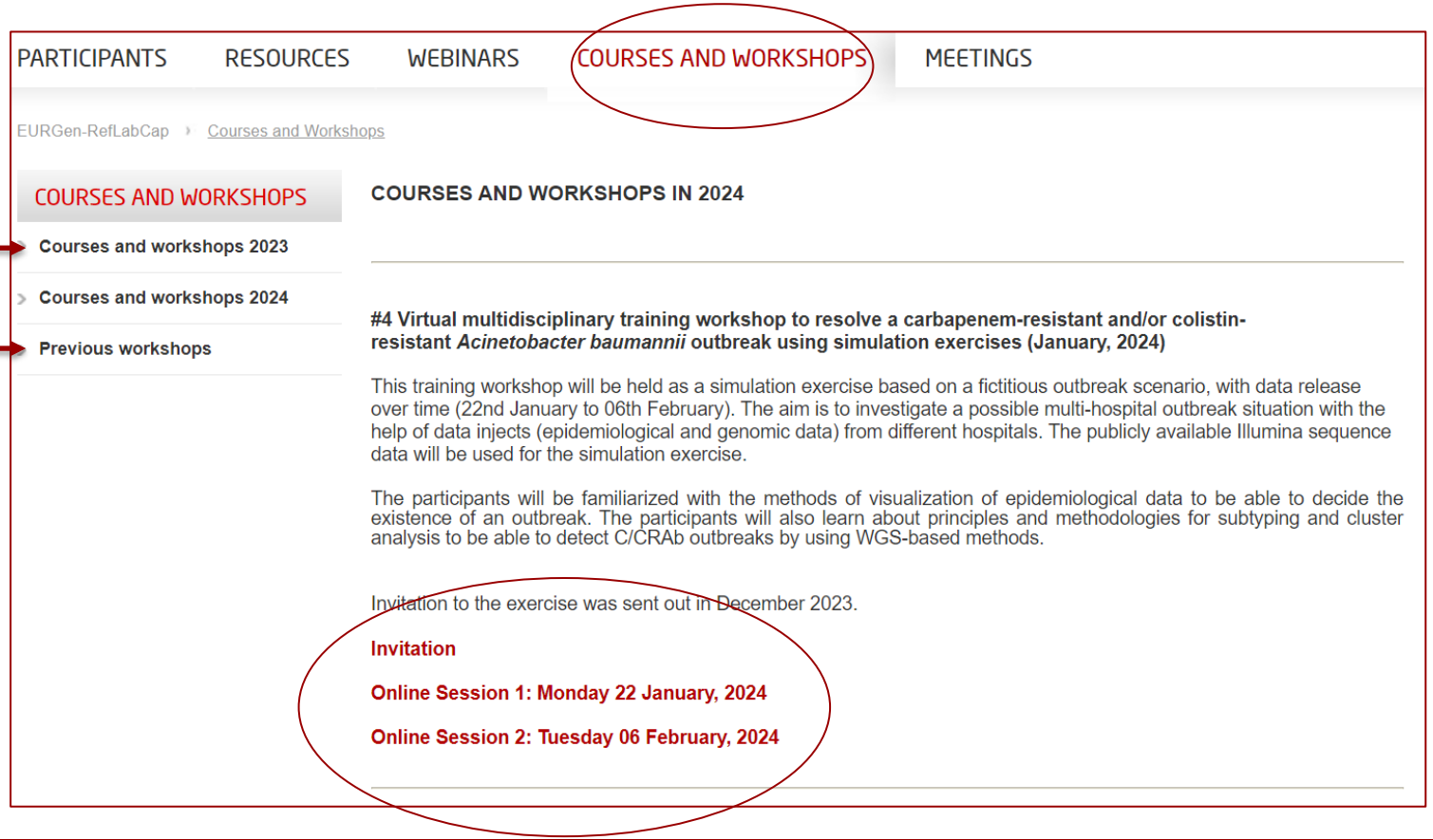
https://www.ecdc.europa.eu/en/publications-data/handbook-simulation-exercises-eu-public-health-settings

Simex structure



Exercise data availability: Presentations

- Presentations are available on EURGen-RefLabCap website (https://www.eurgen-reflabcap.eu/courses-and-workshops)



Exercise data availability: Sequencing data injects

- All the data related to exercises is available on ScienceData
  - Exercise overview
  - inject instructions
  - sequencing data
  - Patient metadata
  - analysis files
  - presentations

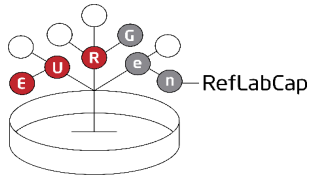
- *K. pneumoniae:* https://sciencedata.dk/shared/3392574dc38c8b5bbb629e024eeda0a0
- *A. baumannii*: https://sciencedata.dk/shared/4418d100e9bda4874b51c70c7ce189a5
- *P. aeruginosa*: https://sciencedata.dk/shared/dd60004f4cccc3452d49f24cfb938af3
- *E. coli/K. pneumoniae*: https://sciencedata.dk/shared/1c29defccaebb09ffc2488b17d04e5e5

Questions/Comments?

- For question you can also reach us via email:
  - Jette (jetk@food.dtu.dk)
  - Faisal (fakh@food.dtu.dk)


DTU

Results from the third External Quality Assessment (EQA) exercise



EURGen-RefLabCap

Faisal Ahmad Khan (fakh@food.dtu.dk)

INTRODUCTION

- OVERVIEW OF THE EURGen-RefLabCap EQAS
- DESIGN OF THE SECOND EQA
- PREPARATION OF EXPECTED RESULTS
- SCORING SYSTEM

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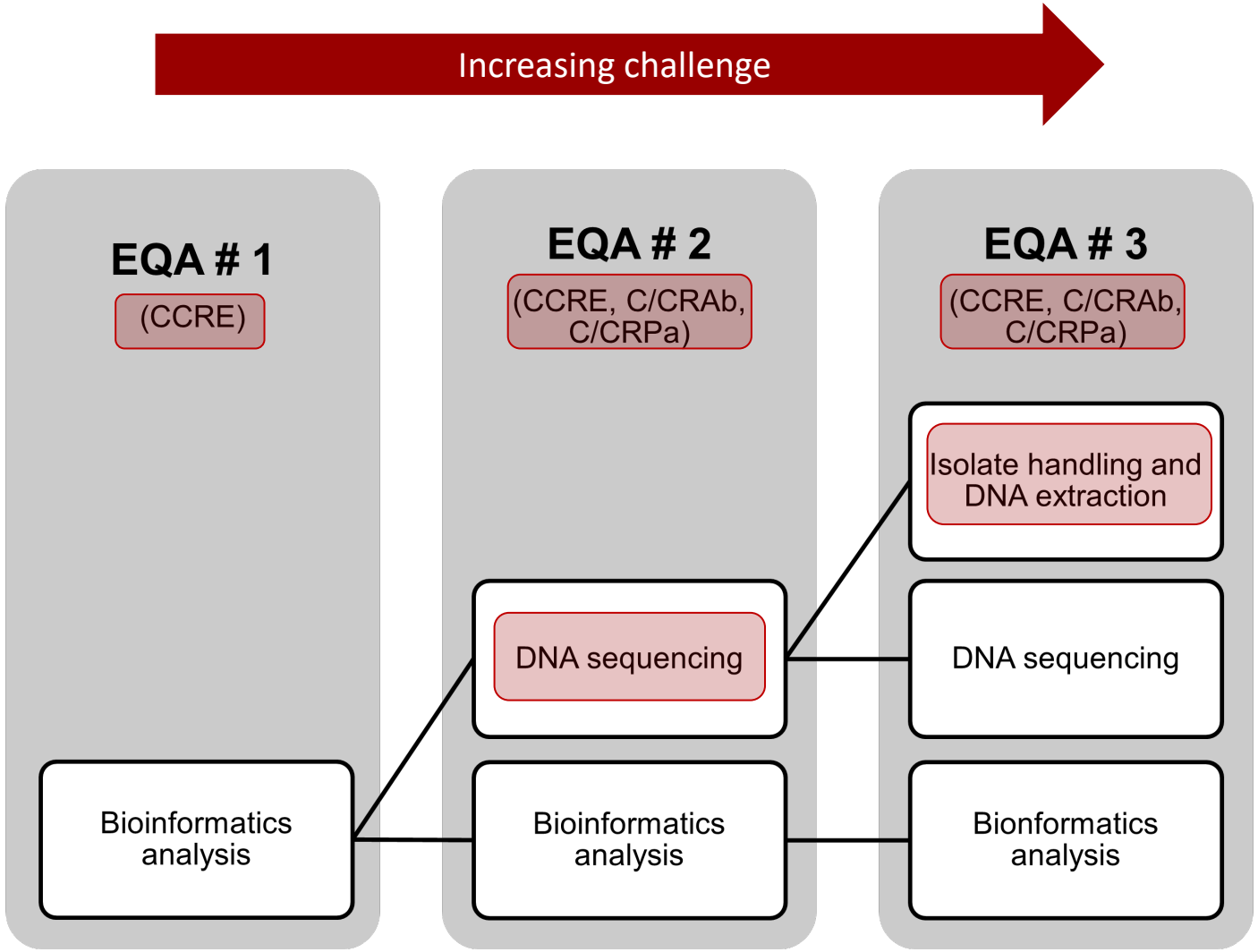
OVERVIEW OF ALL EURGen-RefLabCap EQAs



- Workstream 1 pathogens (WS1)
  - CRE/CCRE
- Workstream 2 pathogens (WS2)
  - C/CRPa
  - C/CRAb

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DESIGN OF THE THIRD EQA

Strains:

- EURGen-2024-01 (*Escherichia coli*)
- EURGen-2024-02 (*Pseudomonas aeruginosa*)
- EURGen-2024-03 (*Acinetobacter baumannii*)
- EURGen-2024-04 (*Klebsiella pneumoniae*)

Materials:

- Purified DNA
- Swabs (bacterial cultures)
- (Raw and assembled reads from Illumina and nanopore sequencing technology)

Bioinformatics analyses included in EQA 2024:

1. Prediction of MLST
2. Prediction of plasmid replicon types
3. Detetcion of genes and chromosomal mutations mediating AMR
4. *In silico* prediction of AMR profiles

Additional Analyses

Quality control of sequences generated by participants

I. *Short-read sequences*

II. *Long-read sequences*

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PREPARATION OF EXPECTED RESULTS

- Consensus results from TWO reference laboratories
  - Sequencing and bioinformatics analysis at DTU
  - Sequencing and bioinformatics analysis at SSI

- Bioinformatics tools used to prepare expected results
  - Mainly CGE tools (MLST, ResFinder, PlasmidFinder)
  - AMRFinder+
  - RGI (CARD database)
  - PathogenWatch

Final set of expected results

Categorical agreement

+

ID ≥ 90%

+

Coverage ≥ 90% (plasmids)/≥ 60% (ARGs)

Expected non mandatory results

- No consensus between reference labs
- Detetcion in only one type of dataset (lr or sr)
- Detection in only one tool

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SCORING SYSTEM IN THE WEBTOOL

Analysis	Submitted result	Score
Prediction of MLST	Correct MLST	1
	Incorrect MLST	0
Detection of plasmid replicons, AMR genes and chromosomal mutations	Genetic determinant correctly identified	1
	Reporting a genetic determinant that was part of the expected results but not mandatory to report	blank
	Missing a genetic determinant	blank
	Reporting an unexpected genetic determinant	0
In-silico AMR profiles	AMR profile correctly reported for the antimicrobial	1
	Reporting an antimicrobial that was part of the expected results but not mandatory to report, or part of intrinsic resistance	blank
	Missing an antimicrobial	blank
	Reporting an AMR profile for an unexpected antimicrobial	0

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SCORING SYSTEM

Maximum possible score of participants

Material and analysis	EURGen-2024-01	EURGen-2024-02	EURGen-2024-03	EURGen-2024-04	Total
Prediction of ST	1	1	1	1	4
Detection of plasmid replicons	5	0	0	6	11
Detection of AMR genes and chromosomal PMs	16	8	4	13	41
In silico prediction of AMR profiles	12	11	5	16	44
Total	**34**	**20**	**10**	**36**	**100**

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RESULTS AND DISCUSSION

- MATERIAL ANALYSED BY PARTICIPANTS
- OVERALL SCORES OF THE PARTICIPANTS
- PREDICTION OF MLST
- DETETCION OF PLASMID REPLIOCN GENES
- DETETCION OF AMR GENES AND MUTATIONS
- *IN SILICO* PREDICTION OF AMR PROFILES

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MATERIAL ANALYSED BY PARTICIPANTS

Total participating laboratories: 31

- WS1: 31 laboratories submitted results
- WS2: 27 laboratories submitted results

	EURGen-2024-01 *(E. coli)*	EURGen-2024-02 (*P. aeruginosa*)	EURGen-2024-03 (*A. baumannii*)	EURGen-2024-04 (*K. pneumoniae*)
Number of Laboratories	31	27	27	31

Test material used:

- Both BACT and DNA: 21 laboratories
- Only BACT: 4 laboratories
- Only DNA: 2 laboratories
- FASTA/FASTQ: 4 laboratories

} Total submissions: 52

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OVERALL SCORES OF THE PARTICIPANTS

Averages of scores (%)

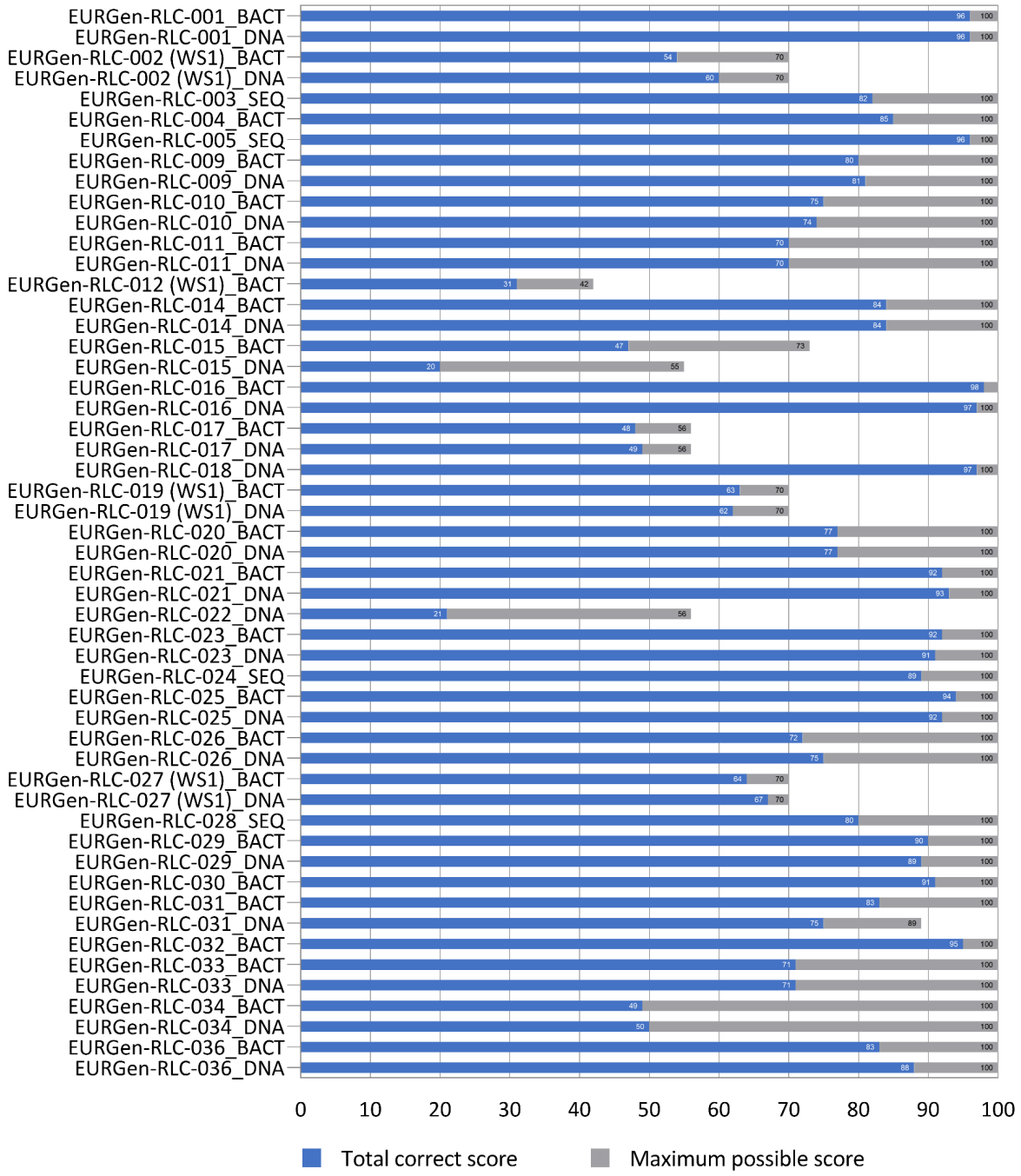
Prediction of MLST: **96%**

Detection of plasmid replicons: **81%**

Prediction of genetic AMR determinants: **79%**

Prediction of AMR profiles: **85%**

Total: 82%



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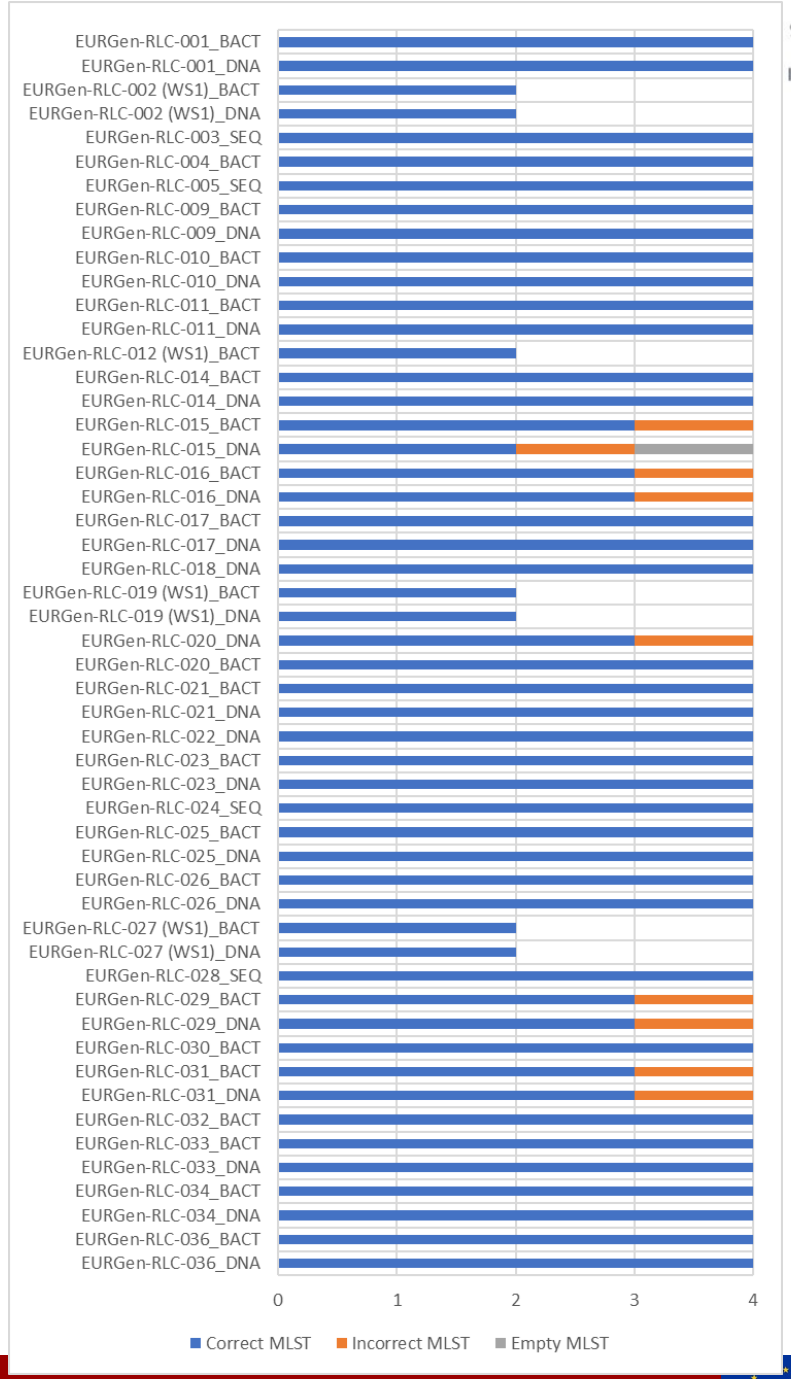
PREDICTION OF MLST – EXPECTED RESULTS

Material	MLST	Alleles assigned to each locus						
EURGen-2024-01 (*E. coli*)*	**457**	*adk*	*fumC*	*gyrB*	*icd*	*mdh*	*purA*	*recA*
		101	88	97	108	26	79	2
EURGen-2024-02 (*P. aeruginosa*)	**644**	*acsA*	*aroE*	*guaA*	*mutL*	*nuoD*	*ppsA*	*trpE*
		28	3	94	13	1	4	10
EURGen-2024-03 (*A. baumannii*)	**1780**	*cpn60*	*gdhB*	*gltA*	*gpi*	*gyrB*	*recA*	*rpoD*
		1	42	1	159	17	12	6
EURGen-2024-04 (*K. pneumoniae*)*	**16**	*gapA*	*infB*	*mdh*	*pgi*	*phoE*	*rpoB*	*tonB*
		2	1	2	1	4	4	4

* For EURGen-2024-01 (E. coli), Achtman scheme was used (E. coli#1, if using CGE MLST tool). For EURGen-2024-03 (A. baumannii), Oxford scheme was used (A. baumannii#1, if using CGE MLST tool).

PREDICTION OF MLST - SUBMITTED RESULTS

- Average score : **96%**
- All MLST were correct for EURGen-2024-01, EURGen-2024-02 and EURGen-2024-04
- 9 Incorrect MLST
  - All for EURGen-2024-03 (*A. baumannii*)



WS1: Only submitted results for workstream 1 pathogens; WS2: Only submitted results for workstream 2 pathogens.

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PREDICTION OF MLST - DISCUSSION

09 Incorrect MLST results for *A. baumannii* (EURGen-2024-03)

- Due to MLST scheme used
  - These participants used Pasteur scheme (ST 764)
  - Oxford scheme used for expected results (ST 1780)

- For the self-evaluation, it should be considered that these discrepancies do not represent a flaw in the bioinformatics analysis performed
- It is important to understand that the bioinformatics capacity and knowledge required for using either MLST scheme is the same

DETECTION OF PLASMID REPLICONS – EXPECTED RESULTS

Material	Plasmid replicons	Nr.
EURGen-2024-01 (*E.coli*)	**Expected**: ColpEC648, IncFIA, IncFIB(AP001918), IncFII, IncI1-I(Alpha)	5
EURGen-2024-02 (*P. aeruginosa*)	No plasmid replicon detected	0
EURGen-2024-03 (*A. baumannii*)	No plasmid replicon detected	0
EURGen-2024-04 (*K. pneumoniae*)	**Expected**: Col440II, IncFIB(K), IncFII, IncFII(K), IncN4, IncX3	6
	Expected but non-mandatory: Col(pHAD28), ColKP3	2

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DETECTION OF PLASMID REPLICONS - SUBMITTED RESULTS

Total submissions: 103

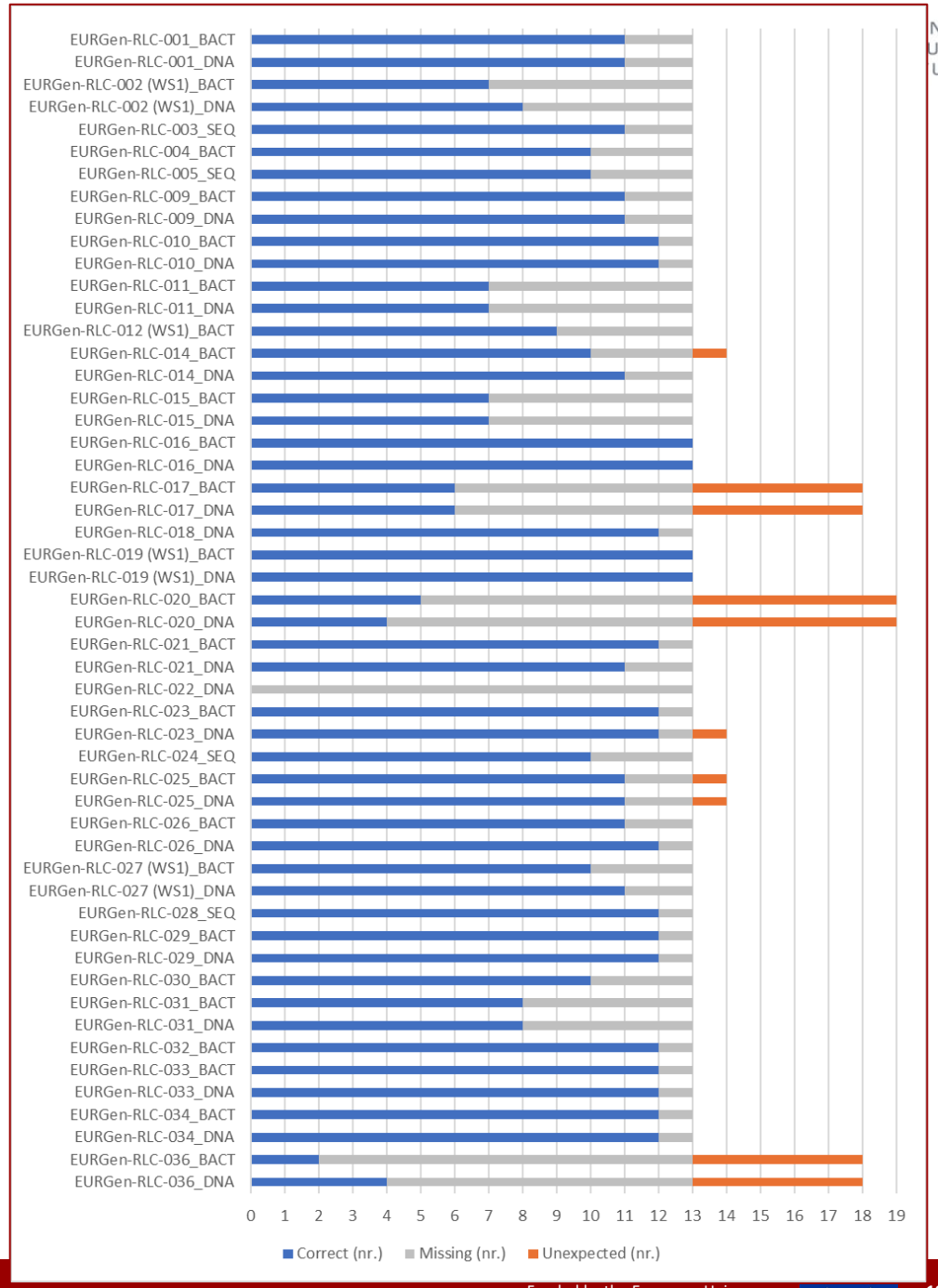
- 50% submissions were fully correct (n=51)
- 33% had missing replicons (n=34)
- 17.5% had unexpected replicons (n=18)

} 16.5% Simultaneous (n=17)

Average score: 81%

- 21 submissions achieved 100% of max. possible score

Clarification on the data in the figure: Each bar represents submissions for all isolates for a particular sample type by a laboratory. For example, EURGen-RLC-001_BACT represents submissions for all isolates (n=2 in this case) by laboratory EURGen-RLC-001 for the BACT sample.



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DETECTION OF PLASMID REPLICONS - SUBMITTED RESULTS

Strain	Missing expected replicons	Unexpected replicons
EURGen-2024-01	ColpEC648 (n=16)	IncFIC(FII) (n=8)
	IncFII (n=16)	IncI(Gamma) (n=6)
	IncI1-I(Alpha) (n=8)	
	IncFIB(AP001918)(n=5)	
EURGen-2024-04	Col(pHAD28)* (n=48)	ColRNAI (n=6)
	colKP3* (n=19)	IncFIA (n=6)
	IncFII(K) (n=22)	IncFIC(FII) (n=6)
	IncN4 (n=16)	IncN (n=6)
	Col440II (n=10)	

* Expected but non-mandatory

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DETECTION OF PLASMID REPLICONS - DISCUSSION

- The non-mandatory replicons were missing in most results
  - Col(pHAD28) (n=48) and ColKP3 (n=19) were only detected in raw reads while preparing the expected results

- The missing plasmid replicons:
  - Choice of different thresholds (?)

Discrepancy between short-and long-read data:

- long-read sequencing is overall more adequate for detection of plasmids
- the assembly process might fail to properly capture sequences that were present in raw data

Different approaches according to purpose:

- Thresholds can be adjusted for different analyses
- Perhaps better to be less strict and manually evaluate results

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DETECTION OF GENES AND MUTATIONS MEDIATING AMR – EXPECTED RESULTS

Material	AMR genes and chromosomal mutations	Nr.
EURGen-2024-01 (*E. coli*)	**Expected**: *aac(3)-IIa*[a], *bla*$_{\text{CTX-M-65}}$, *bla*$_{\text{TEM-1}}$[b], *dfrA12*, *dfrA17*, *sul1*, *sul2*, *sul3*, *fosA3*, *mcr-1.1*[c], *glpT* E448K, *gyrA* D87Y, *gyrA* S83L, *parC* S80I, *parE* S458A, *uhpT* E350Q	16
EURGen-2024-02 (*P. aeruginosa*)	**Expected:** *aph(3')-VI*[d], *aac(6')-Ib*[e], *bla*$_{\text{IMP-62}}$, *bla*$_{\text{NDM-1}}$, *bla*$_{\text{PME-1}}$, *crpP*, *qnrVC1*, *gyrA* T83I	8
	Expected but non-mandatory: *ant(3'')-Ii-aac(6')-Iid*[f], *aac(6')-Ib-cr*[g], *bla*$_{\text{KBL-1}}$, *qepA*[h], *nalC* G71E, *nalC* S209R, *parC* S87L	7
EURGen-2024-03 (*A. baumannii*)	**Expected:** *ant(2'')-Ia*, *bla*$_{\text{OXA-23}}$, *gyrA* S81L, *parC* S84L	4
	Expected but non-mandatory: *parC* D105E, *parC* V104I	2
EURGen-2024-04 (*K. pneumoniae*)	**Expected:** *aac(6')-Ib-cr*[i], *bla*$_{\text{CTX-M-15}}$[j], *bla*$_{\text{NDM-5}}$, *bla*$_{\text{OXA-1}}$, *bla*$_{\text{OXA-181}}$, *bla*$_{\text{TEM-1}}$[b], *dfrA12*, *qnrS1*, *rmtB*[k], *sul1*, *gyrA* D87N, *gyrA* S83F, *parC* E84K	13
	Expected but non-mandatory: *mgrB* W20R	1

[a] Either *aac(3)-IIa or aac(3)-IIe*
[b] Either *bla*$_{\text{TEM-1}}$ or *bla*$_{\text{TEM-1A}}$ or *bla*$_{\text{TEM-1B}}$ or *bla*$_{\text{TEM-1C}}$ or *bla*$_{\text{TEM-1D}}$
[c] Either *mcr1.1* or *mcr-1.26*
[d] Either *aph(3')-VI* or *aph(3')-Via*
[e] Either *aac(6')-Ib* or *aac(6')-Ib-Hangzhou* or *aac(6')-Ib3* or *aac(6')-Ib4* or *aac(6')-Ib9*
[f] Either *ant(3'')-Ii-aac(6')-Iid* or *ant(3'')-Ih/aac(6')-Iid*
[g] Either *aac(6')-Ib-cr* or *aac(6')-Ib-cr5*
[h] Either *qepA* or *qepA1* or *qepA2* or *qepA4*
[i] Either *aac(6')-Ib-cr* or *aac(6')-Ib-cr5* or *aac(6')-Ib-cr6*
[j] Either *bla*$_{\text{CTX-M-15}}$ or *bla*$_{\text{CTX-M-101}}$
[k] Either *rmtB* or *rmtB1*

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DETECTION OF GENES AND MUTATIONS – SUBMITTED RESULTS

Total submissions: 192

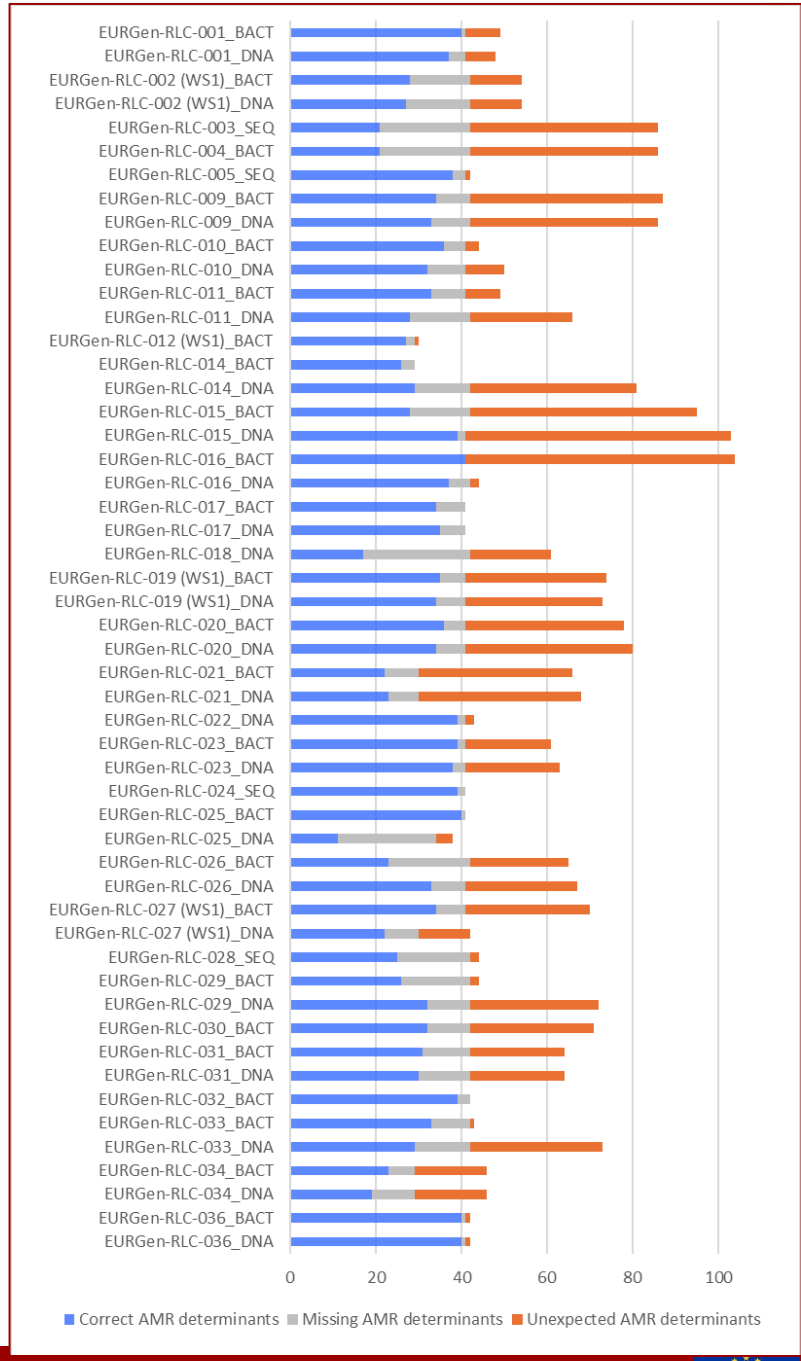
- 9.9% submissions were fully correct (n=19)
- 17% had missing AMR determinants (n=33)
- 73% had unexpected determinants (n=140)

} 54% Simultaneous (n=103)

Average score: 79%

- None of the participants achieved 100% of their max. possible score
- Highest achieved score was 97.5%

Clarification on the data in the figure: Each bar represents submissions for all isolates for a particular sample type by a laboratory. For example, EURGen-RLC-001_BACT represents submissions for all isolates (n=4 in this case) by laboratory EURGen-RLC-001 for the BACT sample.



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DETECTION OF GENES AND MUTATIONS – DISCUSSION

Strain	Examples of problems
01	Missing *glpT* E448K (n=26) or *uhpT* E350Q (n=27)
	Unexpected *aadA1* (n=23), *aadA2* (n=25), *aadA5* (n=24), *tet(A)* (n=20), *tet(M)* (n=16)
02	Missing *aac(6')* (n=19), *crpP* (n=18)
	Unexpected bla_{PAO} (n=10), bla_{PCD} (n=17), $bla_{OXA-486}$ (n=18), $bla_{CARB-2,}$ (n=23), *fosA* (n=25), aph(3')-IIb (n=18)
	Unexpected *tet(G) (n=15), aadA (n=13), aadA2 (n=12)*
03	Missing *gyrA* S81L (n=19), *parC* S84L (n=19)
	Unexpected, $bla_{OXA-429}$ (n=23), $bla_{CARB-2,}$ (n=25), blaPDC-262 (n=16)
	aph(3'')-Ib (n=19), sul2 (n=14), tet(B) (n=18), tet(G) (n=18), aadA2 (n=19)
04	Missing *gyrA* D87N (n=21), *parC* E84K (n=23), *gyrA* S83F (n=21)
	Unexpected *fosA/fosA5* (n=21), *oqxA/oqxB* (n=18)
	Unexpected *aph(3')-Ia (n=24), aadA2 (n=26)*

Missing mutations due to lacking database

- PointFinder can't detect PMs in *A. baumannii* and *P. aeruginosa* – No database!
- *glpT*, *uhpT* mutations not present in PointFinder database (ResFinder)
- Similarly, *gyrA* and *parC* mutations were missing for *A. baumannii*

⇩

Multiple tools and database can be used:

- AMRFinder+
- CARD
- ResFinder
- Other tools (PathogenWatch?)

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DETECTION OF GENES AND MUTATIONS – DISCUSSION

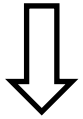
Expected mutations were reported incorrectly

- Many participants reported the expected PMs but in different format than described in EQA protocol
  - E.g., *gyrA* D87Y

- The mutations are present in the isolate

EURGen-2024-001

gyrA	p.D87Y
gyrA	p.S83L
gyrA	S83L;D87Y
parC	p.S80I
parC	parC_S80I
parE	p.S458A
parE	parE_S458A



- For the self-evaluation, it should be considered that these discrepancies do not represent a flaw in the bioinformatics analysis performed

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DETECTION OF GENES AND MUTATIONS – DISCUSSION

Strain	Examples of problems
01	Missing *glpT* E448K (n=26) or *uhpT* E350Q (n=27)
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02	Missing *aac(6')* (n=19), *crpP* (n=18)
	Unexpected bla_{PAO} (n=10), bla_{PCD} (n=17), $bla_{OXA-486}$ (n=18), $bla_{CARB-2,}$ (n=23), *fosA* (n=25), aph(3')-IIb (n=18)
	Unexpected *tet(G) (n=15), aadA (n=13), aadA2 (n=12)*
03	Missing *gyrA* S81L (n=19), *parC* S84L (n=19)
	Unexpected, $bla_{OXA-429}$ (n=23), $bla_{CARB-2,}$ (n=25), blaPDC-262 (n=16)
	aph(3'')-Ib (n=19), sul2 (n=14), tet(B) (n=18), tet(G) (n=18), aadA2 (n=19)
04	Missing *gyrA* D87N (n=21), *parC* E84K (n=23), *gyrA* S83F (n=21)
	Unexpected *fosA/fosA5* (n=21), *oqxA/oqxB* (n=18)
	Unexpected *aph(3')-Ia (n=24), aadA2 (n=26)*

Reporting intrinsic genes

- Present in the strains but do no contribute to the elevated resistance in non-WT phenotype

⇩

<u>Results must be evaluated critically:</u>

- Too much noise can hide the important information
- Insufficient knowledge regarding genetic mechanisms of AMR might lead to incorrect reporting of resistance profiles

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DETECTION OF GENES AND MUTATIONS – DISCUSSION

Strain	Examples of problems
01	Missing *glpT* E448K (n=26) or *uhpT* E350Q (n=27)
	Unexpected *aadA1* (n=23), *aadA2* (n=25), *aadA5* (n=24), *tet(A)* (n=20), *tet(M)* (n=16)
02	Missing *aac(6')* (n=19), *crpP* (n=18)
	Unexpected bla_{PAO} (n=10), bla_{PCD} (n=17), $bla_{OXA-486}$ (n=18), $bla_{CARB-2,}$ (n=23), *fosA* (n=25), aph(3')-IIb (n=18)
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	aph(3'')-Ib (n=19), sul2 (n=14), tet(B) (n=18), tet(G) (n=18), aadA2 (n=19)
04	Missing *gyrA* D87N (n=21), *parC* E84K (n=23), *gyrA* S83F (n=21)
	Unexpected *fosA/fosA5* (n=21), *oqxA/oqxB* (n=18)
	Unexpected *aph(3')-Ia (n=24), aadA2 (n=26)*

Reporting AMR genes for antimicrobials not included in EQA

- These genes are present in the strains but they confer resistance to antimicrobials not relevant for the species
- Streptomycin (*aadA1, aadA2, aadA5, aph(6)-Id, aph(3'')-Ib*) and Kanamycin (*aph(3')-IIb*), Tetracycline (*tet(A), tet(M)*)

⇩

<u>Results must be evaluated critically:</u>

- Too much noise can hide the important information
- Insufficient knowledge regarding genetic mechanisms of AMR might lead to incorrect reporting of resistance profiles

IN SILICO PREDICTION OF AMR PROFILES – EXPECTED REULTS

Material	Associated prediction of AMR profiles	Nr.
EURGen-2024-01 (*E. coli*)	**Expected**: Ampicillin, Aztreonam, Cefepime, Cefotaxime, Ceftazidime, Ciprofloxacin, Colistin, Fosfomycin, Gentamicin, Sulfamethoxazole, Tobramycin, Trimethoprim	12
EURGen-2024-02 (*P. aeruginosa*)	**Expected:** Amikacin, Aztreonam, Cefepime, Ceftazidime, Ceftazidime-avibactam, Ciprofloxacin, Gentamicin, Imipenem, Meropenem, Piperacillin-tazobactam, Tobramycin	11
EURGen-2024-03 (*A. baumannii*)	**Expected:** Ciprofloxacin, Gentamicin, Imipenem, Meropenem, Tobramycin	5
	Intrinsic*: Aztreonam, fosfomycin	2
EURGen-2024-04 (*K. pneumoniae*)	**Expected:** Amikacin, Amoxicillin-clavulanic acid, Aztreonam, Cefepime, Cefotaxime, Ceftazidime, Ceftazidime-avibactam, Ciprofloxacin, Ertapenem, Gentamicin, Imipenem, Meropenem, Piperacillin-tazobactam, Sulfamethoxazole, Tobramycin, Trimethoprim	16
	Expected non-mandatory: Colistin[a]	1
	Intrinsic*: Ampicillin	1

[a] Detection of *mgrB* W20R mutation, and subsequent inclusion of colistin in AMR profile of this strain, were expected results, but not mandatory to report
* Intrinsic resistance (based on EUCAST Expected Phenotypes Version 1.2, January 2023), not part of the expected results

IN SILICO PREDICTION OF AMR PROFILES – EXPECTED REULTS

Total submissions: 173

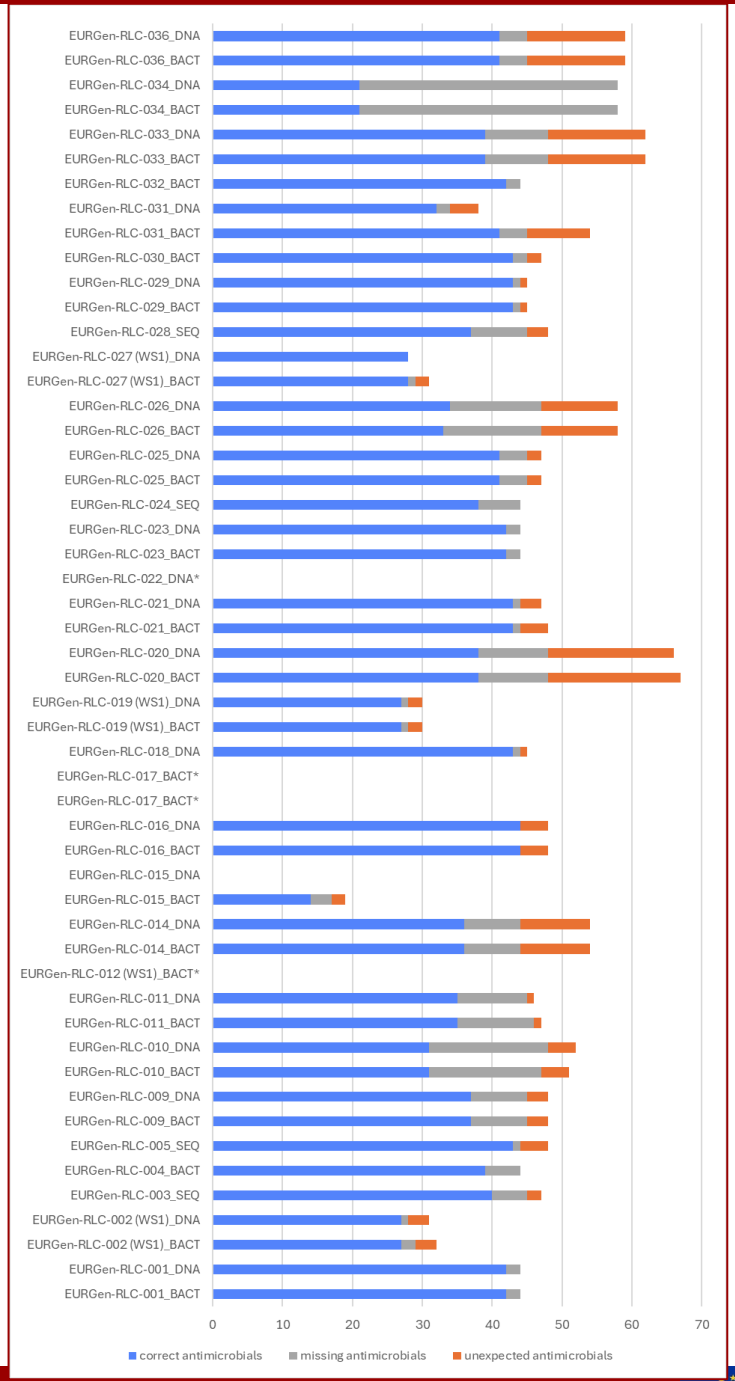
- 24% submissions were fully correct (n=41)
- 32% had missing antimicrobials (n=55)
- 44% had unexpected antimicrobials (n=77)

} 32% Simultaneous (n=56%)

Average score: 85%

- 3 participants achieved 100% of their max. possible score

Clarification on the data in the figure: Each bar represents submissions for all isolates for a particular sample type by a laboratory. For example, EURGen-RLC-001_BACT represents submissions for all isolates (n=4 in this case) by laboratory EURGen-RLC-001 for the BACT sample.



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IN SILICO PREDICTION OF AMR PROFILES – SUBMITTED REULTS

Laboratories	Sample type	Expected: Ampicillin	Aztreonam	Cefepime	Cefotaxime	Ceftazidime	Ciprofloxacin	Colistin	Fosfomycin	Gentamicin	Sulfamethoxazole	Tobramycin	Trimethoprim	Unexpected: Amikacin	Ertapenem	Tigecycline	Correct (nr.)	Missing (nr.)	Unexpected (nr.)
EURGen-RLC-001	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-002	BACT	x	x	x	x	-	x	x	x	x	x	x	x				11	1	0
	DNA	x	x	x	x	-	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-003[b]	SEQ	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-004[c]	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-005[b]	SEQ	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-009	BACT	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
	DNA	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-010	BACT	x	x	x	x	x	-	x	x	x	x	x	x				11	1	0
	DNA	x	x	x	x	x	-	x	x	x	x	x	x				11	1	0
EURGen-RLC-011	BACT	x	-	x	x	x	-	x	x	x	x	x	x				10	2	0
	DNA	x	-	x	x	x	-	x	x	x	x	x	x				10	2	0
EURGen-RLC-014	BACT	-	-	x	x	x	x	x	x	x	x	x	x				10	2	0
	DNA	-	-	x	x	x	x	x	x	x	x	x	x				10	2	0
EURGen-RLC-015	BACT	x	-	x	x	x	x	x	x	x	-	x	x				10	2	0
EURGen-RLC-016	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-018[c]	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-019	BACT	x	x	x	x	x	-	x	x	x	x	x	x				11	1	0
	DNA	x	x	x	x	x	-	x	x	x	x	x	x				11	1	0
EURGen-RLC-020	BACT	x	x	x	x	x	x	x	x	x	-	-	x		x	x	10	2	2
	DNA	x	x	x	x	x	x	x	x	x	-	-	x		x	x	10	2	2
EURGen-RLC-021	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-023	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-024[b]	SEQ	x	x	x	x	x	x	x	x	-	x	-	x				10	2	0
EURGen-RLC-025	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-026	BACT	-	-	x	x	x	-	x	x	-	x	-	x				7	5	0
	DNA	-	-	x	x	x	-	x	x	x	x	-	x				8	4	0
EURGen-RLC-027	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-028[b]	SEQ	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-029	BACT	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
	DNA	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-030[c]	BACT	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-031	BACT	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x				12	0	0
EURGen-RLC-032[c]	BACT	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
EURGen-RLC-033	BACT	x	x	x	x	x	x	x	x	x	-	-	x	x			10	2	1
	DNA	x	x	x	x	x	x	x	x	x	-	-	x	x			10	2	1
EURGen-RLC-034	BACT	-	-	-	-	-	-	x	-	-	-	-	-				1	11	0
	DNA	-	-	-	-	-	-	x	-	-	-	-	-				1	11	0
EURGen-RLC-036	BACT	x	-	x	x	x	x	x	x	x	x	x	x				11	1	0
	DNA	-	x	x	x	x	x	x	x	x	x	x	x				11	1	0
Correct (nr.)		40	29	45	45	43	37	47	45	43	40	38	45	NA	NA	NA	**Total**		
Missing or UN (nr.)		7	18	2	2	4	10	0	2	4	7	9	2	2	2	2	497	67	6

Strain EURGen-2024-01 (*E. coli*)

- Missing from most submitted results
  - Aztreonam (n=18)
    - Only ResFinder reports Aztronam for the R-profile of $bla_{\text{CTX-M-65}}$
  - Ciprofloxacin (n=10)
    - Missing *gyrA* and *parC* mutations in some cases

Results must be evaluated critically:

- Results can / should be confirmed with other tools

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IN SILICO PREDICTION OF AMR PROFILES – SUBMITTED REULTS

Laboratories	Sample type	Expected: Amikacin	Aztreonam	Cefepime	Ceftazidime	Ceftazidime-avibactam	Ciprofloxacin	Gentamicin	Imipenem	Meropenem	Piperacillin-tazobactam	Tobramycin	Unexpected: Amoxicillin-clavulanic acid	Ampicillin	Cefotaxime	Ertapenem	Fosfomycin	Sulfamethoxazole	Tigecycline	Correct (nr.)	Missing (nr.)	Unexpected (nr.)
EURGen-RLC-001	BACT	x	-	x	x	x	x	-	x	x	x	x								9	2	0
	DNA	x	-	x	x	x	x	-	x	x	x	x								9	2	0
EURGen-RLC-003[b]	SEQ	x	-	x	x	-	x	x	x	x	x	x					x			9	2	1
EURGen-RLC-004[c]	BACT	-	-	x	x	x	x	-	x	x	x	-								7	4	0
EURGen-RLC-005[b]	SEQ	x	-	x	x	x	x	x	x	x	x	x								10	1	0
EURGen-RLC-009	BACT	-	-	x	x	-	x	-	x	x	x	-					x			6	5	1
	DNA	-	-	x	x	-	x	-	x	x	x	-					x			6	5	1
EURGen-RLC-010	BACT	x	-	-	-	-	-	x	-	-	-	-					x		x	2	9	2
	DNA	x	-	-	-	-	-	x	-	-	-	-					x		x	2	9	2
EURGen-RLC-011	BACT	-	-	x	x	-	x	-	x	x	x	-								6	5	0
	DNA	-	-	x	x	-	x	-	x	x	x	-								6	5	0
EURGen-RLC-014	BACT	-	-	x	x	x	-	-	x	x	x	-	x	x	x	x	x		x	6	5	6
	DNA	-	-	x	x	x	-	-	x	x	x	-	x	x	x	x	x		x	6	5	6
EURGen-RLC-016	BACT	x	x	x	x	x	x	x	x	x	x	x								11	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x								11	0	0
EURGen-RLC-018[c]	DNA	x	-	x	x	x	x	x	x	x	x	x								10	1	0
EURGen-RLC-020	BACT	x	x	x	x	-	-	x	x	x	-	-		x	x	x	x		x	7	4	5
	DNA	x	x	x	x	-	-	x	x	x	-	-		x	x	x	x		x	7	4	5
EURGen-RLC-021	BACT	x	x	x	x	x	x	x	x	x	x	x					x			11	0	1
	DNA	x	x	x	x	x	x	x	x	x	x	x					x			11	0	1
EURGen-RLC-023	BACT	x	-	x	x	x	x	x	x	x	x	x								10	1	0
	DNA	x	-	x	x	x	x	x	x	x	x	x								10	1	0
EURGen-RLC-024[b]	SEQ	-	x	x	x	-	x	-	x	x	x	-								7	4	0
EURGen-RLC-025	BACT	x	-	x	x	-	x	x	x	x	x	x					x			9	2	1
	DNA	x	-	x	x	-	x	x	x	x	x	x					x			9	2	1
EURGen-RLC-026	BACT	-	-	x	x	-	x	x	x	x	x	-	x	x	x	x	x	x	x	7	4	7
	DNA	-	-	x	x	-	x	x	x	x	x	-	x	x	x	x	x	x	x	7	4	7
EURGen-RLC-028[b]	SEQ	-	-	x	x	-	x	-	x	x	x	-								6	5	0
EURGen-RLC-029	BACT	x	x	x	x	x	x	x	x	x	x	x								11	0	0
	DNA	x	x	x	x	x	x	x	x	x	x	x								11	0	0
EURGen-RLC-030[c]	BACT	x	x	x	x	x	x	x	x	x	x	x								11	0	0
EURGen-RLC-031	BACT	x	-	x	x	-	x	x	x	x	x	x	x	x	x	x	x			9	2	5
EURGen-RLC-032[c]	BACT	x	-	x	x	x	x	x	x	x	x	x								10	1	0
EURGen-RLC-033	BACT	x	x	x	x	-	x	x	x	x	-	-	x	x	x	x	x		x	8	3	6
	DNA	x	x	x	x	-	x	x	x	x	-	-	x	x	x	x	x		x	8	3	6
EURGen-RLC-034	BACT	-	-	-	-	-	-	-	x	x	-	-								2	9	0
	DNA	-	-	-	-	-	-	-	x	x	-	-								2	9	0
EURGen-RLC-036	BACT	x	-	x	x	-	x	x	x	x	x	x	x	x	x	x	x	x	x	9	2	7
	DNA	x	-	x	x	-	x	x	x	x	x	x	x	x	x	x	x	x	x	9	2	7
Correct (nr.)		26	12	35	35	17	31	26	37	37	31	20	NA	NA	NA	NA	NA	NA	NA	**Total**		
Missing or UN (nr.)		13	27	4	4	22	8	13	2	2	8	19	9	11	11	11	20	4	12	307	122	78

Strain EURGen-2024-02 (*P. aeruginosa*)

- **Missing from most submitted results**
  - Aztreonam (n=27)
    - Missing from bla_{PME} R-profile in all three tools
  - Ceftazidime-avibactam (n=22)
    - Missing from $bla_{\text{NDM-1}}$ and $bla_{\text{IMP-62}}$ R-profile in ResFinder database
  - Tobramycin (n=19)
    - Missing in AMRFinder+ for the aminoglycoside resistance genes (*aac(6')-Ib* family)
- **Reporting of intrinsic resistance**
  - Fosfomycin (n=20)
    - *fosA* is intrinsic in *P. aeruginosa*

Results must be evaluated critically:

- Results can / should be confirmed with other tools
- Points to insufficient knowledge of genetic AMR mechanisms

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IN SILICO PREDICTION OF AMR PROFILES – SUBMITTED REULTS

Laboratories	Sample type	Expected: Ciprofloxacin	Gentamicin	Imipenem	Meropenem	Tobramycin	Unexpected: Amoxicillin-clavulanic acid	Ampicillin	Aztreonam	Cefepime	Cefotaxime	Ceftazidime	Ceftazidime-avibactam	Colistin	Ertapenem	Fosfomycin	Piperacillin-tazobactam	Sulfamethoxazole	Tigecycline	Trimethoprim	Correct (nr.)	Missing (nr.)	Unexpected (nr.)
EURGen-RLC-001	BACT	x	x	x	x	x															5	0	0
	DNA	x	x	x	x	x															5	0	0
EURGen-RLC-003[b]	SEQ	-	x	x	x	x															4	1	0
EURGen-RLC-004[c]	BACT	x	-	x	x	x															4	1	0
EURGen-RLC-005[b]	SEQ	x	x	x	x	x				x		x	x				x				5	0	4
EURGen-RLC-009	BACT	-	x	x	x	x															4	1	0
	DNA	-	x	x	x	x															4	1	0
EURGen-RLC-010	BACT	-	x	-	-	x														x	2	3	1
	DNA	-	x	-	-	x														x	2	3	1
EURGen-RLC-011	BACT	-	-	x	x	x															3	2	0
	DNA	-	-	x	x	x															3	2	0
EURGen-RLC-014	BACT	-	x	x	x	x		x										x			4	1	2
	DNA	-	x	x	x	x		x										x			4	1	2
EURGen-RLC-015[c]	BACT	-	x	x	x	x		x										x			4	1	2
EURGen-RLC-016	BACT	x	x	x	x	x				x		x	x				x				5	0	4
	DNA	x	x	x	x	x				x		x	x				x				5	0	4
EURGen-RLC-018[c]	DNA	x	x	x	x	x							x								5	0	1
EURGen-RLC-020	BACT	x	x	x	x	x		x	x	x	x	x			x	x			x	x	5	0	9
	DNA	x	x	x	x	x		x	x	x	x	x			x	x			x		5	0	8
EURGen-RLC-021	BACT	-	x	x	x	x										x					4	1	1
	DNA	-	x	x	x	x										x					4	1	1
EURGen-RLC-023	BACT	-	x	x	x	x															4	1	0
	DNA	-	x	x	x	x															4	1	0
EURGen-RLC-024[b]	SEQ	x	x	x	x	x															5	0	0
EURGen-RLC-025	BACT	-	x	x	x	x															4	1	0
	DNA	-	x	x	x	x															4	1	0
EURGen-RLC-026	BACT	-	x	x	x	-		x										x			3	2	2
	DNA	-	x	x	x	-		x										x			3	2	2
EURGen-RLC-028[b]	SEQ	-	x	x	x	x		x										x			4	1	2
EURGen-RLC-029	BACT	x	x	x	x	x								x							5	0	1
	DNA	x	x	x	x	x								x							5	0	1
EURGen-RLC-030[c]	BACT	x	x	x	x	x															5	0	0
EURGen-RLC-031	BACT	-	x	x	x	x		x										x			4	1	2
	DNA	-	x	x	x	x		x										x			4	1	2
EURGen-RLC-032[c]	BACT	x	x	x	x	x															5	0	0
EURGen-RLC-033	BACT	x	x	x	x	x	x	x							x	x				x	5	0	5
	DNA	x	x	x	x	x	x	x							x	x				x	5	0	5
EURGen-RLC-034	BACT	-	-	x	x	-															2	3	0
	DNA	-	-	x	x	-															2	3	0
EURGen-RLC-036	BACT	x	x	x	x	x	x	x							x		x	x			5	0	5
	DNA	x	x	x	x	x	x	x							x		x	x			5	0	5
EURGen-RLC-012																					NA	NA	NA
Correct (nr.)		18	36	39	39	37	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	**Total**		
Missing or UN (nr.)		23	5	2	2	4	4	14	2	5	2	5	4	2	6	6	5	10	2	5	169	36	72

Strain EURGen-2024-03 (*A. baumannii*)

- Missing from many submitted results
  - Ciprofloxacin (n=23)
    - Due to missing *gyrA* and *parC* mutations (lack of PM database in PointFinder for A. baumannii)
- Reporting of Intrinsic resistance
  - Ampicillin (n=14)
    - $bla_{\text{CARB-2}}$ is intrinsic in *A. baumannii*

Results must be evaluated critically:

- Results can / should be confirmed with other tools
- Points to insufficient knowledge of genetic mechanisms of AMR

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IN SILICO PREDICTION OF AMR PROFILES – SUBMITTED REULTS

Laboratories	Sample type	Amikacin	Amoxicillin-clavulanic acid	Aztreonam	Cefepime	Cefotaxime	Ceftazidime	Ceftazidime-avibactam	Ciprofloxacin	Ertapenem	Gentamicin	Imipenem	Meropenem	Piperacillin-tazobactam	Sulfamethoxazole	Tobramycin	Trimethoprim	Colistin[a]	Ampicillin	Fosfomycin	Tigecycline	Correct (nr.)	Missing (nr.)	Unexpected (nr.)	Expected non-mandatory
		Expected																	Unexpected						
EURGen-RLC-001	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-002	BACT	x	x	-	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	15	1	3	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	16	0	3	1
EURGen-RLC-003[b]	SEQ	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-		x		15	1	1	0
EURGen-RLC-004[c]	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	-				16	0	0	0
EURGen-RLC-005[b]	SEQ	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	-				16	0	0	0
EURGen-RLC-009	BACT	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
	DNA	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
EURGen-RLC-010	BACT	x	x	x	x	x	x	-	x	x	-	x	x	x	x	x	-	-	x			13	3	1	0
	DNA	x	x	x	x	x	x	-	x	x	-	x	x	-	-	x	x	-	x			12	4	1	0
EURGen-RLC-011	BACT	x	x	x	x	x	x	-	x	x	x	x	x	x	-	x	x	-	x			14	2	1	0
	DNA	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x			15	1	1	0
EURGen-RLC-014	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		16	0	2	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		16	0	2	1
EURGen-RLC-016	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-018[c]	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-019	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	-	x	x		16	0	2	0
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	-	x	x		16	0	2	0
EURGen-RLC-020	BACT	x	-	x	x	x	x	-	x	x	x	x	x	-	-	x	x	x	x	x	x	12	4	3	1
	DNA	x	-	x	x	x	x	-	x	x	x	x	x	-	-	x	x	x	x	x	x	12	4	3	1
EURGen-RLC-021	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	16	0	2	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x			16	0	1	1
EURGen-RLC-023	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-024[b]	SEQ	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	-				16	0	0	0
EURGen-RLC-025	BACT	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-		x		15	1	1	0
	DNA	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-		x		15	1	1	0
EURGen-RLC-026	BACT	-	x	x	x	x	x	-	x	x	x	x	x	x	x	-	x	-	x	x		13	3	2	0
	DNA	-	x	x	x	x	x	-	x	x	x	x	x	x	x	-	x	-	x	x		13	3	2	0
EURGen-RLC-027	BACT	x	x	-	x	x	x	x	x	x	x	x	x	x	x	x	x	x		x	x	15	1	2	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-028[b]	SEQ	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x			15	1	1	0
EURGen-RLC-029	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
	DNA	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-030[c]	BACT	x	x	-	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x		15	1	2	1
EURGen-RLC-031	BACT	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
	DNA	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
EURGen-RLC-032[c]	BACT	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x	x				16	0	0	1
EURGen-RLC-033	BACT	x	-	x	x	x	x	-	x	x	x	x	x	-	-	x	x	-	x	x		12	4	2	0
	DNA	x	-	x	x	x	x	-	x	x	x	x	x	-	-	x	x	-	x	x		12	4	2	0
EURGen-RLC-034	BACT	-	-	-	-	-	-	-	-	-	-	x	x	-	-	-	-	-				2	14	0	0
	DNA	-	-	-	-	-	-	-	-	-	-	x	x	-	-	-	-	-				2	14	0	0
EURGen-RLC-036	BACT	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
	DNA	x	x	x	x	x	x	-	x	x	x	x	x	x	x	x	x	-	x	x		15	1	2	0
EURGen-RLC-012																						NA	NA	NA	NA
Correct (nr.)		42	40	41	44	44	44	24	44	44	42	46	46	39	38	42	43	21	NA	NA	NA	**Total**			
Missing or UN (nr.)		4	6	5	2	2	2	22	2	2	4	0	0	7	8	4	3	25	26	23	6	663	73	55	21

Strain EURGen-2024-04 (*K. pneumoniae*)

- Missing from most submitted results
  - Ceftazidime-avibactam (n=22)
    - Missing from $bla_{\text{NDM-5}}$ R-profile in ResFinder database
- Reporting intrinsic resistance
  - Ampicillin (n=26)
    - Listed as expected resistance phenotype by EUCAST (intrinsic blaSHV)
  - Fosfomycin (n=23)
    - *fosA* is intrinsic in *K. pneumoniae*

Results must be evaluated critically:

- Results can / should be confirmed with other tools
- Points to insufficient knowledge of genetic mechanisms of AMR

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GENERAL RECOMMENDATIONS

- For discrepancies due to misinterpretation of the EQA protocol and/or insufficient knowledge about certain genetic elements:
  - Laboratories should ensure sufficient knowledge about the genetic mechanisms mediating AMR and other important genetic elements;
  - Laboratories should ensure the use of multiple bioinformatics tools and databases for the detection of genetic determinants since bioinformatics tools and databases can be limited to the analysis of only a few bacterial species which contributes to the false-negative results;
  - Laboratories should be familiar with the bioinformatics tools they use, and the contents of the respective databases

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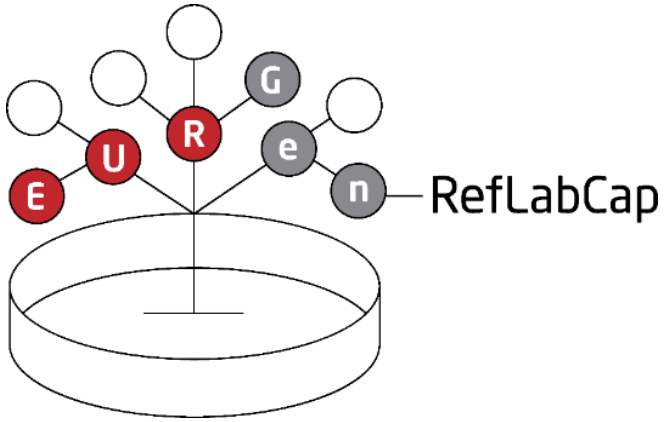
GENERAL RECOMMENDATIONS

- For discrepancies due to variations between the type of data and the chosen bioinformatics tools and databases:
  - Laboratories should implement verification steps such as using multiple bioinformatics approaches to confirm the obtained results;
  - Laboratories should communicate their suggestions, strange observations and potential problems to the curators of bioinformatics tools and databases;
  - Laboratories should be aware of differences between short-and long-read sequencing data and select the most adequate approach depending on their aims.

FEEDBACK SURVEY

- Questions
  - How useful was this EQA to your laboratory? (scale:1-10)
  - Was the preliminary individual EQA evaluation report you received clear and useful? (Yes/No)
  - Did you take any corrective action(s)? (Yes/No)
  - Comment section for suggestions

- Via this link: https://ec.europa.eu/eusurvey/runner/ba959a0a-2d7a-649f-1719-1a61ace0b253



Thank you on behalf of the EURGen-RefLabCap team

EURGen-RefLabCap@food.dtu.dk

EURGen-RefLabCap Network Meeting 2024

Discussion on the usefulness of the EQAs

18-19 September 2024

Ana Rita Rebelo and Faisal Ahman Khan

anrire@food.dtu.dk

Funded by the European Union

Objectives of the session

- Interactive discussion regarding the design and evaluation of the genomic EQAs
- Improvement of potential EQAs to be conducted in the future
- Harmonization of analysis of genomic data

➢ A few questions to be discussed in plenum (min 4 – max 8)

Funded by the European Union

Question 1

- **What is an expected result (how to deal with intrinsic genes and intrinsic resistance profiles)?**

Example:

For *K. pneumoniae*: *fosA* and *blaSHV* are **not part of the expected results** because they are **intrinsic**

Participants should report **susceptibility** to Fosfomycin (unless other determinants are detected)

Participants should report **resistance** to Ampicillin (intrinsic in KPN)

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Question 2

- **Is it useful to do analysis on the isolate AND the reference sequence files for comparison of results, for the same EQA?**

Example:

Have you seen a significant difference in results?

Have you adjusted your protocols or bioinformatics pipelines as a result?

Funded by the European Union

Question 3

- **What is an useful output for the participants?**

Example:

Were the individual report and the final report useful to you? What would you change in those?

Any other outputs that would be important?

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Question 4

- **How to make the protocol more clear? Should it start with one page of very important information?**

Example:

Many participants did not know that they should upload their MD5 checksum files into the ScienceData folders together with their sequence files.

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Question 5

➢ What is an “optional” expected result?

Example:

1) There is an aminoglycoside resistance gene – so it is **mandatory** to report one **gene**

2) However the bioinformatics tools output **different variants** – so the specific variant to be reported is “**optional**”

3) But because there is certainly an aminoglycoside-R gene, reporting **Resistance** towards aminoglycosides is **mandatory**

Example:

1) **Only one** bioinformatics tool detects a mutation conferring resistance towards colistin – therefore it is “**optional**” to report the mutation

2) So it is also “**optional**” to report the **colistin-R** profile – because the participants were encouraged to use two bioinformatics tools and if by chance they choose the two that do not detect the mutation, they still followed the recommended procedure but had no way of arriving at the colistin-R profile

Funded by the European Union

Question 6

- **How to deal with conflicting genomic and phenotypic AST results (in EQAs that include both types of analysis simultaneously)?**

Example:

Evaluate each analysis separately – but how to ensure participants are not influenced by the results of the other type of analysis?

Funded by the European Union

Question 7

- **Any question proposed by the participants**

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Question 8

- **Any question proposed by the participants**

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EURGen-RefLabCap Network Meeting 2024

Impact of the project on national laboratory capacity

18-19 September 2024

Ana Rita Rebelo

anrire@food.dtu.dk

Funded by the European Union

Input from participants on impact of the project on national laboratory capacity

Input from participants on where they started at the beginning of the project, where they are now, what was most useful, development and challenges

- 10 minutes presentations followed by 10 minutes of general discussion

- Estonia
- Slovenia
- Romania
- Spain

Funded by the European Union

EURGen-RefLabCap@food.dtu.dk

Thank you on behalf of the EURGen-RefLabCap team

Funded by the European Union

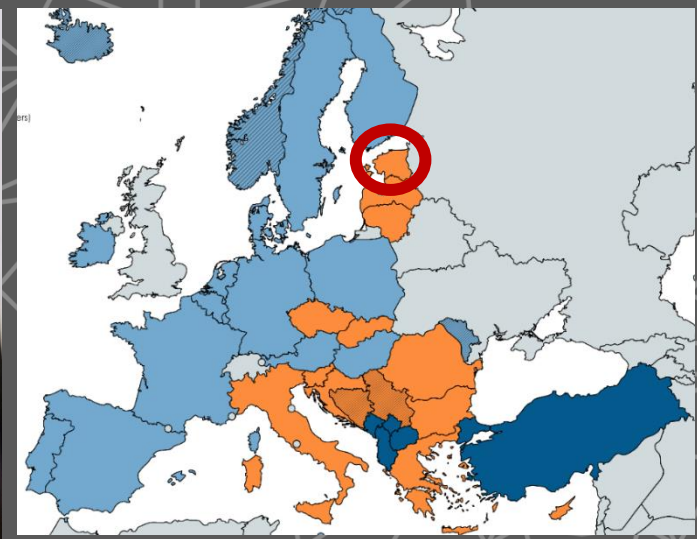
REPUBLIC OF ESTONIA
HEALTH BOARD

EURGen-RefLabCap project impact on Estonian NRL capacity.

Further actions for surveillance and outbreak management of AMR bacteria.

Liisa Lilje
laboratory specialist (AMR)
Laboratory of Communicable Diseases, Health Board
19.09.2024 EURGen-RefLabCap network meeting in Copenhagen, Denmark

Health Board, Laboratory of Communicable Diseases (NRL)



National reference laboratory (ISO 15189) in many areas of research, including antimicrobial resistance of pathogens (NETS § 41)

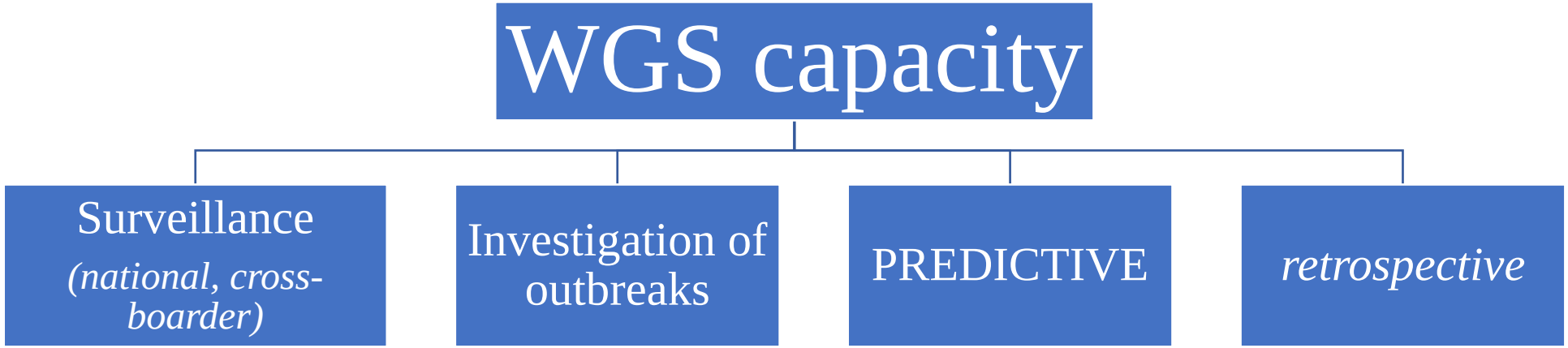
Also determination of salmonella, campylobacter, enteropathogenic E. coli, shigella, pneumo-, meningo- and gonococcal species, (sero)typing and antimicrobial sensitivity, confirmation/determination of resistance mechanisms to nosocomial infections.

AMR surveillance in Estonia started in **2019** coordinated by NRL

(after ECDC country visit)

- Specific positions were created in the Ministry of Social Affairs (1.0) and at Health Board (NRL) (1.0)
- NRL set up methods for molecular detection of AMR genes *(carbapenem-, vancomycin-, methicillin-, colistin-resistance)*
- Hospitals were asked to send their resistent isolates to NRL
- Storage of strains with identified AMR mechanisms
- Active participation in the **Estonian EUCAST and Clinical Microbiology Working Group** (from 2024 regular meetings between NRL and clinical laboratories)

Pilot study (Q1 2023-Q2 2024):



Objectives:

- Build WGS capacity at NRL
- Get an overview of the situation in Estonia (sequence all the stored and newly detected strains)
- Identify possible outbreaks (inc retrospectively)

Long-term objective:

- Increase monitoring capacities at national and EU level
- Increase preparedness to identify and predict outbreaks.

+ biobank (collection, storage, distribution of isolates if necessary) + collection of control strains.

Pilot study (Q1 2023-Q2 2024):

gDNA extraction (manual)

Jan 2023

Tapestation

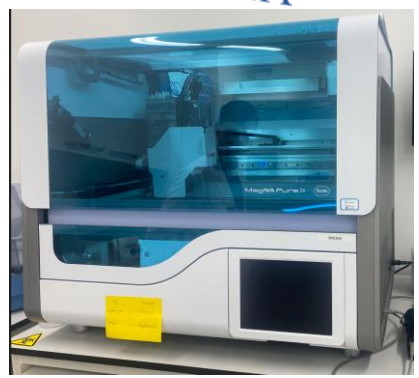
Easy-DNA extraction (manual)

Jan 2023

First sequencing outsourced

Nov 2023

MagNA Pure24 (extraction)automated DNA



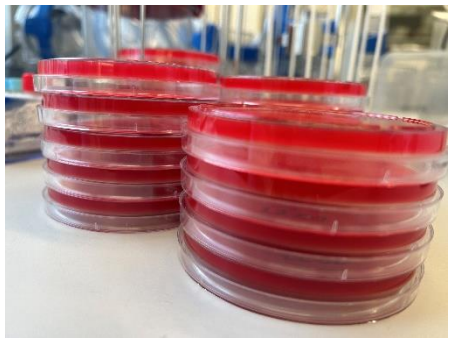
Hamilton

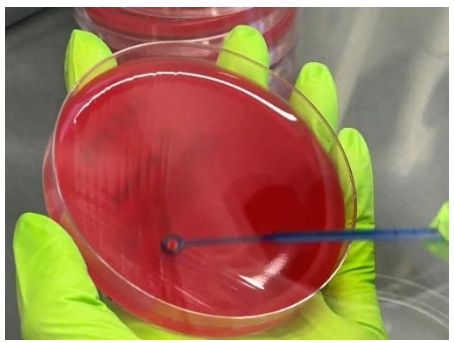
Spring 2024

Aug 2024

Illumina NextSeq2000

Pilot study (Q1 2023-Q2 2024):





Clinical Microbiology labs

- Isolates the pathogen
- Detects resistance
- Sends the isolate NRL (monitoring – res.mechanism det/conf, WGS)

HB NRL

- Identifies culture (MALDI)
- Performs AMR detection/donfirmation PCR

NRL

- Storage of isolate and gDNA
- Additional WGS sequencing (Illumina and/or ONT)
- Bioinformatic analysis (including comparison with previous/EU isolates)

Molecular laboratory workflow

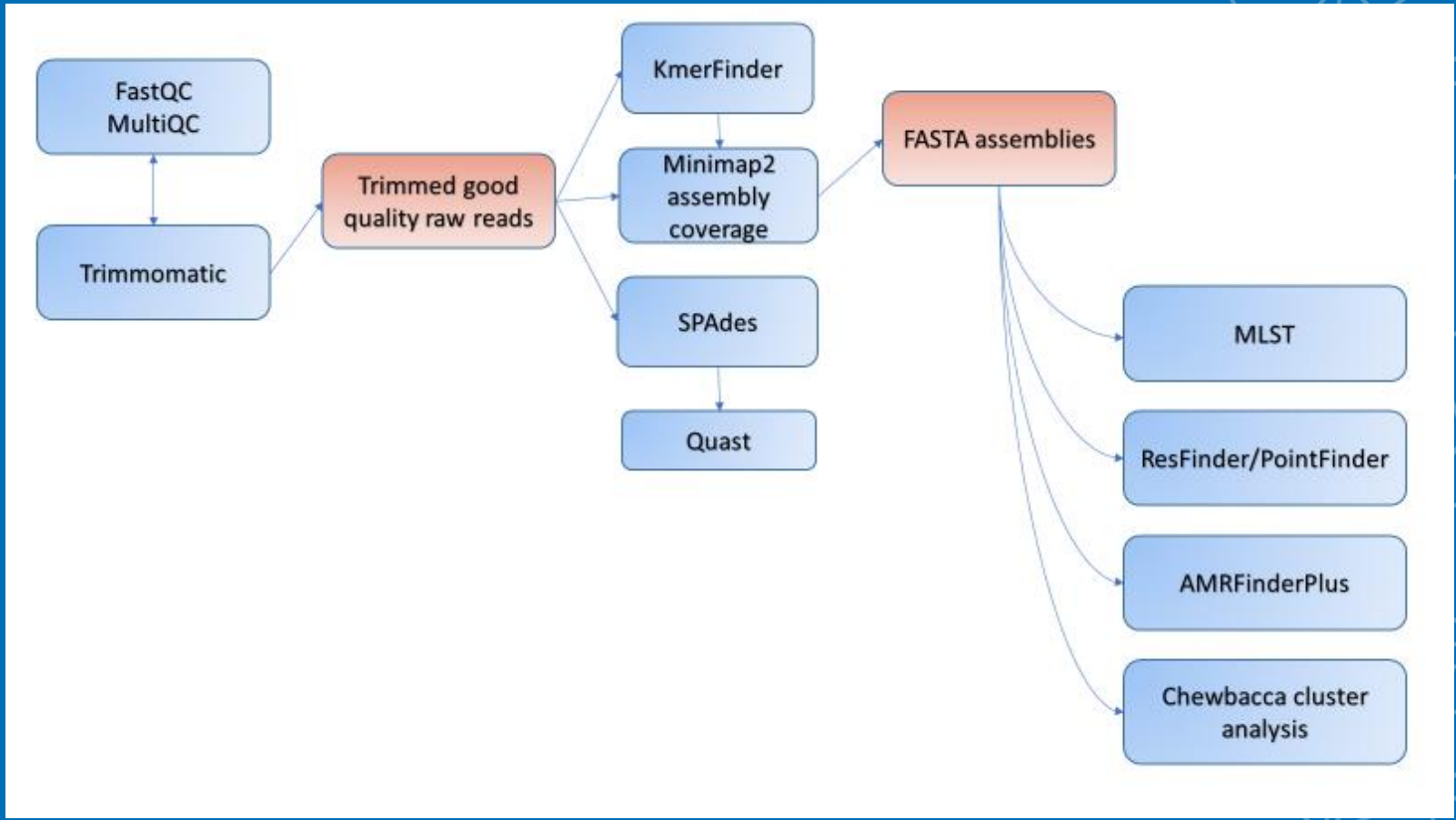
1) Extraction of gDNA and identification of genes
2) Quantification and quality assurance of gDNA

Molecular laboratory workflow

3) WGS performed upon request *(or needs)*

Molecular laboratory workflow

4) Automated bioinformatic analysis

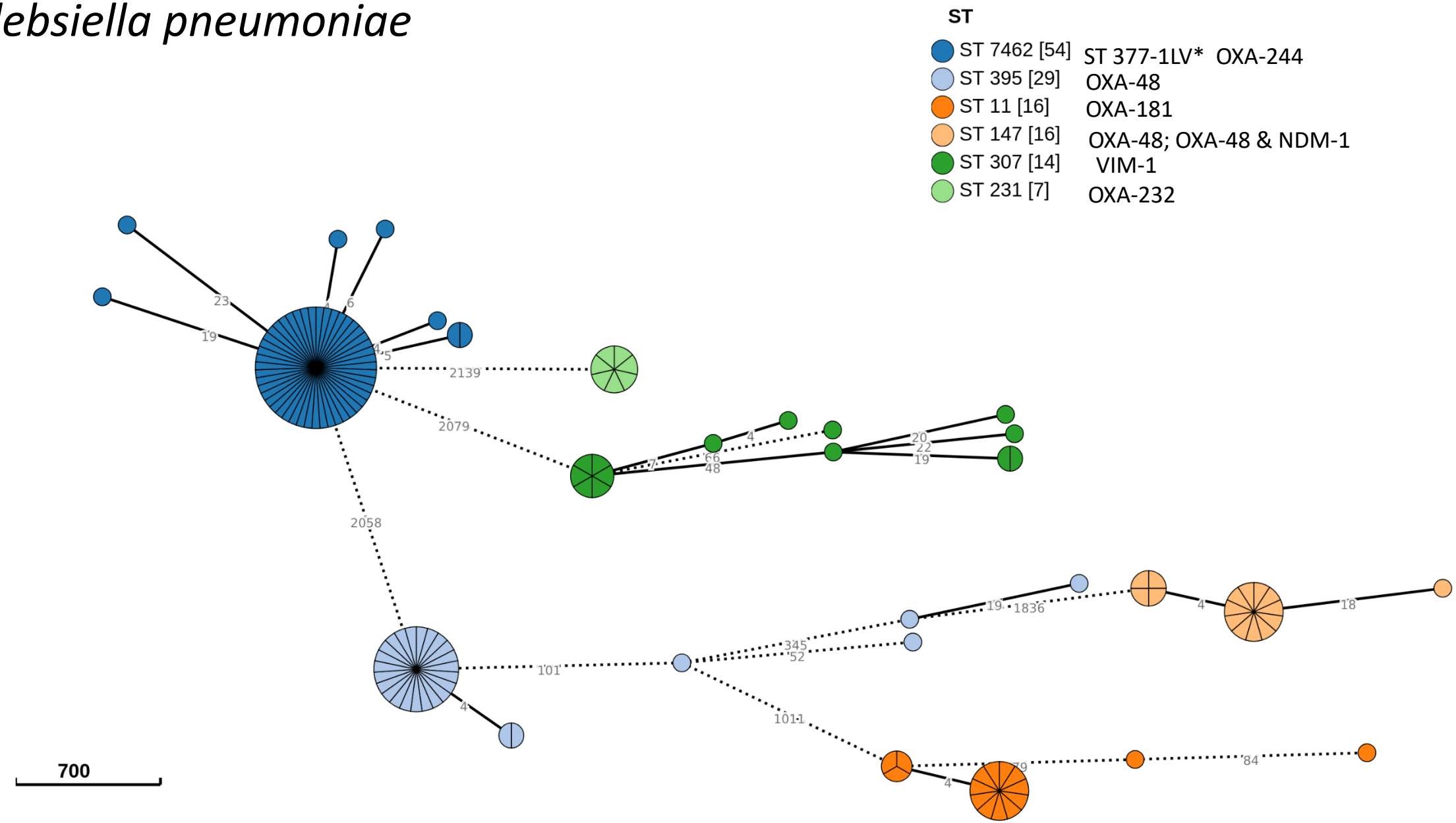


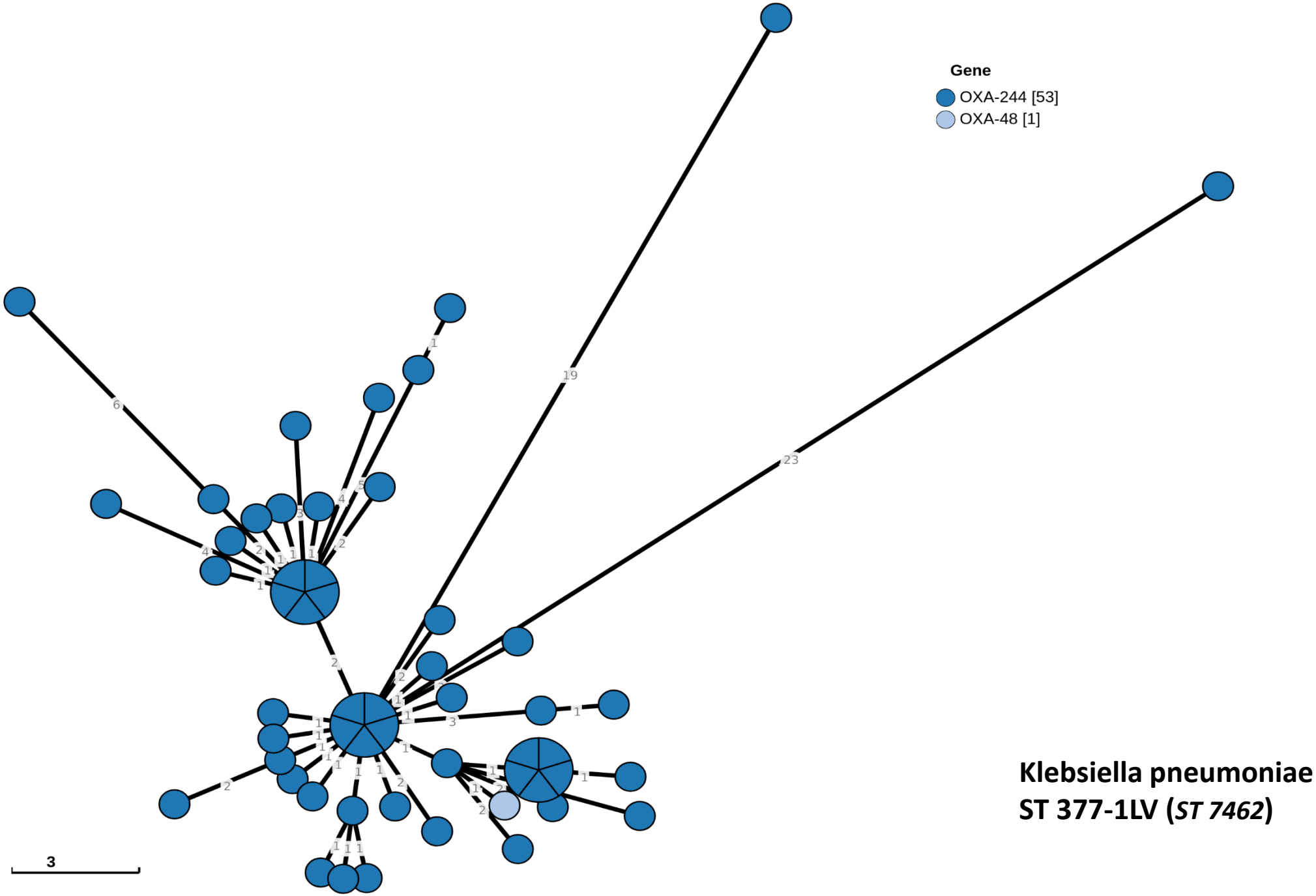
Preliminary findings of the EURGen-RefLabCap pilot genomic surveillance studies

EURGen-RefLabCap pilot study

Species	No of isolates seq
Klebsiella pneumoniae	156 *(90*)*
Acinetobacter baumannii	114
Pseudomonas aeruginosa	32
Enterobacter cloacae complex	21
Escherichia coli	19
Citrobacter freundii	6
Klebsiella oxytoca	5
Klebsiella aerogenes	4
Klebsiella variicola	2

Klebsiella pneumoniae

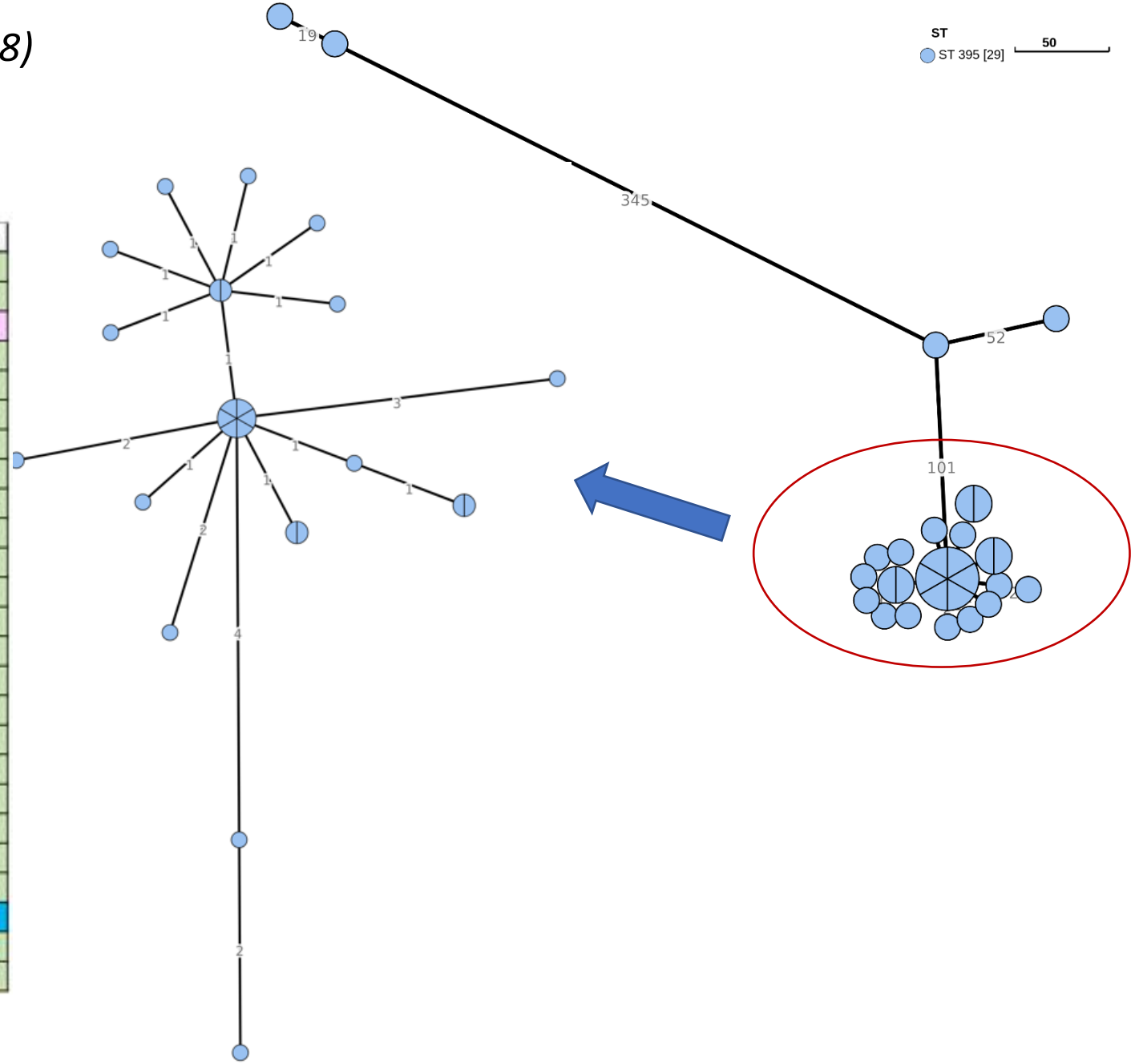


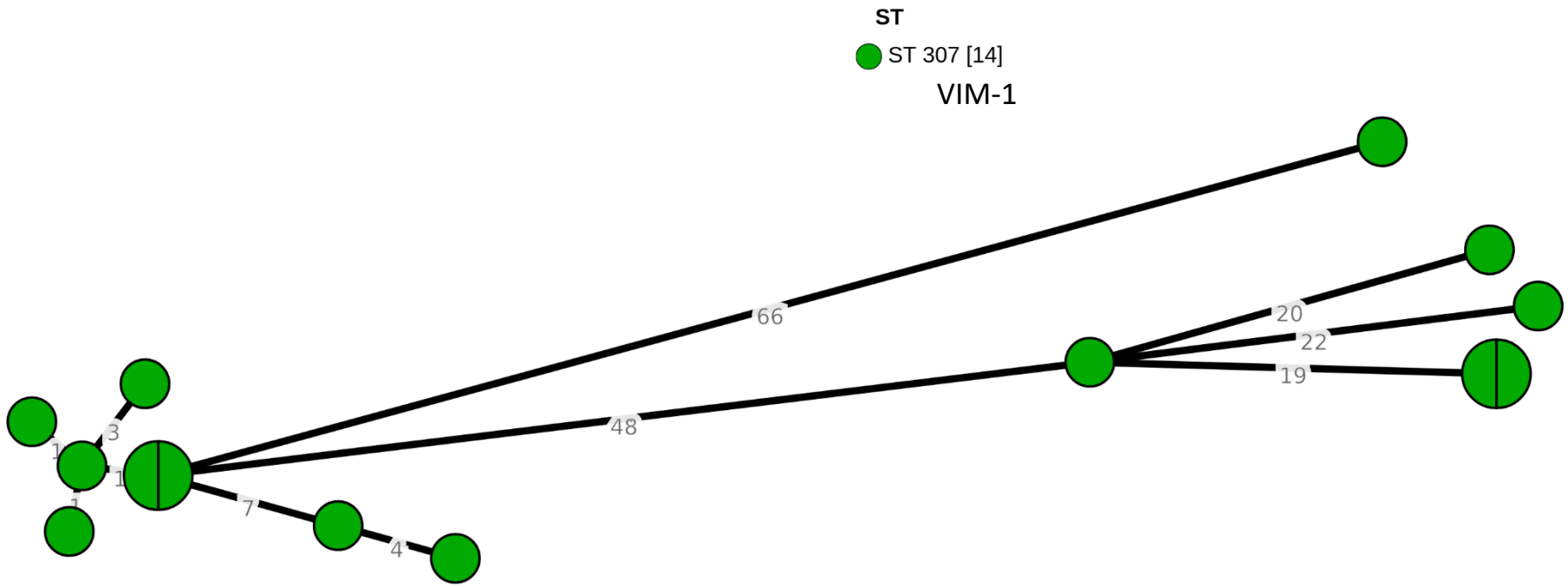


Klebsiella pneumoniae
ST 377-1LV (*ST 7462*)

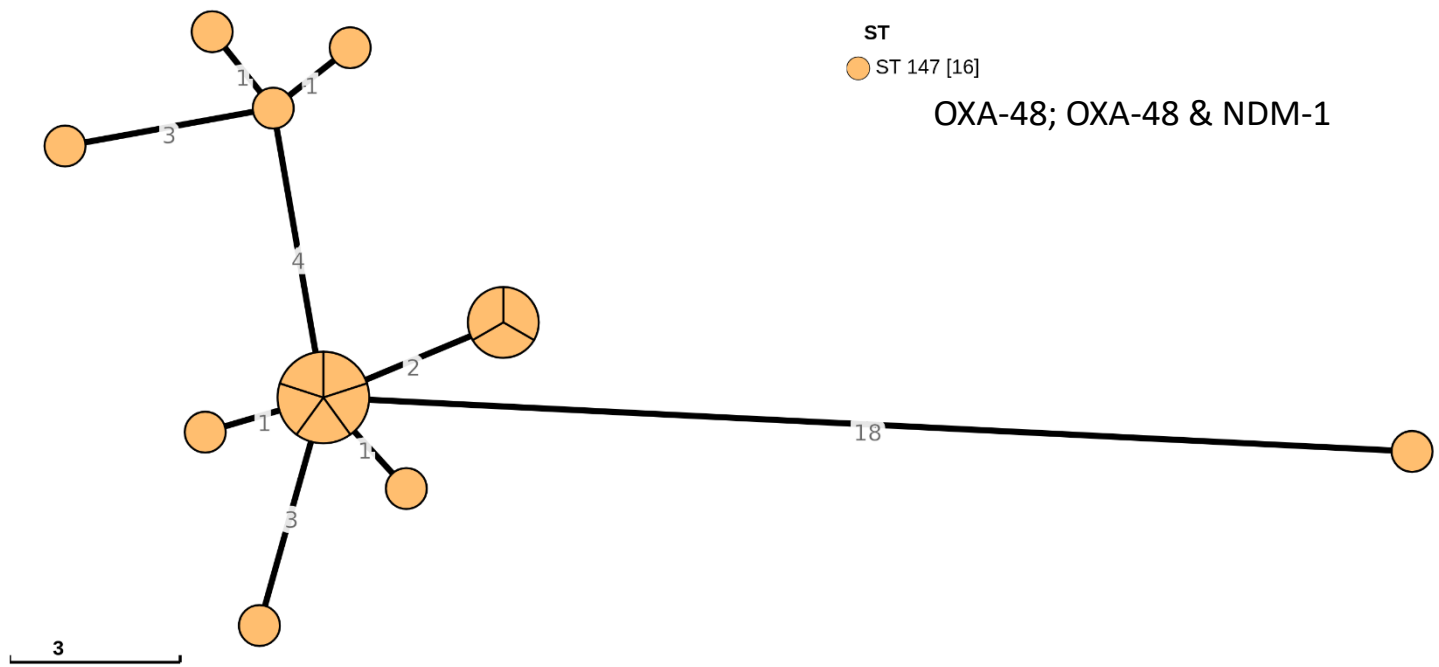
Klebsiella pneumoniae ST395 *(OXA-48)*

Proov	Bakterilliik	Asutu	Proovivõ	Materjal	ST	Cluster
174705	K. pneumoniae	Haigla B	22.05.2023	uriin	395	-
175319	K. pneumoniae	Haigla B	24.07.2023	uriin	395	KD (max 6AD)
175922	K. pneumoniae	Haigla C	12.09.2023		395	KD (max 6AD)
175895	K. pneumoniae	Haigla B	12.09.2023	kurgukaabe	395	KD (max 6AD)
176108	K. pneumoniae	Haigla B	26.09.2023	haavaeritis	395	KD (max 6AD)
176611	K. pneumoniae	Haigla B	20.10.2023	haavaeritis	395	KD (max 6AD)
176839	K. pneumoniae	Haigla B	15.11.2023	kurgukaabe	395	KD (max 6AD)
176841	K. pneumoniae	Haigla B	16.11.2023	kurgukaabe	395	KD (max 6AD)
177743	K. pneumoniae	Haigla B	01.12.2023	kurgukaabe	395	KD (max 6AD)
177744	K. pneumoniae	Haigla B	02.12.2023	kurgukaabe	395	KD (max 6AD)
177749	K. pneumoniae	Haigla B	16.12.2023	uriin	395	KD (max 6AD)
177760	K. pneumoniae	Haigla B	05.01.2024	kõhuõõnevedelik	395	KD (max 6AD)
177762	K. pneumoniae	Haigla B	08.01.2024	uriin	395	KD (max 6AD)
177763	K. pneumoniae	Haigla B	11.01.2024	rektaalkaabe	395	KD (max 6AD)
179475	K. pneumoniae	Haigla B	25.01.2024	kurgukaabe	395	KD (max 6AD)
179483	K. pneumoniae	Haigla B	12.02.2024	uriin	395	KD (max 6AD)
179484	K. pneumoniae	Haigla B	12.02.2024	haavaeritis	395	KD (max 6AD)
179485	K. pneumoniae	Haigla B	19.02.2024	haavaeritis	395	KD (max 6AD)
179486	K. pneumoniae	Haigla B	21.02.2024	rõga	395	KD (max 6AD)
179487	K. pneumoniae	Haigla B	22.02.2024	haavaeritis	395	KD (max 6AD)
178546	K. pneumoniae	Haigla B	01.03.2024	uriin	395	KD (max 6AD)
178547	K. pneumoniae	Haigla B	03.03.2024	uriin	395	KD (max 6AD)
178841	K. pneumoniae	Haigla X	03.04.2024	kateeter (epitsüst	395	KD (max 6AD)
179338	K. pneumoniae	Haigla B	24.04.2024	rõga	395	KD (max 6AD)
179492	K. pneumoniae	Haigla B	20.05.2024	uriin (kateetri)	395	KD (max 6AD)

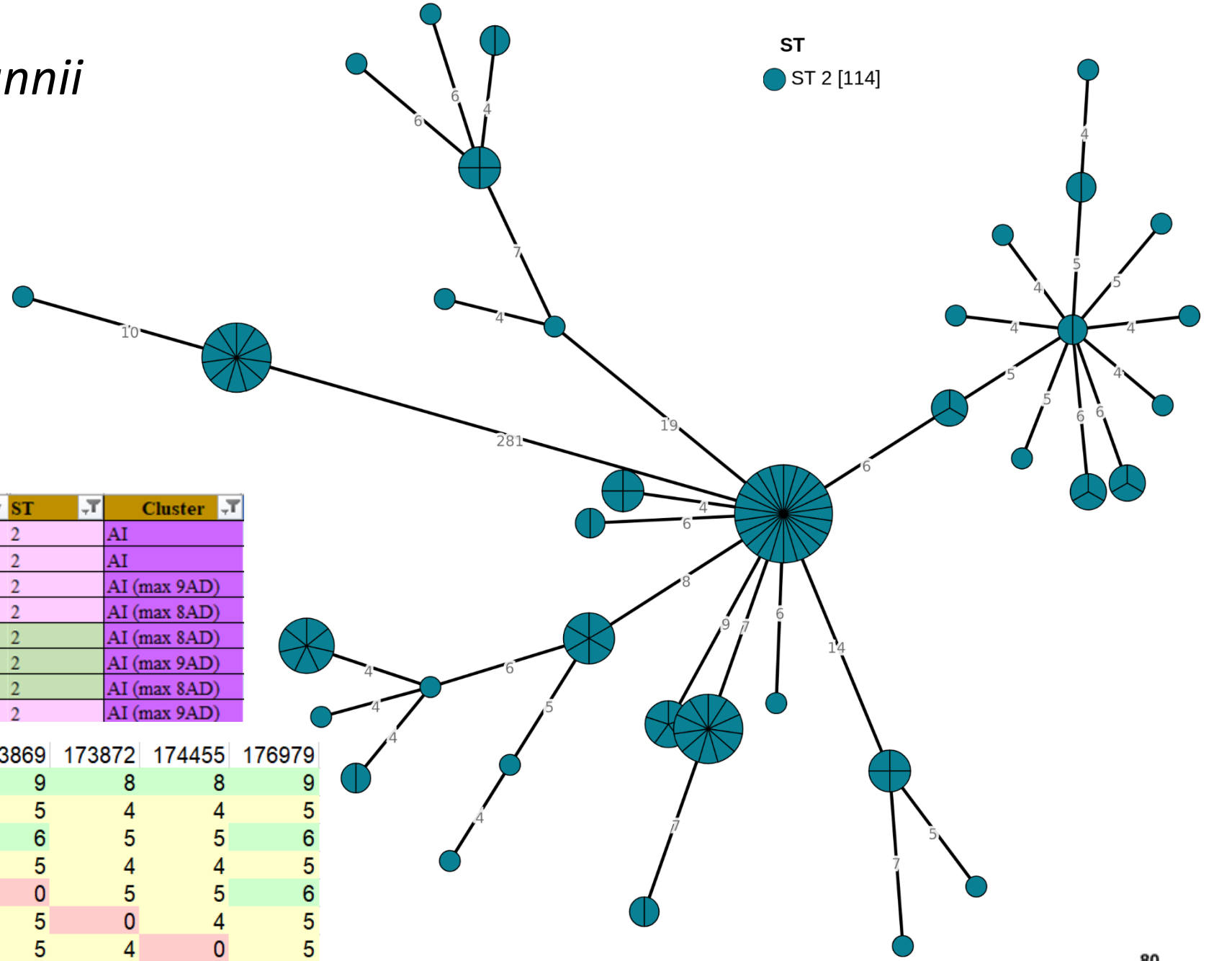




Bakteriliik	Asutus	Proovivõ	Materjal	ST	Cluster
175733 *K. pneumoniae*	Haigla A	30.08.2023	uriin	147	KY (max 6AD)
173329 *K. pneumoniae*	Haigla B	03.02.2023	uriin	147	KY(max 6 AD)
173814 *K. pneumoniae*	Haigla B	06.03.2023	uriin	147	KY(max 6 AD)
173870 *K. pneumoniae*	Haigla B	17.03.2023	uriin	147	KY(max 6 AD)
174702 *K. pneumoniae*	Haigla B	11.05.2023	dreen kõhuõõnes	147	KY(max 6 AD)
175118 *K. pneumoniae*	Haigla B	04.07.2023	haavaeritis	147	KY (max 6AD)
176101 *K. pneumoniae*	Haigla B	15.09.2023	uriin	147	KY(max 6 AD)
176109 *K. pneumoniae*	Haigla B	29.09.2023	uriin	147	KY(max 6 AD)
177750 *K. pneumoniae*	Haigla B	19.12.2023	veri	147	KY(max 6 AD)
178706 *K. pneumoniae*	Haigla B	19.03.2024	trahheaaspiraat	147	KY(max 6 AD)
179339 *K. pneumoniae*	Haigla B	24.04.2024	uriin	147	KY (max 6AD)
179491 *K. pneumoniae*	Haigla B	06.05.2024	uriin (kateetri)	147	KY(max 6 AD)
174281 *K. pneumoniae*	Haigla C	26.04.2023	uriin	147	KY (max 6AD)
176014 *K. pneumoniae*	Haigla C	24.09.2023	uriin	147	KY (max 6AD)
175374 *K. pneumoniae*	Haigla X	02.08.2023	na	147	KY (max 6AD)



Acinetobacter baumannii



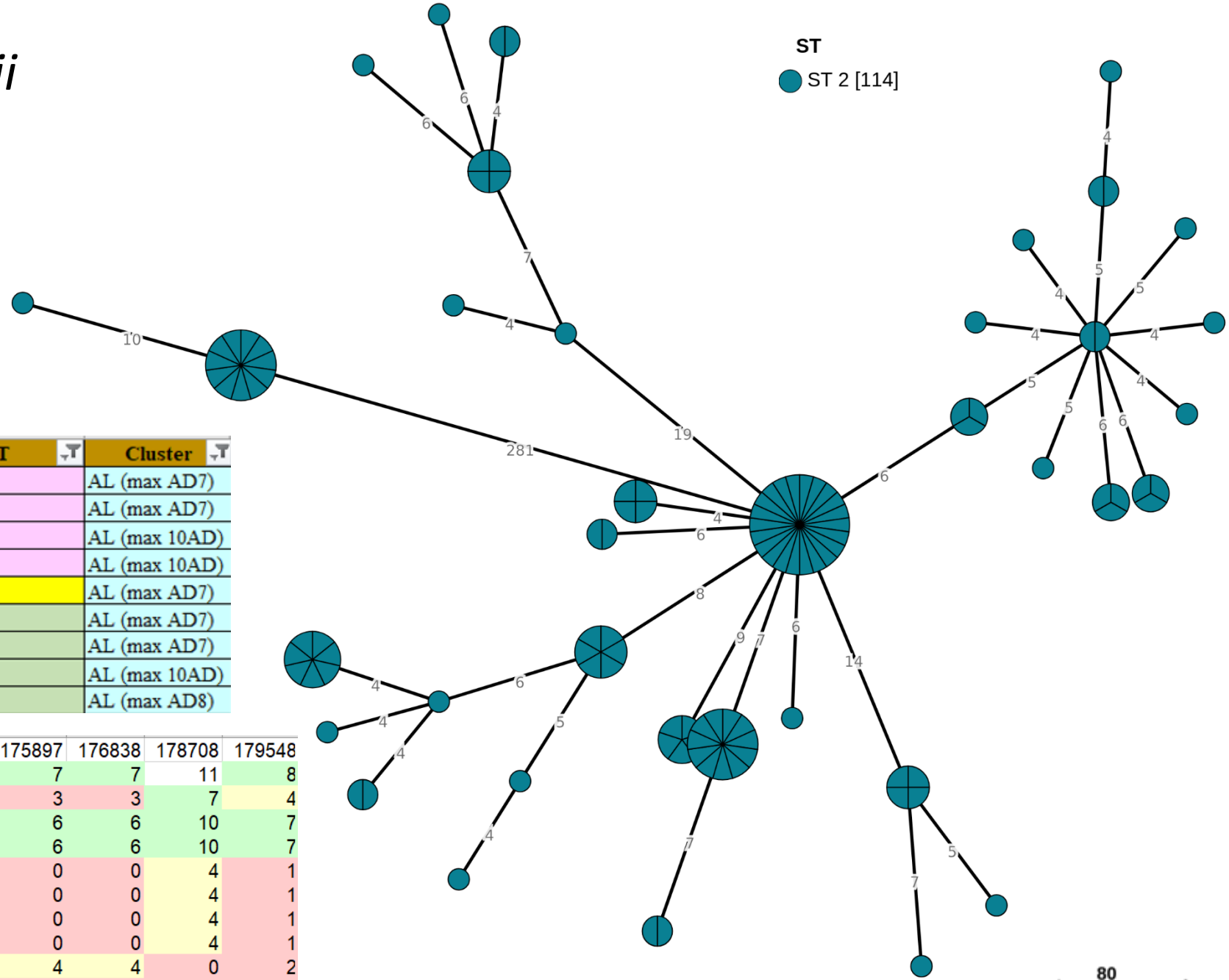
Prooo	Bakteriliik	Asutus	Proovivõ	Materjal	ST	Cluster
172902	*A. baumannii*	Haigla C	27.11.2018	Uriin	2	AI
173226	*A. baumannii*	Haigla C	17.01.2019	Veri	2	AI
172796	*A. baumannii*	Haigla C	07.02.2020	Uriin	2	AI (max 9AD)
172797	*A. baumannii*	Haigla C	09.11.2021	Trahhea	2	AI (max 8AD)
173872	*A. baumannii*	Haigla B	15.03.2023	uriin	2	AI (max 8AD)
173869	*A. baumannii*	Haigla B	17.03.2023	troofiline haav	2	AI (max 9AD)
174455	*A. nosocomialis*	Haigla B	28.04.2023	uriin	2	AI (max 8AD)
176979	*A. baumannii*	Haigla C	04.12.2023		2	AI (max 9AD)

cgmlst-dists	172796	172797	172902	173226	173869	173872	174455	176979
172796	0	8	5	4	9	8	8	9
172797	8	0	5	4	5	4	4	5
172902	5	5	0	1	6	5	5	6
173226	4	4	1	0	5	4	4	5
173869	9	5	6	5	0	5	5	6
173872	8	4	5	4	5	0	4	5
174455	8	4	5	4	5	4	0	5
176979	9	5	6	5	6	5	5	0

Acinetobacter baumannii

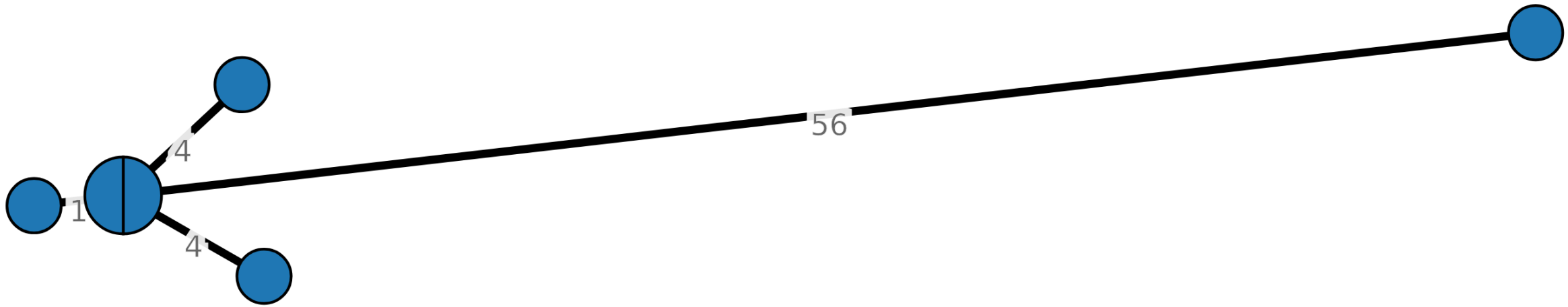
Proov	Bakteriliik	Asutus	Proovivõ	Materjal	ST	Cluster
172798	*A. baumannii*	Haigla C	21.04.2015	Haavaeritis	2	AL (max AD7)
172799	*A. baumannii*	Haigla C	12.11.2016	Uriin	2	AL (max AD7)
173103	*A. baumannii*	Haigla C	19.02.2018	Haav	2	AL (max 10AD)
173102	*A. baumannii*	Haigla C	24.04.2018	Uriin	2	AL (max 10AD)
174253	*A. baumannii*	Haigla A	20.04.2023		2	AL (max AD7)
175897	*A. baumannii*	Haigla B	12.09.2023	haavaeritis	2	AL (max AD7)
176838	*A. baumannii*	Haigla B	10.11.2023	haavaeritis	2	AL (max AD7)
178708	*A. baumannii*	Haigla B	22.03.2024	uriin	2	AL (max 10AD)
179548	*A. baumannii*	Haigla B	29.05.2024	haavaeritis	2	AL (max AD8)

cgmlst-dists	172798	172799	173102	173103	174253	174980	175897	176838	178708	179548
172798	0	4	7	7	7	7	7	7	11	8
172799	4	0	3	3	3	3	3	3	7	4
173102	7	3	0	6	6	6	6	6	10	7
173103	7	3	6	0	6	6	6	6	10	7
174253	7	3	6	6	0	0	0	0	4	1
174980	7	3	6	6	0	0	0	0	4	1
175897	7	3	6	6	0	0	0	0	4	1
176838	7	3	6	6	0	0	0	0	4	1
178708	11	7	10	10	4	4	4	4	0	2
179548	8	4	7	7	1	1	1	1	2	0



Pseudomonas aeruginosa

OXA-904, OXA-932, VIM-1



Plans for actions

Cooperation with epidemiologists (improve metadata)

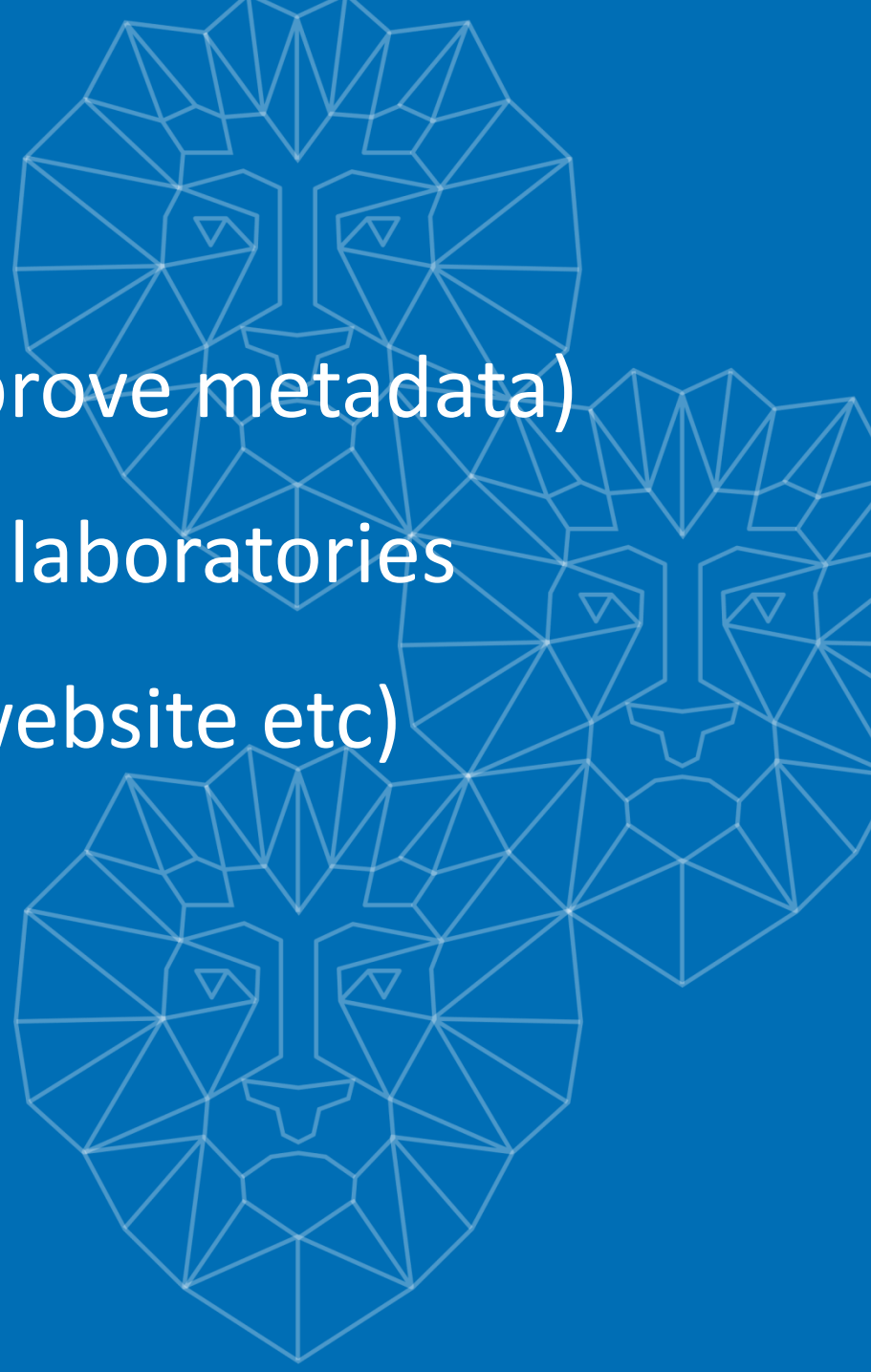
Cooperation with clinical microbiology laboratories

Develop reporting system (to labs, at website etc)

Wider analysis on the data

Routine sequencing

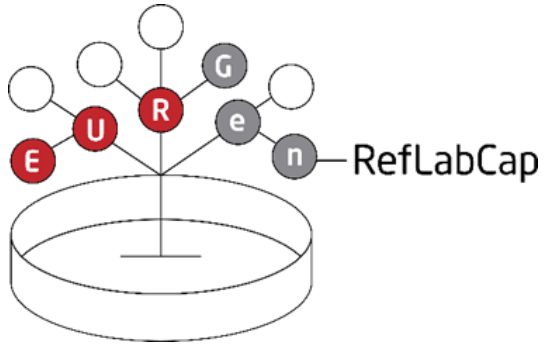
Reporting to EpiPulse



REPUBLIC OF ESTONIA
HEALTH BOARD

Thank you for listening !

liisa.lilje@terviseamet.ee



EURGen-RefLabCap _Pilot study
Carbapenem-resistant *Enterobacterales* in the context of emerging NDM-1 + OXA -48, colistin resistant *Kl. pneumoniae* strains in Romania

Brindusa Lixandru

EURGen-RefLabCap

General objective

- Enhance the accuracy of surveillance AMR data reported at EU level in compliance with the new EU AMR case definitions in order to take concerted actions against AMR at EU, allowing better tracking and managing AMR cases, ultimately aiming to reduce the spread of resistant bacteria.

Specific objective

- Support offered for NRLs networks by providing capacity-building activities (trainings, quality assurance controls, country visits, pilot studies) and validated AMR detection tools to NRLs in compliance with the new EU AMR case definitions.

ROMANIA_2024_EURGen-RefLabCap Pilot study
Recent evidence

- Rapid and continuously spread of *K. pneumoniae* with a combination of *bla*NDM + *bla*OXA-48-like

- 2023- 2024 hospitals investigated outbreaks with *K. pneumoniae* with NDM + OXA-48-like

ROMANIA_2024_EURGen-RefLabCap Pilot study

General aim

✓Developing and capacity building for NEL services concerning genomic surveillance of priority pathogens, by integrating WGS.

- The whole-genome sequencing (WGS) **pilot study** was designed & conducted in Nosocomial Infections & AMR by **addressing a pathogen belonging to the CRE/CCRE group.**

NDM + OXA-48-like dual-producing *Klebsiella pneumoniae* isolates from hospitalized patients.

✓Data confidentiality

- Informations related to the patients, hospitals and laboratories will be anonymized.
- Documents regarding pilot study will be treated as **confidential** and will **not be disclosed** in the public domain.

ROMANIA_2024_EURGen-RefLabCap Pilot study

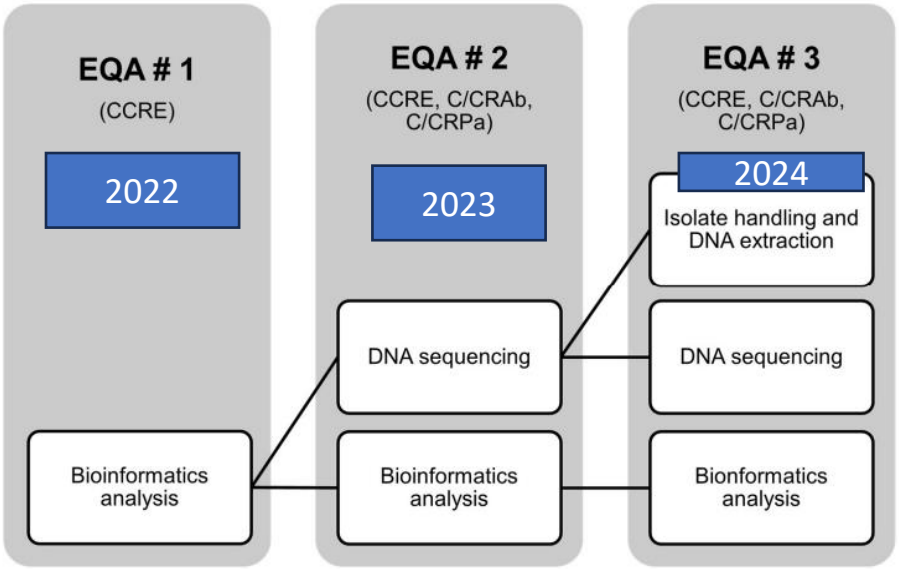
Specific objective

- ✓The pilot study a genomic characterization XDR / PDR *Klebsiella pneumoniae* carbapenems and colistin resistant strains co-harbouring *bla*NDM and *bla*OXA-48-like genes

  - ✓Resistome
  - ✓High-risk clones detection
  - ✓Genomic AMR genes environment (plasmids, mobile genetic elements)
  - ✓Outbreak investigations

Development stages of the pilot study

- December 2023: WGS Training course at DTU
- February- March 2024: MinION device; flow cells and reagents received
- April-May 2024: design of the study and selection/check of the strains from frozen collections
- May 2024: EQA#3 (DNA and bacterial cultures)
- June-August 2024: Sequencing and reporting results (FastQC)
- In progress: data set analysis; results to be published



Romania participation in EURGen-RefLabCap

- 3 participations in EQA controls

Workstream 1 (WS1) pathogens: CRE / CCRE (Carbapenem /Colistin Resistant *Enterobacterales*)

Pilot study bacterial collection

- ✓28 *Klebsiella pneumoniae* clinical isolates collected during the 2023- 2024 from hospitalized patients.
  - ✓Isolates were randomly selected from the frozen stocks
  - ✓Inclusion criteria according to microbiological characteristics:
    - ✓resistance phenotype
    - ✓Identified as NDM +OXA-48 co- producers in NEL using rapid immunochromatographic test (Test NG-Carba 5-Biotech, Guipry, France)
  - ✓Isolates were obtained from different clinical samples:
    - ✓urine (n=16)
    - ✓lower respiratory tract (n=9)
    - ✓wound (n=2)
    - ✓blood (n=1)

Pilot study hospitals involved

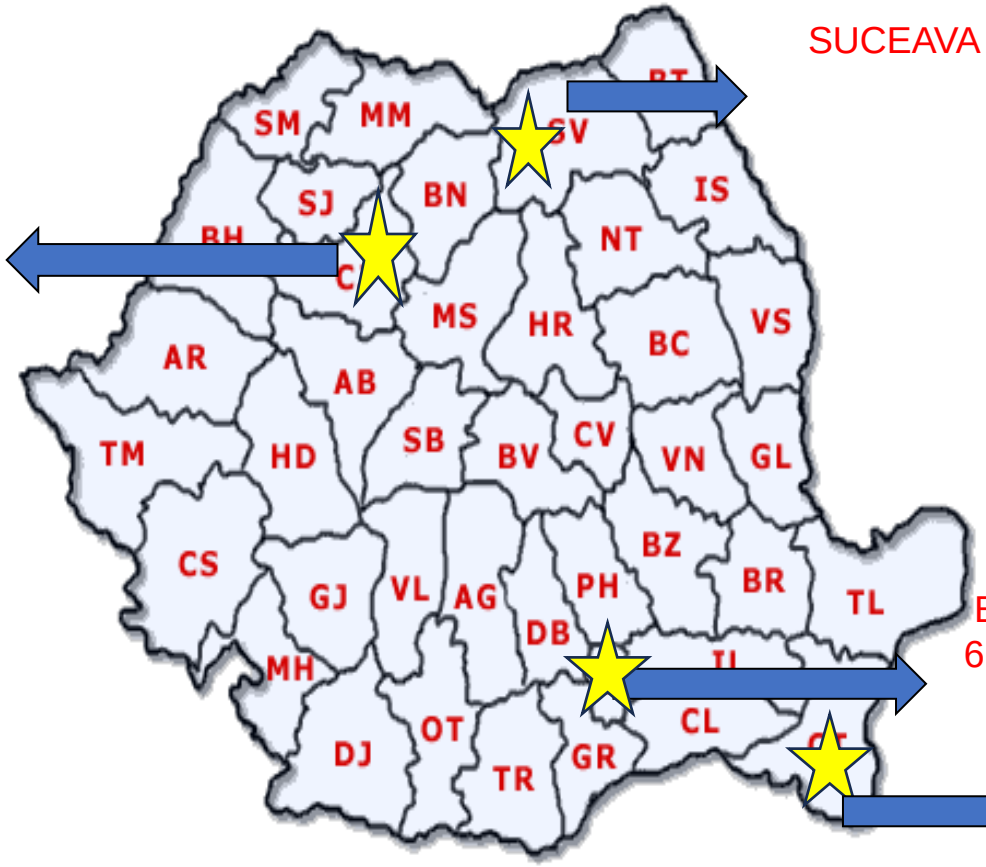
- 9 hospitals isolation sites
  - H1(n=1); H2(n=3); H3(n=1); H4(n=3); H5(n=2); H6(n=2); H7(n=3); H8(n=5); H9(n= 8)

- Isolates recovered from 2 hospitals (H8; H9) came from 2 outbreak investigations

- Hospitals were chosen according to the following criteria
  - Medical services provided for specific clinical manifestations
  - Accessibility to clinical and epidemiological data of patients
  - Voluntary participation and compliance with the AMR active surveillance requirements

Country hospitals distribution

CLUJ MILITARY HOSPITAL (H6)



SUCEAVA COUNTY HOSPITAL (H9)

BUCHAREST CITY AREA:
6 HOSPITALS (H1; H3; H4; H5; H7; H8)

CONSTANTA MILITARY HOSPITAL (H2)

Bacterial isolates and patients data

Isolate no	Patient	Sex	Age	Hospital	Hospital Departament	Specimen type	Isolatio
2/BA	BA	F	92	H1	ICU	urine	2023
3/556603	RN	F	74	H2		urine	2023
22/562036	BC	F	80	H2		urine	2023
23/567252	R.N	F	76	H2		urine	2023
4/PKPN	P.G	M		H3		urine	2023
5/39D		M		H4		urine	2023
6/13A				H4		urine	2023
10/39C				H4		urine	2023
7/519812		M	85	H5		urine	2023
13/546568	MGD	M	36	H5		Traheal	2023
8/551951	TE	F	70	H6		urine	2023
15/ 553749	PL	F	67	H6		urine	2023
9/136S12		M	79	H7		urine	2023
11/5S64		F	73	H7		urine	2023
12/81S64		M	79	H7		urine	2023
559587	BI	M		H8	ICU	Bronchial	2023
559588	VG	F		H8	ICU	Bronchial	2023
559589	IIT	M		H8	ICU	Wound	2023
559590	MG	M		H8	ICU	Bronchial	2023
559591	nn	M		H8	ICU	Bronchial	2023

Isolate	Patient	Sex	Age	Hospital	Department	Specimen type	Isolation date	
568036		F	76	H9	ICU	traheal	2024	
568038		M	56	H9	ICU	traheal	2024	
568040		F	67	H9	ICU	traheal	2024	
568041		M	59	H9	ICU	urine	2024	
568047		M	40	H9	ICU	wound	2024	
569343		M	64	H9	ICU	traheal	2024	
569344		M	81	H9	ICU	blood	2024	
569345		M	54	H9	ICU	urine	2024	

Laboratory methods

Antimicrobial susceptibility tests

- Disk diffusion method (EUCAST standard):
  - Isolates were tested against a standard antimicrobial panel

Aminoglycoside: Gentamicin, Amikacin, Tobramicin

Beta-lactams/monobactams: Aztreonam

Beta-lactams/carbapenems: ertapenem, meropenem, imipenem

Beta-lactams/cephalosporins: ceftazidime, cefepime

Beta-lactams/beta-lactamase inhibitors : amoxicillin / clavulanic ac
Piperaciline/Tazobactam, Ceftazidime/avibactam, Ceftolozane/Tazobactam

Fluoroquinolones: Ciprofloxacin

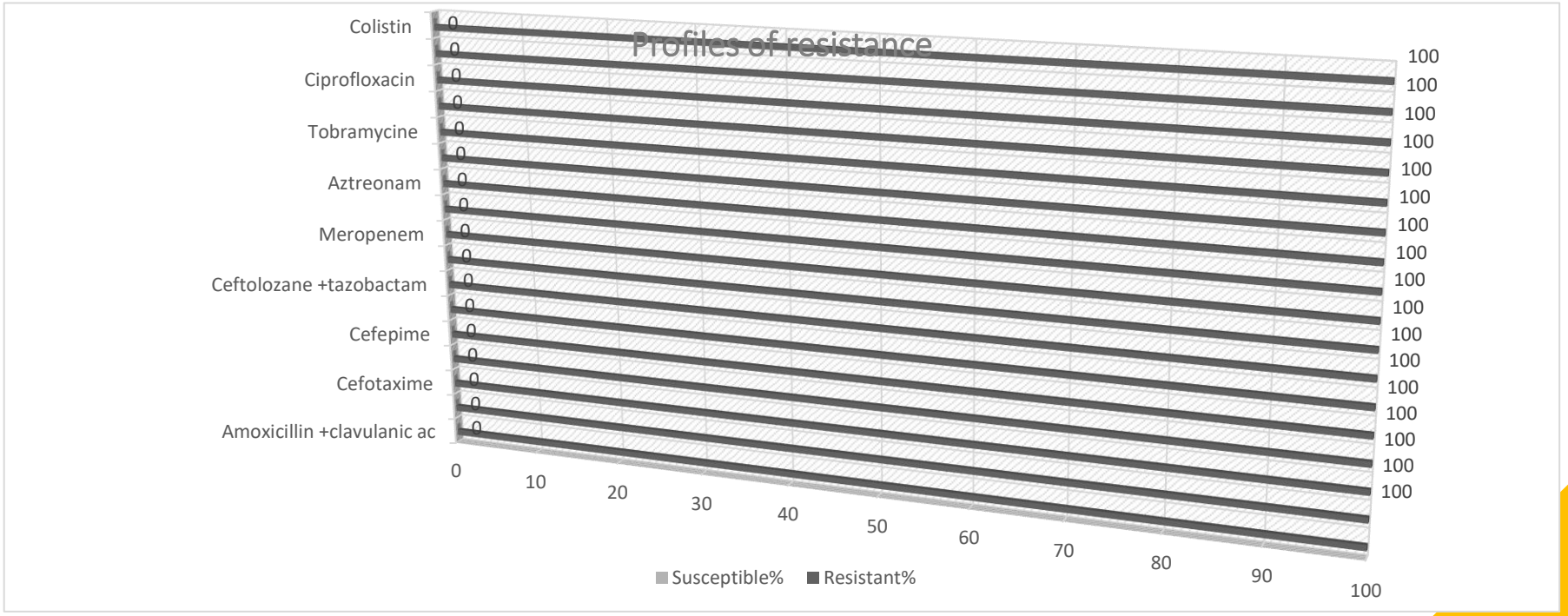
Polymixin: Colistin

- MICs determination using Sensititre System(Thermo Fischer Scientific) EUMDROXF plate and/or DKMGN

AST results

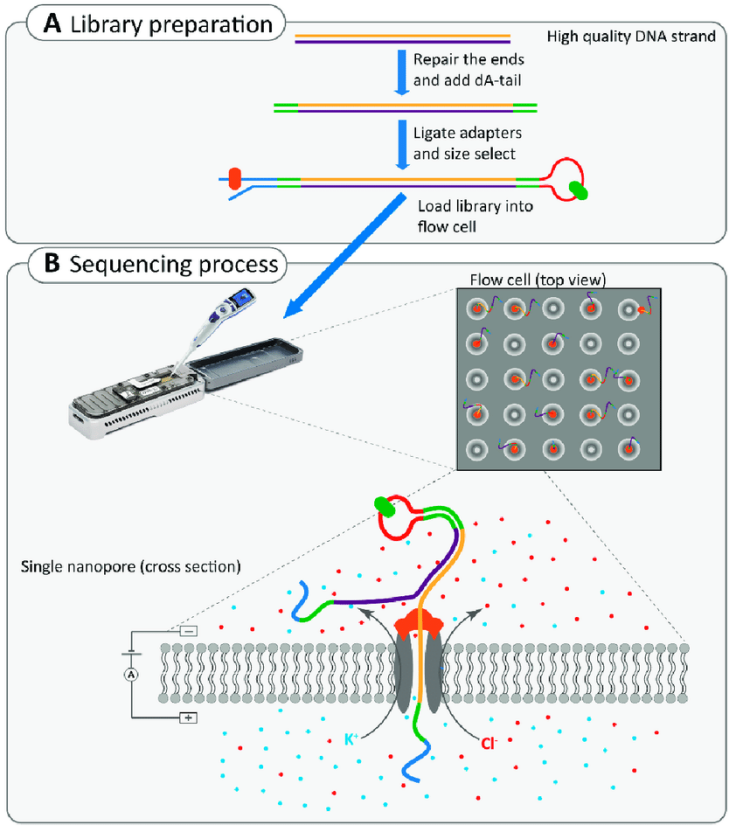
Isolates presented resistance to all antibiotics tested in standard panel

Cefiderocol to be tested with MICs dilution



Molecular tests

- Bacterial DNA extractions:
  - Commercial kit: NEB Monarch® Genomic DNA Extraction Kit (T3010) (New England Biolabs)
- Measurement of DNA purity and integrity
  - UV 260/280 absorbance ratio values: BioAnalyzer (Agilent Technologies)
- DNA quantifications:
  - Qubit fluorometer (ThermoFischer Scientific)
  - dsDNA Quantitation, High Sensitivity kit
- Conventional PCRs for carbapenemases genes:
  - *bla*KPC, *bla*NDM, *bla*VIM, *bla*IMP, blaOXA-48-like



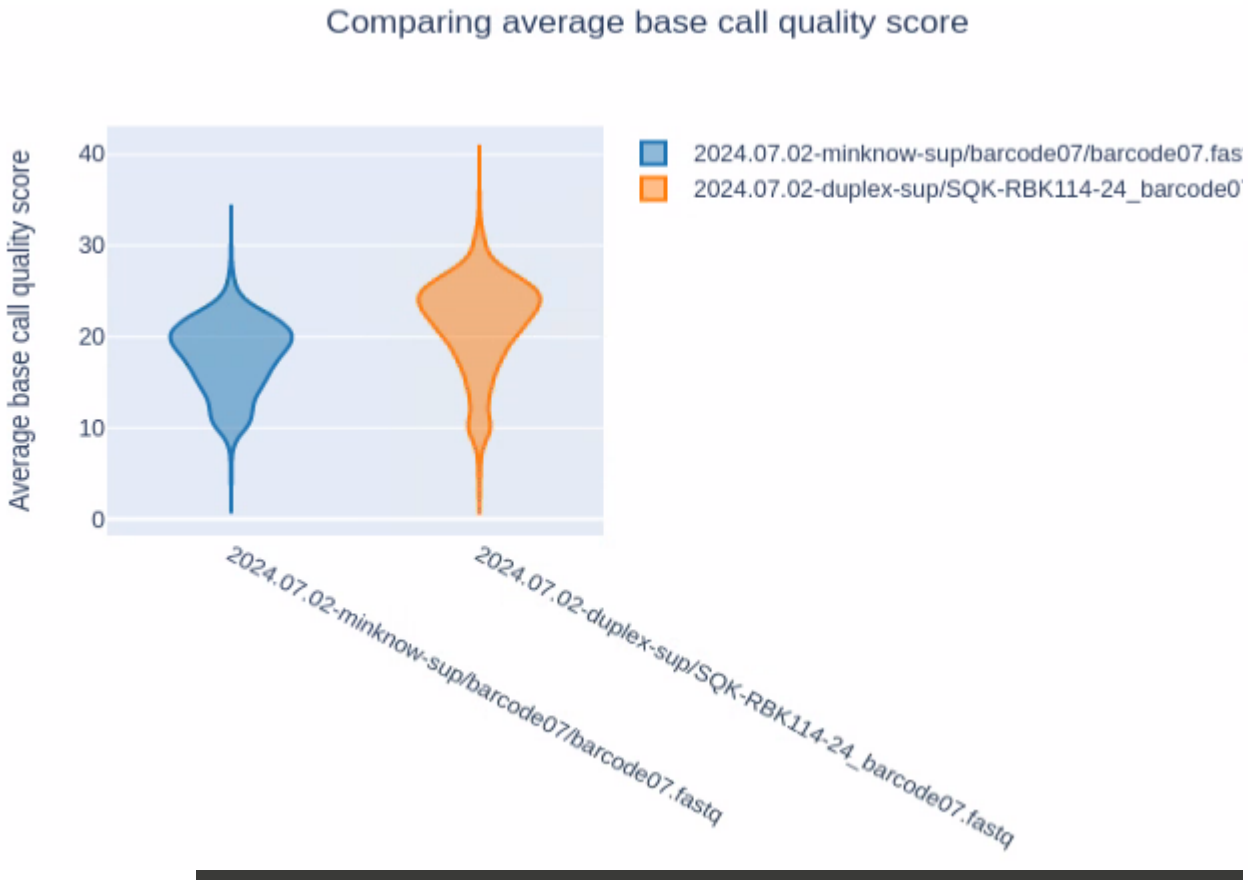
Whole-Genome Sequencing (WGS)

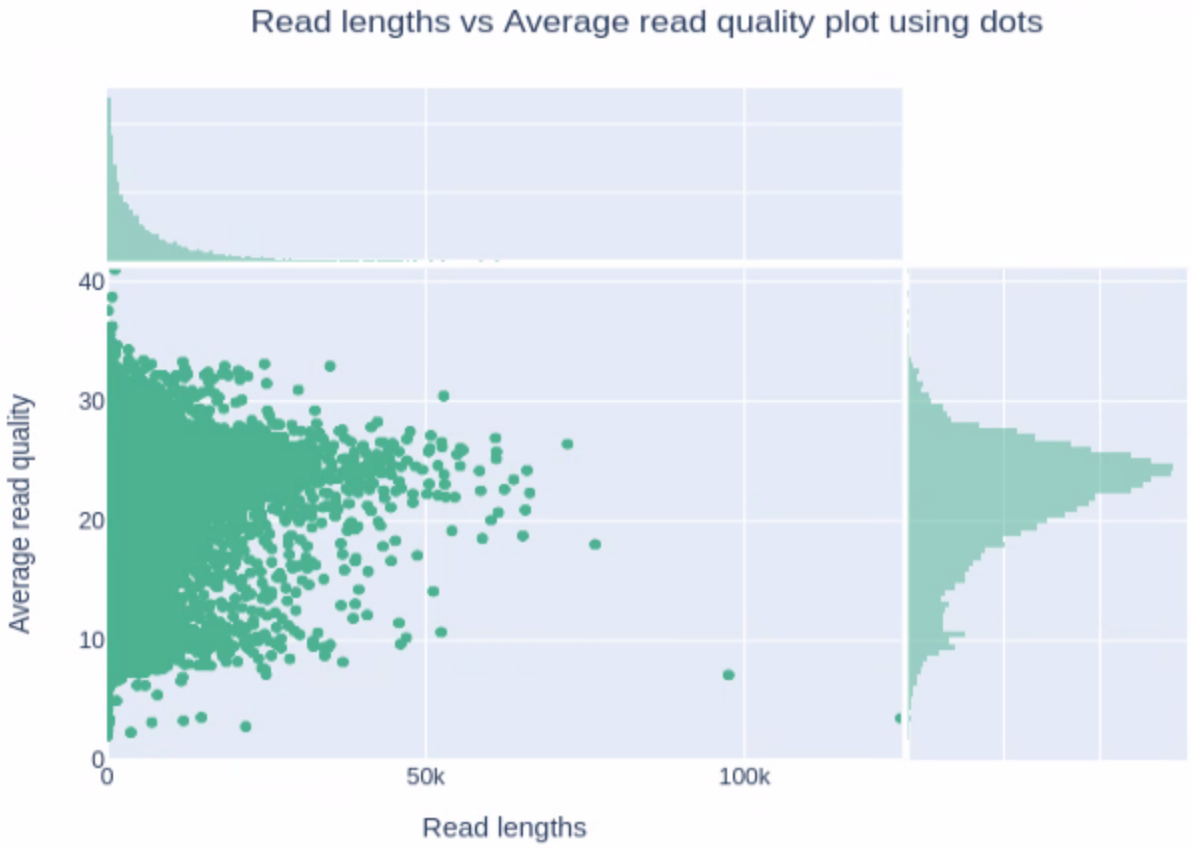
- Nanopore Sequencing was performed in all isolates included in the pilot study at NEL level
- Genomic DNA samples were barcoded with Rapid Barcoding Kit 24 V14 (SQK-RBK114.24)
- Samples were sequenced on R10.4.1 flow cells with a MinION device(FLO-MIN114)

Bioinformatics analysis

- **Duplex** basecalling using command line `dorado`
- Demultiplexing, trimming of adapter sequences
- Evaluation of fastq file with FastQC and NanoQC
- Filtering of sequences < 1000 bp and keeping best 90% of sequences

NanoQC violin plot showing better quality using latest dorado cli and “duplex” basecalling





Bioinformatics pipeline

- Trycycler assembly using
  - Flye, Minimap/miniasm and Raven
  - Reconciliation of contigs
- Polishing using Medaka
- When available, polypolish with Illumina data
- Adnotation with prokka and bakta
- Resfinder, Plasmidfinder, Kleborate
- Visualisation with Geneious Prime

WGS Results

Hospital	Strain	MLST	Carbapenemases genes	ESBLs / AmpC genes	Genes integrated Chromosomal	Plasmids content
H1	BA	ST383	NDM-5; OXA-48	CTX-M -15		IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR) - blaNDM-5, blaCTX-M-15 IncL - blaOXA-48
H2	556603	ST101	NDM-1; OXA-48	CTX-M-15		IncFII(Yp) - blaNDM-1 IncL - blaOXA-48 IncFIB(K), IncFII(K) Col440II
	562036	ST101	NDM-1; OXA-48	CTX-M-15		IncFII(Yp) - blaNDM-1 IncL - blaOXA-48 IncFIB(K), IncFII(K) Col440II CTX-M ?
	567252	ST101	NDM-1; OXA-48	CTX-M-15		IncFII(Yp) - blaNDM-1 IncL - blaOXA-48 IncFIB(K), IncFII(K) Col440II CTX-M ?
H3	P.G	ST2096	NDM-1; OXA232	CMY-2		IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR), IncC - blaNDM-1, CTX-M-15, CMY-6 ColKP3 - blaOXA-232 IncFIB(K)
H4	39D	ST101	NDM-1; OXA-48	CTX-M-15		IncFII(Yp) - blaNDM-1 IncL - blaOXA-48 IncFIA(HI1), IncR, RepB - blaCTX-M-15 IncFIB(K), IncFII(K) Col440II ColpVC
	13A	ST307	NDM-1; OXA-48	CTX-M-15		IncFIB(K), IncFII(K), IncFII(Yp) - blaNDM-1 IncL - blaOXA-48
	39C	ST383	NDM-1; OXA-48	CTX-M-15		IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR) - blaNDM-5, blaCTX-M-15 IncL - blaOXA-48 Col440I Phage?

WGS Results

Hospital	Strain	MLST	Carbapenemases genes	ESBLs / AmpC genes	Chromosomal genes	Plasmids content
H5	519812	ST15	NDM-1; OXA-48	CTX-M-15		IncC - blaNDM-1 IncL - blaOXA-48 Col440II - CTX-M-15
	546568	?	?	?		?
H6	551951	ST395	NDM-5; OXA-232	CTX-M-15		IncFIB(pQil) - blaNDM-5, blaCTX-M-15 IncFII ColKP3 - OXA-232
	553749	ST383	NDM-5; OXA-48	CTX-M -15		
H7	136S12	ST383	NDM-5; OXA-48	CTX-M -15		IncC - blaNDM-1, blaCMY-6 IncL - blaOXA-48 IncFIA(HI1), IncR, RepB IncFIB(pKPHS1) Col440II
	5S64	ST383	NDM-5; OXA-48	CTX-M -15		IncFIB(pNDM-Mar), IncHI1B(pNDM-MAR) - blaNDM-5, blaCTX-M-15 IncL - blaOXA-48 Col440I Phage?
	81S64	ST383	NDM-5; OXA-48	CTX-M -15		
H8	559587-559591 (5)	ST383	NDM-5; OXA-48	CTX-M -15		IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR) - blaNDM-5, blaCTX-M-15 IncL - blaOXA-48
H9	568036-569345	ST383	NDM-5; OXA-48	CTX-M -15		IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR) - blaNDM-5, blaCTX-M-15 IncL - blaOXA-48

High-risk *K.pneumoniae* clones detection

ST383 (n=19)

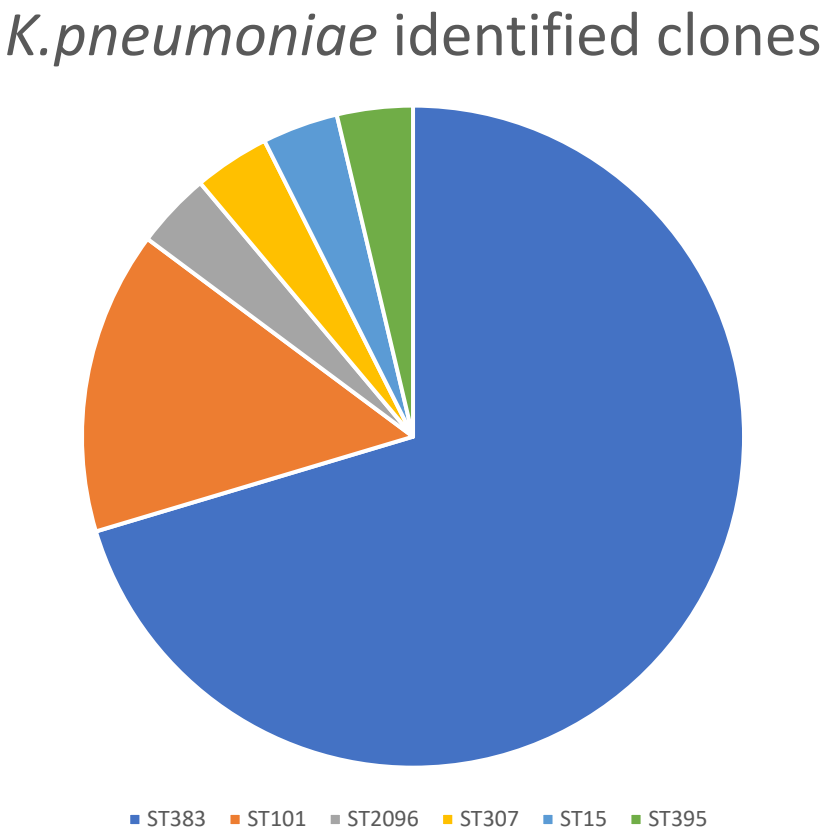
ST101 (n=4)

ST2096 (n=1)

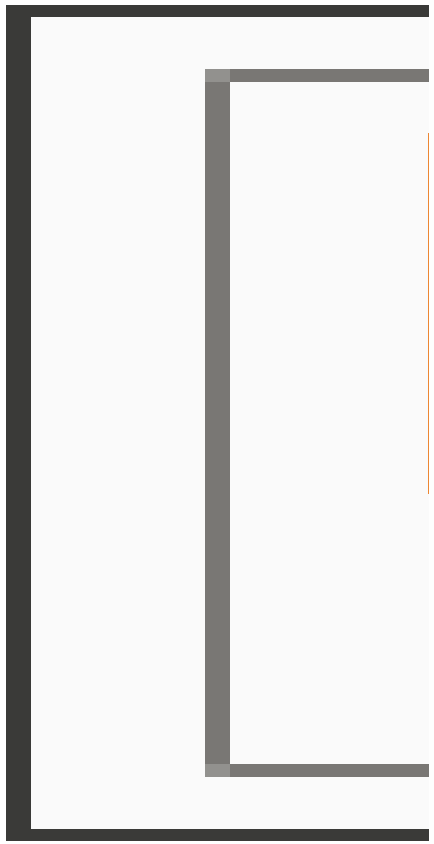
ST307 (n=1)

ST15 (n=1)

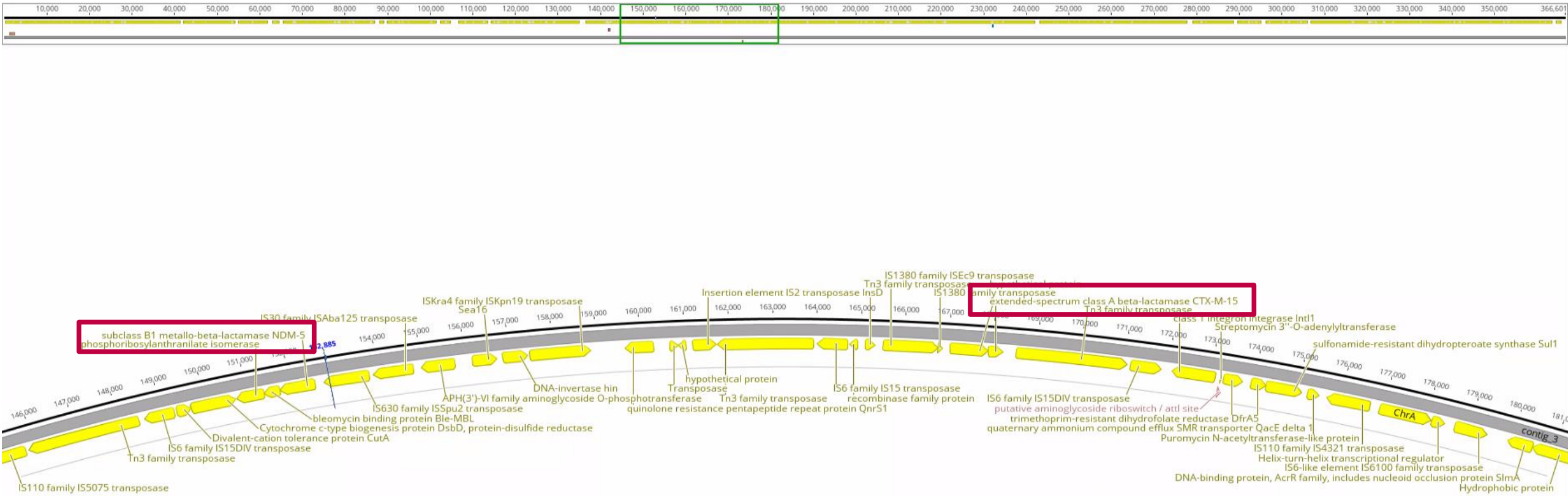
ST395 (n=1)



IncL - blaOXA-48

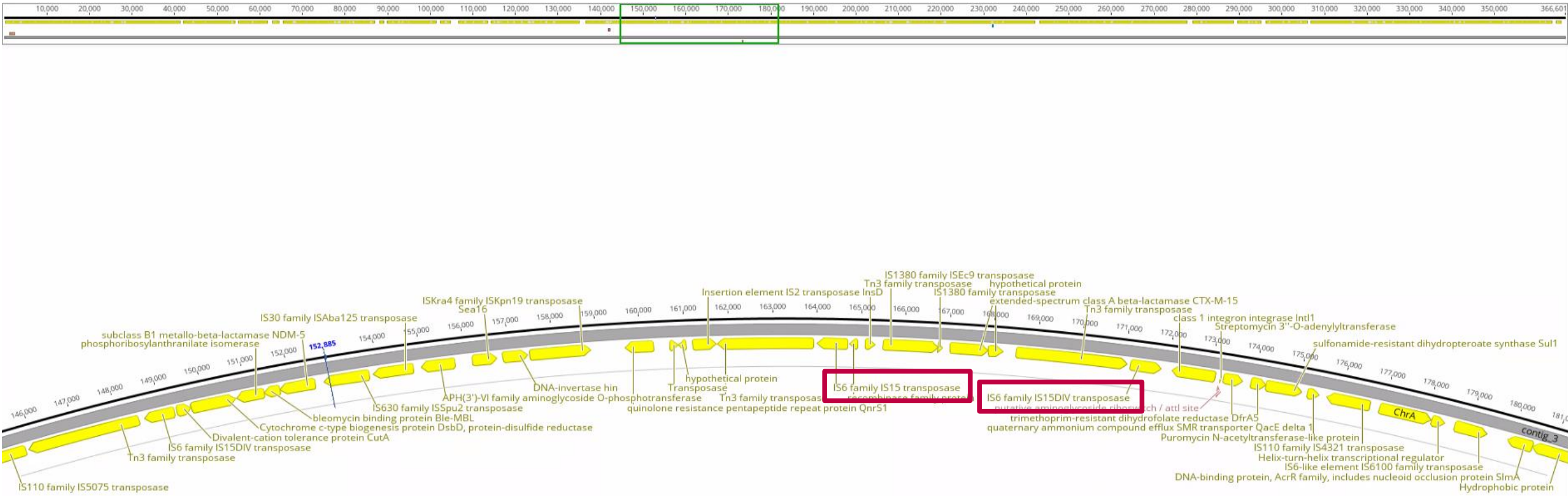


IncFIB(pNDM-Mar)/IncHI1B(pNDM-MAR) – NDM-5, CTX-M-15



contig_3 - IncFIB - 2024.06.25-barcode02-KPN-PBEC
366,601 bp

IncFIB(pNDM-Mar), IncHI1B(pNDM-MAR) – NDM-5, CTX-M-15



contig_3 - IncFIB - 2024.06.25-barcode02-KPN-PBEC
366,601 bp

ST383 *Kl. pneumoniae*

- Detected in 5 hospitals included in the pilot study
- Associated with *bla*NDM-5 gene
- The plasmid carring blaNDM-5 and CTX-M-15 genes : IncFIB(pNDM-Mar)/ IncHI1B(pNDM-MAR)

MDR Kpn associated with virulence

- Some clones are presenting genetic hallmarks of hvKp.
- Besides a high resistance level, the collection also included multiple virulence factor genes associated with the hypervirulent phenotype
- ST2096 presented
  - *iuc* locus
  - Yersiniabactin gene cluster (*ybt*)
  - integrative conjugative elements (ICEKp5)

Challenges for participation in pilot study

- Laboratory investigations:
  - Sometimes there are compromised Nanopore flow cells provided by representative, replaced with time consuming
  - Insufficient metadata provided from hospital teams
- Staff:
  - Bioinformatic data analyst missing (obtained data are interpreting by a MD, microbiologist)
- Laboratory digital infrastructure without sufficient WGS capacity

Conclusions

- The emergence of multidrug-resistant *K. pneumoniae* is a fundamental reason for enhanced efforts towards genomic surveillance of this microorganism.
- Despite the fact that WGS is a useful tool for reaching the goal of knowing all the aspects regarding antibiotic resistance, the following aspects remained in the current context in Romania, and it would be necessary to investigate further:

  A) replacement and increasing resistance;

  B) what will be the contribution by this pilot study to reduction of antibiotic-resistant bacteria on long term?

- There is an urgent need for further genomic epidemiological investigations

3rd EURGen-RefLabCap Network Meeting
18-19th Sepetember 2024

Impact of the EURGen-RefLabCap in Spanish LRA

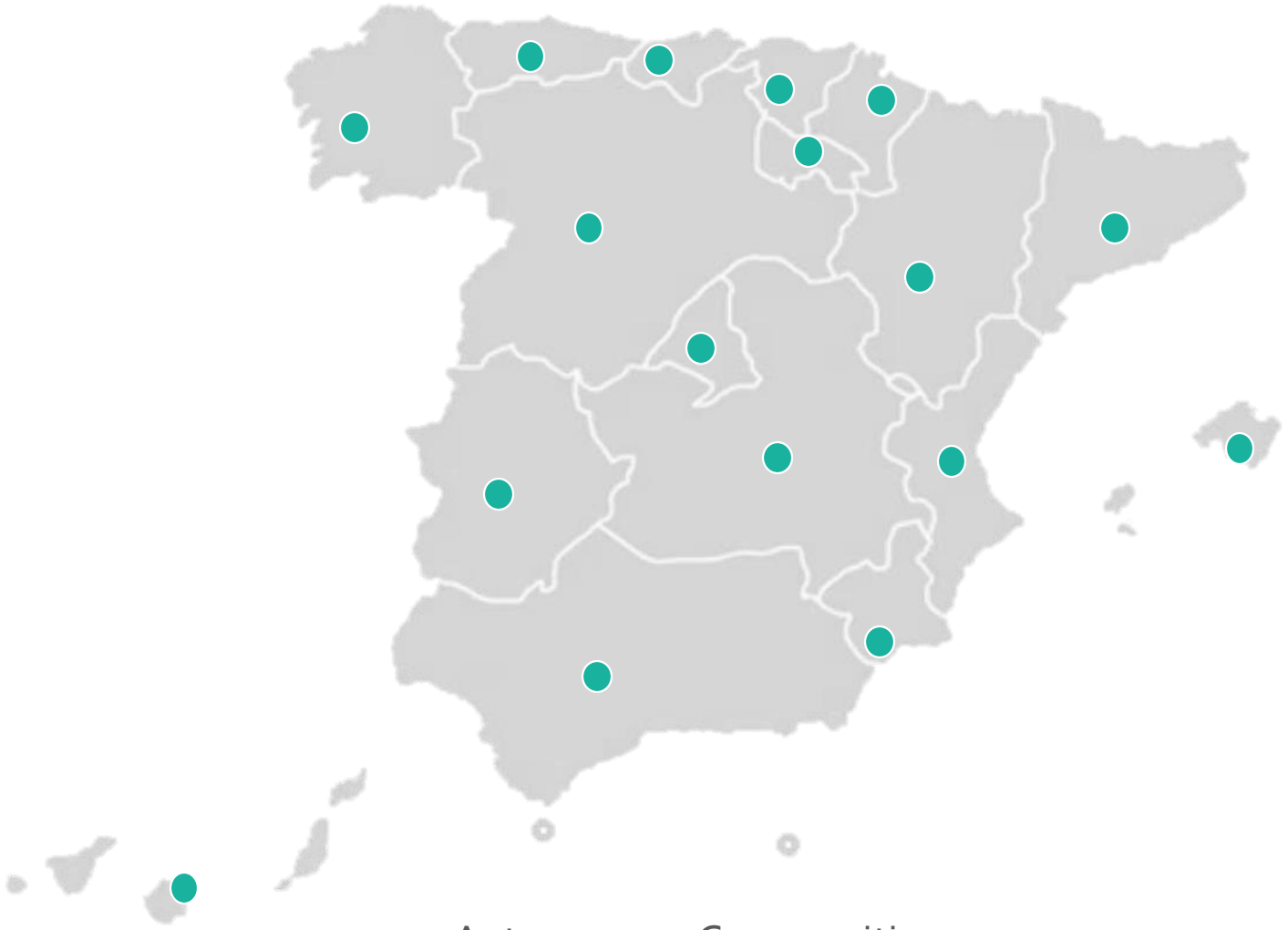
Reference and Research Laboratory on Antimicrobial Resistance and Healthcare-Associated Infections

National Centre of Microbiology, Instituto de Salud Carlos III

María Pérez-Vázquez/Silvia García Cobos

GOBIERNO DE ESPAÑA
MINISTERIO DE CIENCIA E INNOVACIÓN

Instituto de Salud Carlos III



17 Autonomous Communities

Public Healthcare System

Ministry of Health

National laws and regulations

Regional - 17 AC – local administration

Political and administrative division, and Healthcare System

National Laboratory Network for the genomic surveillance of Antibiotic Resistant Microorganisms

How is this network organized?

How we provide advisory to the network?

Our capacity to colaborate with the network?

Instituto de Salud Carlos III

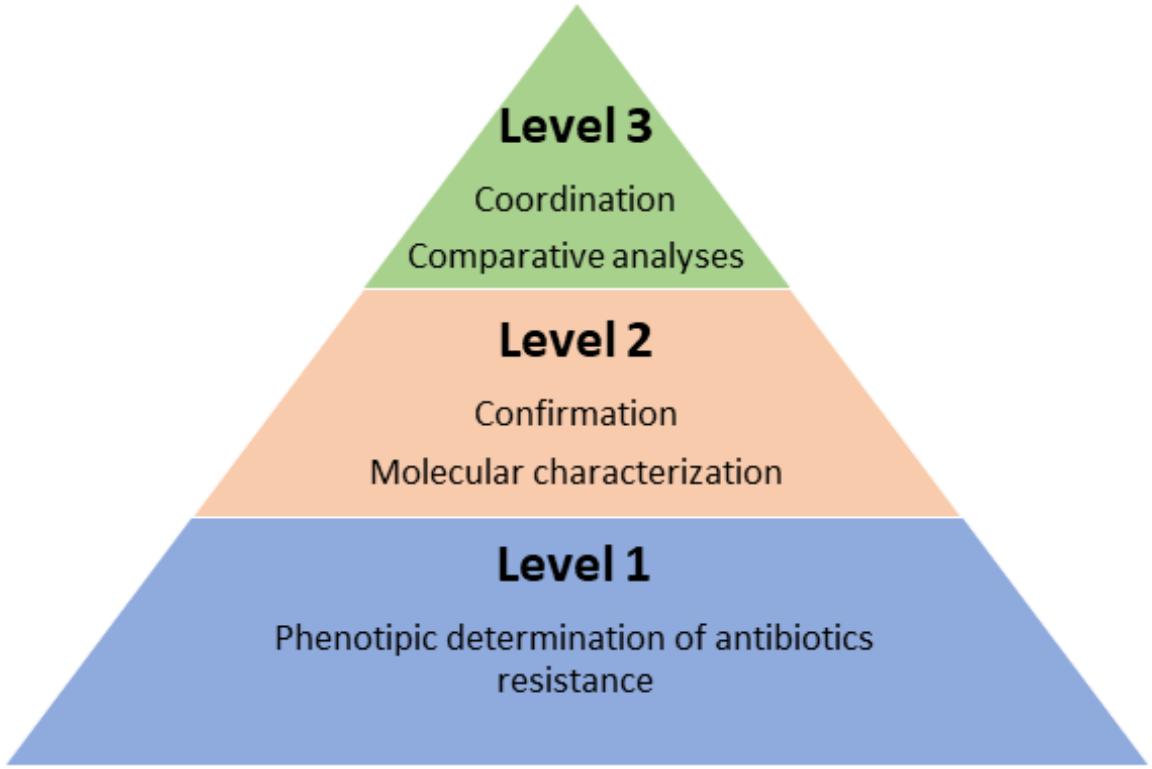
PRAN

RedlabRA

Red de Laboratorios para la Vigilancia de Microorganismos Resistentes

Integrated network of laboratories

- Level 1 laboratories
  Phenotypic detection
  Outbreak detection
  Refer isolates to Level 2
- Level 2 laboratories
  Molecular characterization (resistance mechanism, MLST, specie)
  Reception of strains from Level1 and comunication
- Level 3 laboratory (LRA)
  Reference and support Level 2, coordination, WGS global analysis

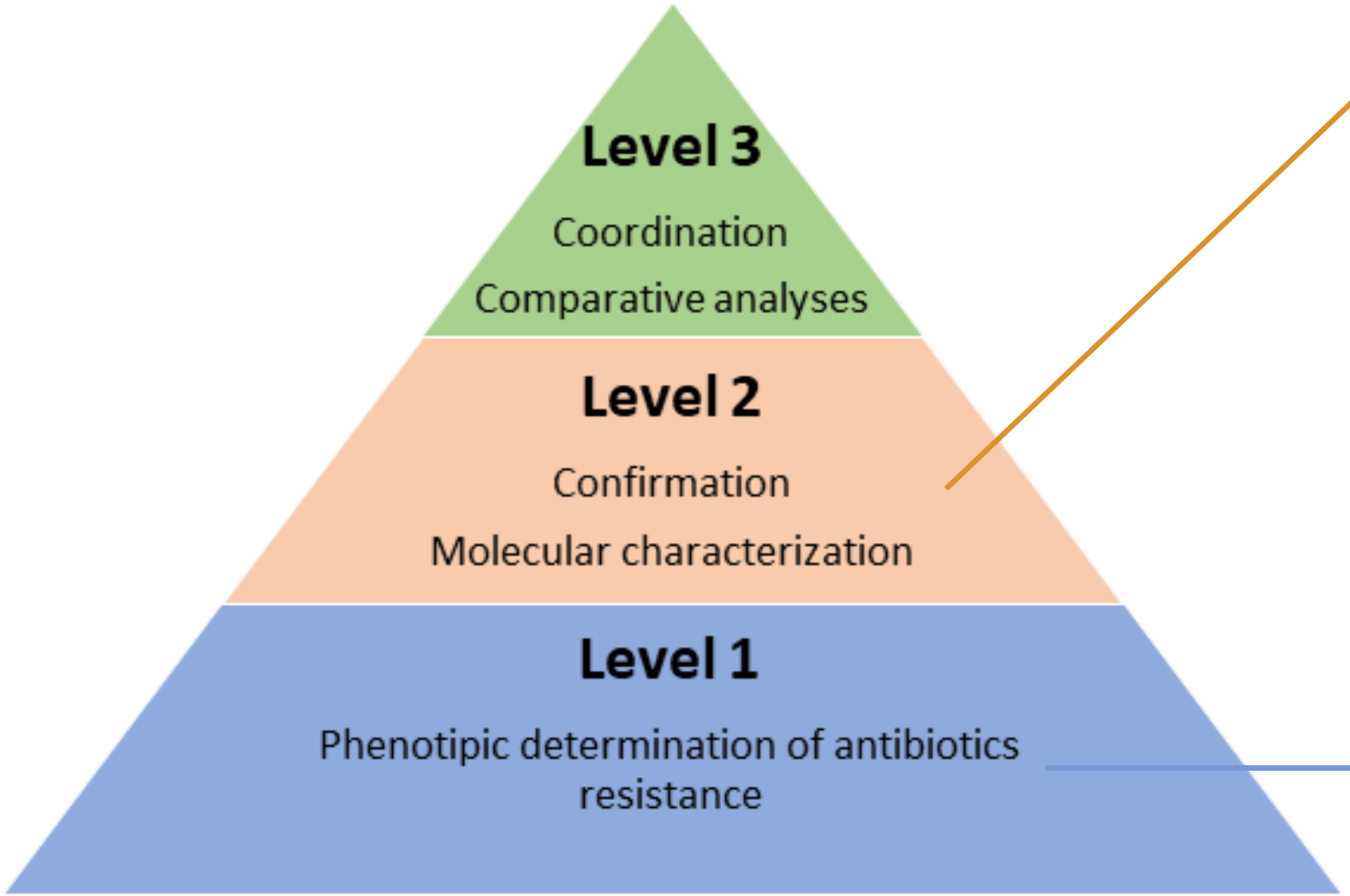


PRAN

RedlabRA
Red de Laboratorios para la Vigilancia de Microorganismos Resistentes

Cañada-García JE, et al. *Rev Esp Quimioter*. 2021

Network coverage



38 LN2

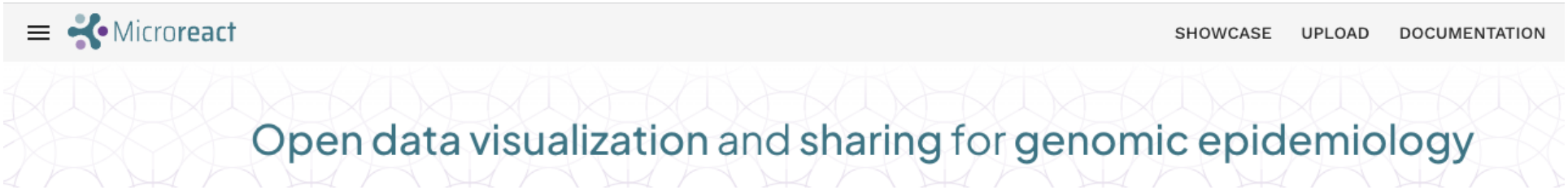
104 LN1 17 CC. AA. + Melilla

RedLabRA
Organizative comitte

Advisory to the network

Colaboration with the network

Interactive tool for notification, visualization and analysis



Enlace microreact

Colaboration with the network

Implementation of WGS in our laboratory

Sequencing and bioinformatic analysis

Short sequencing
Genomic unit (2013)

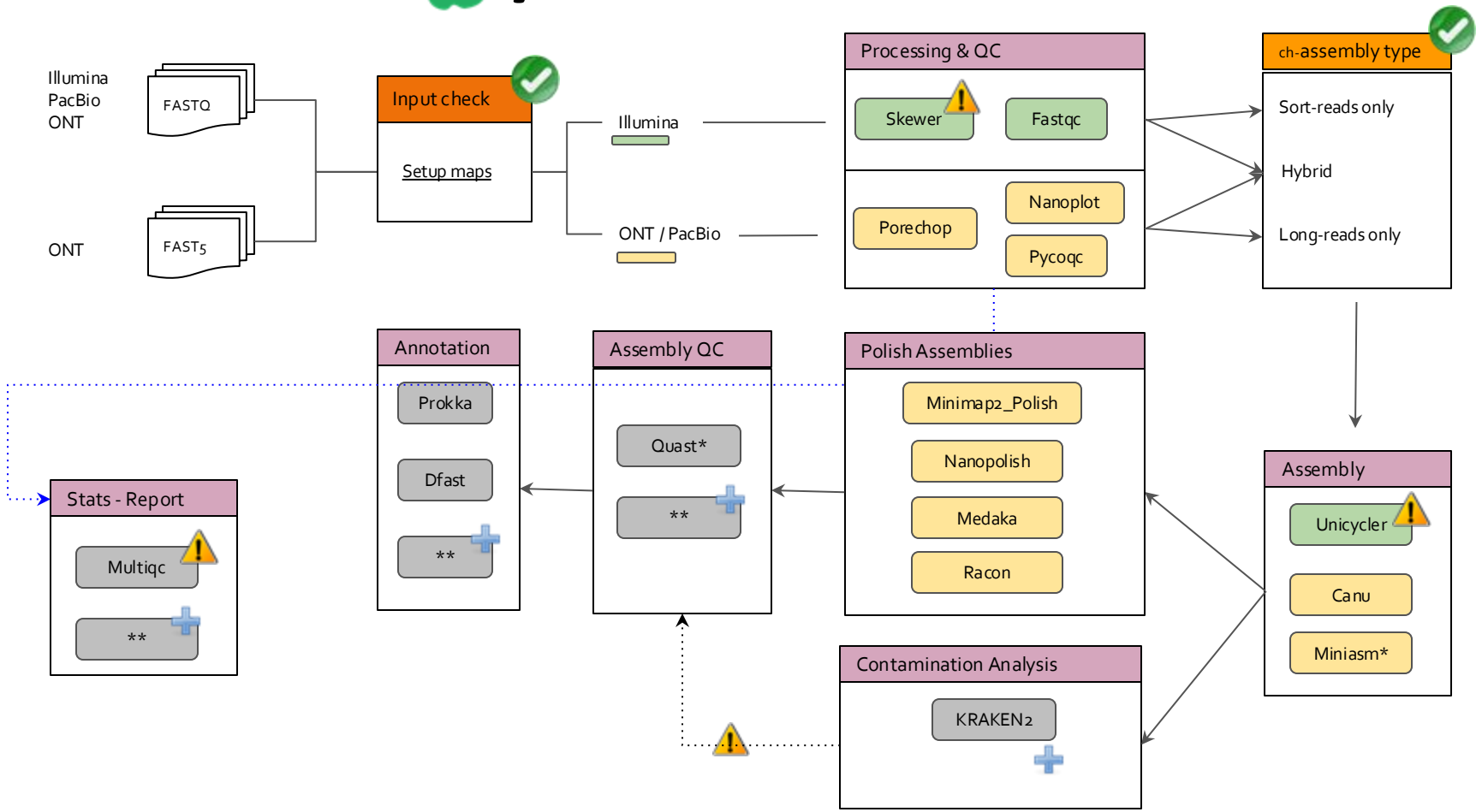
illumina®

Long sequencing

Oxford NANOPORE Technologies

Methodology of sequencing developed in our laboratory

nf-core /bacass



slurm workload manager

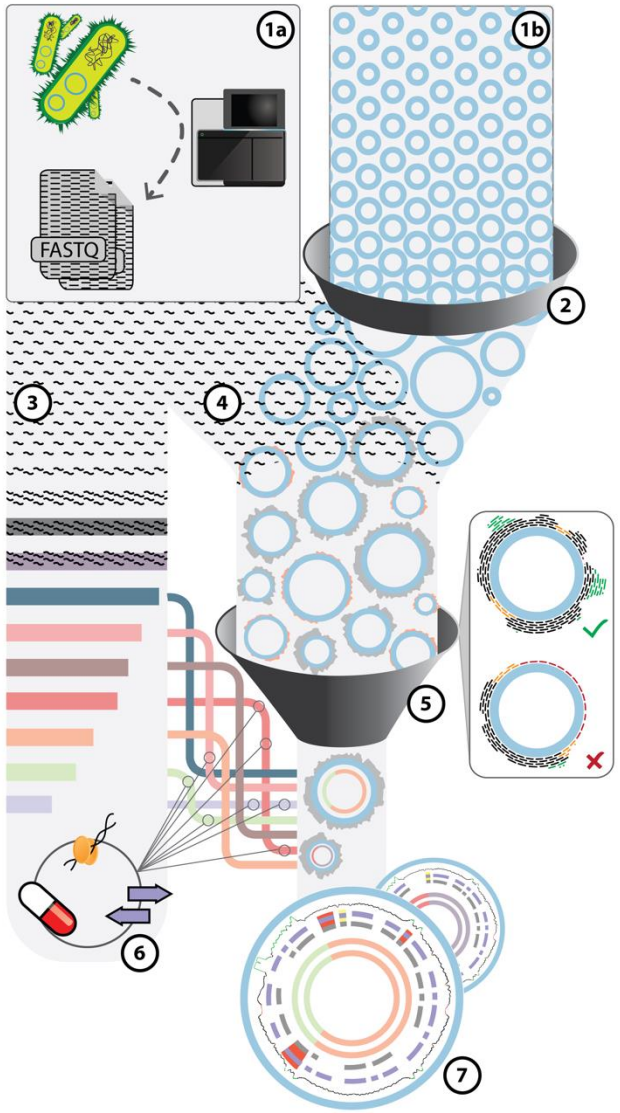
- Número de nodos: 34
- Cores/CPUs totales: 768
- Memoria total: ~12.6 TB
- GPGPU: 4 x NVIDIA Tesla P100
- Conexión almacenamiento: Ethernet de 10 Gbps
- Almacenamiento principal: 100 TB
- Almacenamiento interno nodo: ~800 GB

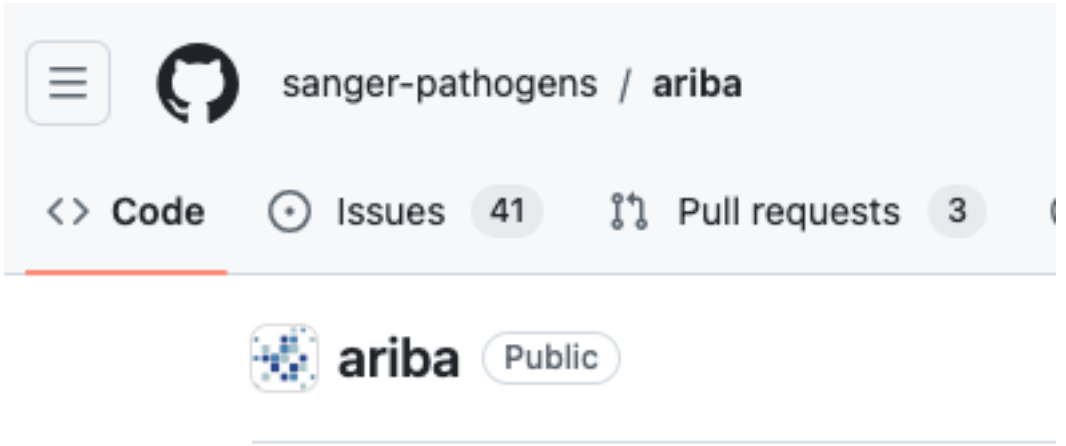
XTutatis computación HPC

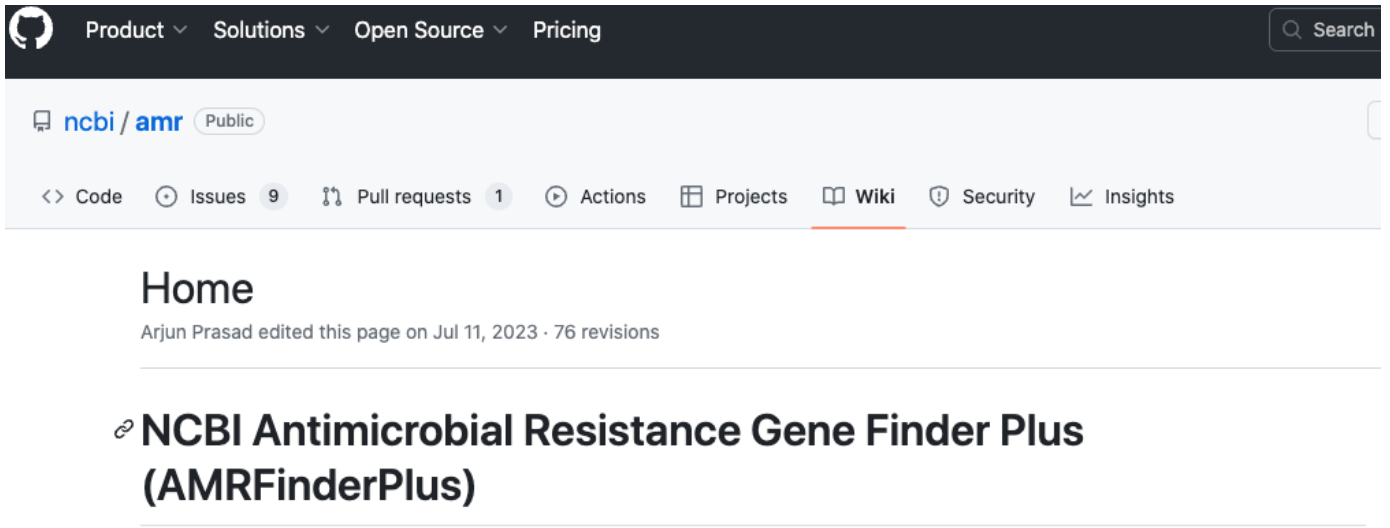
Bioinformatic unit

Genomic unit

Bioinformatic tools used in our laboratory (Bioinformatic Unit)







Resfinder, Card, NCBI

https://github.com/BU-ISCIII/plasmidID, PlasmidFinder

Bioinformatic tools used in our laboratory

Efforts in reporting laboratory results at European level?

European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net)

RAPID COMMUNICATION

Cross-border spread of *bla*$_{NDM-1}$- and *bla*$_{OXA-48}$ positive *Klebsiella pneumoniae*: a European collaborative analysis of whole genome sequencing and epidemiological data, 2014 to 2019

Catherine Ludden[1], Felix Lötsch[1], Erik Alm[1], Narender Kumar[2], Karin Johansson[1], Barbara Albiger[1], Te-Din Huang[3], Olivier Denis[3], Anette M Hammerum[4], Henrik Hasman[4], Jari Jalava[5], Kati Räisänen[5], Laurent Dortet[6], Agnès B Jousset[6], Sören Gatermann[7], Sebastian Haller[8], Martin Cormican[9], Wendy Brennan[9], Maria Del Grosso[10], Monica Monaco[10], Leo Schouls[11], Ørjan Samuelsen[12,13], Mateja Pirš[14], Tjaša Cerar[14], Jésus Oteo-Iglesias[15], Maria Pérez-Vázquez[15], Karin Sjöström[16], Petra Edquist[16], Katie L Hopkins[17], Marc J Struelens[1], Daniel Palm[1], Dominique L Monnet[1], Anke Kohlenberg[1]

RAPID COMMUNICATION

Rapid cross-border emergence of NDM-5-producing *Escherichia coli* in the European Union/European Economic Area, 2012 to June 2022

Marius Linkevicius[1], Rémy A Bonnin[2], Erik Alm[1], Olov Svartström[1], Petra Apfalter[3], Rainer Hartl[3], Henrik Hasman[4], Louise Roer[4], Kati Räisänen[5], Laurent Dortet[2], Niels Pfennigwerth[6], Jörg B Hans[6], Ákos Tóth[7], Lilla Buzgó[7], Martin Cormican[8], Niall Delappe[8], Monica Monaco[9], Maria Giufrè[9], Antoni PA Hendrickx[10], Ørjan Samuelsen[11,12], Anna K Pöntinen[11,13], Manuela Caniça[14], Vera Manageiro[14], Jesús Oteo-Iglesias[15], María Pérez-Vázquez[15], Karin Westmo[16], Barbro Mäkitalo[16], Daniel Palm[1], Dominique L Monnet[1], Anke Kohlenberg[1]

International level
ECDC

TESSy
The European Surveillance System

EARS-Net
European Antimicrobial Resistance Surveillance Network

Participation (EUSKAPE, CAR-Survey, CP-Aba Survey…….

Thanks

Jesús Oteo Iglesias
Silvia García Cobos
María Pérez Vázquez
Belén Aracil García
Eva Ramírez de Arellano
Javier E. Cañada
Noelia Lara Fuella
Jared Sotelo
Verónica Bautista Sánchez
Verónica Casquero García

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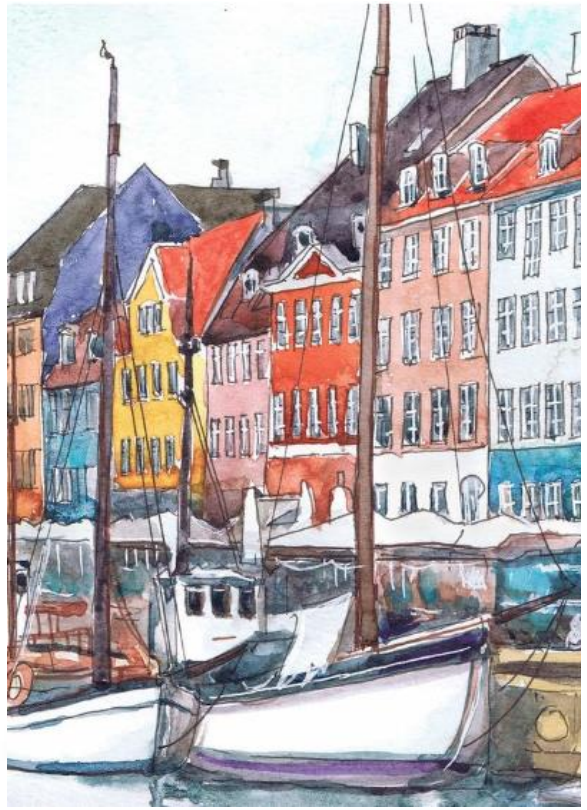
Instituto de Salud Carlos III

Thank you for your attention



EURL-PH-AMR

Camilla Coia
Anders Rhod Larsen

Call for Applications for the Designation of an EU Reference Laboratory for Public Health in the field of Antimicrobial Resistance (AMR) in bacteria

EU4Health Programme (EU4H)

Application Form

Administrative Forms (Part A)
Technical Description (Part B)

(EU4H Standard)

EURGen-RefLabCap Network meeting 19 September 2024

The legal base

- **Entered into force 26 December 2022:**
  - REGULATION (EU) 2022/2371 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 23 November 2022 on **serious cross-border threats to health** and repealing Decision No 1082/2013/EU
    - Regulations are binding in their entirety and directly applicable in all EU Member States
    - **Article 15 – EU reference laboratories**
  - REGULATION (EU) 2022/2370 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 23 November 2022 amending Regulation (EC) No 851/2004 **establishing a European centre for disease prevention and control**
    - **Article 5** - Operation of dedicated networks and networking activities
    - **Article 11** - Support for international and field preparedness and response

REINFORCED MANDATE OF ECDC SINCE 2022

EDITORIAL

Preparing Europe for future health threats and crises – key elements of the European Centre for Disease Prevention and Control's reinforced mandate

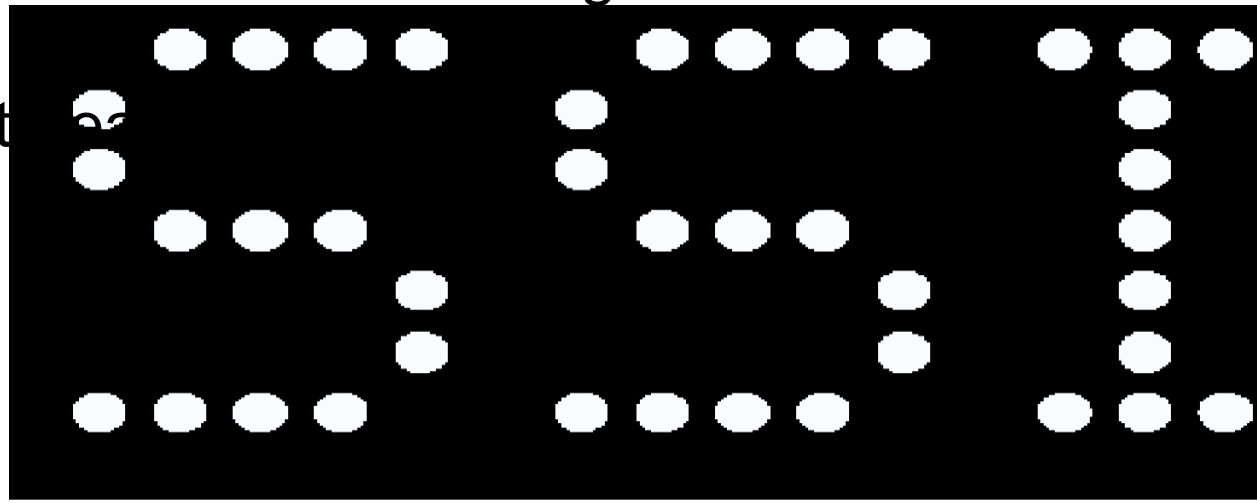
Maarit Kokki[1] , Andrea Ammon[1]
1. European Centre for Disease Prevention and Control (ECDC), Stockholm, Sweden
Correspondence: Andrea Ammon(andrea.ammon@ecdc.europa.eu)

Citation style for this article:
Kokki Maarit, Ammon Andrea. Preparing Europe for future health threats and crises – key elements of the European Centre for Disease Prevention and Control's reinforced mandate. Euro Surveill. 2023;28(3):pii=2300033. https://doi.org/10.2807/1560-7917.ES.2023.28.3.2300033

Article submitted on 17 Jan 2023 / accepted on 19 Jan 2023 / published on 19 Jan 2023

.. to provide science-based recommendations for management and control of communicable diseases; and

- building capacity for detection of t
- develop digital systems,
- epidemiological modelling, and
- **coordinate the new Network of**



Networking of NRLs bolsters Europes defenses against infectious diseases - - Albiger et al.

Networking of Public Health Microbiology Laboratories Bolsters Europe's Defenses against Infectious Diseases

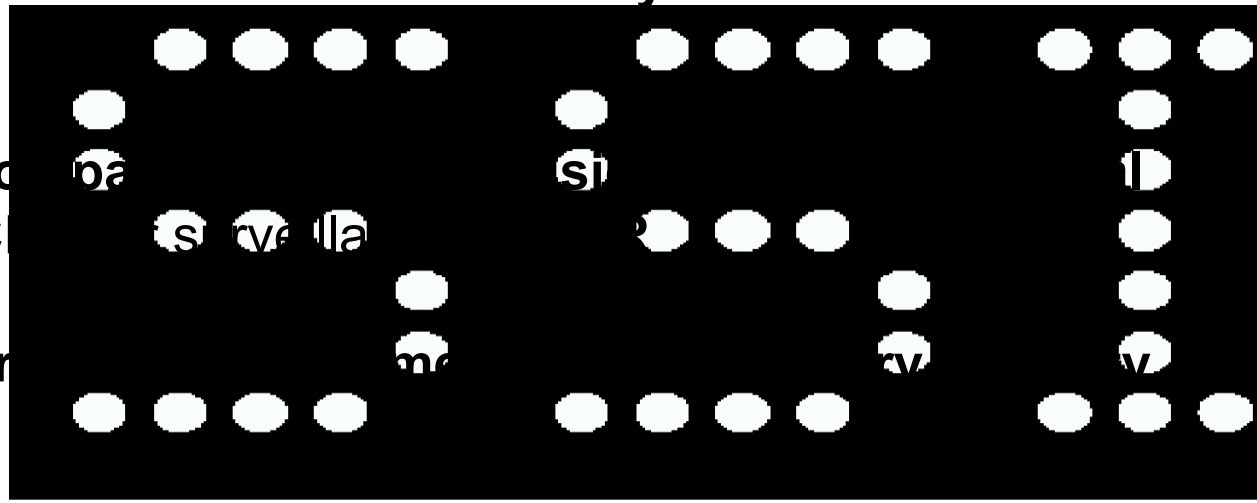
Barbara Albiger[1], Joana Revez[1], Katrin Claire Leitmeyer[1] and Marc J. Struelens[1]*

[1]Scientific Advice Coordination Section, Office of the Chief Scientist, European Centre for Disease Prevention and Control, Stockholm, Sweden, [2]Microbiology Coordination Section, Office of the Chief Scientist, European Centre for Disease Prevention and Control, Stockholm, Sweden

frontiers in Public Health

PERSPECTIVE
published: 26 February 2018
doi: 10.3389/fpubh.2018.00046

- Setting up laboratory networks has been succesful in strengthening **epidemic preparedness** by enabling adaptive capabilities for rapid detection of emerging pathogens
- Networks have **progressed harmonisation of routinely used AST and molecular typing methods**
- Has advanced the **quality, co** **information** gathered for EC
- Has resulted in **continous pr** **across Europe**



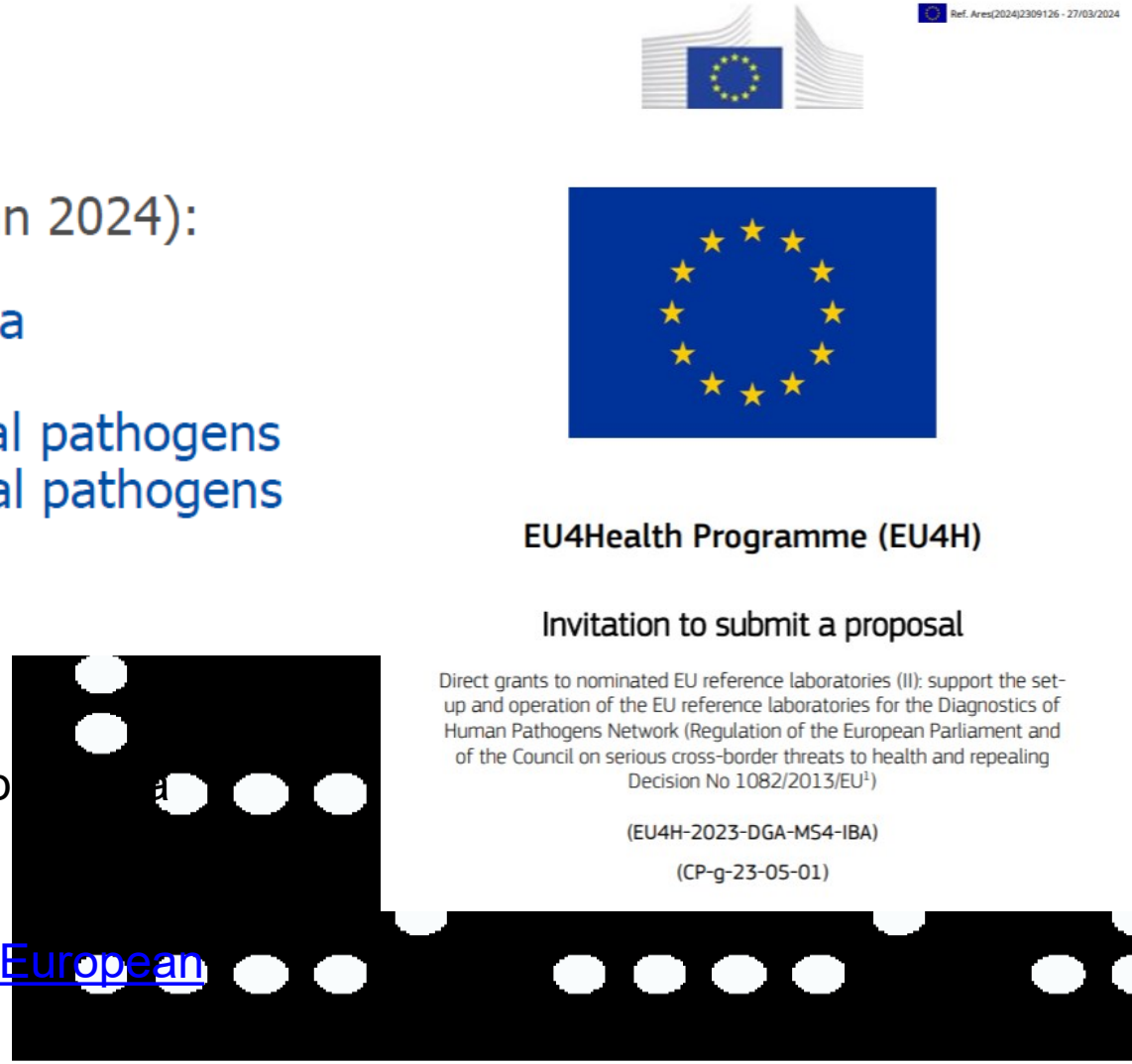
GRANT PROPOSAL – SUBMITTED 23 MAY 2024

- EU4H Direct grant

- DG SANTE published six calls (2 Oct 2023 – 5 Jan 2024):
  - ❑ Antimicrobial Resistance (AMR) in bacteria
  - ❑ Vector-borne viral pathogens
  - ❑ Emerging, rodent-borne and zoonotic viral pathogens
  - ❑ High-risk, emerging and zoonotic bacterial pathogens
  - ❑ *Legionella*
  - ❑ Diphtheria and pertussis

•Food- and water-borne bacteria
•Food-, water-, and vector-borne helminths and p[illegible]a
•Food- and water-borne viruses

[EU Reference Laboratories for public health - European Commission (europa.eu)]



APPLICATION FOR DESIGNATION AS EURL-PH-AMR

- For a seven year period each area of support, required activities are defined, number of participants, repetitions of activities, number of tests, number of reports etc.

List of mandatory EURL tasks and activities

Task no	Task / Activity	Timing	Minimum volume over the two-year scenario period
Reference diagnostics, including test protocols			
1	Provision of phenotypic and functional reference testing including confirmation of resistance mechanisms (EURGen-Net)	Upon request	Testing of 1000 isolates per year, i.e., approx. 2000 isolates to be tested for the scenario period
External quality assessments (EQAs)			
4	Conducting phenotypic AMR EQA for local clinical laboratories (EARS-Net)	Annually	EQA for approx. 1000 network laboratories per year i.e., 2 EQAs for approx. 2000 laboratories over the scenario period
5	Provision of phenotypic EQAs and genomic proficiency testing (PT) to the national reference laboratories (EURGen-Net)	Annually	EQA and PT combined for approx. 37 network laboratories per year i.e., 2 rounds of EQA and PT combined for approx. 74 laboratories over the scenario period

- 15 mandatory pre-defined tasks
- 5 innovative tasks
- 48 (84) months of detailed planning

Scientific advice and technical assistance			
6	Assessment of laboratory capacity and development of plans for capacity strengthening (EURGen-Net)	Biennially	1 capacity survey report and 1 capacity building plan over the scenario period
7	Support to capacity building through bespoke consultations and advice, including remote or on-site visits as required (EURGen-Net)	Annually	At least 8 hours of support / country and year for 37 countries i.e., 16 hours of support / country over the scenario period covering 37 countries

REGULATION (EU) 2024/892 – DESIGNATION OF EURL-PH-AMR

Official Journal
of the European Union

EN
L series

2024/892

25.3.2024

COMMISSION IMPLEMENTING REGULATION (EU) 2024/892

of 22 March 2024

designating European Union reference laboratories for certain specific areas of public health

(Text with EEA relevance)

ANNEX I

THE EU REFERENCE LABORATORY FOR PUBLIC HEALTH ON ANTIMICROBIAL RESISTANCE (AMR) IN BACTERIA, ITS RESPONSIBILITIES AND TASKS

1. THE CONSORTIUM DESIGNATED AS THE EU REFERENCE LABORATORY FOR PUBLIC HEALTH ON ANTIMICROBIAL RESISTANCE (AMR) IN BACTERIA (HEREINAFTER 'EURL')

Consortium led by:

Statens Serum Institut, Artillerivej 5, 2300 København S, DENMARK

Also composed of:

Danmarks Tekniske Universitet, Anker Engelunds Vej 101, 2800 Kongens Lyngby, DENMARK

Clinical Microbiology Region Kronoberg, Central Hospital Växjö, Värendsgatan 7, SE-351 85 Växjö, SWEDEN

2. RESPONSIBILITIES AND TASKS

The EURL shall provide support to national reference laboratories and promote good practice and quality to st
public health microbiology in the field of AMR in bacteria, with the exception of AMR issues related to *S.*
species, *Campylobacter* species and *Neisseria gonorrhoeae*.

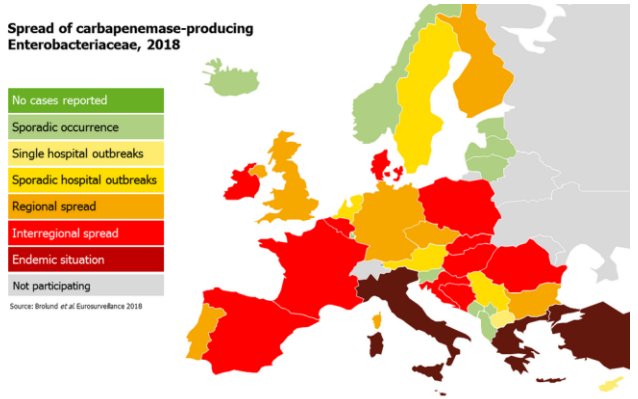
The EURL shall provide support to the members of the laboratory networks of the European Centre for
Prevention and Control (ECDC)'s European Antimicrobial Resistance Surveillance Network (EARS-Net) (1)
European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net) (2) on aspects related to dia
testing methods, use of certain tests for the uniform surveillance, notification and reporting of diseases.

For the implementation of the activities under the EURL's work plan which the EURL shall develop and agree
ECDC, the EURL shall coordinate the laboratory networks of EARS-Net and EURGen-Net consisting of the
Focal Points (NFPs) for AMR and the Operational Contact Points (OCPs) for Microbiology for the pathogens co
EARS-Net and EURGen-Net.

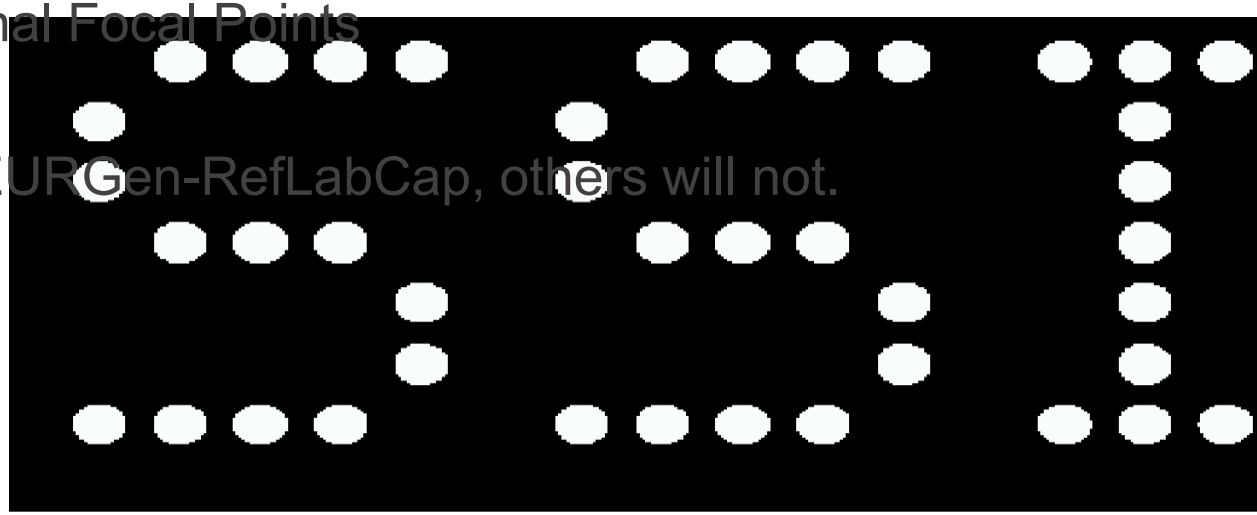
Upon request from the ECDC, the EURL shall participate in relevant ECDC networks and structures. The EU
participate in the network of EU reference laboratories that is to be operated and coordinated by the
accordance with Article 15(3) of Regulation (EU) 2022/2371.

NETWORKS OF LABORATORIES RECEIVING THE SUPPORT

- **EURGen-Net** (Genomic PT + **all support activities**)
- **EARS-Net** (mainly phenotypic EQA)



- Country coordinators are selected through ECDC Stakeholder Relationship Management (SRM) System and their interaction with National Focal Points
- Some country teams will stay the same as in EURGen-RefLabCap, others will not.

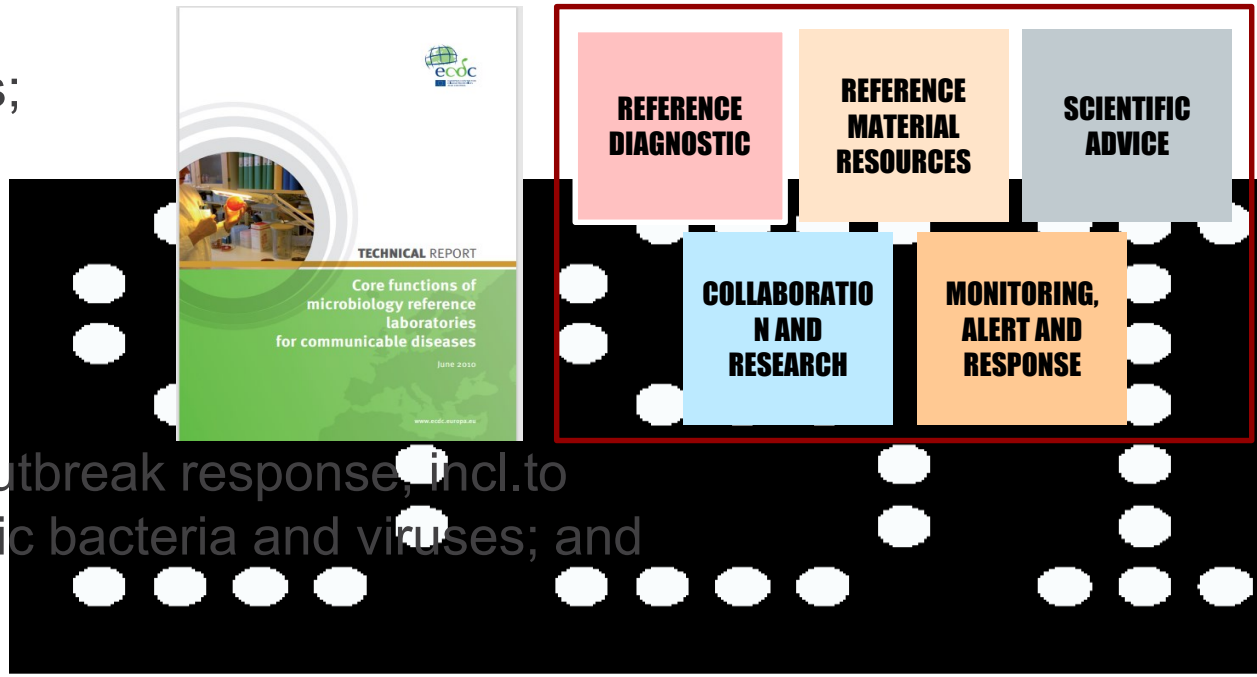


EURL SUPPORT TO NETWORKS

EURLs should provide support to disease and laboratory networks to promote good practice and alignment by Member States on a voluntary basis on diagnostics, testing methods, use of certain tests for the uniform surveillance, notification and reporting of diseases by Member States.

EURL shall be responsible for coordinating the network of NRLs, in particular, in the following areas:

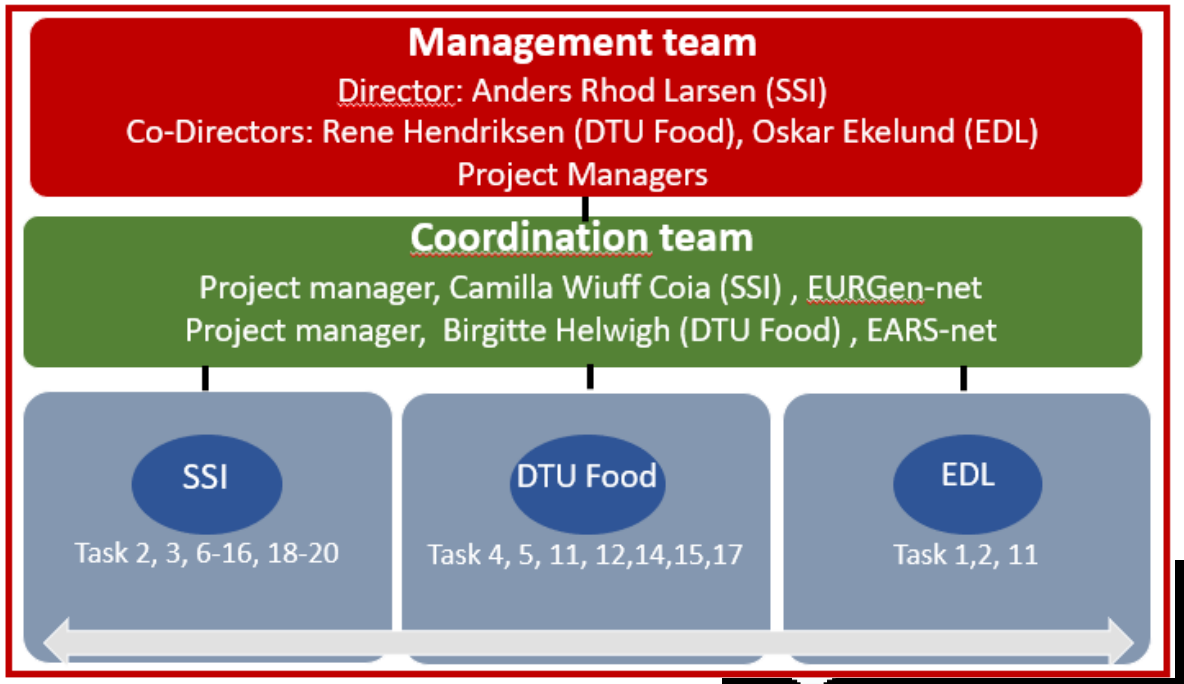
- (a) reference diagnostics, including test protocols;
- (b) reference material resources;
- (c) external quality assessments;
- (d) scientific advice and technical assistance;
- (e) collaboration and research;
- (f) monitoring, alert notifications and support in outbreak response, incl.to emerging communicable diseases and pathogenic bacteria and viruses; and
- (g) training



NEW CONSORTIUM SETUP AND SUPPORT ACTIVITIES FOR EURL-PH-AMR

SSI

- Coordination
- Project management
- Communication
- Reporting on activities
- Providing reference material
- Genomic testing for AMR
- Outbreak investigation support to ECDC
- EQAs/PTs for EURGen-Net
- Capacity building activities
- Collaborative research studies
- Training

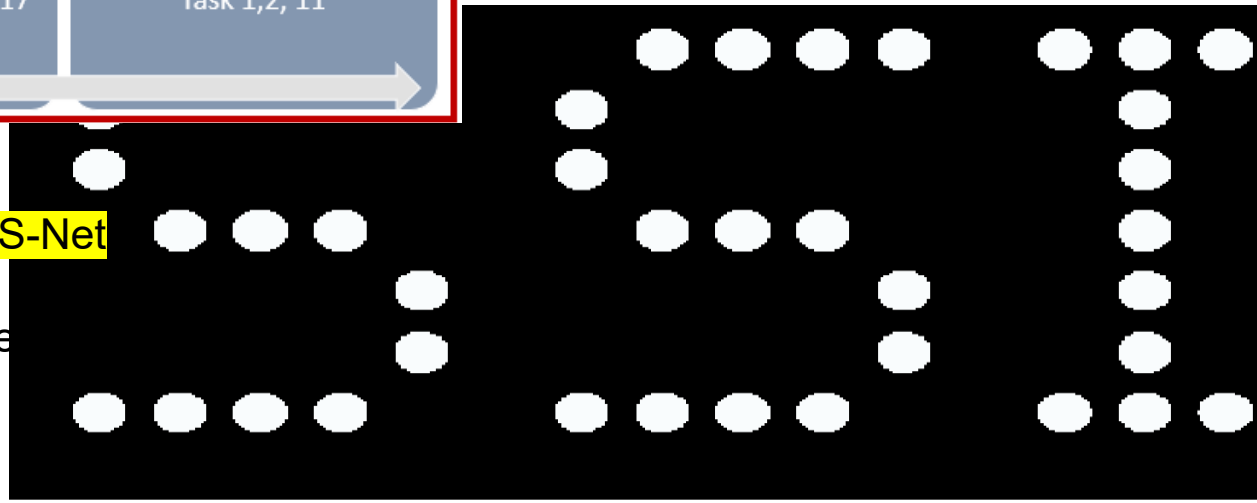


EDL

- Reference testing (phenotypic and functional AMR)
- Guidance/protocols
- Support to other activities

DTU

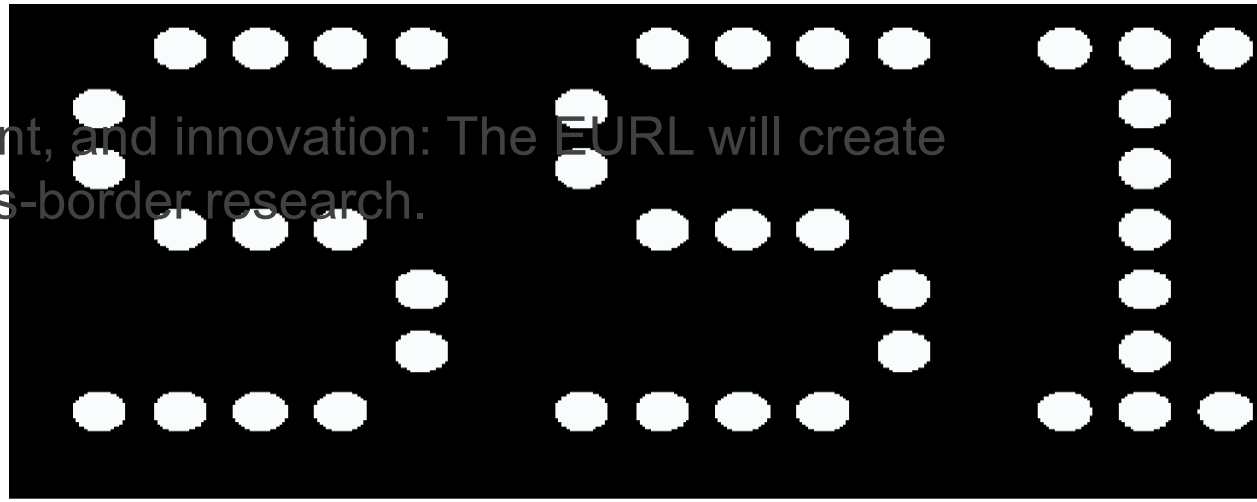
- EQAs for EARS-Net
- Training
- Support to othe



EURL functions not in EURGen-RefLabCap (in yellow)

THE NETWORK WILL ADD VALUE BY:

- Strengthening the role of **NRLs to build capacities** through networks of local/regional laboratories in the health systems of their countries.
- Modernising of **diagnostic and molecular typing** tests using **WGS** for genomic surveillance, providing capacity and competences to improve detection, diagnosis and treatment of infectious diseases.
- Closing current knowledge gaps: **spread of high-risk clones** to enable EU to act and control emerging clones more rapidly.
- Encouraging and **boosting research**, development, and innovation: The EURL will create opportunities for laboratories to participate in cross-border research.



Overview of European Commission/ECDC* activities to boost genomic epidemiology

Access to high-capacity, rapid turn-around time WGS services

HERA Incubator

Cross-border capacity-building support programme

Ensure WGS capacity in NRLs (EURGen-RefLabCap & FWD-AMR-RefLabCap)

Increase bioinformatic capacity and integration of WGS in Public Health

Training of Bioinformaticians and non- bioinformaticians in implementation of WGS in public Health (GenEpi-BioTrain)

EU-RL public health

EURL-AMR

2021 2022 2023 2024 2025

*: Either implemented directly by ECDC, or implemented by HERA/HaDEA with ECDC technical input and support

Thank you!

Acknowledgements

- Anders Rhod Larsen, SSI
- Oskar Ekelund, EDL
- Gunnar Kahlmeter, EDL
- Rene S. Hendriksen, DTU
- Birgitte Helwigh, DTU
- DG SANTE
- HaDEA
- ECDC

EU-JAMRAI Joint Action Antimicrobial Resistance and Healthcare-Associated Infections

Co-funded by the European Union

Presentation of the EU-JAMRAI 2 project

Network Meeting EURGen-RefLabCap

at DTU

JAMRAI 2 is co-funded by the European Union under Grant Agreement No 101127787

"Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them"

19. September 2024

Asja Kunøe, MD, National Center for Infection Control (CEI), Statens Serum Institut, Denmark

Background

- The AMR challenge, EC council recommendations, EU-JAMRAI 1

Objectives of the project

Work package 1-10

- and "the EU-JAMRAI-liason"

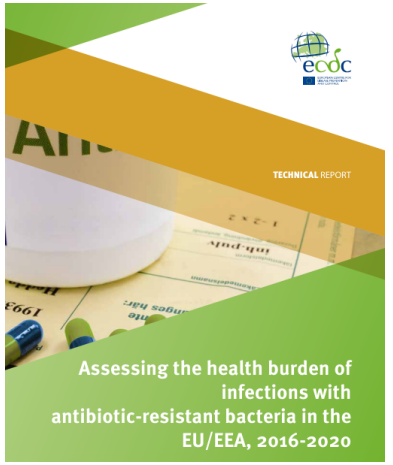
The Danish involvement

AMR is a global challenge for public health

<u>Antibiotic resistance at "a glace" in Europe:</u>

- 35,000 deaths yearly caused by an infection with a AB-resistant bacteria
- 70% of infections with AB-resistant bacteria are HAI
- 1,005,388 million lost years (DALY) yearly
- Estimated societal cost of about €1.5 billion each year, ref.:

https://webgate.ec.europa.eu/amr/



<u>Microbes know no borders:</u>

- Can cross ecosystems and countries borders

EUROPEAN COMMISION Council recommendation on stepping up EU actions to combat antimicrobial resistance in a One Health approach, June 2023

- Urge the MS to have in place (1 year after the recommendations) and regurlarly update, implement and evaluate **NAPs against AMR**
- Close existing surveillance and monitoring gaps and **ensure completeness of data, including real-time data and timely access to data** where appropriate by 2030, on both **AMR and AMC** at all levels
- Ensure that **IPC measures in human health are put in place** and continuously monitored to contribute to limiting the spread of antimicrobial resistant pathogens
- Take measures to **improve the health and welfare of food-producing animals** in order to decrease the occurrence and spread of infectious diseases in farming
- Ensure that measures are put in place in human health to **support the prudent use of antimicrobial agents**, in health care settings, including primary health care settings and long-term care facilities, and community care
- Recommended **targets by 2030 for antimicrobial consumption and antimicrobial resistance** - see the specific reduction targets per country in the appendix
- **And much more**: https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32023H0622(01)

EU-JAMRAI 1 (2017-2021):

10 POLICY BRIEFS with "several recommendations including the need to define targets and indicators for monitoring the National Action Plans (NAP), core competencies for AMS and IPC in EU, and actions to increase European access to important antibiotics"

Need to strengthen the AMR networking in Europe

Need to focus on sustainability (e.g. lack of workforce in health care)

Need to focus on implementation of concrete actions

- Antimicrobial stewardship
- Infection Prevention and Control

30 countries work together in EU-JAMRAI 2

- Co-financed by EU (80%)
- Total grant: 50,000,000 €
- 4-year-project: 01-01-2024 to 31-12-2027
- 30 countries (27 MS, Iceland, Norway and Ukraine), 128 partners, 40 stakeholders
- https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/projects-details/43332642/101127787/EU4H
- https://globalamrhub.org/news/eu-jamrai-2-meeting-european-union-joint-action-on-antimicrobial-resistance-and-healthcare-associated-infections/

EU-JAMRAI 2: Objectives

- https://eu-jamrai.eu/about/#general-objectives
- https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/projects-details/43332642/101127787/EU4H

WP6 Antimicrobial stewardship in humans, animals and environment

- https://eu-jamrai.eu/stewardship/

WP7 Improve the Infection Prevention and Control (IPC) actions with a One Health approach

- https://eu-jamrai.eu/prevention-control/

WP8 Integrated One Health surveillance

- https://eu-jamrai.eu/surveillance/

WP9 Access

https://eu-jamrai.eu/access/

THE DANISH INVOLVEMENT:

Statens Serum Institut represents Denmark as "competent authority" in the second EU Joint action on Antimicrobial Resistance and Healthcare Associated Infections

Statens Serum Institut (National Center for Infection Control (CEI), Bacteria, Parasites & Fungi(BPS)) – Infection Prevention and Control, Surveillance and Acces (WP7, WP8, WP9) – *Human sector*

National Health Authority (Sundhedsstyrelsen): NAP and AMS (WP5 and WP6) – *Human sector*

University of Copenhagen (KU): AMS, IPC and Surveillance (WP6, WP7, WP8) – *Veterinary sector (and environmental sector in WP6)*

Danish Technical University (DTU): Surveillance (WP8) – *Human sector*

EU-JAMRAI Joint Action Antimicrobial Resistance and Healthcare-Associated Infections

Co-funded by the European Union

Asja Kunøe

asku@ssi.dk

EU-JAMRAI 2 receives funding from the European Union's EU4Health programme under grant agreement No 101127787. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

BUILDING A ONE HEALTH WORLD

to reduce Antimicrobial Resistance (AMR)