



TERVISEAMET

EURGen-RefLabCap projekt

CRE, CCRE seire täiustamine

Nakkushaiguste labor

Terviseamet

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AVATUD

HOOLIV

EURGen-RefLabCap projekt

* *European Antimicrobial Resistance Genes Surveillance Network (EURGen-Net)*

37 riiki Euroopas

* *EURGen-RefLabCap - 4a projekt (12.2020-12.2024) – fookuses CRE/CCRE**

* *Rahastatud ECDC poolt. Projekti töövõtjaks (contractor) Taani Tehnika Ülikool (DTU Food) ja Statens Serum Institut (SSI)*

* *Eesti poolt osalevad: TA, ITK ja PERH-i esindajad*

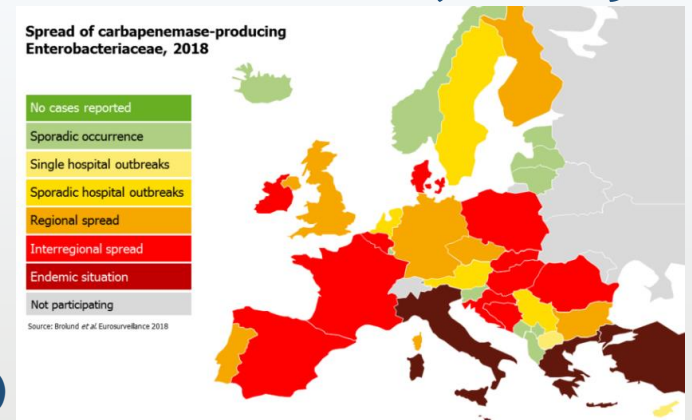
* **Projekti eesmärk: tugevdada ref.laborite võimekust määrata ja efektiivselt kontrollida CRE ja/või CCRE* levikut tervishoiuasutustes rahvuslikul, EU ja globaalsel tasandil.**

* **Peamised ülesanded:**

* **ref.laborite võimekuse suurendamine;**

* **AMR määramisvõimekuse parandamine;**

* **diagnostiliste, molekulaarse tüpiseerimise testide kaasajastamine (WGS)**



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* **CRE/CCRE – carbapenem/carbapenem and colistin resistand Enterobacterales**

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*Juuli-sept 2021 täitsid EL riigid küsimustiku 5 põhifunktsiooni kohta defineeritud ECDC poolt:



The questions were aimed at **gaining more detailed and up-to-date information on the current situation** in each of the participating countries in order to **plan the activities of the entire network** and to identify a **number of priority countries**



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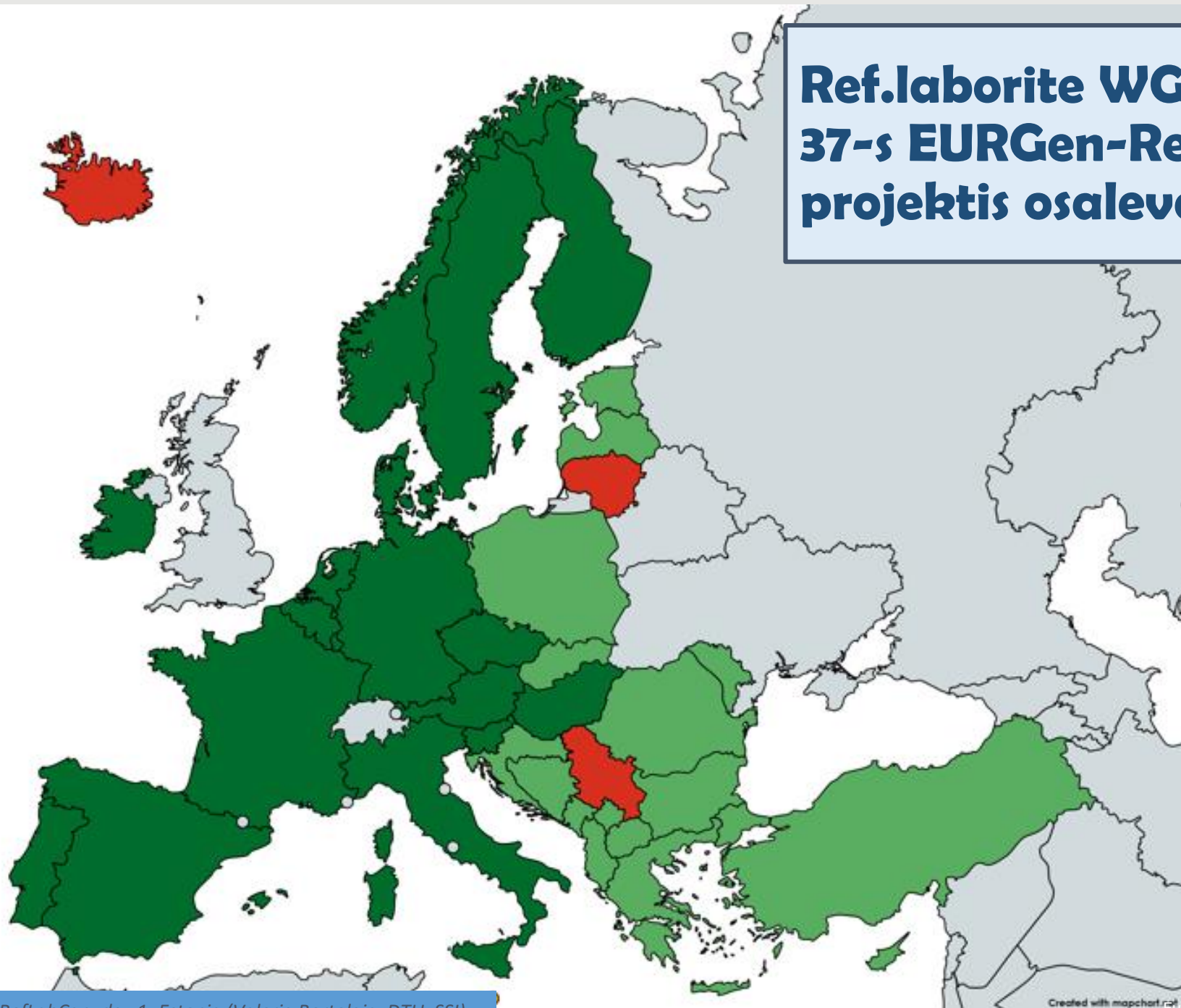
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Capacity for WGS

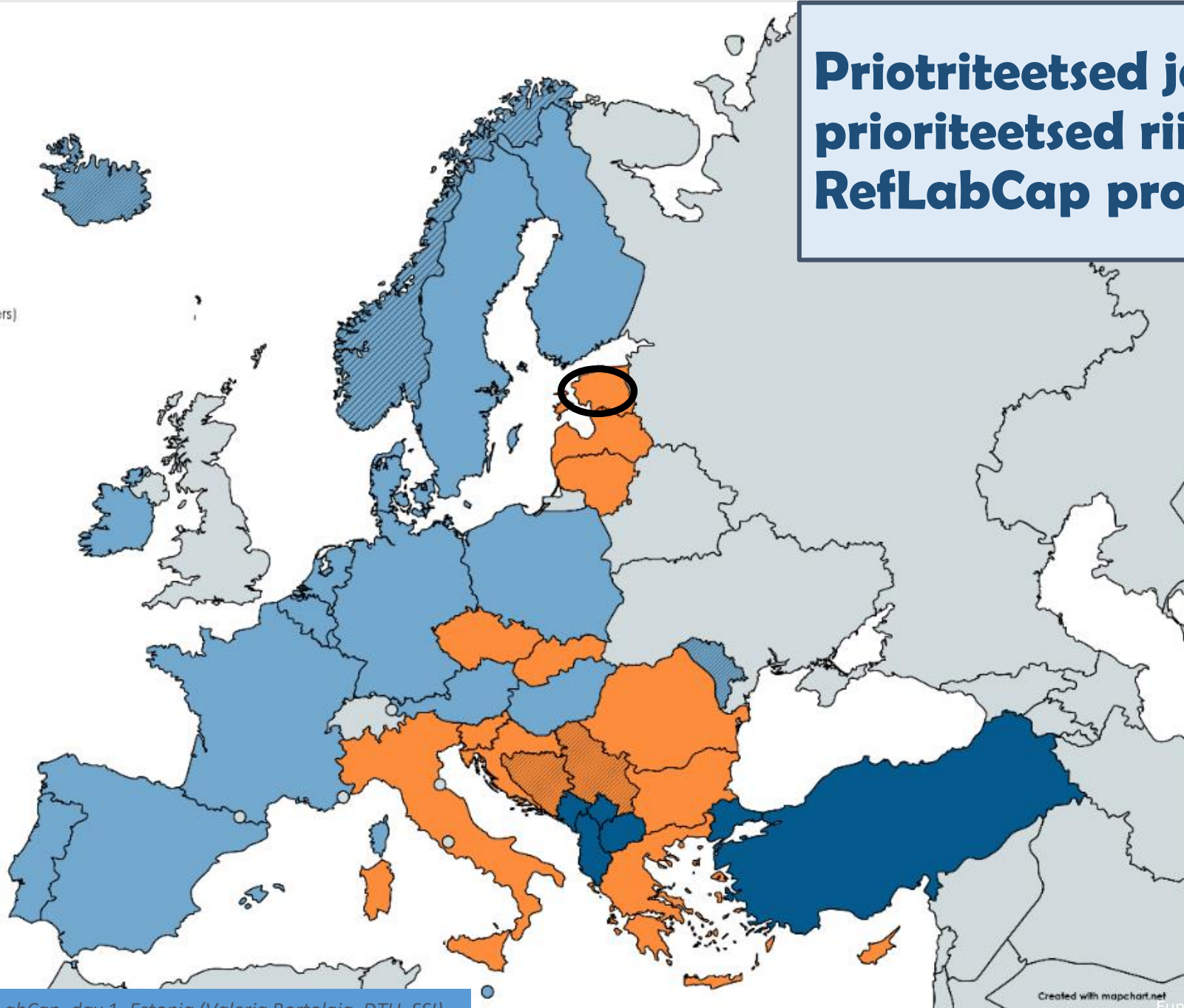
- WGS is employed
- WGS is planned
- WGS is not employed nor planned
- Need for clarification



**Ref.laborite WGS võimekus
37-s EURGen-RefLabCap
projektis osalevas riigis**

Participating countries

- Identified Priority Countries (EU members)
- Identified Priority Countries (non EU members)
- Countries included in the Third EU Health Programme (EU members)
- Countries included in the Third EU Health Programme (non EU members)
- Countries not included in the Third EU Health Programme (non EU members)



Priortiteetsed ja mitte-priortiteetsed riigid EURGen-RefLabCap projektis



EURGen-RefLabCap – projekti ülevaade

Pakkuda ELi võrgustikku ja toetust rahvatervise ref.labori funktsioonide osas AMR uurimiseks tervishoiuga seotud prioriteetsete nakkuste puhul.



Tugevdada ref.labori rolli rahvatervise valdkonnas, et parandada piirkondlike ja kohalike laborite võimekust.



Diagnostiliste ja molekulaarsete testide ajakohastamine kasutades WGS-i.



Kiirem reageerimine tekkivatele või epideemilistele AMR-seotud infektsioonidele, vähendades AMR- infektsioonidega seotud suremust ja haigestumust ning suurendades patsiendi ohutust.

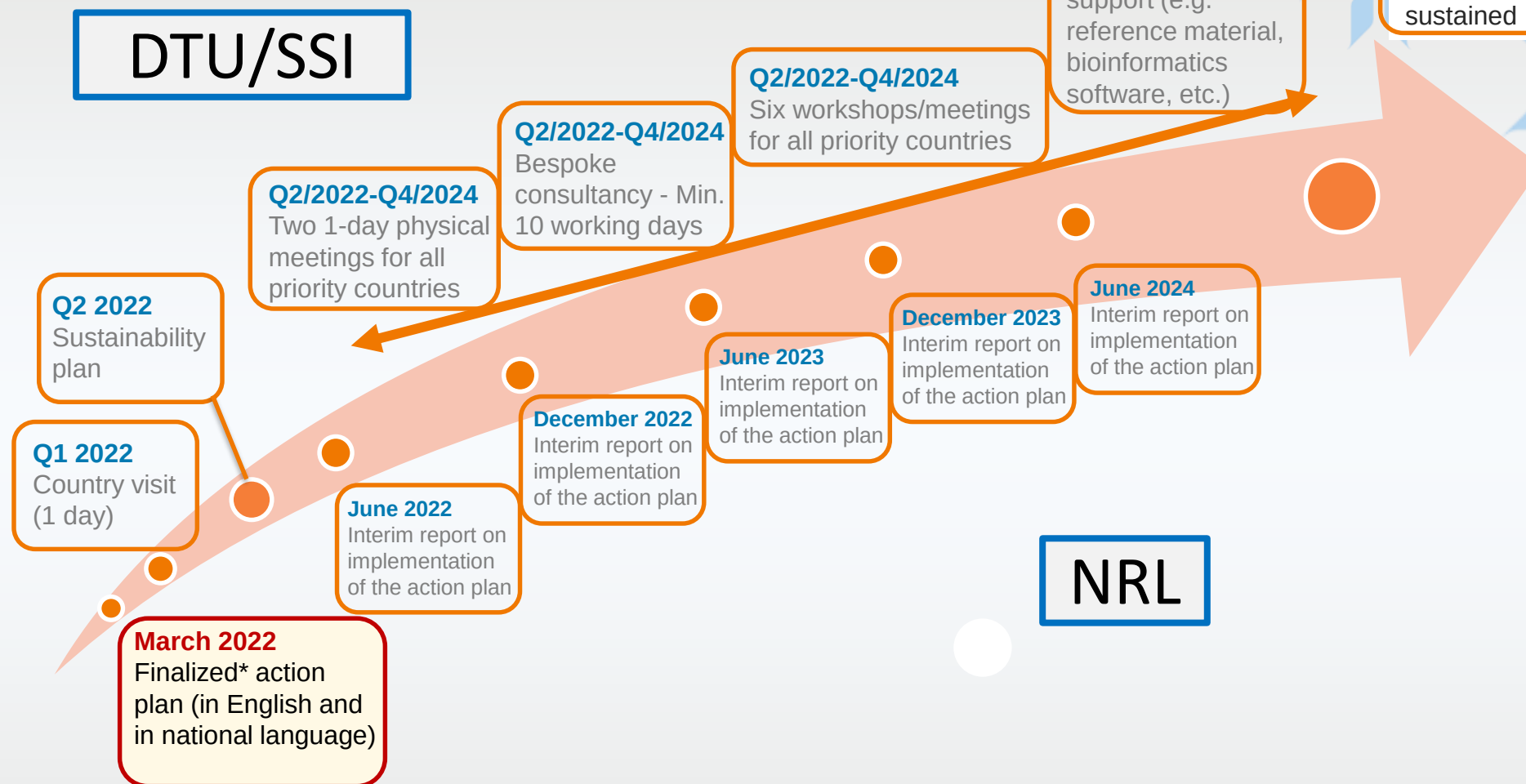
Projekti eesmärk

Üldeesmärk on suurendada ELi tasandil edastatud seireandmete täpsust kooskõlas ELi uute AMR juhtumite määratlustega, et anda teavet kooskõlastatud meetmetest AMR osas ning võimaldada paremini avastada ja kontrollida AMR põhjustatud piiriüleseid ohte inimeste tervisele.

Projekti oodatav tulemus

Tugevdada AMR seiresüsteemide katvust, õigeaegsust ja kasutatavust AMR-i edastamise kontrollimiseks kohalikul, piirkondlikul ja riiklikul tasandil, mis parandab AMR-i varajase hoiatamise ja sihipärase kontrolli tõhusust, suurendab valmisolekut ja annab täiendavat teavet AMR ohjeldamise tegevuste ja poliitikate hindamiseks.

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*Important! It will be possible to revise and reassess the action plan during the project



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Resistentsete *K. pneumoniae* ning *E. coli* tüvede esinemine Euroopas



- * **ECDC Sureillance Atlas of Infectious Diseases**
- * **Data on antimicrobial resistance in *Klebsiella pneumoniae* collected by the European Antimicrobial Resistance Surveillance Network (EARS-Net). Only data from invasive (blood and cerebrospinal fluid) isolates are included in EARS-Net.**

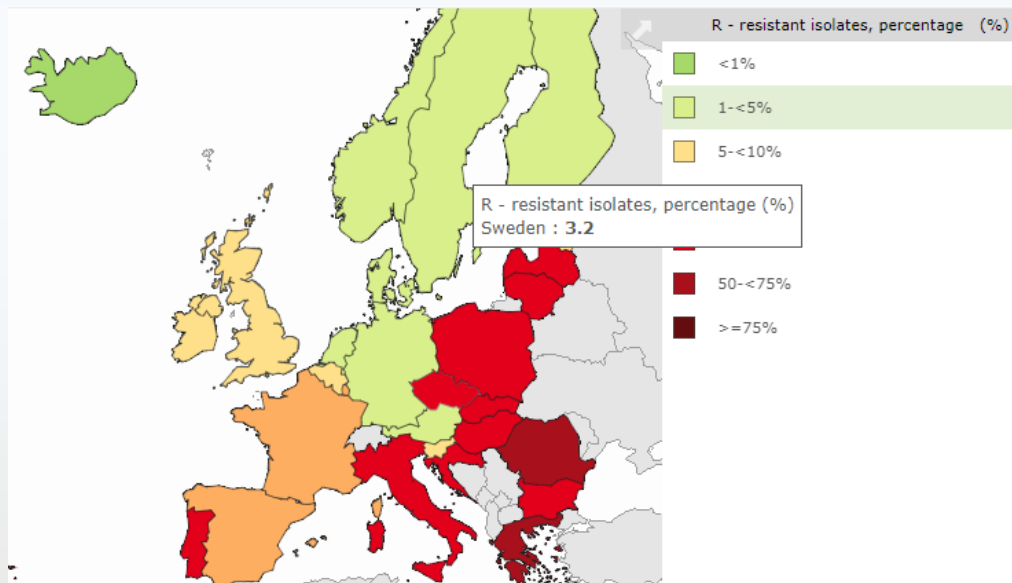


Klebsiella pneumoniae

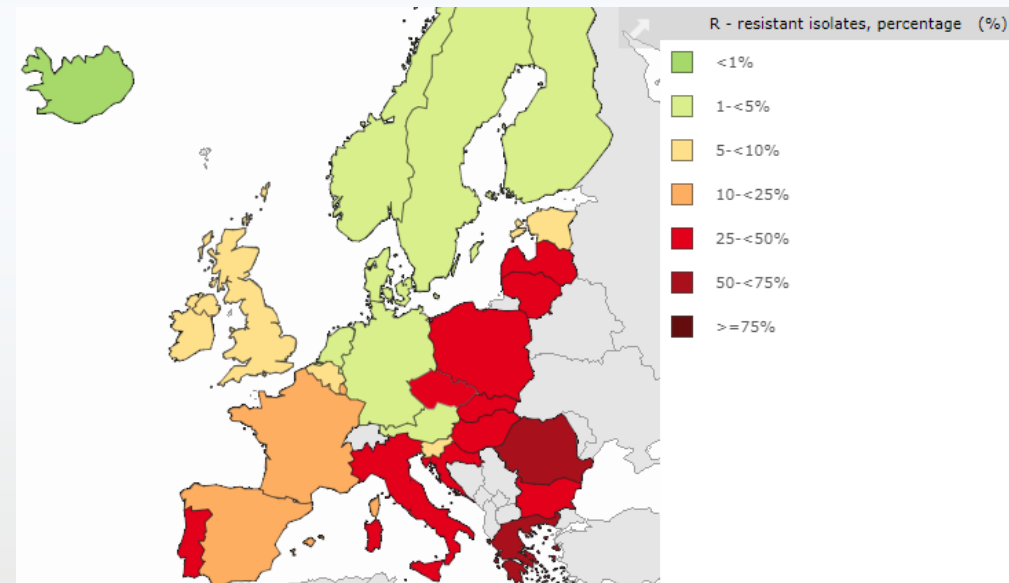


✱ **Combined resistance (third-generation cephalosporin, fluoroquinolones and aminoglycoside)**

✱ **2019. Eesti – 5,6%**



2020. Eesti – 7,1%



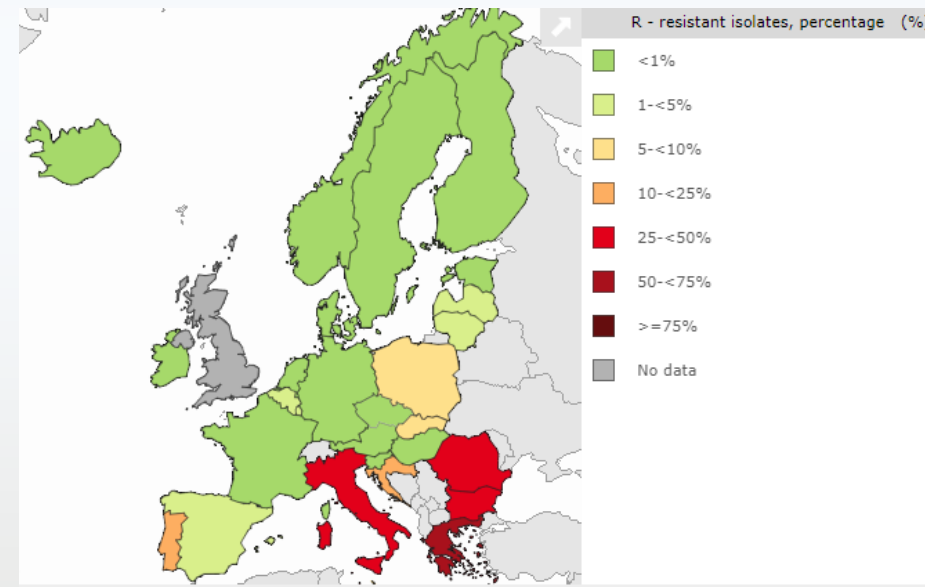
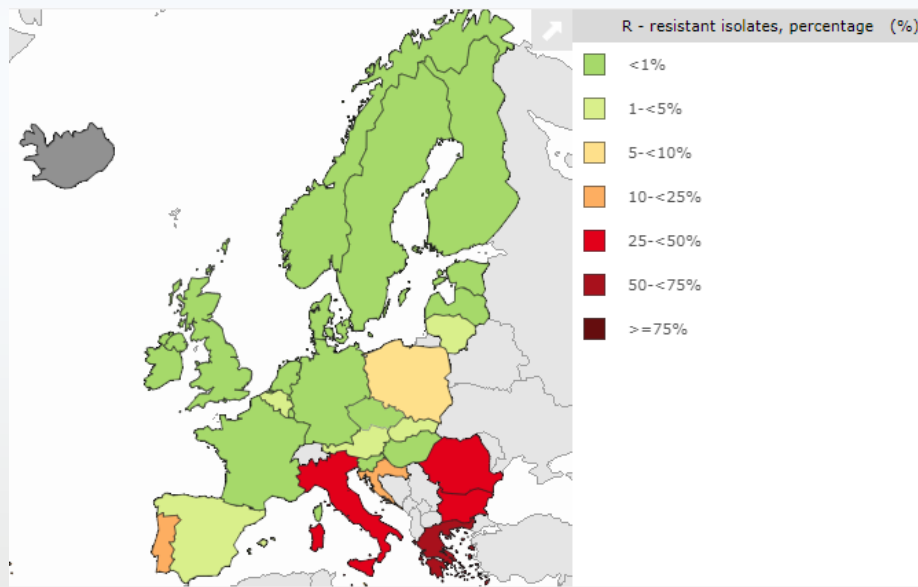
Klebsiella pneumoniae



* Carbapenem resistance

* 2019. Eesti – 0,0%

2020. Eesti – 0,0%



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Projekti *action plan alus* (template) , kust iga riik valib enda jaoks olulisimad eesmärgid:

		CORE FUNCTION 1 - Reference diagnostics							Risks				PROGRESS MONITORING			
OBJECTIVES	ACTIVITIES / SOLUTIONS	INDICATORS /COMMENT S	NEEDED RESOURCES (personnel, knowledge, financial)	TIMEFRAME	STATUS	ORGANIZATION and CONTACT	D: Deliverables	M: Milestone	O: Ongoing activity							
To participate in EQAs	EQA for phenotypic testing methods: EQA for WGS and bioinformatics pipelines. Participate in international interlaboratory EQA exercise in silico. Performs corrective actions (in the NRL) when EQA performance criteria re not met															
To facilitate EQA for clinical laboratories	NRL arranges EQA for clinical laboratories. NRL feedbacks regarding corrective actions when EQA performance criteria are not met															
To hold accreditation for characterisation of CRE and/or CCRE																
To perform phenotypic AST according to reference methods including use of control strains from a reliable source																
To have an internal quality control scheme/quality management systems (QMS)																
To have defined laboratory and bioinformatic approaches and methods		Personnel is trained or hired, and/or service is outsourced. Analytical pipeline is build using open source or commercial software														
To perform quality control testing of WGS	The NRL performs quality control testing on WGS runs and bioinformatic analysis	E.g. list of quality parameters that are used for quality control testing (e.g. number of reads, PHRED scores, average read depth, etc.)														
To upload WGS data for sharing purposes	The NRL uploads WGS data to repositories for sharing purposes (with/without metadata)	Data-sharing protocol has been developed														
To report WGS data to the clinical laboratories	The NRL reports WGS data and interpreted WGS data to the clinical laboratories	Reports to clinical laboratories includes: AST patterns, plasmid typing, changes in occurrence, outbreak detection, etc.														
To use controls from a reliable source for methods other than WGS (ONLY RELEVANT WHEN PCR IS USED)																
To provide reference services for CRE/CCRE	Establish service agreement(s) between the NRL and the public health authorities and clinical laboratories (including how to ship the samples, metadata required, etc.). Develop user handbook that guides the users' (clinical laboratories, others) on how to use the NRL services. Monitor referral of CRE, CCRE and other AMR isolates, testing of isolates and associated cost and time spent. Ensure adequate resourcing.	Hospitals, clinical laboratories and other stakeholders have been identified														
To ensure correct species identification	The NRL performs confirmatory species identification and/or supports the clinical laboratories on performing correct species identification															
To use international guidelines for confirmatory testing and further characterisation of CRE/CCRE at the NRL																
To offer WGS-based reference services	Define the objectives of NRL WGS services (e.g. surveillance and outbreak puposes, species ID, antimicrobial resistance genotyping, prediction of susceptibility)															
	Named genes and pathogens are characterised by WGS at the NRL (develop documentation that defines remit of reference testing by WGS)															
To create a standard operating procedure to identify profiles of atypical and unusual CRE/CCRE isolates																
To collect and test profiles of atypical and unusual CRE/CCRE isolates																

Ref	Diagn (1)	Reference material (2)	Monitoring-Alert (5)
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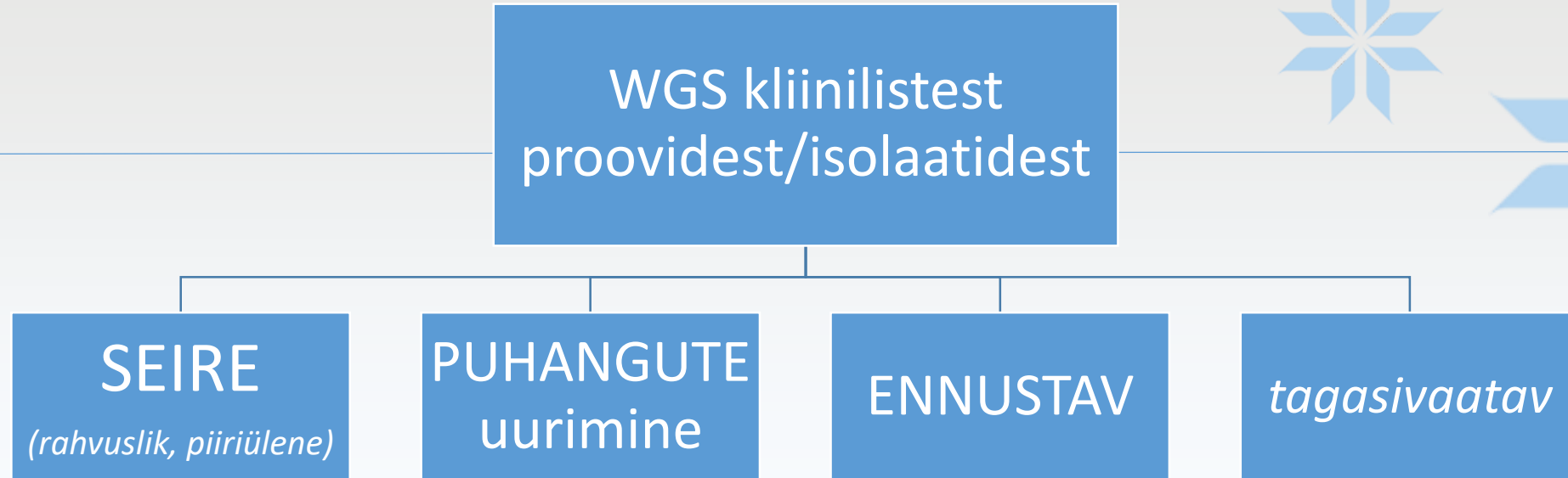
Planeeritud eesmärgid projektis osalemisel:

*Lähituleviku eesmärgid:

- ***sekveneerimise võimekuse loomine, selle kasutamine nii käesoleval kui ka eelmistel aastatel ringlevate tüvede kaardistamiseks ning puhangute tuvastamiseks.**
- ***biopank (tüvede kogumine, säilitamine ja vajadusel jagamine) + kontrolltüvede kogum.**
- ***juhiste koostamine ja avalikustamine TA kodulehel: *CRE/CCRE referral criteria*. Küsitluse korraldamine eesmärgiga kaardistada Eesti kliiniliste laborite CRE/CCRE diagnostiline võimekus (sellest tulenevalt kaardistada vajadused ning planeerida ref. labori tegevust).**
- ***2021. a AMR laboriandmete analüüs lähtudes TIS-st ning ülevaade avalikustamine.**



CRE/CCRE sekveneerimise peamised eesmärgid:



* Lühiajaline eesmärk:

- * Sekveneerida hetkel ringlevaid tüvesid
- * Saada ülevaade ringluses olevatest tüvedest ja nende seotusest

* Pikaajaline eesmärk:

- * Suurendada seire võimekust rahvuslikul ja EU tasandil
- * Suurendada valmisolekut haiguspuhanguteks



NHL sekvenaator – minION ja gridION (Oxford Nanopore Technologies)

- *kulutõhus, kiire, pikk „lugemine“, vastupidav tehnoloogia, reaajas, ülitäpne DNA ja RNA järjestus, hõlpsasti rakendatav pilvepõhine platvorm (EPI2ME).
- *sekveneerimist saab teha paljude lähteproovide puhul, genoomne DNA ja cDNA – sh sihipärane sekveneerimine ja DNA modifikatsioonide tuvastamine.



	Flongle	MiniON	GridION (5 flow cells)
			
Maximum run time	16 hours	72 hours	72 hours
Theoretical 1D maximum yield	Up to 3.3 Gb	Up to 40 Gb	Up to 200 Gb
Current 1D maximum yield	Up to 2 Gb	Up to 30 Gb	Up to 150 Gb
Available channels 850 × 371	Up to 126	Up to 512	Up to 2,560



Kliinised proovid/isolaadid (CRE/CCRE)

-> MaldiTOF + PCR (*vajadusel*)



gDNA eraldamine



QC

Sekveneerimiseks ette valmistamine
(raamatukogu valmistamine)



Server
Andmete säilitamine



Bioinformatika

QC

Computation

Databases, alignment

...



Report



LIS

**Report to clinical
laboratories**

**Results to public
health system**

ENA – European Nucleotide Archive



Other relevant International database

ECDC, TESSy



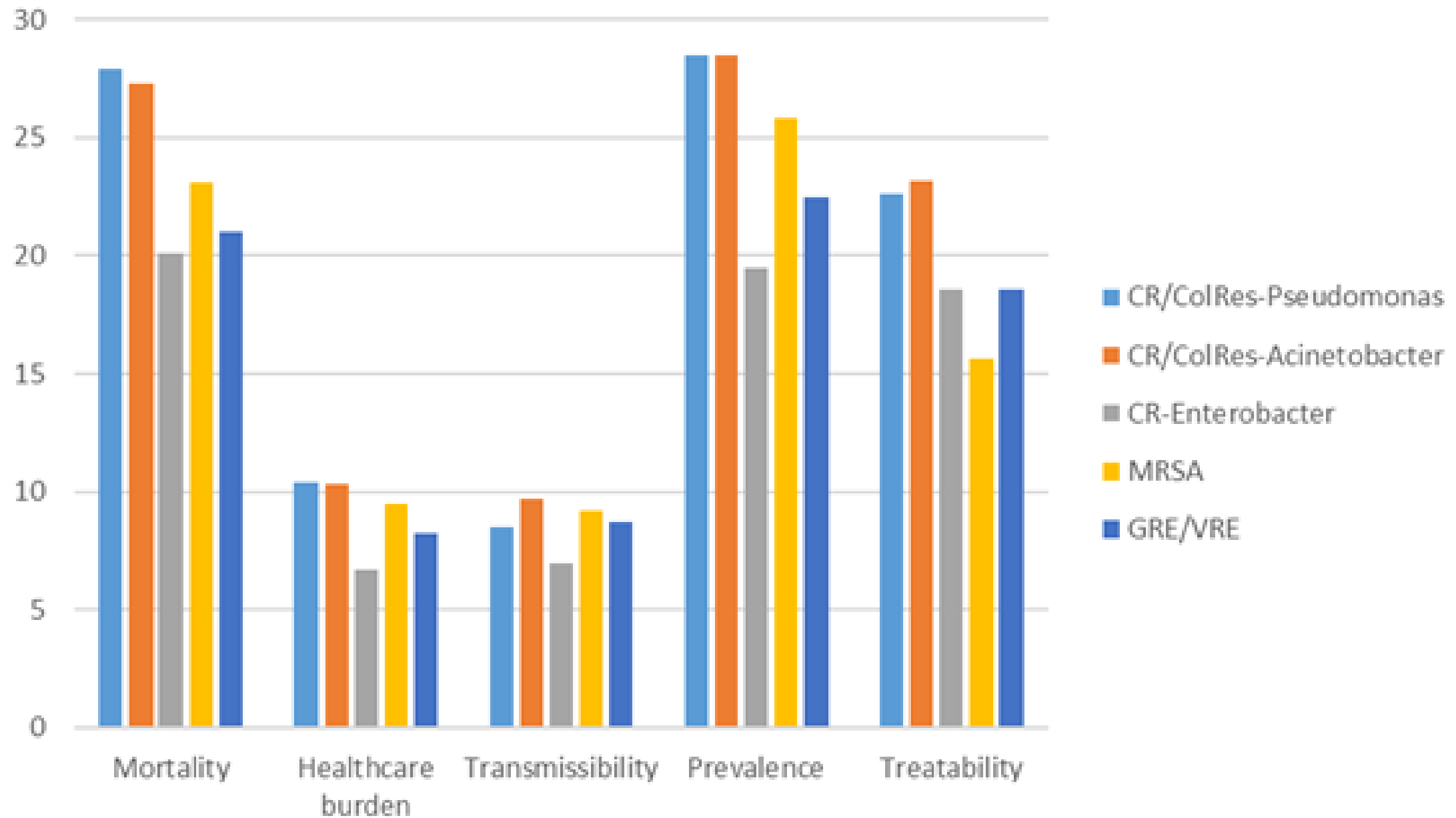
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WEIGHTED scores across 25 countries (by category)





Täna kuulamast!



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