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Enhanced data sharing and coordination to ensure Australia can address the threat of extensively drug-resistant *Shigella* – a case study for consideration by the Australian Centre for Disease Control

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Original article

Abstract

Increasing antimicrobial resistance and changing epidemiological risk groups for shigellosis pose a threat to Australian public health. Integrated surveillance, enhanced through pathogen genomics data, represents an opportunity to improve the precision of public health responses to drug-resistant shigellosis in Australia and a compelling case study for the new Australian Centre for Disease Control. Here we describe a national public health laboratory scoping study and propose a model for enhanced surveillance of shigellosis that will improve national responses to this emerging public health threat.

Keywords: shigellosis; surveillance; antimicrobial resistance

Introduction

Shigellosis is a gastrointestinal infection in humans that is caused by one of four *Shigella* species (*S. sonnei*, *S. flexneri*, *S. boydii* and *S. dysenteriae*).[1] It is highly transmissible and can be spread through faecal-oral route or by direct or indirect contact. Symptoms of shigellosis range from mild diarrhoea to severe dysentery, with treatment focusing on rehydration as the mainstay of therapy. Antibiotic therapy may be required for patients with severe disease or those that are immunocompromised.[2]

Increasing antimicrobial resistance (AMR) in *Shigella* species has been observed over the past decade.[3,4] The Australian CARAlert Annual Report showed a ten-fold increase in multi-drug resistant (MDR) *Shigella* numbers between 2021 and 2023, across all jurisdictions.[5] Extensively drug resistant (XDR) strains with limited treatment options have been identified globally and within Australia, including in men who have sex with men and in Indigenous populations.[6,7] An XDR *S. sonnei* strain was initially identified in the United Kingdom in 2021 before rapidly disseminating across the European Union.[8] A large outbreak of XDR *Shigella sonnei* occurred in Victoria in 2024; the outbreak was related to a music festival and led to many hospital presentations, with patients requiring very broad-spectrum antibiotics for treatment.

Comprehensive antimicrobial susceptibility testing (AST) and whole genome sequencing (WGS) of *Shigella* isolates is critical to inform treatment guidelines, to identify transmission of XDR strains, to understand the genomic elements driving the spread of resistance genes and to implement targeted control measures. However, current laboratory guidelines for shigellosis in Australia do not address emerging AMR issues.[9] Additionally, AST alone (or with whole genome sequencing) and limited to a single state or territory can't achieve optimal public health surveillance and actions; rather, this data needs to be rapidly and comprehensively shared and linked to key risk factor data.

As shigellosis is a nationally notifiable disease in Australia, all cases of shigellosis must be reported to the public health unit (PHU) in the relevant state or territory. Additionally, diagnostic microbiology laboratories are required to send any isolates of *Shigella* to a reference or public health laboratory (PHL) for further typing and reporting to the jurisdictional PHU. These results are reported to the PHU, and collated case-level data are reported up to the National Notifiable Diseases Surveillance System (NNDSS), noting that different jurisdictions may hold additional epidemiologic data. Although AST is often performed by PHLs, no AST data are reported as part of this national surveillance.

However, high-level AMR data are collected by the national Critical Antimicrobial Resistance Alert system (CARAlert). CARAlert collects laboratory-based data on AST, including limited genomic data (resistance mechanisms) where available, but does not include any patient or case-level metadata. As such, there is currently no integrated national data including both AMR and epidemiologic case data (such as risk factors) available for monitoring AMR in *Shigella* in Australia.

In light of recent discussions and consultations regarding enhanced national and international coordination of public health activities and the Australian Centre for Disease Control (CDC), mapping the current and ideal systems for effective surveillance and control of XDR shigellosis provides an intriguing 'case study' for genomics-enabled surveillance in the re-imagining of Australia's public health surveillance and response systems. Here we survey Australian public health laboratories to investigate current practices around *Shigella* and AMR, to examine Australia's capability to systematically detect and monitor the spread of XDR *Shigella* and explore potential enhancements to public health.

Methods

In December 2021, the Public Health Laboratory Network (PHLN) Expert Reference Panel on AMR undertook a scoping survey of Australian PHLs to explore laboratory capacity and use of new technologies for surveillance of XDR *Shigella* in Australia. These surveys are voluntary and frequently undertaken at the laboratory level (rather than individual participants) to understand the current state of surveillance in PHLs. As such, ethics approval was not sought. The survey was distributed on an electronic platform (Qualtrics) to laboratory heads, and results collated for further analysis. The survey questions are included in Appendix A.

Results of the scoping survey

Responses were received from seven PHLs in seven different jurisdictions across Australia (Table 1). All seven PHLs reported that all *Shigella* isolates notified to jurisdictional public health authorities were referred to a PHL. Isolates are referred to the PHL located within the jurisdiction of notification in 4/7 jurisdictions. The remaining 3/7 jurisdictions have relationships in place with other jurisdictional PHLs for the referral of isolates.

Testing

Six of the seven PHLs in Australia indicated that they were able to conduct AST for *Shigella* species, using automated susceptibility testing platforms (3/7 labs), broth microdilution (1/7 labs), or disk diffusion (2/7 labs), with one lab performing no susceptibility testing. The European Committee for Antimicrobial Susceptibility Testing (EUCAST) was the most common interpretive guidelines used to interpret AST results (5/7), with Clinical and Laboratory Standards Institute (CLSI) used by the minority (2/7). The range of antibiotics tested and reported routinely varied widely between jurisdictions, but nevertheless, all phenotypic and/or genotypic AST results were routinely reported back to jurisdictional public health authorities.

Almost all PHLs performed serotyping on all *Shigella* isolates received at their laboratories (6/7), with the remaining PHL referring isolates to an interstate PHL for testing. Fewer PHLs provided biotyping (4/7). Serotyping turnaround times from receipt of an isolate at the reference Public Health Laboratory to reporting of results to the referring laboratory and public health authority ranged from 5–10 hours to over 3 weeks.

At the time of the survey, only 4/7 of the responding PHLs had in-house capacity to conduct WGS for *Shigella*. Three of the four PHLs with genomic sequencing capacity carried out sequencing on all *Shigella* isolates received, while one PHL restricted sequencing to a particular strain (*Shigella sonnei* biotype G). All four PHLs reported on sequence type, with three PHLs routinely reporting phylogeny and AST targets, and two reporting on *in silico* serotyping. Of the three PHLs without genomics capability (all from jurisdictions with smaller populations), two had protocols in place to refer isolates for sequencing. The turnaround time for genotypic AMR ranged from 80+ hours to over 3 weeks.

Reporting and data sharing

At a national level, MDR *Shigella* isolates were reported to the Critical Antimicrobial Resistance Alert (CARAlert) system by almost all PHLs (6/7). The remaining PHL not undertaking this reporting noted that this activity was undertaken by referring laboratories. Reporting to the Australian Passive Antimicrobial Surveillance (APAS) system was also undertaken by 3/7 PHLs in their functions as primary referral laboratories. No laboratories were routinely sharing genomic data within Australia, and only one laboratory was routinely sharing genomic data internationally.

Table 1: Results of jurisdictional Public Health Laboratory scoping survey on shigellosis testing and reporting, Australia, December 2021

Shigella laboratory characteristic[a]	Category[b]	Number of laboratories[c]		
		n	Percentage	Comments
AST performed	—	6	86%	—
AST method	Automated AST platforms	3	43%	—
	Broth microdilution	1	14%	—
	Disk diffusion	2	29%	—
Interpretive criteria used	EUCAST	5	71%	—
	CLSI	2	29%	—
Antibiotics tested (phenotypic AST)	Amoxicillin/ampicillin	5	71%	—
	Ceftriaxone/cefotaxime	5	71%	—
	Azithromycin	4	57%	—
	Fluroquinolone	6	86%	—
	Cotrimoxazole	6	86%	—
Isolate typing	Performed in lab	6	86%	—
	Samples referred to other PHL for typing	1	14%	—
	Biotyping performed	4	57%	—
	Serotyping turnaround times	—	—	Range: 5 hours – 3+ weeks
Genomic sequencing – conducted in house	PHLs conducting in-house sequencing	4	57%	—
	All *Shigella* isolates sequenced	3[d]	75%	—
	Only *Shigella sonnei* biotype g sequenced	1[d]	25%	—
	Multi-locus sequence type (MLST) reported	4[d]	100%	—
	AMR	3[d]	75%	—
	Genomic clustering	3[d]	75%	—
Genomic sequencing – samples referred to other PHL	—	2	29%	—
Genomic sequencing turnaround times	—	—	—	Range: 80+ hours – 3+ weeks
Reporting of MDR/XDR *Shigella* isolates	Reported to CARAlert (directly or by secondary referral lab)	7	100%	—
	Reported to APAS	3	43%	—

a AST: antimicrobial susceptibility testing; PHL: public health laboratory; MDR: multi-drug resistant; XDR: extensively drug resistant.

b EUCAST: European Committee for Antimicrobial Susceptibility Testing; CLSI: Clinical and Laboratory Standards Institute; AMR: Antimicrobial resistance; CARAlert: Critical Antimicrobial Resistance Alert system; APAS: Australian Passive Antimicrobial Surveillance.

c Unless otherwise specified, denominator for percentage calculation is N = 7.

d N = 4.

Future opportunities

Many PHLs identified additional activities they would like to perform outside of their current work, including the provision of in-house (2/7) or increased (1/7) genomic sequencing capacity. Barriers identified to undertaking these activities included funding, capability, and capacity issues.

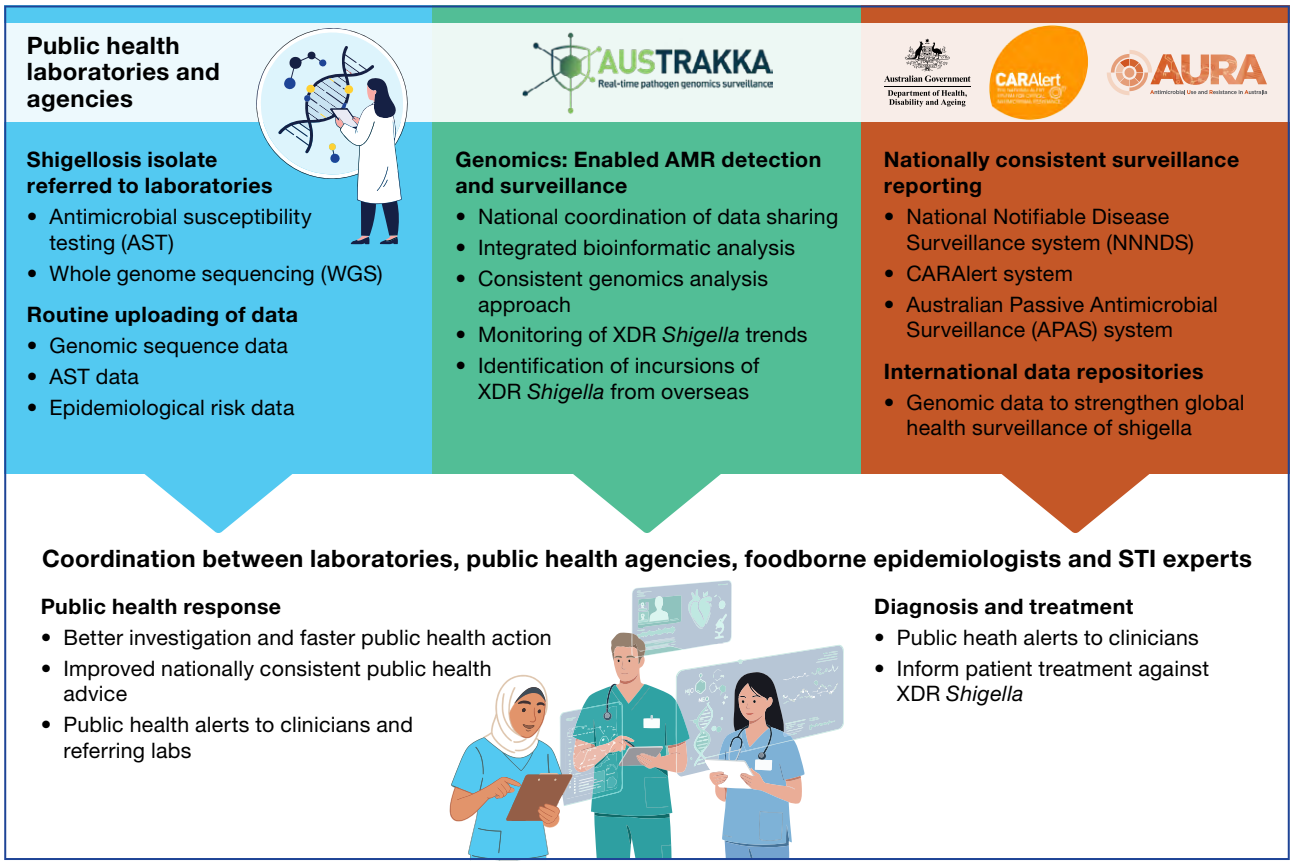
Discussion

The results of this scoping survey (performed in 2021) demonstrate that the basic building blocks of laboratory AMR surveillance of *Shigella* are already in place in PHLs in most jurisdictions in Australia. However, national case-based shigellosis surveillance through NNDSS, including critical data on risk factors, is currently disconnected from AMR surveillance (through CARAlert). This means that we do not currently have the data required to identify incursions and spread of epidemic XDR *Shigella* strains from overseas. Some states and territories have identified particular risk groups associated with MDR *Shigella*, and have issued jurisdictional public health alerts to clinicians and referring laboratories. However, it is not possible at present to do this on a national level, as we do not currently have the integrated case-level laboratory, genomic and epidemiologic data to sufficiently inform public health interventions in real-time on a national level.

While *Shigella* was previously seen primarily as a population health issue or foodborne pathogen, XDR *Shigella* now represents a major AMR risk. The presence of XDR *Shigella* in men who have sex with men represents a new epidemiological risk group for *Shigella* and further highlights the complexity of understanding and responding to potential outbreaks, which requires national coordination across expert groups (laboratories, foodborne disease epidemiologists and STI experts).

Notably, Chief Health Officer alerts have been released, highlighting the risks of XDR *Shigella* outbreaks in Victoria and New South Wales;[10,11] however, no national alerts or guidance have been released. We propose utilising integrated national genomics to enhance our understanding of the problem posed by *Shigella*, including the molecular mechanisms responsible for XDR emergence, leading to better investigation, faster action and improved nationally consistent public health advice (Figure 1).

Figure 1: Proposed model for nationally coordinated, genomics enabled surveillance of Shigellosis in Australia



Our experiences from the coronavirus disease 2019 (COVID-19) public health response has shown that genomics-based surveillance is not just possible but is fundamental to effective infectious diseases surveillance at a national level.[12,13] Australia has benefitted from the formation of the Communicable Diseases Genomics Network (CDGN) in 2015,[i] which has promoted the development and deployment of the national pathogen genomics surveillance platform, AusTrakka, enabling rapid, secure sharing of genomic data for integrated analysis.[13] Australia also has dedicated funding for the integration of genomics into public health responses through the Australian Pathogen Genomics (AusPathoGen) Program,[ii] which is establishing nationally consistent and equitable approaches to genomic surveillance,[14] including a national surveillance system for XDR *Shigella* that can be integrated into the AusTrakka platform. Since this survey was performed, the AusPathoGen program has supported the smaller jurisdictions to develop in-house genomic sequencing capacity, with all labs now having routine or emerging genomic sequencing capacity.

Given the complex nature of *Shigella*—as a foodborne pathogen, a sexually transmitted infection and a MDR/XDR AMR pathogen—clear national guidance, communication and coordination will be required to ensure data is sufficiently comprehensive to enable linkage to public health actions. As current systems such as the National Notifiable Diseases Surveillance System do not capture *Shigella* AMR phenotype data, alternative approaches, such as genomics-enabled AMR detection and surveillance, may be required to address this national need.

We propose a model to add AMR data into the existing national surveillance system for shigellosis, taking advantage of the laboratory capacities that are largely already in place and routinely being collected for other pathogens. At a minimum, phenotypic AST data currently submitted to CARAlert should be connected with case-level data (submitted to NNDSS) to identify risk factors for infection with XDR *Shigella*. Ideally, to maximise our ability to identify and respond to the threat of XDR *Shigella*, we propose a national genomic surveillance program supported by appropriate national governance.

This would involve (i) harmonisation of AST panels and reporting; (ii) routine performance of genomic sequencing on isolates; (iii) uploading of genomic sequences and defined limited metadata to AusTrakka (after agreement and approvals from jurisdictions) with centralised analysis and reporting; and (iv) nationally consistent surveillance reporting. Key to the success of this proposed model is partnerships with PHU teams, including those involved in both foodborne pathogen and sexually transmitted infection surveillance, to maximise the understanding and impact of the data.

Conclusion

As the threat of infectious diseases and antimicrobial resistance increases, Australia is well placed to enhance the surveillance and response to emerging issues, such as XDR shigellosis, through the use of integrated pathogen genomics, representing an ideal case study for the future Australian Centre for Disease Control. The results of this survey demonstrate that the 'building blocks' are already in place but some critical issues remain to be solved.

So, are we ready to address the threat of XDR *Shigella* in Australia? Not quite yet, but there is a clear path forward towards integrated national surveillance, and we are optimistic that the support of the CDC to coordinate these developments would enable us to identify XDR *Shigella* and to link into public health responses in the near future.

i https://www.cdgn.org.au/.

ii https://www.auspathogen.org.au/.

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Appendix A: Survey questions

1. Name, Email (Optional)
2. Organisation
3. In general, are there satisfactory protocols in place for the referral of isolates to a reference laboratory in your jurisdiction? – Yes/No
4. Are all *Shigella* isolates notified in your jurisdiction referred to a reference laboratory? If not, what is the criteria for referral? – Yes/No
5. Are all *Shigella* isolates notified in your jurisdiction referred to a reference laboratory? If not, what is the criteria for referral? – a. If not, what is the criteria for referral?
6. Which laboratory(ies) are *Shigella* isolates referred to?
    i. Which laboratory(ies) are *Shigella* isolates referred to?
    ii. If multiple laboratories, please provide an explanation for why.
    b. Is this different for private pathology providers? – Yes/No
    i. If yes, which laboratories?
7. Do you conduct typing testing of all *Shigella* isolates? – Yes/No
    a. If yes, briefly describe the procedure for typing.
    b. If no, what isolates are selected for typing?
8. If the reference laboratory is in a different jurisdiction, does your laboratory receive a report on referred *Shigella* isolates? – Yes/No
    a. If yes, what results are reported on?
9. Do you conduct phenotypic antibiotic susceptibility testing (AST) of all *Shigella* isolates? – Yes/No
    a. If yes, briefly describe the procedure for typing.
    b. If yes, is typing performed on all samples/isolates?
    c. If no, what isolates are selected for typing?
    d. If yes, what is the typical antimicrobial profile you test?
    e. If yes, what is the typical antimicrobial profile you report?
10. Do you conduct genomic sequencing of *Shigella* isolates? – Yes/No
    a. If yes, briefly describe the procedure for genomic sequencing.
    b. If yes, what sequencing data are reported on (e.g. phylogeny, ST, AST targets, in silico serotyping)?
11. If whole genome sequencing is performed for *Shigella* isolates:
    a. Are the data shared within Australia or internationally? – Yes/No
    i. If yes, are the data shared within Australia or internationally?
    1. If yes, what platforms or networks are data shared with?
    2. If yes, what associated metadata are shared with the genomic data?
    ii. If yes, is genomic sequencing performed on all *Shigella* samples/isolates? – Yes/No
    1. If no, what isolates are selected for genomic sequencing?

b. If no sequencing is being conducted by you, do you refer isolates to another reference laboratory for sequencing? – Yes/No

    i. If yes, do you refer all *Shigella* isolates for genomic sequencing or just a selection (if the latter, please explain the selection process)?

12. Is there any further testing performed on any *Shigella* isolates? – Yes/No

    a. If yes, please briefly describe the procedure and which selection of isolates undergo this testing.

13. Are there any specific funding arrangements for *Shigella* referral, testing or surveillance? – Free text

14. Does your laboratory use EUCAST or CLSI for AMR (including multidrug resistant (MDR)) *Shigella*? – Select all that apply

15. What laboratory information system do you currently use to store information? – Free text

16. Is there any additional testing you are currently not performing on *Shigella* that you would like to, and if so, what are the barriers to implementing this? – Free text

17. What is considered a positive case of *Shigella* for laboratory purposes in your jurisdiction? – Select all that apply

    a. IpaH gene positive PCR

    b. pINV

    c. Bacterial culture positive

    d. In line with the CDNA Shigellosis Surveillance Case Definition

18. What is the turnaround time from receipt of isolate in the reference laboratory to reporting of results to referring laboratory and/or public health authority in the following situations? – Select appropriate timeframe for each

    a. Serotyping

    b. Phenotypic AST

    c. Genotypic AST

    d. Further characterisation from genomic data (e.g. genomic clustering/lineage)

19. Do you report all *Shigella* results to your local public health authority/jurisdictional health department? – Yes/No

    a. If yes, what exactly is reported?

    b. If yes, how do you report results for the following?

        i. Serotyping

        ii. Phenotypic AST

        iii. Genotypic AST

        iv. Sequencing (see comments on question 24)

    c. If yes, who are results reported to?

    d. Do any of the above reporting practices (19a, 19b, 19c) differ between MDR and non-MDR *Shigella*? – Yes/No

        i. If yes, how?

    e. Do you report regular or sporadic integrated analytical reports for MDR *Shigella*? – Yes/No

        i. If yes, what is included in these reports?

20. Are you provided with additional metadata (e.g. epidemiological data) from the public health authorities for *Shigella* isolates/cases? – Yes/No
    a. If yes, please provide the details of what metadata are captured.
21. Do you report on all MDR *Shigella* in the Australian Passive AMR Surveillance (APAS) system, formally OrgTrx? – Yes/No
22. Do you report all MDR *Shigella* results to Critical Antimicrobial Resistance Alert (CARAlert)? – Yes/No
23. Are you the only CARAlert confirming laboratory for *Shigella* in your jurisdiction? – Yes/No
    a. If no, are there any protocols in place for the referral of confirmed CARAlert MDR *Shigella* isolates for further testing, characterisation and/or sequencing?
24. Do you report *Shigella* results to other jurisdictions? – Yes/No
    a. If yes, is this for isolates they have referred to you?
    b. How do you report *Shigella* results to other jurisdictions? – Select all that apply:
        i. Electronic notification
        ii. Fax
        iii. Letter
    c. If yes, do you include data on cross-jurisdictional isolates in your routine reporting to your local public health authority/jurisdictional health department
    d. If you report *Shigella* results to other jurisdictions, is this different for MDR and non-MDR *Shigella*? – Yes/No
        i. If yes, how?
25. What public health actions have occurred as a result of laboratories reporting antibiotic susceptibility testing (AST) data for *Shigella*? – Free text
26. Has the reporting on antibiotic susceptibility testing (AST) data for *Shigella* resulted in any changes to policy and/or practices (e.g. prescribing guidelines in your institution, jurisdiction or nationally)? – Yes/No
    a. If yes, do you think these changes could be used to influence broader policies?
27. What areas (inside or outside your lab) did you consult with when completing this survey? – Free text