Harnessing Genomics for Antimicrobial Resistance Surveillance 3

Genomics for public health and international surveillance of antimicrobial resistance

Kate S Baker, Elita Jauneikaite, Katie L Hopkins, Stephanie W Lo, Leonor Sánchez-Busó, Maria Getino, Benjamin P Howden, Kathryn E Holt, Lillian A Musila, Rene S Hendriksen, Daniel G Amoako, David M Aanensen, Iruka N Okeke, Beverly Egyir, Jamie G Nunn, Janet T Midega, Nicholas A Feasey, Sharon J Peacock, for the SEDRIC Genomics Surveillance Working Group

Historically, epidemiological investigation and surveillance for bacterial antimicrobial resistance (AMR) has relied on low-resolution isolate-based phenotypic analyses undertaken at local and national reference laboratories. Genomic sequencing has the potential to provide a far more high-resolution picture of AMR evolution and transmission, and is already beginning to revolutionise how public health surveillance networks monitor and tackle bacterial AMR. However, the routine integration of genomics in surveillance pipelines still has considerable barriers to overcome. In 2022, a workshop series and online consultation brought together international experts in AMR and pathogen genomics to assess the status of genomic applications for AMR surveillance in a range of settings. Here we focus on discussions around the use of genomics for public health and international AMR surveillance, noting the potential advantages of, and barriers to, implementation, and proposing recommendations from the working group to help to drive the adoption of genomics in public health AMR surveillance. These recommendations include the need to build capacity for genome sequencing and analysis, harmonising and standardising surveillance systems, developing equitable data sharing and governance frameworks, and strengthening interactions and relationships among stakeholders at multiple levels.

Lancet Microbe 2023

Published Online November 14, 2023 https://doi.org/10.1016/S2666-5247(23)00283-5

This is the third in a Series of five papers about harnessing genomics for antimicrobial resistance surveillance. All papers in the Series are available at www.thelancet.com/microbe.

Department for Clinical Infection, Microbiology, and Immunology, University of Liverpool, Liverpool, UK (Prof K S Baker PhD); **Department of Genetics** (Prof K S Baker), **and Department of Medicine** (Prof S J Peacock PhD), **University of Cambridge, Cambridge, UK; Department of Infectious Disease Epidemiology, School of Public Health, Imperial College London, London, UK** (E Jauneikaite PhD); **NIHR Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance, Department of Infectious Disease, Imperial College London, Hammersmith Hospital, London, UK** (E Jauneikaite, M Getino PhD); **HCAI, Fungal, AMR, AMU & Sepsis Division** (K L Hopkins PhD) **and Antimicrobial Resistance and Healthcare Associated Infections Reference Unit** (K L Hopkins), **UK Health Security Agency, London, UK; Parasites and Microbes, Wellcome Sanger Institute, Hinxton, UK** (S W Lo PhD); **Genomics and Health Area, Foundation for the Promotion of Health and Biomedical Research in the Valencian Community (FISABIO-Public Health), Valencia, Spain** (L Sánchez-Busó PhD); **CIBERESP, ISCIII, Madrid, Spain**

Background

In early 2022, the Surveillance and Epidemiology of Drug-resistant Infections Consortium (SEDRIC) convened a working group to evaluate the use of genomics for conducting surveillance of antimicrobial resistance (AMR) in bacterial pathogens. The second in a series of workshops (see the first paper in this Series[1]) entitled Public Health and International was held on March 29, 2022, and aimed to conduct a situational analysis of the use of genomics for AMR surveillance across public health surveillance networks (ie, at national and international levels); reach a consensus on where the use of genomics for AMR surveillance adds value in these settings; and develop and prioritise stakeholder recommendations for the implementation or enhancement of genomics for AMR surveillance.[1] Here, we summarise the discussion, highlighting general advantages and specific use cases for genomic AMR surveillance for public health, and elaborate on the working group's recommendations for overcoming barriers to unlock the considerable potential of genomics to improve public health AMR surveillance.

Advantages and applications of genomics for AMR surveillance in public health

Historically, bacteria causing disease in humans have been identified to species or serotype level in clinical laboratories. To describe bacteria in greater depth to aid epidemiological investigation and regional surveillance, they are sometimes also sent on to reference laboratories for further subtyping. This process is highly specialised for each pathogen and includes both extensive phenotypic and, more recently, molecular or subgenomic methods such as pulse field gel electrophoresis or multilocus sequence typing. However, it is now possible to characterise and distinguish bacteria through genomic sequencing, making some of these laboratory processes redundant and harmonising other aspects of the workflow. Sequencing platforms are an adaptable infrastructure that can be tailored to any pathogen, including those causing emerging infectious diseases, in support of pandemic preparedness and responses. Unlike earlier typing approaches, which were usually only feasible in reference laboratories, genomic surveillance is technically possible using a bench-top sequencing machine in any laboratory. However, some infrastructural change might be needed to accommodate compartmentation of activities and housing of specialist equipment (eg, as noted by Kekre and colleagues[2]), particularly if diagnostic PCR is not routine, as is the case in some low-income and middle-income countries (LMICs). Thus, there are some advantages in centralising sequencing services in reference laboratories, including the higher scale and throughput, making sequencing more cost-effective than implementation of genomics in smaller, more local laboratories. However, this needs to be balanced with the potential disadvantages, such as the increased turnaround times associated with moving isolates from one location to another. Ultimately, the right implementation model will depend on the

(L Sánchez-Busó); **The Centre for Pathogen Genomics, Doherty Institute, The University of Melbourne, Melbourne, VIC, Australia** (Prof B P Howden PhD); **Department of Infection Biology, London School of Hygiene & Tropical Medicine, London, UK** (Prof K E Holt PhD); **Department of Infectious Diseases, Central Clinical School, Monash University, Melbourne, VIC, Australia** (Prof K E Holt); **Department of Emerging Infectious Diseases, United States Army Medical Research Directorate – Africa, Nairobi, Kenya** (L A Musila PhD); **Kenya Medical Research Institute, Nairobi, Kenya** (L A Musila); **National Food Institute, Technical University of Denmark, Lyngby, Denmark** (Prof R S Hendriksen PhD); **Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases, Johannesburg, South Africa** (D G Amoako PhD); **School of Health Sciences, University of KwaZulu-Natal, Durban, South Africa** (D G Amoako); **Department of Pathobiology, University of Guelph, Guelph, ON, Canada** (D G Amoako); **Centre for Genomic Pathogen Surveillance, Nuffield Department of Medicine, University of Oxford, Big Data Institute, Oxford, UK** (Prof D M Aanensen PhD); **Department of Pharmaceutical Microbiology, Faculty of Pharmacy, University of Ibadan, Ibadan, Oyo State, Nigeria** (Prof I N Okeke PhD); **Department of Bacteriology, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon-Accra, Ghana, West Africa** (B Egyir PhD); **Infectious Disease Challenge Area** (J G Nunn MSc), **and Drug Resistant Infections** (J T Midega PhD), **Wellcome Trust, London, UK; Clinical Sciences, Liverpool School of Tropical Medicine, Liverpool, UK** (Prof N A Feasey PhD); **Malawi Liverpool Wellcome Research Programme, Malawi** (Prof N A Feasey)

Correspondence to:
Prof Kate S Baker, Department of Genetics, University of Cambridge, Cambridge CB2 3EH, UK
kb827@cam.ac.uk

For more on the **SEDRIC working groups** see https://sedric.org.uk/working-groups/

sensitivity for rapid turnaround time for a given indication, the broader public health infrastructure, and funding levels (see the second paper in this Series[3]).

Regardless of where and how the data are generated, the level of detail provided by genomics is superior to that provided by previous methods, while also allowing some data processing steps to be streamlined. Genomic data supports the surveillance of pathogens at levels ranging from lineage (used here to refer to all genomic-informed nomenclature; eg, clone, sublineage, clade, core genome multilocus sequence type, and HierCC groupings) to the highly granular ability to identify genomically identical isolates. Genomics also facilitates the detection of genetic determinants of AMR (and their vehicles; eg, plasmids), virulence, and other relevant phenotypic markers that were previously only explored using molecular techniques, such as PCR. The electronic nature of genomic data also allows sequencing outputs to be shared and analysed among laboratories and in bioinformatic hubs (either physical or cloud based), for retrospective and international data comparison and for external quality assessments of genomic and bioinformatic processes.

Among the working group there was strong consensus that better advocacy and articulation of the use cases for genomic AMR surveillance were needed. The two main use cases for genomic surveillance of AMR in the public health setting were proposed to be detecting and understanding novel and emerging threats, and informing and assessing public health interventions. To better articulate these use cases, we provide examples of each of the applications below.

Genomics for detecting and understanding emerging public health threats

High-resolution views of bacterial populations and AMR determinants offered by genomic analyses have greatly enhanced our ability to detect and monitor emerging AMR threats over time, by geographical location, and through public health or laboratory networks and patient communities. However, genomic AMR surveillance mechanisms are not yet integrated as standard in most countries or regions. As such, there are numerous examples of substantial recent epidemics or pandemics that have been missed owing to the inability to resolve new or rapidly spreading variants of bacterial species that might have met the criteria for a Public Health Emergency of International Concern had they been detected. These variants include globally circulating $bla_{CTX\text{-}M15}$-producing *Escherichia coli*, multidrug-resistant *Salmonella typhimurium* ST313 in Africa, and fluoroquinolone-resistant *Shigella sonnei*.[4–6]

Food microbiology reference laboratories have been early adopters of genomic surveillance. Some of these laboratories and networks (typically in high-income countries) have already implemented routine sequencing, and, thus, offer an ideal opportunity from which to learn and leverage best practices and platforms for introducing and enhancing genomic AMR surveillance in other contexts.[7–10] A large body of evidence on *Salmonella* spp, *Shigella* spp, *Listeria monocytogenes*, shiga-toxigenic *E coli*, and *Campylobacter* spp ably shows the enhanced ability of genomic epidemiology to detect outbreaks in dispersed geographical areas and identify the source of outbreaks.[11–17] Some of these studies focused explicitly on the detection of newly emergent lineages with AMR[16,18–21] and the spread of mobilisable AMR.[22,23] These datasets not only contribute to AMR monitoring,[7,24] but also help to validate the use of genomics for the surveillance of AMR determinants, with multiple studies showing reliable genotypic prediction of AMR[25,26] (although this is not true for all pathogens—see later, and the fifth paper in this Series[27]) and other relevant phenotypes (eg, serotype and virulence).[28–30]

PulseNet, one of the largest international foodborne disease surveillance networks, previously relied on pulse field gel electrophoresis for typing, but is transitioning to use genomics to enhance international surveillance, largely through the GenomeTrakr distributed network of laboratories.[31,32] However, a survey of PulseNet laboratories identified a lack of funding, as well as gaps in expertise and training (especially for data analysis and interpretation), as the main barriers preventing the widespread uptake of genomics for surveillance, particularly in LMICs.[33] Importantly, foodborne illness surveillance in highly developed agricultural settings is frequently coupled with clear public health interventions to address outbreaks, but this is less often the case in informal agricultural systems found in many LMICs. The ability to detect threats from AMR and inform interventions in near real time is an important factor in accelerating the uptake of genomic surveillance. The UK experience already suggests that implementation of routine genomic sequencing for *Salmonella* has identified a greater number of outbreaks than would have been detected using routine microbiology.[34,35] Thus, as genomic surveillance is adopted more widely, we anticipate a substantial increase in the number of outbreaks detected, highlighting the need to be able to prioritise outbreaks for intervention based on features of the causal bacterial pathogen.

There have also been substantial global efforts to harmonise AMR surveillance of health-care-associated infections (HCAIs) across networks.[36,37] Multiple large studies of *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa*, and *Enterobacter* spp and other HCAI pathogens have identified regionally dominant lineages and placed them in a global context.[38–40] The identification of globally emerging or dominant lineages with AMR (eg, *E coli* ST131, *K pneumoniae* ST258, and *S aureus* USA300) have helped to focus research and control efforts.[41] Similar to foodborne illnesses, genomic surveillance of HCAIs can illuminate the genetic basis

and spread of new or concerning AMR bug–drug combinations[42–49] and characterise other phenotypes of interest (eg, serotype and virulence).[38,50,51] Genomics has also been used to investigate changes in the bacterial lineages occurring across health and social care networks[52–54] and in multihospital surveillance to identify hidden transmission patterns and previously undetected outbreaks.[55–57] The enhanced resolution of genomics has also enabled more detailed epidemiological studies, such as the identification of potential *Clostridioides difficile* transmissions in north Wales and the demonstration that a failure to meet cleaning targets was not associated with higher-than-expected transmissions.[58] Highlighting such use cases for genomic data (whether generated in reference or front-line laboratories) is vital as genomics for HCAI is often in competition with automated clinical diagnostic antimicrobial susceptibility testing tools, which offer enhanced turnaround times, but comparatively little additional information to inform broader surveillance efforts, understand transmission dynamics, and prevent HCAIs.[59]

Genomics for shaping and monitoring public health interventions

Numerous longitudinal studies of AMR have shown the value of routine genomic surveillance in shaping public health interventions at national and international levels, including informing treatment recommendations and influencing vaccination regimens.

Longitudinal genomic surveillance of *Neisseria gonorrhoeae*, the causative agent of the sexually transmitted infection gonorrhoea, and a WHO priority 2 pathogen for which antimicrobials are urgently needed,[60] has been used to shape treatment recommendations. An early global study[61] identified major sublineages with different AMR profiles, including a multidrug-resistant lineage associated with men who have sex with men that has sequentially evolved resistance to last-line treatment options azithromycin and ceftriaxone.[62] Ongoing genomic surveillance has shown that *N gonorrhoeae* rapidly evolves in response to changing treatment recommendations. For example, a rise in cefixime resistance led to a change in EU–European Economic Area treatment recommendations in 2012 to dual therapy with ceftriaxone and azithromycin,[63] which was followed by a decrease in resistance to extended-spectrum cephalosporins but an increase in azithromycin resistance.[64,65] In turn, this led some countries to recommend ceftriaxone monotherapy for treating uncomplicated gonorrhoea.[66,67] Genomic analyses of isolates from the European Gonococcal Antimicrobial Surveillance Programme identified the basis for these shifting phenotypes.[68] Specifically, lineage G1407 (previously associated with decreased susceptibility and resistance to extended-spectrum cephalosporins[69]) is now being replaced by G12302, an azithromycin-resistant lineage. Genomic analysis of European Gonococcal Antimicrobial Surveillance Programme data has also revealed the absence of resistance mutations to zoliflodacin and gepotidacin, which are currently in phase 3 randomised controlled trials for the treatment of gonorrhoea.[68,70] This cyclical use of genomic AMR surveillance to shape and assess new and prospective treatment regimens highlights a key use case for ongoing genomic surveillance to tackle AMR.

Similar value has been seen in using genomic surveillance of *Streptococcus pneumoniae* for informing vaccination programmes, an increasingly prominent preventive strategy against AMR.[71] Specifically, the global deployment of the pneumococcal conjugate vaccine (PCV) has been effective in reducing pneumococcal disease worldwide[72] and has had a positive impact on reducing AMR.[73] However, the current PCVs only target 13 of more than 100 distinct capsule types (ie, serotypes). Incomplete coverage of all serotypes in the vaccine has allowed the pneumococcal population to evolve and evade the vaccine resulting in serotype replacement.[74] The global pneumococcal sequencing (GPS) project has shown the utility for genomics in evaluating changes in *S pneumoniae* populations following the roll-out of PCV by detecting shifts in serotypes, and relating these to the genomic lineages and AMR use data from more than 50 countries.[75] The outputs of these studies have guided the choice of future vaccines and treatment options. Specifically, analyses have identified vaccine-evading subtypes like the multidrug-resistant global pneumococcal sequence cluster 10 (GPSC10) that expressed 17 different serotypes. After the introduction of PCV13, GPSC10 rapidly adapted to the vaccine-selective pressure and caused invasive disease by expressing a high invasive disease potential serotype 24F (not included in PCV13) in multiple countries.[76] This information has subsequently guided the inclusion of serotype 24F in the upcoming PCV formulation. The availability of genome data faciliated the modelling of the prospective effect of new PCV formulations to guide public health agencies in vaccine formulation to maximise the reduction in pneumococcal disease.[77] These retrospective analyses and prospective scenario modelling provide evidence of the value of genomic surveillance in cycles of shaping interventions, evaluating their effect, and monitoring the resulting changes in bacterial populations.

Barriers to genomics implementation at a public health level

The types of barriers to implementation of genomics for AMR surveillance differ depending on the setting. However, the examples provided by food microbiology reference laboratory surveillance and SARS-CoV-2 surveillance systems offer lessons for overcoming these barriers and finding pathways to adoption. Some settings are more advanced in this process than others. In LMICs, poor supply chains, unfavourable costing models for

consumables, and unreliable equipment maintenance support have hampered the establishment of sustained operations and deterred investment (as experienced by the working group and reported by Davedow and colleagues[33]). Other practical barriers identified included concerns around harmonisation and standardisation, and lack of sufficient isolates, epidemiological data, infrastructure, or political will (or a combination of these) to implement, sustain, or improve genomic AMR surveillance. Additional barriers include inadequate funding to establish and support ongoing genomic surveillance, insufficient knowledge exchange between academia and public health institutes leading to a duplication of effort, problems with epidemiological data linkage, and a lack of training in genomic and bioinformatic analysis (the latter is addressed more thoroughly in the second paper in this Series[3]). Many of these barriers probably result from imperfect relationships and poorly defined expectations among policy makers, the research community, the private sector, and public health providers, highlighting the importance of building trust, cooperation, and common goals in these areas.

Recommendations from the working group

Based on workshop discussions, the working group made a series of recommendations centred around five main areas: (1) building capacity in hub and spoke models (also covered in the second paper in this Series[3]); (2) harmonising and standardising surveillance systems; (3) developing and agreeing equitable data sharing and governance frameworks; and (4) improving stakeholder interactions and relationships. The fifth area of focus was delivering training to strengthen genomic surveillance competence among the health scientist workforce which is reported more thoroughly in the second paper in this Series. Recommendations from the working group are captured in a stakeholder focused interaction map (figure).

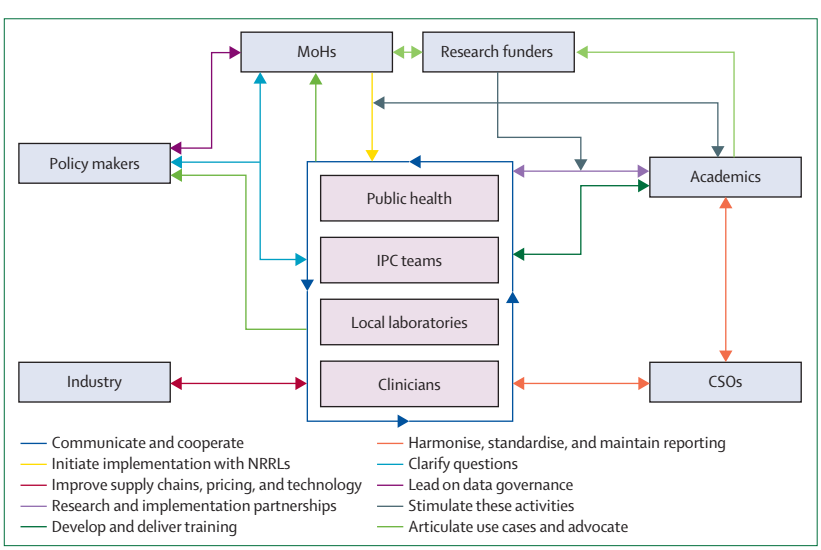

Figure: **Stakeholder interaction map for improvement of the application of genomics for antimicrobial resistance surveillance**
Stakeholders within health delivery are in lighter pink encircled in a box. MoHs=ministries of health. IPC=infection prevention and control. CSOs=clinical standards organisations. NRRLs=national and regional reference laboratories.

Building capacity with hub and spoke models

Where not already in existence, health policy makers and national ministries and departments of health should establish and equip national or regional reference laboratories to act as hubs in hub and spoke models. Local laboratories can then submit bacterial isolates or locally generated sequence data to enable analysis of the national or regional context (covered further in the second paper in this Series[3]). National or regional reference laboratories can provide community services by acting as hubs for aggregated data analysis, and centralised expertise to provide training and external quality assurance schemes and materials—eg, well characterised bacterial strains or genomic DNA, such as those shared by the Danish Technical University with UK AID Fleming Fund SEQAFRICA and the EU Reference Laboratory for antimicrobial resistance network.[78,79] They might also host computational or web-based platforms that allow other laboratories undertaking whole-genome sequencing to submit data to conduct their own analyses or receive an output that places their data into context. National or regional reference laboratories could also offer centralised sequencing services that benefit from the economy of scale for results that might be less dependent on rapid turnaround times (eg, those requiring clinically actionable timeframes), but the appropriate model for distribution of sequencing depends on the resources of the system (see the second paper in this Series[3]).

Harmonising and standardising surveillance systems

Define pathogens and AMR focus to help implement whole-genome sequencing systems

There was general agreement that organism-specific analysis pipelines were needed and that the WHO priority pathogens[60] and Global Antimicrobial Surveillance System[80] pathogen lists provide a good starting point for identifying target organisms. However, for practical implementation, these lists should be initially focused on attainable use cases addressing specific bug–drug combinations, contexts, or objectives, before devoting existing capacity or building new dedicated surveillance pipelines. Pathogen prioritisation should take into consideration how the data output can be used in interventions, such as improved antimicrobial stewardship, outbreak and infection prevention and control measures, or vaccine use. It should also be further refined based on country-specific or region-specific health priorities.

Greater involvement of clinical standards organisations

The European Committee on Antimicrobial Susceptibility Testing (EUCAST) and WHO have already published reports on the role of genomics for bacterial antimicrobial

susceptibility testing and for AMR surveillance.[80,81] These and other international organisations, such as the Clinical Laboratories Standards Institute, can still have a valuable role in the development of standards for genomics for AMR surveillance. Such organisations are well placed to develop consensus protocols and quality control metrics for the use of genomics in AMR surveillance. Some of this work has already commenced. Harmonising organism-specific analytic approaches, as well as interpretive and reporting criteria (as currently done for phenotypic susceptibility testing), is essential for data comparison across countries and with other parts of the One Health triumvirate (ie, surveillance in animals and the environment). Ideally, standards would be produced using an open model (as used by EUCAST) rather than a pay-to-access model (as typically used by the Clinical Laboratories Standards Institute). Standards are also needed for the initial assessment of new analytical pipelines, akin to the International Standardization Organization standard 20776-2 or US Food and Drug Administration guidance that outline acceptable performance criteria for new susceptibility testing devices, and downstream external quality assessment processes. In this regard, some headway has been made for laboratory proficiency testing of genomics in the GenomeTrakr network.[82,83] Achieving consensus on analytical tools and reference databases around which to build pipelines will be challenging as protocols are rapidly evolving. However, meeting regulatory standards for the use of genomic data in public health microbiology (eg, International Standardization Organization 15189 accreditation) needs to be progressed, and in one case has recently been achieved for AMR in *Salmonella* spp.[84] One approach would be a standardised pipeline for species identification, followed by organism-specific pipelines for AMR detection, but that are accessed through a single-user portal (eg, Galaxy, Pathogenwatch, Center for Genomic Epidemiology, and the Pathosystems Resource Integration Centre).[83,85] Decisions about updating organism-specific databases should be guided by steering groups consisting of research groups and reference laboratories with organism-specific expertise (like the model developing in Pathogenwatch)[86,87] and with endorsement of health policy makers.

Improving academic, research, and public health institution partnerships

Genomics researchers need well defined questions from clinicians and public health specialists to properly assess the feasibility of genomics to produce actionable outputs. There are good examples of partnerships between academic and public health institutes (eg, England's National Institute for Health and Care Research [NIHR] Health Protection Research Units; African public health institutes; the Network for Genomic Surveillance in South Africa; Global Pneumococcal Sequencing project public health partners; and, in Australia, the Doherty Institute, AusTrakka, and the Australian Pathogen Genomics Program).[88] However, not all public health institutes or researchers have such partnerships. Researchers will benefit from implementation of their genomics protocols and tools by public health institutes and evaluation by health economists to show their impact and cost-effectiveness in a real-world setting,[89–91] with this impact supplementing and potentially superseding publication as a metric for success. Such partnerships can enable genomic data to be fully exploited by answering specific public health questions, such as shaping vaccination programmes.[92–94] To date, a shortage of trained bioinformatic staff has impeded technology transfer into public health, yet academic–public health partnerships clearly benefit from the availability of bioinformatics expertise for improving service provision through analysis pipeline development, improving genotype–phenotype concordance, and delivering training (see the second paper in this Series[3]).

Interpretability and richness of information derived from genomic data

As the mechanisms that mediate AMR can differ between bacterial genera, different AMR determinant databases and analytical standards are required. There is a lack of evidence on the agreement between AMR phenotype and genotype for some bug–drug combinations, and researchers at the interface between public health and academia will be vital for resolving this discordance, because existing resistance mechanisms become better understood and novel AMR-associated genes and mutations are identified and added to existing curated databases (see the fifth paper in this Series[27]). Many currently used AMR pipelines and databases are supported by the academic sector, but will require ongoing financial support and investment from health budgets in the future. Consideration needs to be given to ensuring that analytic pipelines not only detect the presence or absence of known AMR genes and mutations, but are also designed such that they can detect and characterise emerging novel, and more complex[95] AMR mechanisms. To achieve this outcome, benchmarking and the use of machine learning will be required (see the fifth paper in this Series[27]), as will maximising interpretation of genomics data for other actionable health information (eg, virulence factor profiles and their relationship with disease severity).

For more on **Galaxy** see https://galaxytrakr.org

For more on **Pathogenwatch** see https://pathogen.watch

For more on the **Center for Genomic Epidemiology** see https://www.genomicepidemiology.org/services/

For more on the **Pathosystems Resource Integration Centre** see https://www.bv-brc.org/portal/portal/patric/home

Developing and agreeing equitable data sharing and governance frameworks

Developing agreed data sharing standards is a crucial early step, with reference where appropriate to the Nagoya protocol on the sharing of non-human genomic resources, and ethical considerations.[96] Data with the most serious of implications that require urgent action by public health officials and clinicians (eg, a newly emerging AMR pathogen with pandemic potential) should be

shared openly, with countries being lauded rather than stigmatised for reporting AMR issues. Other than to fulfil legal requirements, data sharing can be inadequately incentivised and so the benefits of data sharing need to be promoted. There is sometimes a reluctance to share data in public archives among laboratories and countries newly adopting genomics over concern this might lead to publication and monetarisation of data by others. Establishing governance structures around data sharing, such as those being developed in the field of biodiversity,[97] is crucial in building trust and ensuring that any benefits are appropriately shared among stakeholders (alongside a focus on supporting end-to-end capacity development in both sequencing and bioinformatics.[3] A lot can be learned and adopted from the experiences of various national sequencing consortia established during the COVID-19 pandemic[98–102] and the Public Health Alliance for Genomic Epidemiology, which has an ethics and data sharing subgroup focused on improving equitable data governance.[103] WHO, the Africa Centers for Disease Control and Prevention (CDC) Pathogen Genomics Initiative, the US CDC, and the European Centre for Disease Prevention and Control could also play leading roles in promoting communication in this area, with WHO highlighting the critical role of a strong governance foundation in their recent global genomic surveillance strategy.[104] Furthermore, WHO have recently published a set of 13 guiding principles for pathogen genome data sharing, which cover many of the same areas and recommendations included in our genomic AMR surveillance workshops, in particular in relation to equitable data sharing and governance.[105]

Improving stakeholder interactions and relationships

At present, a lack of commitment or political will to support adoption of genomics for surveillance can be seen in many countries, including some where the availability of funding might not be prohibitive. Addressing this problem will be key for translation into routine public health use. Policy makers are continually challenged to invest in public health services, yet often focus on services for specific conditions or groups of conditions that have effective advocacy groups, rather than prioritising preventive services, which might have a greater long-term impact on health, albeit in an indirect manner that can be challenging to quantify. Large-scale sequencing of the SARS-CoV-2 virus has helped policy makers understand the utility of genomics for tracking the transmission and evolution of pathogens. This new understanding should be capitalised on, and the capabilities established during the COVID-19 pandemic should be expanded to AMR surveillance. Identifying and developing suitable case studies that show the benefits of genomics will help with advocacy efforts, but will also illustrate how AMR surveillance is more complex (eg, multipathogen and more dynamic) in nature than SARS-CoV-2, requiring more financial commitment and investment to develop and optimise methods.

Strengthening efforts to communicate the value of genomic surveillance among scientists in local, national, and regional laboratories, clinicians, and infection prevention and control teams should be prioritised by health organisations so that genomic outputs are used to their maximum benefit. Furthermore, reporting formats should be established to transform complex data into actionable information for public health practitioners, as has been achieved effectively for SARS-CoV-2 variants of concern.[106] This improvement will help to guide decision making by integrating knowledge of the specific strain of pathogen behind an infection, the broader epidemiological context (eg, linkage to an outbreak), the likelihood for AMR transmissibility, and the selection pressure behind emergence.

Conclusions

The need for increased bioinformatic training and better interaction and communication to raise awareness of the benefits of genomic AMR surveillance among stakeholders were repeating themes in both workshops 1 and 2, which related primarily to AMR surveillance in human health (although many of the findings are equally relevant for animal and environmental AMR surveillance, which are covered in the fourth paper in this Series[107]). There is a clear need for further research and partnership among policy makers, health providers, and academics to harmonise the generation and interpretation of genomic data and to build and maintain standards. While implementation of genomic AMR surveillance in clinical settings will have its challenges, the knowledge exchange, cooperation, and trust required to facilitate buy-in for contributing and sharing data at a public health level will be much harder, meaning that establishing good relationships underpinned by strong governance and agreed goals will be essential for meaningful progress.

Contributors

SJP, NAF, KSB, EJ, JGN, and JTM conceptualised the study. KSB, EJ, and JGN curated data. SJP, NAF, JGN, and JTM acquired funding. All authors did the investigation. SJP, NAF, KSB, and EJ developed the methods. SJP, NAF, KSB, EJ, JGN, and JTM were responsible for project administration. SJP, NAF, KSB, and EJ were responsible for supervision. KSB prepared the original data visualisations. KSB, EJ, KLH, SWL, and LS-B wrote the original draft. All authors reviewed and edited the paper, and engaged and participated in the workshop.

Declaration of interests

KSB reports funding from the Biotechnology and Biological Sciences Research Council and Medical Research Council (MRC) and partial salary cover from Wellcome Trust and the UK Health Security Agency (UKHSA) over the course of this work. EJ had partial salary cover from Wellcome Trust over the course of this work. SWL has received the Robert Austrian Research Award sponsored by Pfizer in 2022. DGA reports funding from the NIHR. INO reports funding from the Bill & Melinda Gates Foundation, Joint Programming Intiative on Antimicrobial Resistance, Wellcome Trust, Grand Challenges Africa Award, and UK MRC; royalties for *Genetics: Genes, Genomes and Evolution* (Oxford University Press), and *Divining Without Seeds and for Antimicrobial Resistance in Developing Countries* (Springer); consulting fees from Wellcome Trust; honoraria for Harvard University seminars; and the Peter Wildy Lecture Award 2023. DGA, BE, RSH, and INO report receiving funding from the UK Department of Health and Social

Care in the form of a grant managed by the Fleming Fund and work performed under the auspices of the SEQAFRICA project. LS-B reports funding by Conselleria de Sanitat Universal i Salut Pública, Generalitat Valenciana, Valencia (Spain), under Plan GenT (reference number CDEI-06/20-B). NAF reports funding from the Gates Foundation, UK Research and Innovation, and NIHR. SJP is a member of the Scientific Advisory Board of Next Gen Diagnostics and was supported by Illumina to attend the European Congress of Clinical Microbiology and Infectious Disease conference. All other authors declare no competing interests.

Acknowledgments

This research was funded by Wellcome Trust. The funding source had no role in study or workshop design, data collection, analysis, interpretation, writing of the Series paper, or in the decision to submit the Series paper for publication. Developmental editing support for this work was provided by Germinate Science Consulting. KSB is affiliated with the NIHR Health Protection Research Unit (HPRU) in Gastrointestinal Infections at the University of Liverpool in partnership with the UKHSA, in collaboration with the University of Warwick. EJ is an Imperial College Research Fellow, funded by Rosetrees Trust and the Stoneygate Trust; and is affiliated with the NIHR HPRU in Healthcare Associated Infections and Antimicrobial Resistance at Imperial College London in partnership with the UKHSA, in collaboration with Imperial Healthcare Partners, the University of Cambridge, and the University of Warwick. The views expressed are those of the authors and not necessarily those of the National Health Service, the NIHR, the Department of Health and Social Care, or the UKHSA. Members of the SEDRIC Genomics Surveillance Working Group are listed in the appendix of the first paper in this Series.[1]

References

1 Baker KS, Jauneikaite E, Nunn JG, et al. Evidence review and recommendations for the implementation of genomics for antimicrobial resistance surveillance: reports from an international expert group. *Lancet Microbe* 2023; published online Nov 14. https://doi.org/10.1016/S2666-5247(23)00281-1.

2 Kekre M, Arevalo SA, Valencia MF, et al. Integrating scalable genome sequencing into microbiology laboratories for routine antimicrobial resistance surveillance. *Clin Infect Dis* 2021; **73** (suppl 4)**:** S258–66.

3 Jauneikate E, Baker KS, Nunn JG, et al. Genomics for antimicrobial resistance surveillance to support infection prevention and control in health-care facilities. *Lancet Microbe* 2023; published online Nov 14. https://doi.org/10.1016/S2666-5247(23)00282-3.

4 Stoesser N, Sheppard AE, Pankhurst L, et al. Evolutionary history of the global emergence of the *Escherichia coli* epidemic clone ST131. *MBio* 2016; **7:** e02162.

5 Okoro CK, Kingsley RA, Connor TR, et al. Intracontinental spread of human invasive *Salmonella typhimurium* pathovariants in sub-Saharan Africa. *Nat Genet* 2012; **44:** 1215–21.

6 Chung The H, Boinett C, Pham Thanh D, et al. Dissecting the molecular evolution of fluoroquinolone-resistant *Shigella sonnei*. *Nat Commun* 2019; **10:** 4828.

7 Karp BE, Tate H, Plumblee JR, et al. National antimicrobial resistance monitoring system: two decades of advancing public health through integrated surveillance of antimicrobial resistance. *Foodborne Pathog Dis* 2017; **14:** 545–57.

8 Li W, Cui Q, Bai L, et al. Application of whole-genome sequencing in the national molecular tracing network for foodborne disease surveillance in China. *Foodborne Pathog Dis* 2021; **18:** 538–46.

9 Chattaway MA, Dallman TJ, Larkin L, et al. The transformation of reference microbiology methods and surveillance for *Salmonella* with the use of whole genome sequencing in England and Wales. *Front Public Health* 2019; **7:** 317.

10 Gattuso A, Cella E, Fillo S, et al. Phylogenetic and evolutionary genomic analysis of *Listeria monocytogenes* clinical strains in the framework of foodborne listeriosis risk assessment. *Front Microbiol* 2022; **13:** 816880.

11 Ashton PM, Owen SV, Kaindama L, et al. Public health surveillance in the UK revolutionises our understanding of the invasive *Salmonella typhimurium* epidemic in Africa. *Genome Med* 2017; **9:** 92.

12 Park CJ, Li J, Zhang X, Gao F, Benton CS, Andam CP. Diverse lineages of multidrug resistant clinical *Salmonella enterica* and a cryptic outbreak in New Hampshire, USA revealed from a year-long genomic surveillance. *Infect Genet Evol* 2021; **87:** 104645.

13 Siira L, Naseer U, Alfsnes K, Hermansen NO, Lange H, Brandal LT. Whole genome sequencing of *Salmonella* Chester reveals geographically distinct clusters, Norway, 2000 to 2016. *Euro surveill* 2019; **24:** 1800186.

14 Baker KS, Campos J, Pichel M, et al. Whole genome sequencing of *Shigella sonnei* through PulseNet Latin America and Caribbean: advancing global surveillance of foodborne illnesses. *Clin Microbiol Infect* 2017; **23:** 845–53.

15 Bottichio L, Keaton A, Thomas D, et al. Shiga toxin-producing *Escherichia coli* infections associated with romaine lettuce-United States, 2018. *Clin Infect Dis* 2020; **71:** e323–30.

16 Self JL, Conrad A, Stroika S, et al. Multistate outbreak of listeriosis associated with packaged leafy green salads, United States and Canada, 2015–2016. *Emerg Infect Dis* 2019; **25:** 1461–68.

17 Carvalho JP, Benusic M, Codat R, Gruescu R, Haydu L, Loh LC. Health risks of frozen raw breaded chicken products: a local health unit perspective. *CCDR* 2020; **46**: 403–08.

18 Gaudreau C, Bernaquez I, Pilon PA, Goyette A, Yared N, Bekal S. Clinical and genomic investigation of an international ceftriaxone- and azithromycin-resistant *Shigella sonnei* cluster among men who have sex with men, Montréal, Canada 2017-2019. *Microbiol Spectr* 2022; **10:** e0233721.

19 Alba P, Leekitcharoenphon P, Franco A, et al. Molecular epidemiology of *mcr*-encoded colistin resistance in *Enterobacteriaceae* from food-producing animals in Italy revealed through the EU harmonized antimicrobial resistance monitoring. *Front Microbiol* 2018; **9:** 1217.

20 Conesa A, Garofolo G, Di Pasquale A, Cammà C. Monitoring AMR in *Campylobacter jejuni* from Italy in the last 10 years (2011–2021): microbiological and WGS data risk assessment. *EFSA J* 2022; **20** (suppl 1)**:** e200406.

21 Baker KS, Dallman TJ, Ashton PM, et al. Intercontinental dissemination of azithromycin-resistant shigellosis through sexual transmission: a cross-sectional study. *Lancet Infect Dis* 2015; **15:** 913–21.

22 Baker KS, Dallman TJ, Field N, et al. Horizontal antimicrobial resistance transfer drives epidemics of multiple *Shigella* species. *Nat Commun* 2018; **9:** 1462.

23 Moreno-Switt AI, Pezoa D, Sepúlveda V, et al. Transduction as a potential dissemination mechanism of a clonal *qnrB19*-carrying plasmid isolated from *Salmonella* of multiple serotypes and isolation sources. *Front Microbiol* 2019; **10:** 2503.

24 Feldgarden M, Brover V, Haft DH, et al. Validating the AMRFinder tool and resistance gene database by using antimicrobial resistance genotype-phenotype correlations in a collection of isolates. *Antimicrob Agents Chemother* 2019; **63:** e00483-19.

25 Rokney A, Valinsky L, Vranckx K, et al. WGS-based prediction and analysis of antimicrobial resistance in *Campylobacter jejuni* isolates from Israel. *Front Cell Infect Microbiol* 2020; **10:** 365.

26 Neuert S, Nair S, Day MR, et al. Prediction of phenotypic antimicrobial resistance profiles from whole genome sequences of non-typhoidal *Salmonella enterica*. *Front Microbiol* 2018; **9:** 592.

27 Wheeler NE, Price V, Cunningham-Oakes E, et al. Innovations in genomic antimicrobial resistance surveillance. *Lancet Microbe* 2023; published online Nov 14. https://doi.org/10.1016/S2666-5247(23)00285-9.

28 Bogaerts B, Nouws S, Verhaegen B, et al. Validation strategy of a bioinformatics whole genome sequencing workflow for Shiga toxin-producing *Escherichia coli* using a reference collection extensively characterized with conventional methods. *Microb Genom* 2021; **7:** mgen000531.

29 Bessonov K, Laing C, Robertson J, et al. ECTyper: in silico *Escherichia coli* serotype and species prediction from raw and assembled whole-genome sequence data. *Microb Genom* 2021; **7:** 000728.

30 Cooper AL, Low AJ, Koziol AG, et al. Systematic evaluation of whole genome sequence-based predictions of *Salmonella* serotype and antimicrobial resistance. *Front Microbiol* 2020; **11:** 549.

31 Timme RE, Sanchez Leon M, Allard MW. Utilizing the public GenomeTrakr database for foodborne pathogen traceback. *Methods Mol Biol* 2019; **1918:** 201–12.

32 Chinen I, Campos J, Dorji T, Pérez Gutiérrez E. PulseNet Latin America and the Caribbean Network: present and future. *Foodborne Pathog Dis* 2019; **16:** 489–97.

33 Davedow T, Carleton H, Kubota K, et al. PulseNet international survey on the implementation of whole genome sequencing in low and middle-income countries for foodborne disease surveillance. *Foodborne Pathog Dis* 2022; **19:** 332–40.

34 Mook P, Gardiner D, Verlander NQ, et al. Operational burden of implementing *Salmonella enteritidis* and *typhimurium* cluster detection using whole genome sequencing surveillance data in England: a retrospective assessment. *Epidemiol Infect* 2018; **146:** 1452–60.

35 Paranthaman K, Mook P, Curtis D, et al. Development and evaluation of an outbreak surveillance system integrating whole genome sequencing data for non-typhoidal *Salmonella* in London and south east of England, 2016–17. *Epidemiol Infect* 2021; **149:** e164.

36 European Centre for Disease Prevention and Control. European Antimicrobial Resistance Surveillance Network. 2023. https://www.ecdc.europa.eu/en/about-us/networks/disease-networks-and-laboratory-networks/ears-net-data (accessed Sept 24, 2023).

37 WHO. Global antimicrobial resistance and use surveillance system. 2018. https://www.who.int/initiatives/glass (accessed Sept 24, 2023).

38 Kongthai P, Thummeepak R, Leungtongkam U, et al. Insight into molecular epidemiology, antimicrobial resistance, and virulence genes of extensively drug-resistant *Acinetobacter baumannii* in Thailand. *Microb Drug Resist* 2021; **27:** 350–59.

39 Di Gregorio S, Haim MS, Vielma Vallenilla J, et al. Genomic epidemiology of CC30 methicillin-resistant *Staphylococcus aureus* strains from Argentina reveals four major clades with distinctive genetic features. *MSphere* 2021; **6:** e01297-20.

40 Karlsson M, Lutgring JD, Ansari U, et al. Molecular characterization of carbapenem-resistant Enterobacterales collected in the United States. *Microb Drug Resist* 2022; **28:** 389–97.

41 Baker KS. Microbe hunting in the modern era: reflecting on a decade of microbial genomic epidemiology. *Curr Biol* 2020; **30:** R1124–30.

42 McKay SL, Vlachos N, Daniels JB, et al. Molecular epidemiology of carbapenem-resistant *Acinetobacter baumannii* in the United States, 2013-2017. *Microb Drug Resist* 2022; **28:** 645–53.

43 Afolayan AO, Oaikhena AO, Aboderin AO, et al. Clones and clusters of antimicrobial-resistant *Klebsiella* from southwestern Nigeria. *Clin Infect Dis* 2021; **73** (suppl 4)**:** S308–15.

44 Yao Y, Falgenhauer L, Falgenhauer J, et al. Carbapenem-resistant *Citrobacter* spp. as an emerging concern in the hospital-setting: results from a genome-based regional surveillance study. *Front Cell Infect Microbiol* 2021; **11:** 744431.

45 Chen C, Xu H, Liu R, et al. Emergence of neonatal sepsis caused by MCR-9- and NDM-1-co-producing *Enterobacter hormaechei* in China. *Front Cell Infect Microbiol* 2022; **12:** 879409.

46 Shropshire WC, Dinh AQ, Earley M, et al. Accessory genomes drive independent spread of carbapenem-resistant *Klebsiella pneumoniae* clonal groups 258 and 307 in Houston, TX. *MBio* 2022; **13:** e0049722.

47 Dong H, Li Y, Cheng J, et al. Genomic epidemiology insights on NDM-producing pathogens revealed the pivotal role of plasmids on bla_{NDM} transmission. *Microbiol Spectr* 2022; **10:** e0215621.

48 Legese MH, Asrat D, Aseffa A, Hasan B, Mihret A, Swedberg G. Molecular epidemiology of extended-spectrum beta-lactamase and AmpC producing Enterobacteriaceae among sepsis patients in Ethiopia: a prospective multicenter study. *Antibiotics* 2022; **11:** 131.

49 Stoesser N, Phan HTT, Seale AC, et al. Genomic epidemiology of complex, multispecies, plasmid-borne bla_{KPC} carbapenemase in Enterobacterales in the United Kingdom from 2009 to 2014. *Antimicrob Agents Chemother* 2020; **64:** e02244-19.

50 Aguilar-Zamora E, Weimer BC, Torres RC, et al. Molecular epidemiology and antimicrobial resistance of *Clostridioides difficile* in hospitalized patients from Mexico. *Front Microbiol* 2022; **12:** 787451.

51 Lam MMC, Wick RR, Watts SC, Cerdeira LT, Wyres KL, Holt KE. A genomic surveillance framework and genotyping tool for *Klebsiella pneumoniae* and its related species complex. *Nat Commun* 2021; **12:** 4188.

52 Guthrie JL, Teatero S, Hirai S, et al. Genomic epidemiology of invasive methicillin-resistant *Staphylococcus aureus* infections among hospitalized individuals in Ontario, Canada. *J Infect Dis* 2020; **222:** 2071–81.

53 Lee RS, Gonçalves da Silva A, Baines SL, et al. The changing landscape of vancomycin-resistant *Enterococcus faecium* in Australia: a population-level genomic study. *J Antimicrob Chemother* 2018; **73:** 3268–78.

54 Zhou K, Tang X, Wang L, et al. An emerging clone (ST457) of *Acinetobacter baumannii* clonal complex 92 with enhanced virulence and increasing endemicity in south China. *Clin Infect Dis* 2018; **67** (suppl 2)**:** S179–88.

55 Jamal AJ, Mataseje LF, Williams V, et al. Genomic Epidemiology of carbapenemase-producing enterobacterales at a hospital system in Toronto, Ontario, Canada, 2007 to 2018. *Antimicrob Agents Chemother* 2021; **65:** e0036021.

56 Carlos CC, Masim MAL, Lagrada ML, et al. Genome sequencing identifies previously unrecognized *Klebsiella pneumoniae* outbreaks in neonatal intensive care units in the Philippines. *Clin Infect Dis* 2021; **73** (suppl 4)**:** S316–24.

57 Viehweger A, Blumenscheit C, Lippmann N, et al. Context-aware genomic surveillance reveals hidden transmission of a carbapenemase-producing *Klebsiella pneumoniae*. *Microb Genom* 2021; **7:** 000741.

58 Eyre DW, Shaw R, Adams H, et al. WGS to determine the extent of *Clostridioides difficile* transmission in a high incidence setting in north Wales in 2015. *J Antimicrob Chemother* 2019; **74:** 1092–100.

59 Halpin AL, McDonald LC, Elkins CA. Framing bacterial genomics for public health (care). *J Clin Microbiol* 2021; **59:** e0013521.

60 WHO. WHO publishes list of bacteria for which new antibiotics are urgently needed. Feb 27, 2017. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed (accessed Sept 24, 2023).

61 Sánchez-Busó L, Golparian D, Corander J, et al. The impact of antimicrobials on gonococcal evolution. *Nat Microbiol* 2019; **4:** 1941–50.

62 Golparian D, Harris SR, Sánchez-Busó L, et al. Genomic evolution of *Neisseria gonorrhoeae* since the preantibiotic era (1928–2013): antimicrobial use/misuse selects for resistance and drives evolution. *BMC Genomics* 2020; **21:** 116.

63 Bignell C, Unemo M, Radcliffe K, et al. 2012 European guideline on the diagnosis and treatment of gonorrhoea in adults. *Int J STD AIDS* 2013; **24:** 85–92.

64 European Centre for Disease Prevention and Control. Gonococcal antimicrobial susceptibility surveillance in Europe. Results summary 2018. European Centre for Disease Prevention and Control, 2020. https://www.ecdc.europa.eu/sites/default/files/documents/gonococcal-antimicrobial-susceptibility-Euro-GASP-2018.pdf (accessed Sept 28, 2023).

65 Cole MJ, Spiteri G, Jacobsson S, et al. Overall low extended-spectrum cephalosporin resistance but high azithromycin resistance in *Neisseria gonorrhoeae* in 24 European countries, 2015. *BMC Infect Dis* 2017; **17:** 617.

66 Fifer H, Saunders J, Soni S, Sadiq ST, FitzGerald M. 2018 UK national guideline for the management of infection with *Neisseria gonorrhoeae*. *Int J STD AIDS* 2020; **31:** 4–15.

67 St Cyr S, Barbee L, Workowski KA, et al. Update to CDC's treatment guidelines for gonococcal infection, 2020. *MMWR Morb Mortal Wkly Rep* 2020; **69:** 1911–16.

68 Sánchez-Busó L, Cole MJ, Spiteri G, et al. Europe-wide expansion and eradication of multidrug-resistant *Neisseria gonorrhoeae* lineages: a genomic surveillance study. *Lancet Microbe* 2022; **3:** e452–63.

69 Harris SR, Cole MJ, Spiteri G, et al. Public health surveillance of multidrug-resistant clones of *Neisseria gonorrhoeae* in Europe: a genomic survey. *Lancet Infect Dis* 2018; **18:** 758–68.

70 Unemo M, Ahlstrand J, Sánchez-Busó L, et al. High susceptibility to zoliflodacin and conserved target (GyrB) for zoliflodacin among 1209 consecutive clinical *Neisseria gonorrhoeae* isolates from 25 European countries, 2018. *J Antimicrob Chemother* 2021; **76:** 1221–28.

71 Wellcome, The Boston Consulting Group. Vaccines to tackle drug resistant infections: an evaluation of R&D opportunities, 2021. https://vaccinesforamr.org/wp-content/uploads/2018/09/Vaccines_for_AMR.pdf (accessed Sept 24, 2023).

72 Wahl B, O'Brien KL, Greenbaum A, et al. Burden of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b disease in children in the era of conjugate vaccines: global, regional, and national estimates for 2000–15. *Lancet Glob Health* 2018; **6:** e744–57.

73 Klugman KP, Black S. Impact of existing vaccines in reducing antibiotic resistance: primary and secondary effects. *Proc Natl Acad Sci USA* 2018; **115:** 12896–901.

74 Lo SW, Gladstone RA, van Tonder AJ, et al. Pneumococcal lineages associated with serotype replacement and antibiotic resistance in childhood invasive pneumococcal disease in the post-PCV13 era: an international whole-genome sequencing study. *Lancet Infect Dis* 2019; **19:** 759–69.

75 Microbiology Society. Global pneumococcal sequencing collection. 2022. https://www.microbiologyresearch.org/content/global-pneumococcal-sequencing-collection (accessed July 19, 2022).

76 Lo SW, Mellor K, Cohen R, et al. Emergence of a multidrug-resistant and virulent *Streptococcus pneumoniae* lineage mediates serotype replacement after PCV13: an international whole-genome sequencing study. *Lancet Microbe* 2022; **3:** e735–43.

77 Colijn C, Corander J, Croucher NJ. Designing ecologically optimized pneumococcal vaccines using population genomics. *Nat Microbiol* 2020; **5:** 473–85.

78 Technical University of Denmark, National Food Institute. Extending whole genome capacity for AMR surveillance: Fleming Fund regional grant SEQAFRICA. 2023. https://antimicrobialresistance.dk/seqafrica.aspx (accessed Jan 20, 2023).

79 Global Surveillance. About the DTU genomic proficiency test. 2023. https://www.globalsurveillance.eu/projects/genomic-proficiency-test-2021 (accessed Jan 20, 2023).

80 Antimicrobial Resistance Division, Global Antimicrobial Resistance Surveillance System (GLASS), Research for Health, Surveillance & Evidence and Laboratory Strengthening, Surveillance, Prevention and Control. GLASS whole genome sequencing for surveillance of antimicrobial resistance, 2020. https://iris.who.int/bitstream/handle/10665/334354/9789240011007-eng.pdf?sequence=1 (accessed Sept 23, 2023).

81 Ellington MJ, Ekelund O, Aarestrup FM, et al. The role of whole genome sequencing in antimicrobial susceptibility testing of bacteria: report from the EUCAST subcommittee. *Clin Microbiol Infect* 2017; **23:** 2–22.

82 Mitchell PK, Wang L, Stanhope BJ, et al. Multi-laboratory evaluation of the Illumina iSeq platform for whole genome sequencing of *Salmonella*, *Escherichia coli* and *Listeria*. *Microb Genom* 2022; **8:** 000717.

83 Timme RE, Lafon PC, Balkey M, et al. Gen-FS coordinated proficiency test data for genomic foodborne pathogen surveillance, 2017 and 2018 exercises. *Sci Data* 2020; **7:** 402.

84 Sherry NL, Horan KA, Ballard SA, et al. An ISO-certified genomics workflow for identification and surveillance of antimicrobial resistance. *Nat Commun* 2023; **14:** 60.

85 Gangiredla J, Rand H, Benisatto D, et al. GalaxyTrakr: a distributed analysis tool for public health whole genome sequence data accessible to non-bioinformaticians. *BMC Genomics* 2021; **22:** 114.

86 Argimón S, David S, Underwood A, et al. Rapid genomic characterization and global surveillance of *Klebsiella* using pathogenwatch. *Clin Infect Dis* 2021; **73** (suppl 4): S325–35.

87 Sánchez-Busó L, Yeats CA, Taylor B, et al. A community-driven resource for genomic epidemiology and antimicrobial resistance prediction of *Neisseria gonorrhoeae* at Pathogenwatch. *Genome Med* 2021; **13:** 61.

88 Hoang T, da Silva AG, Jennison AV, Williamson DA, Howden BP, Seemann T. AusTrakka: fast-tracking nationalized genomics surveillance in response to the COVID-19 pandemic. *Nat Commun* 2022; **13:** 865.

89 Gordon LG, Elliott TM, Forde B, et al. Budget impact analysis of routinely using whole-genomic sequencing of six multidrug-resistant bacterial pathogens in Queensland, Australia. *BMJ Open* 2021; **11:** e041968.

90 Brown B, Allard M, Bazaco MC, Blankenship J, Minor T. An economic evaluation of the Whole Genome Sequencing source tracking program in the U.S. *PLoS One* 2021; **16:** e0258262.

91 Alleweldt F, Kara S, Best K, et al. Economic evaluation of whole genome sequencing for pathogen identification and surveillance—results of case studies in Europe and the Americas 2016 to 2019. *Euro Surveill* 2021; **26:** 1900606.

92 Bengtsson RJ, Simpkin AJ, Pulford CV, et al. Pathogenomic analyses of *Shigella* isolates inform factors limiting shigellosis prevention and control across LMICs. *Nat Microbiol* 2022; **7:** 251–61.

93 Lefrancq N, Bouchez V, Fernandes N, et al. Global spatial dynamics and vaccine-induced fitness changes of *Bordetella pertussis*. *Sci Transl Med* 2022; **14:** eabn3253.

94 Wyres KL, Nguyen TNT, Lam MMC, et al. Genomic surveillance for hypervirulence and multi-drug resistance in invasive *Klebsiella pneumoniae* from south and southeast Asia. *Genome Med* 2020; **12:** 11.

95 Davies TJ, Stoesser N, Sheppard AE, et al. Reconciling the potentially irreconcilable? Genotypic and phenotypic amoxicillin-clavulanate resistance in *Escherichia coli*. *Antimicrob Agents Chemother* 2020; **64:** e02026–19.

96 Milne R, Patch C. Ethical challenges associated with pathogen and host genetics in infectious disease. *New Bioeth* 2023; **29:** 24–36.

97 Scholz AH, Freitag J, Lyal CHC, et al. Multilateral benefit-sharing from digital sequence information will support both science and biodiversity conservation. *Nat Commun* 2022; **13:** 1086.

98 Msomi N, Mlisana K, de Oliveira T, et al. A genomics network established to respond rapidly to public health threats in South Africa. *Lancet Microbe* 2020; **1:** e229–30.

99 Griffiths EJ, Timme RE, Mendes CI, et al. Future-proofing and maximizing the utility of metadata: the PHA4GE SARS-CoV-2 contextual data specification package. *Gigascience* 2022; **11:** 11.

100 Chen Z, Azman AS, Chen X, et al. Global landscape of SARS-CoV-2 genomic surveillance and data sharing. *Nat Genet* 2022; **54:** 499–507.

101 Brito AF, Semenova E, Dudas G, et al. Global disparities in SARS-CoV-2 genomic surveillance. *Nat Commun* 2022; **13:** 7003.

102 The COVID-19 Genomics UK (COG-UK) consortium. An integrated national scale SARS-CoV-2 genomic surveillance network. *Lancet Microbe* 2020; **1:** e99–100.

103 Bedeker A, Nichols M, Allie T, et al. A framework for the promotion of ethical benefit sharing in health research. *BMJ Glob Health* 2022; **7:** e008096.

104 WHO. Global genomic surveillance strategy for pathogens with pandemic and epidemic potential 2022–2032. World Health Organization, 2022. https://iris.who.int/bitstream/handle/10665/352580/9789240046979-eng.pdf?sequence=1 (accessed Sept 24, 2023).

105 WHO. WHO guiding principles for pathogen genome data sharing. World Health Organization, 2022. https://iris.who.int/bitstream/handle/10665/364222/9789240061743-eng.pdf?sequence=1 (accessed Sept 24, 2023).

106 WHO. Tracking SARS-CoV-2 variants. 2023. https://www.who.int/activities/tracking-SARS-CoV-2-variants (accessed Jan 20, 2023).

107 Muloi DM, Jauneikaite E, Anjum MF, et al. Exploiting genomics for antimicrobial resistance surveillance at One Health interfaces. *Lancet Microbe* 2023; published online Nov 14. https://doi.org/10.1016/S2666-5247(23)00284-7.