The importance of public health genomics for ensuring health security for Australia

Coordination is required to future-proof Australia's capacity and leadership in public health genomics

Infectious diseases are an ever-present risk to society, particularly because of globalisation and the threat of antimicrobial-resistant organisms. Recently, a World Health Organization (WHO) team conducted a joint external evaluation of Australia's core capacities under the International Health Regulations. The evaluation gave Australia a high scorecard in all areas relevant to protecting health from emerging infectious disease threats.[1] However, an area that the evaluation team highlighted for critical improvement was the integration of whole genome sequencing-based surveillance into existing communicable diseases control systems in the Australian setting.[1] While Australia scored highly for laboratory testing of priority diseases, the team recommended "integration of laboratory testing data with epidemiological data particularly in the context of whole genome sequencing".[1]

Whole genome sequencing involves sequencing the entire genome of a pathogen, and the genomic information gleaned can be used to determine pathogen identity, predict antimicrobial resistance and virulence traits, and understand relationships between pathogens.[2] The use of whole genome sequencing has the potential to transform the investigation and surveillance of communicable diseases by providing the highest possible characterisation of pathogens, enabling earlier and accurate detection of outbreaks and a timely and targeted public health response.[2] One key advantage of whole genome sequencing-based approaches is that they provide a one-stop shop for microbiological analyses, rather than multiple, iterative laboratory tests.

Similar to the WHO joint external evaluation report, the National Framework for Communicable Disease Control previously noted that a coordinated and strategic approach to infectious diseases surveillance and outbreak investigation is vital to improve communicable diseases control across Australia, and to limit costs to human health and the economy.[3] Outbreaks of infectious diseases routinely cross state and territory borders, and require strategic national coordination. Recent examples of nationally disseminated outbreaks include listeriosis from contaminated rockmelon, salmonellosis in contaminated fresh produce such as lettuce and bean sprouts, and a large outbreak of serogroup W *Neisseria meningitidis* extending into central Australia. All of these outbreaks have required rapid whole genome sequencing to confirm relatedness of strains in different geographical locations.

To ensure the best health outcomes and keep pace internationally, implementation of a practical national strategy for microbial genomics is required, consistent with that of the implementation of human genomics into medicine.[4] In the absence of a national communicable disease agency, Australia has developed a complex series of networks and committees for epidemiological and laboratory investigation of communicable diseases, including those caused by antimicrobial-resistant pathogens. However, there remain considerable constraints in sharing epidemiological and laboratory data at a national level (eg, privacy concerns about sharing data across state borders), along with jurisdictional differences in laboratory testing and reporting. Further, smaller jurisdictions often do not have access to timely whole genome sequencing and associated bioinformatic expertise, leading to an inequity of resource and infrastructure across the country.

Whole genome sequencing: international successes

In the United States, the Food and Drug Administration has developed the GenomeTrakr project for whole genome sequencing-based surveillance of foodborne pathogens. This initiative has helped US state public health laboratories build the capacity necessary to collect and share whole genome sequencing data.[5] GenomeTrakr collects raw DNA sequence data for foodborne pathogens centrally in real time, which are immediately uploaded to a publicly available DNA sequence archive housed at the National Center for Biotechnology Information at the National Institutes of Health. Contextual information (metadata), such as name of microbial species, sample collection date, state or country, and sample source, are included with genomic data. Nightly centralised analyses identify genetic linkages among isolates to alert relevant authorities. When required, there is collaboration between public health agencies to share more detailed metadata. Estimating the public health impact of this system is complex, although it has led to faster detection of foodborne disease outbreaks, and regulatory interventions such as closing contaminated facilities and product recalls.[5] Similarly, Australia has experienced the benefits of international data sharing when human *Listeria monocytogenes* sequences were submitted to GenomeTrakr, which identified an identical strain in an Australian man and Californian stone fruit that was corroborated epidemiologically.[6]

In the United Kingdom, Public Health England has implemented genomics into public health microbiology nationally. The model of delivery is highly centralised, with a large sequencing facility and a core bioinformatics unit for processing and analysing

Deborah A Williamson[1]
Martyn D Kirk[2]
Vitali Sintchenko[3]
Benjamin P Howden[1]

1 University of Melbourne, Melbourne, VIC.
2 National Centre for Epidemiology and Population Health, Australian National University, Canberra, ACT.
3 University of Sydney, Sydney, NSW.

deborah.williamson@unimelb.edu.au; bhowden@unimelb.edu.au

doi: 10.5694/mja2.50063

1 Overview of challenges and opportunities relating to implementation of microbial genomics in Australia

Major challenges in implementation	Opportunities afforded by microbial genomics
• Sustained funding for maintaining a nationally coordinated microbial genomics service • Improving bioinformatics expertise in some jurisdictions • Improving infrastructure in relation to data storage and computational capacity • Standardisation of bioinformatic analysis between jurisdictions through a common platform • Coordination of genomics activities at a national level • Improving capacity to share sequence data and epidemiological data across jurisdictions	• Providing the highest resolution typing data, which is superior to current approaches • Earlier detection and more rapid response to disease outbreaks (eg, foodborne disease) • Assessment of disease transmission and spread (eg, tuberculosis) • Accurate and rapid source attribution of food and waterborne outbreaks • Rapid detection and characterisation of emerging pathogens or new mechanisms of antibiotic resistance • Monitor and predict effectiveness of vaccines for communicable diseases pathogens (eg, *Neisseria meningitidis*, influenza)

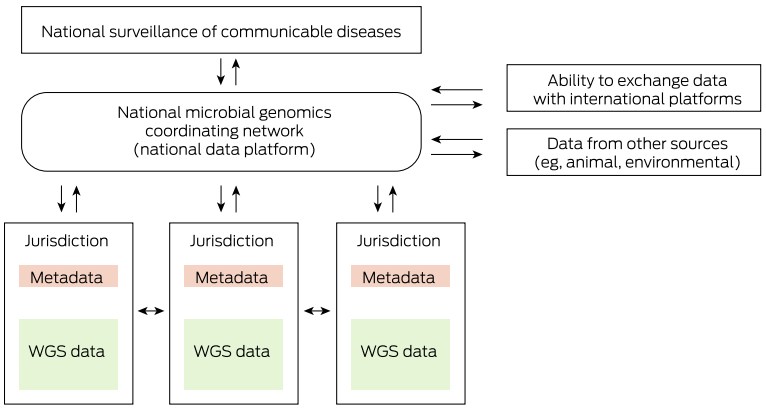
all samples. Domain specialists, such as laboratory scientists and epidemiologists, are integrally involved in analysis to ensure meaningful interpretation of results and enact a suitable public health response.[7] This centralised approach has demonstrated utility for improving national surveillance of enteric pathogens in the UK. For example, when applied to surveillance of Shiga toxin-producing *Escherichia coli* serotype O157, whole genome sequencing detected twice as many disease clusters than traditional typing methods, including common source outbreaks that were geographically distributed across the country.[8] Similarly, routine whole genome sequencing of *Salmonella enterica* and *Shigella* isolates in England and Wales has generated a rich repository of genomic data, providing unparalleled levels of strain discrimination and a wealth of information on the emergence and spread of antimicrobial-resistant pathogens.[9,10]

Whole genome sequencing implementation in Australia

Public health agencies in Australia have already made good use of whole genome sequencing for outbreak investigations; for example, in a recent outbreak of *Mycobacterium chimaera* infections associated with cardiac surgery,[11] a large outbreak of Shiga toxin-producing *E. coli* in Queensland,[12] and numerous multijurisdictional *Salmonella* outbreaks. Further, jurisdictions have been successfully employing whole genome sequencing for routine public health surveillance of several other diseases with epidemic potential, including those caused by antimicrobial-resistant pathogens.[13–15] However, implementation of microbial genomics in public health laboratories in Australia remains sporadic, with varying resources, capacities and capabilities across jurisdictions. Moreover, sharing of both whole genome sequencing and epidemiological data for surveillance purposes across Australia is problematic due to complex governance arrangements and lack of a consistent data management framework. Until recently, the use of whole genome sequencing as an investigative tool in Australian public health laboratories has largely focused on research, rather than being embedded in routine public health practice — an observation highlighted in the recent WHO joint external evaluation report.[1]

To help address these issues, laboratories have recently established a Communicable Diseases Genomic Network — a collaborative public health, clinical microbiology and infectious diseases partnership — that aims to facilitate the implementation of whole genome sequencing into infectious diseases surveillance and response in Australia (Box 1). This group forms the basis for improved and scalable genomics-based surveillance and outbreak response, but there is still a pressing need for effective implementation through clear designation of a coordinating network that ensures access to technology across the country, protocols for national data sharing, a sustainable national bioinformatics platform, and standardised approaches to analysis. The most appropriate structural model for coordination of microbial genomics in Australia is still evolving (and may differ according to domain), but overseas experience has highlighted the benefits of a centralised service (even

2 A proposed schematic model for microbial genomics coordination in Australia



WGS = whole genome sequencing. In this structure, jurisdictions could exchange genomic (and relevant epidemiological data) through a secure national data storage and analysis platform. Centralised daily analysis of jurisdictional genomic data would provide information on relatedness of pathogens, which would subsequently inform timely public health responses at both jurisdictional and national levels. ◆

in federated countries), with a networked "hub and spoke" model for national laboratory surveillance that is effective and capable of resolving national level outbreaks in a timely fashion.[7] Importantly, centralising microbial genomic analysis in Australia would facilitate both intra-jurisdictional surveillance and outbreak investigations, while enabling concurrent national surveillance. One proposed structural model is shown in Box 2.

Currently, the unifying nature of whole genome sequencing data offers a unique opportunity to help overcome many of the historic issues that have hampered public health responses to communicable diseases in Australia. The key challenge for those involved in public health delivery is how to convert this significant potential into reality, particularly for real-time and actionable national surveillance. Despite having high laboratory capacity in Australia, national surveillance and control of infectious diseases is not reaping the full benefits from the power of whole genome sequencing. We believe that national resourcing, coordination and transparent collaboration between state and territory microbial genomics systems is critical to increase Australia's capacity to detect, respond to and control infectious threats, and to improve regional health security.

Competing interests: No relevant disclosures

Provenance: Not commissioned, externally peer reviewed. ■

References are available online.

1 World Health Organization. Joint external evaluation of IHR core capacities of Australia: mission report, 24 November - 1 December 2017. Geneva: WHO, 2018. http://apps.who.int/iris/handle/10665/272362 (viewed Feb 2019).

2 Gardy JL, Loman NJ. Towards a genomics-informed, real-time, global pathogen surveillance system. *Nat Rev Genet* 2018; 19: 9–20.

3 Australian Government Department of Health. National Framework for Communicable Disease Control Canberra: Commonwealth of Australia, 2014. http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-nat-frame-communic-disease-control.htm (viewed Feb 2019).

4 Australian Government Department of Health. National Health Genomics Policy Framework 2018-2021. http://www.health.gov.au/internet/main/publishing.nsf/Content/national-health-genomics-policy-framework-2018-2021 (viewed Feb 2018).

5 Allard MW, Strain E, Melka D, et al. Practical value of food pathogen traceability through building a whole-genome sequencing network and database. *J Clin Microbiol* 2016; 54: 1975–1983.

6 Kwong JC, Stafford R, Strain E, et al. Sharing is caring: international sharing of data enhances genomic surveillance of *Listeria monocytogenes*. *Clin Infect Dis* 2016; 63: 846–848.

7 Grant K, Jenkins C, Arnold C, et al. Implementing pathogen genomics: a case study. London: Public Health England, 2018. https://www.gov.uk/government/publications/implementing-pathogen-genomics-a-case-study (viewed Feb 2018).

8 Dallman TJ, Byrne L, Ashton PM, et al. Whole-genome sequencing for national surveillance of Shiga toxin-producing *Escherichia coli* O157. *Clin Infect Dis* 2015; 61: 305–312.

9 Baker KS, Dallman TJ, Field N, et al. Genomic epidemiology of *Shigella* in the United Kingdom shows transmission of pathogen sublineages and determinants of antimicrobial resistance. *Sci Rep* 2018; 8: 7389.

10 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.

11 Williamson D, Howden B, Stinear T. *Mycobacterium chimaera* spread from heating and cooling units in heart surgery. *N Engl J Med* 2017; 376: 600–602.

12 Vasant BR, Stafford RJ, Jennison AV, et al. Mild Illness during outbreak of Shiga toxin-producing *Escherichia coli* O157 infections associated with agricultural show, Australia. *Emerg Infect Dis* 2017; 23: 1686–1689.

13 Gurjav U, Outhred AC, Jelfs P, et al. Whole genome sequencing demonstrates limited transmission within identified *Mycobacterium tuberculosis* clusters in New South Wales, Australia. *PLOS One* 2016; 11: e0163612.

14 Kwong JC, Mercoulia K, Tomita T, et al. Prospective whole-genome sequencing enhances national surveillance of *Listeria monocytogenes*. *J Clin Microbiol* 2016; 54: 333–342.

15 Kwong JC, Lane CR, Romanes F, et al. Translating genomics into practice for real-time surveillance and response to carbapenemase-producing Enterobacteriaceae: evidence from a complex multi-institutional KPC outbreak. *PeerJ* 2018; 6: e4210. ■