



Food- and Waterborne Diseases Antimicrobial Resistance – Reference Laboratory Capacity

FWD AMR-RefLabCap

Eva Møller Nielsen, Statens Serum Institut, Denmark





Provision of EU networking and support for public health reference laboratory functions for antimicrobial resistance in *Salmonella* and *Campylobacter* in human samples

- The project is run under a contract with HaDEA on behalf of DG SANTE and in close cooperation with ECDC
- 4-year project: 2021-2024
- Contractors:
 - Statens Serum Institut (SSI)
 - Project leader: Eva Møller Nielsen, Section of Foodborne Infections
 - National Food Institute, Technical University of Denmark (DTU)
 - René Hendriksen, Research group for global capacity building

OBJECTIVES



- Support countries to enhance the validity and accuracy of surveillance data in order to inform concerted actions against AMR at EU level and enable better detection and control of cross border threats to human health from AMR
- AMR in Salmonella spp and Campylobacter spp in human samples
- Participants:
 - Countries participating in the EU Health programme
 - Candidate and potential candidate countries, other funding
- Cooperation with ECDC, DG SANTE and when relevant also EFSA and EURLs in the food safety area
 - EURL-AR, -Campylobacter, -Salmonella + inter-EURL working group on NGS

OVERVIEW OF TASKS



Networking and capacity building activities provided to national public health reference laboratories to improve their functions for AMR surveillance of human *Salmonella* and *Campylobacter* infections

Modernisation of methods for diagnostics, typing and AMR by using whole genome sequencing (WGS)

Activities to support the role of NRLs for public health to work with and **build capacities in the regional and local laboratories** in their own countries

Two pathogens: Salmonella spp and Campylobacter spp in humans

A specific focus on countries where capacities are less well developed

Establishing a laboratory network



Network meetings, workshops, online presentations

- exhange of experience, best practice, inspiration
- discussions on NRL requirements, protocols, feedback on activities
- complementarity with work carried out by the relevant EURLs in the food safety area

Capacity building

Networking

Website: Protocols, guidance docs, training material, links

Training

Methods

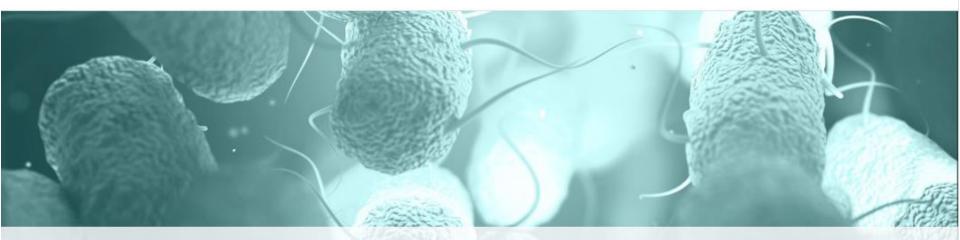
Project website: www.fwdamr-reflabcap.eu







Resources EQAs Events Participants News Q



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FWD AMR· RefLabCap

12 May 2021 Welcome to FWD AMR-RefLabCap

News

30 November - 1 December 2021 (tentative) - Network meeting at SSI, Copenhagen, Denmark 10 September 2021

7 September - online meeting 10 September 2021

Welcome to FWD AMR-RefLabCap 12 May 2021

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Home / Participants

Participants

Laboratories participating in the FWD AMR-RefLabCap network

Updated 8 July 2021

Albania

Institute of Public Health Laboratory of Enterobacteriology

Austria

Austrian Agency for Health and Food Safety, Institute for Medical Microbiology and Hygiene Graz National Reference Centre for Salmonella

Austrian Agency for Health and Food Safety, Institute for Medical Microbiology & Hygiene, Centre for Foodborne Infectious Diseases National Reference Centre for Campylobacter

Belglum

Sciensano Sciensano - NRC salmonella

NRC Campylobacter - University Laboratory Brussels LHUB-ULB - NRC Campylobacter

Bosnia and Herzegovina

Public Health Institute of The Republic of Srpska Department of Microbiology

Bulgaria

National Center for Infectious and Parasitic Diseases NRL of Enteric Infections, Pathogenic cocci and Diphtheria

Croatla

Croatian Institute of Public Health

43 laboratories from 36 countries



- Laboratories in 32 EU/EEA countries + EU Health Programme invited to participate
 - Participation of 38 laboratories in 31 countries
- Laboratories in 5 candidate/potential candidate countries are invited as "observers" (separate funding)
 - 5 laboratories in 5 countries
- Total of 38 laboratories in EU/EEA + EU Health Programme countries
 - 22 NRLs cover both Campylobacter and Salmonella
 - 7 NRLs of Campylobacter
 - 9 NRLs of Salmonella
- Western Balkans and Turkey (enlargement countries)
 - 5 NRLs of both Campylobacter and Salmonella

NRL functions and gap analysis



Minimum and optimal requirements in PH NRL functions

- Recommended coverage of surveillance
- Sampling and testing frequency
- Epi-situations for isolation & referral of isolates from primary to national level
- Methodological and resource capacity and capability requirements at all levels
- Identify capacity/capability gaps in all countries
 - Existing information
 - Survey in network







Capacity building



- Capacity building activities for all NRLs
 - Lab training courses
 - Workshops and surveillance exercises on integrated WGS-based surveillance

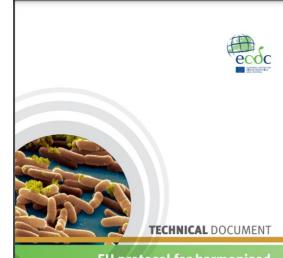
- Tailored support to 'priority countries'
 - country visits
 - action plans



Modernisation of methods



- Propose optimal methodologies for AMR detection, integrated into WGS-based surveillance for cluster detection
 - Existing guidance and literature, incl. bioinformatics and databases
 - Seek consensus experts/ECDC/EFSA/EUCAST
 - Set of common methods and standard protocols for national surveillance
 - Agreement in network
- Any relevant methodologies developed by EURLs shall be taken into account to ensure complementarity
- Review/amend existing EU protocol for AMR surveillance to include genetic AMR determinants



EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates

June 2016

Scientific papers on WGS-based AMR and typing



European Journal of Clinical Microbiology & Infectious Diseases (2021) 40:673-682 https://doi.org/10.1007/s10096-020-04043-y

ORIGINAL ARTICLE



Prediction of antimicrobial resistance in clinical Campylobacter jejuni isolates from whole-genome sequencing data

Louise Gade Dahl¹ · Katrine Grimstrup Joensen¹ · Mark Thomas Østerlund¹ · Kristoffer Kiil¹ · Eva Møller Nielsen¹

Received: 14 July 2020 / Accepted: 17 September 2020 / Published online: 24 September 2020 (© The Author(s) 2020

Abstract

Campylobacter jejuni is recognised as the leading cause of bacterial gastroenteritis in industrialised countries. Although the majority of *Campylobacter* infections are self-limiting, antimicrobial treatment is necessary in severe cases. Therefore, the development of antimicrobial resistance (AMR) in *Campylobacter* is a growing public health challenge and surveillance of AMR is important for bacterial disease control. The aim of this study was to predict antimicrobial resistance in *C. jejuni* from whole-genome sequencing data. A total of 516 clinical *C. jejuni* isolates collected between 2014 and 2017 were subjected to WGS. Resistance phenotypes were determined by standard broth dilution, categorising isolates as either susceptible or resistant based on epidemiological cutoffs for six antimicrobials: ciprofloxacin, nalidixic acid, erythromycin, gentamicin, streptomycin, and tetracycline. Resistance genotypes were identified using an in-house database containing reference genes with known point mutations and the presence of resistance genes was determined using the ResFinder database and four bioinformatical methods (modified KMA, ABRicate, ARIBA, and ResFinder Batch Upload). We identified seven resistance genes including *tet(O)*, *tet(O/32/O)*, *ant(6)-la*, *aph(2")-lf*, *blaOXA*, *aph(3")-III*, and *cat* as well as mutations in three genes: *gyrA*, *23S rRNA*, and *rpsL*. There was a high correlation between phenotypic resistance and the presence of known resistance genes and/or point mutations. A correlation above 98% was seen for all antimicrobials except streptomycin with a correlation of 92%. In conclusion, we found that WGS can predict antimicrobial resistance with a high degree of accuracy and have the potential to be a powerful tool for AMR surveillance.

Whole-Genome Sequencing to Detect Numerous *Campylobacter jejuni* Outbreaks and Match Patient Isolates to Sources, Denmark, 2015–2017

Katrine G. Joensen, Kristoffer Kiil, Mette R. Gantzhorn, Birgitte Nauerby, Jørgen Engberg, Hanne M. Holt, Hans L. Nielsen, Andreas M. Petersen, Katrin G. Kuhn, Gudrun Sandø, Steen Ethelberg, Eva M. Nielsen

Emerging Infectious Diseases Vol. 26, No. 3, March 2020

Whole genome sequencing data used for surveillance of *Campylobacter* infections: detection of a large continuous outbreak, Denmark, 2019

Katrine Grimstrup Joensen¹, Susanne Schjørring¹, Mette Rørbæk Gantzhorn², Camilla Thougaard Vester², Hans Linde Nielsen^{3,4}, Jørgen Harald Engberg⁵, Hanne Marie Holt⁶, Steen Ethelberg⁷, Luise Müller⁷, Gudrun Sandø², Eva Møller Nielsen¹

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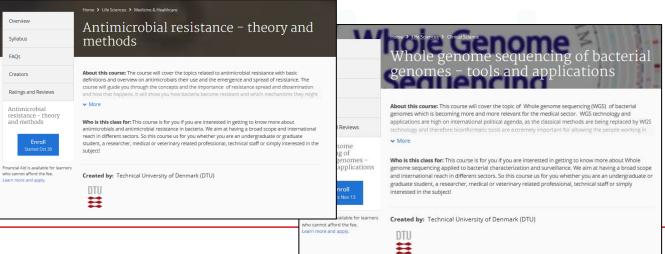
Euro Surveill. 2021;26(22):pii=2001396

Implementation of WGS – training and EQAs



- Multi-disciplinary training workshops and webinars for PH epidemiologists
 - integration of WGS into national AMR surveillance and outbreak investigation
- EQAs of WGS-based resistome profiling
 - complement ongoing EQA schemes
 - 3 rounds for all NRLs

Inter-laboratory ring-trials of bioinformatics pipelines for prediction of AMR



EQAs on antimicrobial susceptibility testing (ECDC)

- Support the implementation of the harmonized EU AST protocol for Salmonella and Campylobacter in NPHRLs
- Assess the quality of the AST data (MIC and DD methods) across Europe
- Allow evaluation of new molecular based methodologies

EQA 2020 round: 21 EU/EEA countries participated

- 13 reported disk diffusion results
- 12 reported MIC results, broth dilution or gradient strip
- 4 reported predicted results based on WGS





TECHNICAL DOCUMENT

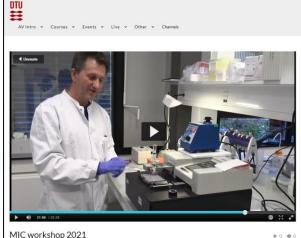
EU protocol for harmonised monitoring of antimicrobial resistance in human *Salmonella* and *Campylobacter* isolates

June 2016

Support NRLs to build capacities in local/regional labs

- Support all NRLs in mapping the regional/local labs' capacities for detection and characterization of Salmonella and Campylobacter
 - Strengths/weaknesses and gaps/further needs for each country
- Support NRLs to carry out regional capacity building (≥16 MSs)
 - Physical and online meetings and workshops
 - Learning material
 - Ongoing individual support

- Support NRLs to establish national network of labs
- Model protocol for national surveillance of AMR in Salm/Campy
- Suidance for internal QC schemes for reference AMR testing





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WWW. FWDAMR-RefLabCap.EU

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