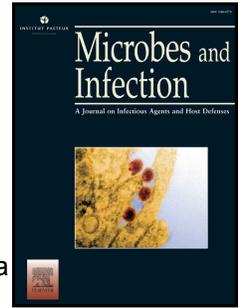


# Journal Pre-proof

Conference report: The second Bacterial Genome Sequencing Pan-European Network conference

Kuangyi Charles Wei, Srinithi Purushothaman, Francesca Azzato, Kate S. Baker, Kira Waagner Birkeland, Sofia Brunet, Josefina Campos, Thomas R. Connor, Christian G. Giske, Gilbert Greub, Erika Tång Hallbäck, Dag Harmsen, Emma B. Hodcroft, Matthew T.G. Holden, Jobin Jacob, Andre Kahles, Amaya Campillay Lagos, Samuel Lipworth, Elin Loo, Paolo Miotto, Richard A. Neher, Aitana Neves, Derren Ready, Tim Roloff, Ashley Rooney, Emilie Rousseau, Jacques Schrenzel, Martin Sundqvist, Sofia Viegas, Fanny Wegner, Hege Vangstein Aamot, Stefan Niemann, Deborah A. Williamson, Paula Mölling, Adrian Egli



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1 **Conference report:**2 **The second Bacterial Genome Sequencing Pan-European Network conference**

3

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## 59 Introduction

60 Advancements in sequencing technologies have transformed the diagnostic and public health  
61 landscape of microbiology, particularly in the areas of antimicrobial resistance (AMR)  
62 surveillance, outbreak monitoring, and pandemic preparedness. Each technological leap  
63 introduces both new opportunities and challenges, emphasizing the need for collaborative  
64 scientific efforts to establish standardized frameworks that ensure accuracy, reproducibility,  
65 cost-effectiveness, and clinical utility.

66  
67 Standardization and data sharing have emerged as critical enablers for the successful  
68 integration of whole genome sequencing (WGS) into healthcare systems. Harmonized  
69 methodologies ensure reproducibility across laboratories and geographies, laying the  
70 groundwork for global research, regulatory compliance, clinical accreditation, and policy  
71 development. Sequenced data is increasingly shared in multi-country outbreaks e.g., as  
72 recently shown in a large European *Corynebacterium diphtheriae* outbreak [1] and acts as the  
73 vital fuel for machine learning (ML) algorithms, which increasingly underpin predictive tools in  
74 microbial genomics [2]. To achieve their full potential, access to FAIR (Findable, Accessible,  
75 Interoperable, Reusable) data is required [3]. The availability of large, diverse, and well-  
76 annotated datasets enhances genotype-to-phenotype prediction, supports real-time outbreak  
77 tracking, local infection prevention and control measurements, and strengthens antimicrobial  
78 stewardship (AMS). In this context, fostering a culture of data sharing is essential for  
79 progressing resilient public health infrastructure, e.g., the Swiss Pathogen Surveillance  
80 Platform [4] or the National Genomics Platform developed by Genomic Medicine Sweden [5].  
81 The initiatives of national data sharing are in the next step paving the way for international  
82 data sharing.

83 International collaboration is essential to align scientific expectations, identify operational  
84 needs, and navigate the regulatory frameworks governing sequencing-based diagnostics and  
85 surveillance. The “Bacterial Genome Sequencing Pan-European Network” was launched to  
86 foster such collaboration and to catalyse the integration of genomics into routine clinical and  
87 public health settings. Following the success of its inaugural edition [6], the second edition of  
88 the conference was convened in Engelberg, Switzerland, from March 13<sup>th</sup> to 16<sup>th</sup>, 2025.

89 Co-organized by Adrian Egli (Switzerland), Paula Mölling (Sweden), Deborah Williamson  
90 (UK), Hege Vangstein Aamot (Norway), and Stefan Nieman (Germany), the event brought  
91 together a diverse, international and interdisciplinary group of researchers, clinicians, and  
92 public health experts. The conference hosted a total of 35 speakers (**Table 1**) and featured  
93 scientific presentations from diverse, early-career scientists to senior researchers, panel  
94 discussions, an interactive workshop and brainstorming session, and networking opportunities  
95 (**Figure 1**). Our aim was to advance the use of WGS in clinical microbiology and to drive  
96 consensus around key challenges such as the implementation of sequencing for clinical  
97 diagnostics and surveillance, ethical data-sharing policies, learning about ML models, and the  
98 role of sequencing in shaping public health policy. This report provides a structured summary  
99 of the sessions and collaborative outcomes from the four-day meeting.

100

101

## 102 **Surveillance and AMR**

103 Day 1 of the conference highlighted advancements in genomic surveillance methods and  
104 AMR, exploring the innovative sequencing technologies, pipeline developments, and strategic  
105 frameworks aimed at enhancing bacterial pathogen tracking, outbreak management, and  
106 AMR monitoring at national and international scales.

107

### 108 **1.1 *Reliable and reproducible whole-genome genotyping for bacterial genomic*** 109 ***surveillance with Nanopore sequencing data***

110 Dag Harmsen evaluated the Oxford Nanopore sequencing (ONT) method for genotyping 80  
111 ESKAPE bacterial isolates [7]. Results demonstrated substantial improvements in accuracy  
112 and reproducibility when combining Dorado 5.0 model base calling, Medaka v2.0 with a  
113 bacterial methylation-aware model, and a novel ONT core genome multi-locus sequence  
114 typing (cgMLST)-polisher algorithm. This approach showed superior identification and  
115 localization of AMR genes compared to Illumina sequencing. A multicentre ring-trial further  
116 validated these methods, potentially showing that ONT sequencing may become sufficiently  
117 reliable for genomic surveillance purposes.

118

### 119 **1.2 *Evidence review and recommendations for implementation of genomic AMR*** 120 ***surveillance***

121

122 Kate S. Baker highlighted AMR as a complex, multi-pathogen challenge for surveillance,  
123 emphasizing the critical role genomics can play compared to traditional methods. Baker  
124 summarized findings from the Surveillance and Epidemiology of Drug-Resistant Infections  
125 Consortium (SEDRIC) genomics working group, outlining key recommendations including  
126 standardized surveillance frameworks, capacity building, data governance, improving  
127 stakeholder interactions, funding for cost-effectiveness studies, and investing in genomic  
128 innovations [8]. Baker also discussed ongoing United Kingdom initiatives, like TargetAMR  
129 (<https://www.targetamr.org.uk/>), designed to foster transdisciplinary collaborations and  
130 strategic alignment to enhance real-world genomic AMR surveillance and address  
131 implementation barriers.

132

### 133 **1.3 *National and international WGS surveillance and outbreak alerts***

134

135 Martin Sundqvist emphasized the transformative potential of WGS for real-time surveillance  
136 of infectious diseases and AMR, highlighting successful platforms such as EpiPulse, European  
137 Gonococcal Antimicrobial Surveillance Programme (Euro-GASP), and GISAID. Sundqvist  
138 underscored the necessity of robust infrastructure, timely data sharing, and cross-sector  
139 collaboration exemplified by Sweden's Genomic Medicine platform  
140 (<https://genomicmedicine.se>) and Swiss Pathogen Surveillance Platform (<https://spsp.ch>).  
141 Sundqvist concluded by illustrating how prospective WGS combined with machine learning  
142 offers an avenue to enhance outbreak detection, promoting faster, more precise public health  
143 interventions internationally.

144

### 145 **1.4 *Evolution of Mycobacterium tuberculosis multidrug-resistant lineage strains toward*** 146 ***global epidemic success***

147

148 Emilie Rousseau demonstrated the rapid global emergence of multidrug-resistant tuberculosis  
149 (MDR-TB), focusing on lineage-specific evolutionary traits that underpin its success. Using  
150 genomic and *in vitro* approaches, Rousseau revealed that lineage-2 strains acquire resistance  
151 mutations, particularly to rifampicin, at rates significantly faster than lineage-4 strains  
152 (unpublished). Rousseau highlighted that recent lineage-2 outbreaks have increasingly  
153 displaced endemic strains in Central Asia during humanitarian crises, suggesting these  
154 genetic traits confer substantial advantages in drug resistance acquisition and global  
155 dissemination.

156

### 157 **1.5 Targeted capture-based sequencing: bridging the gap in *Neisseria gonorrhoeae*** 158 **genomic surveillance**

159

160 Francesca Azzato evaluated the effectiveness of targeted metagenomic next-generation  
161 sequencing (capture-based mNGS) for directly detecting and characterizing AMR in clinical  
162 samples of *N. gonorrhoeae*. Utilizing a modified RNA bait-based enrichment used in the  
163 detection of other sexually transmitted infections [9] to selectively capture *N.*  
164 *gonorrhoeae* directly from clinical samples. Azzato demonstrated high concordance between  
165 direct sequencing and traditional culture methods in identifying AMR determinants and  
166 genomic diversity. Given its practical challenges like cost and bioinformatics complexity,  
167 targeted mNGS was shown to be highly suitable for reflexed testing, focusing on  
168 characterizing pathogens that are relevant to public health, rather than using it as a single  
169 approach for identification and surveillance.

170

### 171 **1.6 Genomic characterization of *Pseudomonas aeruginosa* from Swedish cystic** 172 **fibrosis patients**

173

174 Elin Loo investigated genomic and phenotypic characteristics of *P. aeruginosa* isolates (n=26)  
175 from cystic fibrosis patients at Karolinska University Hospital. Using WGS and cgMLST-based  
176 phylogenetics, she identified significant genomic diversity with the presence of an epidemic  
177 strain ST-242 (AUST-03). Phenotypically, the isolates showed high AMR rates, driven by the  
178 accumulation of chromosomal mutations under high selective pressure (unpublished). These  
179 findings show potential genetic diversity and evolutionary pressures shaping AMR in *P.*  
180 *aeruginosa* within a cystic fibrosis population in Sweden. However, these are samples from a  
181 single centre and need to be confirmed.

182

### 183 **1.7 Predicting drug-resistant bacteria from WGS data**

184

185 Christian G. Giske evaluated the capability of WGS to accurately predict AMR across various  
186 bacterial pathogens. He emphasized the complexity of the genotype-phenotype relationship,  
187 detailing successes with species like *Mycobacterium tuberculosis* and *Staphylococcus*  
188 *aureus*, while noting significant predictive challenges in species like *Acinetobacter baumannii*,  
189 *P. aeruginosa*, and *N. gonorrhoeae*. Giske highlighted advancements in databases, machine  
190 learning methods, and standardized regulatory frameworks essential for integrating genomic  
191 predictions into clinical practice, advocating further international coordination to refine  
192 genomic antimicrobial susceptibility for routine clinical implementation.

193

### 194 **1.8 Designing, validating, and implementing an AMR pipeline into a local and national** 195 **framework**

196  
197 Tim Roloff described the development of IMMense  
198 (<https://gitlab.uzh.ch/appliedmicrobiologyresearch/immense>, [10]), a modular nextflow-based  
199 sequencing pipeline designed to enhance reproducibility, scalability, and flexibility in AMR  
200 monitoring. Initially tailored for local clinical microbiology needs, the pipeline expanded  
201 nationally via the Swiss Pathogen Surveillance Platform (<https://spsp.ch/>, [4]), incorporating  
202 comprehensive benchmarking against phenotypic resistant profiles. Roloff emphasized key  
203 implementation challenges, including standardisation, stakeholder alignment, and resource  
204 management, underscoring the importance of rigorous quality control and stakeholder-driven  
205 iterative development for effective national integration and sustainability.

206

### 207 ***Panel discussion: What is needed for efficient molecular surveillance?***

208 Gilbert Greub and Hege Vangstein Aamot co-moderated a panel themed "Key requirements  
209 for efficient molecular surveillance", during which panelists outlined the essential elements for  
210 an effective surveillance framework. They noted that "rapid detection" timelines are context-  
211 dependent, ranging from one to two days for hospital outbreaks to slightly longer for  
212 community scenarios. Real-time sequencing was highlighted as critical for outbreak  
213 management, along with promptly identifying virulent and epidemiologically distinct  
214 pathogens.

215 The panel advocated streamlined, interoperable, and automated reporting systems tailored  
216 specifically for clinicians, bioinformaticians, and public health authorities. Emphasis was  
217 placed on maintaining trust through rigorous quality control and skilled personnel verifying  
218 data accuracy, while cautioning against oversimplification in electronic medical records.

219 Data sharing should follow a proactive, default-public approach with clear governance  
220 frameworks for privacy, anonymization, and ethics. This concept signifies a fundamental  
221 philosophical shift towards making molecular surveillance data, particularly genomic and  
222 associated epidemiological information, publicly available by default. This is critical in  
223 supporting public health measurements.

224 A practical "traffic light" system (green, yellow, red) was recommended to manage data  
225 sensitivity, especially regarding genomic data and associated metadata.

226 Training emerged as essential, with panelists proposing mandatory genomic microbiology  
227 certification and comprehensive education for laboratory staff, clinicians, public health officials,  
228 and regulators. Continuous training and skill updates were emphasized as crucial for  
229 maintaining surveillance standards despite stakeholder resistance.

230

### 231 **Emerging concepts**

232 Day 2 focused on the integration of genomic sequencing technologies, specifically long-read  
233 sequencing and ML models. The speakers highlighted how the combination of cutting-edge  
234 genomic technologies and advanced computational methods can significantly improve real-  
235 time outbreak investigations, rapid AMR detection, and predictive analytics in clinical settings.

236

## 237 **2.1 Long-read shotgun metagenomic sequencing in CNS infections**

238 Kira Waagner Birkeland presented on the use of long-read shotgun metagenomic sequencing  
239 (mNGS) to investigate central nervous system infections [11]. The study aims to develop a  
240 protocol for pathogen identification in cerebrospinal fluid (CSF) samples using ONT and  
241 validate it against commercially available ZymoBIOMICS Microbial Community Standard with  
242 MS2 phage and Cytomegalovirus, and AMPLIRUN® TOTAL SARS-COV-2/FLUA/FLUB/RSV  
243 CONTROL (SWAB) with ZymoBIOMICS Spike-in Control II (Low-microbial load). Initial testing  
244 of a new protocol demonstrated the ability to detect viruses (Enterovirus B and Varicella-zoster  
245 virus) in CSF samples to reduce diagnostic turnaround time, offering a promising alternative  
246 to traditional methods. The integration of ONT sequencing into diagnostic workflows could  
247 serve as a model for hospitals, enhancing infection management capabilities.

## 248 **2.2 Long-read whole-genome sequencing to highlight MRSA's adaptive potential within** 249 **host**

250 Amaya Campillay Lagos discussed the genomic plasticity of methicillin resistant *S. aureus*  
251 (MRSA) in long-term carriers [12]. By using long-read sequencing, the study observed the  
252 evolution of MRSA within hosts, revealing a mutation rate of 10 SNPs per year and significant  
253 genomic diversity. This project was part of a broader genomic medicine initiative, focusing on  
254 integrating genomics into a broad national clinical diagnostic [13]. This research highlights  
255 MRSA's adaptive potential, emphasizing the need for personalized surveillance for long-term  
256 carriers. The importance of genomic medicine initiatives lies in improving patient-specific data  
257 integration, which could reshape treatment approaches for chronic infections.

## 258 259 **2.3 Long-read shotgun metagenomics to rapidly detect colonization with AMR directly** 260 **from rectal swabs**

261 Srinithi Purushothaman explored the use of long-read shotgun metagenomics to detect  
262 Antimicrobial Resistance Genes (ARGs) directly from rectal swabs [14]. The study achieved  
263 significant reductions in turnaround time (TAT) to 24 hours, focusing on high-risk patients.  
264 However, there is still the need to further improve the sensitivity of certain resistance  
265 mechanisms in the current applied protocol. The research highlighted ONT sequencing as a  
266 potential tool for AMR surveillance in clinical settings. By reducing the TAT for detecting ARGs  
267 and pathogens, the study emphasizes the role of culture-independent genomic sequencing in  
268 improving the TAT for clinical diagnosis and surveillance [15].

## 269 270 **2.4 Integration of long-read sequencing for rapid whole-genome analysis in outbreak** 271 **investigations**

272 Hege Vangstein Aamot discussed integrating long-read sequencing for outbreak  
273 investigations of multidrug-resistant pathogens (ESBL-producing *K. pneumoniae* and  
274 Methicillin-resistant *S. aureus*) and surveillance of *Pseudomonas spp.*, *C. difficile*, and  
275 *Stenotrophomonas spp.* The use of ONT sequencing enabled real-time identification of  
276 pathogen transmission in healthcare-associated infections, providing a rapid and accurate  
277 method for outbreak control. The implementation of ONT sequencing as part of genomic  
278 diagnostics networks is crucial for rapid outbreak response. Different genomic sequencing

279 pipelines can streamline public health efforts by quickly identifying clusters and transmission  
280 routes, which is essential for controlling outbreaks.

281

## 282 **2.5 Holistic approach to unravel AMR in East Africa (HATUA)**

283 Matt Holden presented the HATUA project, an interdisciplinary initiative aimed at investigating  
284 AMR drivers in East Africa. The project combines genomic data with socioeconomic factors,  
285 analysing patterns in urinary tract infection pathogens from Kenya, Uganda, and Tanzania  
286 [16]. By integrating genomic surveillance with social science research, HATUA provides a  
287 holistic approach to understanding AMR. The HATUA project exemplifies the importance of  
288 interdisciplinary approaches to combat AMR, blending genomics with social and  
289 environmental factors. It shows the need for global collaborations that address AMR through  
290 a multifaceted lens, connecting microbiological, clinical, and societal data.

291

## 292 **2.6 Machine learning for bacterial genomics**

293 Andre Kahles discussed the role of ML in bacterial genomics, focusing on how ML models are  
294 applied to genomic data for predicting AMR, virulence, and pathogen characterization. The  
295 talk highlighted the various ML approaches for analysing genomic sequences and emphasized  
296 the importance of large, well-curated datasets for training effective models. ML is becoming  
297 increasingly important in bacterial genomics, particularly in AMR prediction. The ability to  
298 predict resistance patterns using genomic data is enhanced by ML algorithms, which could  
299 ultimately support more personalized treatment strategies for infections.

300

## 301 **2.7 What is the role of machine learning in AMR prediction?**

302 Samuel Lipworth explored ML's role in predicting AMR in *Escherichia coli* and *Klebsiella spp.*  
303 in bloodstream infections. The study utilized ONT sequencing and ML models to predict  
304 antibiotic resistance and optimize therapy. Lipworth emphasized the importance of large,  
305 diverse datasets and external validation for the effectiveness of ML models. Lipworth's  
306 research illustrates the promise of ML in improving AMS through better prediction of resistance  
307 patterns [17]. However, challenges in data quality and label accuracy underscore the need for  
308 more comprehensive, validated datasets to improve the reliability of ML predictions. While  
309 genotypic data is crucial for predicting AMR, challenges remain in accurately linking it to  
310 phenotypic resistance, requiring refined models and better catalogues of mutations.

311

## 312 **Panel discussion: How can we implement long-read sequencing and machine learning** 313 **in clinical practice?**

314 Moderated by Ashley Rooney and Jacques Schrenzel, the panel including Hege Vangstein  
315 Aamot, Matt Holden, Andre Kahles, and Samuel Lipworth discussed integrating long-read  
316 sequencing and ML clinically.

317 The panel identified key implementation hurdles, particularly selecting high-yield cases and  
318 clinician hesitation due to a lack of validated tools and standardized workflows. Examples from  
319 oncology precision medicine and HIV antiviral treatment underscored the value of successful  
320 integration models. Long-read sequencing was highlighted for its potential in community

321 surveillance through wastewater and saliva, emphasizing the need for rapid, actionable, point-  
322 of-care data delivery and robust local bioinformatics infrastructure.

323 Immediate clinical applications include infection control, outbreak prediction, and resistance  
324 tracking, with bacterial population genetics poised as an emerging clinical tool. Despite  
325 enthusiasm, challenges persist, especially the gap between technological capacity and clinical  
326 uptake. Harmonizing genotype-to-phenotype datasets remains a critical task. The panel urged  
327 focusing on identifying and harmonizing relevant data locally.

328 Regulatory hurdles remain significant, suggesting infection control as a feasible starting point.  
329 Panelists recommended initiating a focused pilot project on a specific pathogen or disease to  
330 generate localized evidence, demonstrate cost-effectiveness, and effectively engage  
331 stakeholders and regulatory bodies.

332

### 333 **Routine diagnostics**

334 Day 3 focused on the critical aspects of implementing WGS in routine diagnostics, highlighting  
335 the challenges and importance of standardization, quality control, and efficient data sharing.  
336 Speakers presented innovative methods and real-world experiences from diverse international  
337 settings, emphasizing the need for streamlined robust systems.

338

#### 339 ***3.1 National implementation of 16S Nanopore sequencing***

340 Sofia Brunet reported findings from a nationwide Swedish multicentre study, including 20  
341 different laboratories, evaluating 16S ONT sequencing for bacterial identification, highlighting  
342 protocol harmonization and bioinformatics pipeline comparisons. Results showed varying  
343 success in species identification linked to primer specificity and database selection.  
344 Optimization with enzymatic pretreatment enhanced detection sensitivity. Nanopore  
345 sequencing via GMS-16S demonstrated user-friendliness and accuracy suitable for clinical  
346 diagnostics [18].

347

#### 348 ***3.2 Exploring algorithms for outbreak detection for AMR bacteria***

349 Charles Wei examined current genotyping methods for pathogen surveillance, identifying  
350 limitations such as suboptimal resolution. Using a dataset of *Shigella sonnei* isolates, Wei  
351 highlighted the clustering inaccuracies arising from static thresholds and single-linkage  
352 methods. Wei proposed adaptive threshold clustering to improve outbreak detection,  
353 emphasizing that integrating genotyping with AMR data enhances actionable surveillance.  
354 Wei concluded that refined, adaptive algorithms could significantly advance public health  
355 response capabilities, balancing resolution, speed, and accuracy.

356

#### 357 ***3.3 Leveraging microbial genomics for diagnosis and public health: the Indian*** 358 ***perspective***

359 Jobin Jacob detailed high infectious disease and AMR burden in India, highlighting challenges  
360 including fragmented surveillance and diagnostic limitations. Jacob showcased institutional  
361 efforts to integrate genomics into clinical diagnostics, notably using rapid Nanopore  
362 sequencing for real-time diagnosis and outbreak management. Jacob stressed genomics' role

363 in identifying resistance mechanisms, optimizing antimicrobial therapy, and supporting  
364 vaccination strategies, underscoring its transformative potential for public health in resource-  
365 limited settings facing extensive disease burdens.

366

### 367 **3.4 Genomic applications in public health bacteriology**

368 Derren Ready discussed genomic sequencing's crucial role within the UK's public health  
369 services, particularly emphasizing outbreak detection and AMR profiling. Through case  
370 studies of *Klebsiella pneumoniae* and STEC O145:H28 outbreaks [19], Ready illustrated  
371 genomics' powerful capabilities in identifying transmission pathways, informing clinical  
372 interventions, and shaping public health policies. Genomic methods offer superior resolution  
373 over traditional typing techniques, significantly refining epidemiological investigations and  
374 response actions, thereby enhancing patient care and outbreak management at both local and  
375 national levels.

376

### 377 **3.5 Necessary quality steps for implementing whole genome sequencing in routine** 378 **diagnostics**

379 Erika Tång Hallbäck outlined essential quality control stages for integrating genomic  
380 sequencing into clinical microbiology, including meticulous validation of DNA extraction, library  
381 construction, sequencing quality, bioinformatics analysis, and external quality assessments.  
382 Hallbäck emphasized challenges such as bioinformatics expertise, IT infrastructure, data  
383 security, and standardized data sharing. Hallbäck highlighted the importance of harmonized  
384 national strategies for genomic implementation, advocating rigorous quality management and  
385 comprehensive staff training to ensure reliable diagnostic and surveillance outcomes across  
386 Sweden [13].

387

### 388 **3.6 Ten simple rules for the sharing of bacterial genotype-phenotype data on AMR**

389 Aitana Neves emphasized the importance of structured, standardized, and machine-readable  
390 formats for sharing AMR genotype-phenotype data. Highlighting platforms such as SPSP,  
391 COMPARE (<https://www.compare-europe.eu/>), ANRESIS (<https://www.anresis.ch/#>), and  
392 CARD (<https://card.mcmaster.ca/>), she outlined guidelines for metadata standardization,  
393 ontology utilization, and transparent reporting of resistance determinants. Neves advocated  
394 for open, accurate, and interoperable data sharing to enhance AMR surveillance,  
395 recommending clear licensing, consistent versioning, and efficient data accessibility  
396 mechanisms (**Table 2**).

397

398

399

400

### 401 **3.7 Realising national, end-to-end accredited, pathogen genomics services for** 402 **diagnostics and surveillance**

403 Tom Connor described Wales's successful development and accreditation of comprehensive  
404 pathogen genomic services, from sequencing to clinical action. Through detailed examples  
405 such as SARS-CoV-2 and *Clostridioides difficile*, Connor demonstrated the impact of

406 integrated genomics on public health surveillance, outbreak management, and patient care  
407 [20]. Connor emphasized modularization, robust bioinformatics infrastructure, and close  
408 integration with public health authorities as critical success factors, highlighting the significant  
409 public health benefits derived from streamlined genomic data use and interdisciplinary  
410 collaboration.

411

#### 412 ***Workshop: Key steps to translate sequencing into routine diagnostics***

413 The 2-hour workshop addressed critical aspects for integrating genomic sequencing into  
414 routine diagnostics, emphasizing five main areas: bioinformatics, validation and accreditation,  
415 automation, artificial intelligence (AI), and reporting strategies.

416 Bioinformatics emphasized reproducibility, secure backups, metadata integration, and  
417 sustainable IT platforms with user-friendly interfaces. Community engagement among  
418 academia, industry, and clinics was vital for broad genomic adoption. Validation discussions  
419 prioritized clear SOPs, modular workflows for flexibility, adherence to ISO standards, regular  
420 external quality assessments (EQAs), audits, and workforce training. Automation was  
421 acknowledged for error reduction and efficiency, though cost and maintenance challenges  
422 persist. Integrated sequencing systems were recommended for smaller labs. AI was  
423 particularly valued for outbreak prediction, AMR forecasting, and identifying novel resistance  
424 mechanisms, despite challenges with prospective validation. Developing unbiased AI models  
425 was crucial for generalizable results. Effective reporting tailored to various stakeholders, with  
426 clear confidence indicators, was key for clinical integration. Multidisciplinary teams were  
427 proposed to enhance genomic report interpretation and clinical decision-making.

428

429

#### 430 **Sequencing meets politics**

431 Day 4 focused on the integration and long-term sustainability of sequencing in public health,  
432 emphasizing its crucial role in monitoring and controlling infectious diseases. The discussions  
433 centered on how WGS can be implemented into routine surveillance systems, with a particular  
434 focus on financial sustainability, workforce development, data management, and policy  
435 integration. Sustainability, scalability, and global collaboration emerged as key drivers for  
436 ensuring the success and longevity of genomic surveillance programs.

437

#### 438 ***4.1 Translation of pathogen genomics to public health policy***

439 Deborah Williamson underscored that effective translation of genomic research into evidence-  
440 based policies is essential for influencing decision-making at governmental, institutional, and  
441 societal levels. Such translation ensures real-world applications that impact public health and  
442 healthcare practices. Williamson presented the application of genomic sequencing to track  
443 SARS-CoV-2 variants that played a pivotal role in the development of vaccines and the  
444 implementation of public health interventions such as border controls, lockdowns, and  
445 vaccination strategies, along with the integration of real-time genomic epidemiology in sexually  
446 transmitted infection control which faces challenges in balancing data sharing, privacy  
447 concerns, and clinical integration, but offers a unique opportunity to enhance public health  
448 interventions.

449

#### 450 **4.2 Integrating sequencing into local TB control guidelines in high incidence settings**

451 Sofia Viegas presented on the integration of WGS into National TB testing algorithms in  
452 Mozambique. She highlighted the country's high TB burden and the role sequencing can play  
453 in providing more accurate drug resistance profiles and faster diagnostics. Viegas also  
454 discussed the establishment of local capacity for sequencing and the strategic partnerships  
455 necessary to support sustainable sequencing programs. Viegas' talk emphasizes the  
456 importance of building local sequencing capacity to enhance TB management in high-burden  
457 settings. The integration of WGS in Mozambique is a crucial step towards improving drug-  
458 resistant TB diagnosis and treatment, requiring both infrastructure investment and global  
459 partnerships for long-term success.

460

#### 461 **4.3 Pathoplexus - building a new kind of pathogen database**

462 Emma Hodcroft discussed the limitations of existing pathogen sequence-sharing platforms, in  
463 particular difficulty of data upload and access, sometimes untransparent governance, and  
464 limitations in ensuring sequence generators are protected from 'scooping.' These issues  
465 hinder reproducibility, broader data integration, and the development of open analysis  
466 ecosystems. Hodcroft introduced Pathoplexus (<https://pathoplexus.org/>) as a new open-  
467 source, community-driven database designed to address these issues [21]. Pathoplexus  
468 focuses on ease of submission, improving data accessibility, clear data use terms, transparent  
469 governance, and the ability for researchers to submit pathogen sequences while reserving the  
470 right to publish first. Hodcroft's presentation highlighted the need for more transparent and  
471 accessible pathogen databases to encourage quick data sharing for public health response  
472 and foster a collaborative sharing environment. Pathoplexus is positioned as a solution to  
473 enhance data sharing, aid global collaboration and promote ethical use of genomic data, which  
474 is crucial for accelerating research and improving public health responses.

475

#### 476 **4.4 Sustainability of sequencing programs**

477 Paolo Miotto explored the key components necessary for the sustainability of sequencing  
478 programs, which requires a multifaceted approach that balances financial stability, robust  
479 infrastructure, skilled workforce retention, and the ability to adapt to evolving technological and  
480 public health needs. Central to this is the adoption of standardized frameworks. Miotto outlined  
481 the role of the WHO TB mutation catalogue in standardizing drug-resistant TB sequencing and  
482 discussed the importance of international collaborations and capacity-building efforts to  
483 ensure the long-term viability of sequencing programs. When integrated with public health  
484 systems, these efforts ensure genomic data informs real-time diagnosis, surveillance, and  
485 treatment. Miotto's talk emphasized that sustainability in sequencing programs depends on  
486 interdisciplinary collaboration, cost-efficiency, and workforce training. By integrating  
487 sequencing into routine diagnostic algorithms, especially for TB, sequencing programs can  
488 become a cornerstone for improving public health surveillance and disease management. Yet  
489 challenges remain, particularly in procurement, data sharing, and aligning stakeholders  
490 around clear, measurable goals. Embracing a One Health approach and fostering cross-sector  
491 collaboration can help overcome these gaps and ensure sequencing becomes a sustainable  
492 tool for global health.

493

494

495 **Conclusion**

496 The second edition of the four-day “Bacterial Genome Sequencing Pan-European Network”  
497 conference successfully gathered international experts to discuss recent advances and  
498 address critical challenges in bacterial genome sequencing. Central themes included  
499 standardization, quality assurance, and efficient implementation of genomic methods,  
500 especially long-read sequencing technology into routine diagnostics and public health  
501 surveillance. Discussions underlined the necessity of rigorous validation, standardized  
502 reporting, and effective data sharing frameworks to facilitate accurate genomic interpretation  
503 and meaningful clinical translation. Importantly, the conference highlighted the transformative  
504 potential of emerging technologies such as long-read sequencing and AI, alongside  
505 considerations for sustainable practices and ethical guidelines.

506 **Declarations.** ChatGPT4 with the GPT-4-turbo model (April 2024) version is used to support  
507 writing and editing the first draft of the manuscript. The manuscript has substantially changed  
508 during the human writing course. Every author checked and edited the manuscript.

509

510 **Declaration of generative AI and AI-assisted technologies in the writing process**

511 During the preparation of this work the authors used ChatGPT4 with the GPT-4-turbo model  
512 (April 2024) version in order to support writing and editing the first draft of the manuscript.  
513 After using this tool/service, the authors reviewed and edited the content as needed and takes  
514 full responsibility for the content of the publication. The manuscript has substantially changed  
515 during the human writing course. Every author checked and edited the manuscript.

516

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522

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527

528 **Figure and table legends**

529

530 **Figure 1:** The international participants of the second Bacterial Genome Sequencing Pan-  
531 European Network conference from eight different countries.

532

533 **Table 1.** List of participants and their corresponding affiliations.

534

535 **Table 2:** Ten recommendations for good data sharing practice for bacterial genotype-  
536 phenotype data. EUCAST, European Committee on Antimicrobial Susceptibility Testing  
537 (<https://www.eucast.org/>); CLSI, Clinical and Laboratory Standards Institute (<https://clsi.org/>);  
538 API, application programming interface; SPARQL, standard query language and protocol for  
539 Linked Open Data on the web or for RDF triplestores; IRI, Internationalized Resource Identifier  
540 (<https://lincsproject.ca/docs/terms/internationalized-resource-identifier>).

541

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**Table 1.** List of participants and their corresponding affiliations.

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Rule	Rule Content
1	For phenotypic AMR, use ontologies/CVs, if possible, defined within European/global consortia
2	Use standardised resistance definitions (global standards (EUCAST, CLSI) and specify versions (e.g., year) for susceptible/intermediate/resistant (S/I/R) interpretation.
3	For bioinformatics results, follow PHA4GE specifications
4	For genotypic to phenotypic predictions, document the source of information (e.g., knowledge base and date of accession, or tool + version)
5	Provide minimal contextual metadata (e.g. strain name, collection date, location (country), host, compartment (human, animal, food, environment)
6	Publish phenotypic data openly on the INSDC (under BioSample)
7	Ensure data is accurate (correct/update where needed)
8	Make data findable, also for machines (API or SPARQL endpoints + use IRIs)
9	Make data accessible and reusable (i.e., define clear access models, explicit license)
10	Version data and metadata

**Table 2:** Ten recommendations for good data sharing practice for bacterial genotype-phenotype data. EUCAST, European Committee on Antimicrobial Susceptibility Testing (<https://www.eucast.org/>); CLSI, Clinical and Laboratory Standards Institute (<https://clsi.org/>); API, application programming interface; SPARQL, standard query language and protocol for Linked Open Data on the web or for RDF triplestores; IRI, Internationalized Resource Identifier (<https://lincsproject.ca/docs/terms/internationalized-resource-identifier>).



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