Timeliness of *Salmonella* Typhimurium notifications after the introduction of routine MLVA typing in NSW

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Abstract: *Salmonella* Typhimurium is the most common bacterial cause of gastrointestinal disease in NSW. Regular review of surveillance procedures ensures system objectives are met and informs improvements in system utility and efficiency. This paper assesses the timeliness and data completeness of NSW *Salmonella* Typhimurium surveillance after the routine introduction of multilocus variable repeat analysis (MLVA), a rapid sub-typing technique. MLVA results were available significantly earlier than alternate sub-typing techniques over the 2 years of this review. Accordingly, from a timeliness perspective, MLVA offers a favourable *Salmonella* Typhimurium sub-typing option in NSW. Further opportunities to improve timeliness and data completeness are identified. This paper was produced as part of a review of *Salmonella* Typhimurium surveillance in NSW for the period 2008–2009 by members of OzFoodNet based at Hunter New England Population Health. OzFoodNet is a national network established by the then Commonwealth Department of Health and Ageing in 2000 to enhance foodborne disease surveillance in Australia.

Salmonella Typhimurium (STm) is the most common *Salmonella* serotype in New South Wales (NSW); in 2009 STm accounted for 54% of all NSW *Salmonella* notifications[1] and 77% of Australian foodborne outbreaks with an identified causative agent.[2] STm is a heterogeneous *Salmonella* serovar, requiring additional sub-typing to identify outbreak-specific strains. Research exploring sub-typing techniques proffers multilocus variable repeat analysis (MLVA) as a rapid alternative to phage typing,[3,4] the sub-typing technique historically used in Australia. MLVA typing has been shown to successfully differentiate strains within phage types 135a and 170 that comprise more than half the STm isolates in NSW.[5] In 2006 and 2007, routine STm MLVA sub-typing was implemented in Queensland and NSW, respectively.

Regular review of public health surveillance determines the success of system objectives and informs refinement of system utility and efficiency.[6,7] The NSW *Salmonella* surveillance system involves a complex network of local and interstate laboratories and notification processes. Local primary laboratories identify *Salmonella* species (spp.), while serovar confirmation and MLVA typing occur at the closest reference laboratory, and phage typing at one of the two national phage typing laboratories (Institute of Medical and Veterinary Science (IMVS), Adelaide and Medical Diagnostic Unit (MDU), Melbourne). The NSW *Public Health Act 1991 (*and its subsequent revision in 2010) mandates laboratories to notify all confirmed *Salmonella* cases. In 2008 and 2009 notifications were entered into the NSW Notifiable Diseases Database (NDD) by Public Health Units (PHUs) for data collation, timely outbreak detection and disease control, key objectives of the NSW surveillance system.[8]
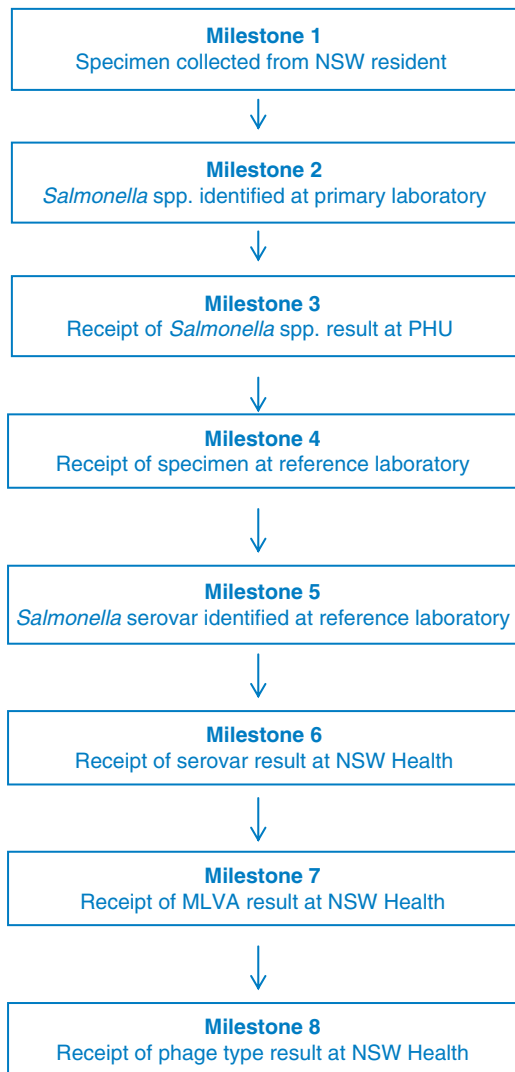
This paper assesses the timeliness and completeness of NSW *Salmonella* Typhimurium surveillance data after the routine introduction of MLVA. Serovar and MLVA notifications received in 2008 and 2009 were reviewed to identify opportunities for minimising delays.

Methods
The Centers for Disease Control and Prevention's Updated Guidelines for Evaluating Public Health Surveillance Systems[6] were used as an evaluation framework for this investigation.
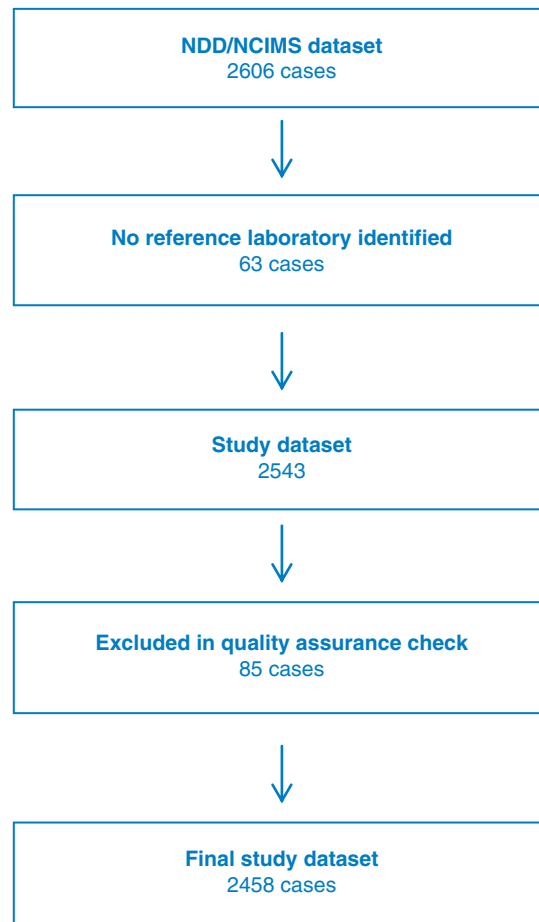
Data sources
STm notifications of NSW residents with a specimen collection date from 1 January 2008 to 31 December 2009 were identified and extracted in August 2010. As a

Milestone 1
Specimen collected from NSW resident

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Milestone 2
Salmonella spp. identified at primary laboratory

↓

Milestone 3
Receipt of *Salmonella* spp. result at PHU

↓

Milestone 4
Receipt of specimen at reference laboratory

↓

Milestone 5
Salmonella serovar identified at reference laboratory

↓

Milestone 6
Receipt of serovar result at NSW Health

↓

Milestone 7
Receipt of MLVA result at NSW Health

↓

Milestone 8
Receipt of phage type result at NSW Health

Figure 1. Milestones in the NSW *Salmonella* Typhimurium surveillance system

MLVA: multilocus variable repeat analysis; PHU: Public Health Unit.

new data management system (Notifiable Conditions Information Management System (NCIMS)) was instituted in May 2010, notifications were entered into the NDD during 2008 and 2009, but data were extracted from NCIMS in 2010. Additional milestone dates were obtained from the Institute for Clinical Pathology and Medical Research (ICPMR) electronic notifications and Queensland Health Forensic and Scientific Services (QHFSS), the NSW and Queensland reference laboratories, respectively. Other state reference laboratories were excluded as MLVA typing was not routinely conducted during the period of interest. NDD data comprised primary laboratory name and the date of *Salmonella* spp. receipt at the relevant PHU. ICPMR data included the following dates: specimen collection, *Salmonella* spp. identification, isolate receipt at ICPMR, and the electronic notification of serovar, MLVA and phage typing. The QHFSS dataset provided specimen collection date and the electronic notification dates of serovar and MLVA typing.

NDD/NCIMS dataset
2606 cases

↓

No reference laboratory identified
63 cases

↓

Study dataset
2543

↓

Excluded in quality assurance check
85 cases

↓

Final study dataset
2458 cases

Figure 2. Timeliness review of the NSW *Salmonella* Typhimurium surveillance system, 2008–2009: dataset derivation and case exclusion

NCIMS: Notifiable Conditions Information Management System; NDD: Notifiable Diseases Database.

Data management and analysis

The relevant ICPMR and QHFSS dates were added to the NDD data extraction using SAS software (version 9.2, SAS Institute, Cary, NC, USA).

Eight milestones of public health importance were used in the analysis (Figure 1). Completeness and accuracy of milestones affected the number of cases available for timeliness evaluation; accordingly, a review of data completeness was conducted. Data cleaning verified the accuracy of extracted data and guided exclusion of duplicate cases and repeat specimens (specimens less than 14 days apart).[8] Additional quality assurance checks involved scrutiny and possible exclusion of unexpected dates, established by negative time between sequential surveillance milestones. Time intervals greater than 365 days were reviewed to determine validity and excluded where appropriate. A total of 2458 cases (94.3% of all STm notifications) were included in the analysis (Figure 2).

SAS software and Microsoft Excel 2010 were used for quality assurance checks, calculation of time intervals between milestones, and significance testing, using Wilcoxon rank sum test methodology.

Table 1. Elapsed days from specimen collection to *Salmonella* Typhimurium surveillance milestones, NSW residents, 2008–2009

Milestone	2008		2009	
	Available records (*n*)	Median days (range)	Available records (*n*)	Median days (range)
Salmonella spp. identified at primary laboratory	1047	3 (1–31)	1364	3 (1–13)
Salmonella spp. result received by PHU	812	7 (3–156)	1168	6[a] (3–69)
Specimen received by reference laboratory	1036	6 (3–13)	1358	6 (3–39)
Salmonella serovar identification	1039	8 (4–32)	1274	7[a] (4–41)
Salmonella serovar result received[b]	1060[c]	10 (4–377)	1380[c]	9 (5–54)
MLVA result received[b]	1047	23 (8–384)	1377	21[a] (7–376)
Phage type result received[b]	1007	46 (21–786)	1362	65[a] (20–307)

MLVA: multilocus variable repeat analysis; PHU: Public Health Unit.
[a]Difference in 2008 and 2009 median (days), *p* < 0.001.
[b]Reference laboratory results are emailed to NSW Health; subsequent dissemination to the relevant PHU.
[c]Includes Queensland Health Forensic and Scientific Services (QHFSS) specimens where earlier milestone dates unavailable (QHFSS results notified on serovar identification).
Source: Notifiable Conditions Information Management System (SAPHaRI), NSW Ministry of Health.

Table 2. Missing and invalid *Salmonella* Typhimurium surveillance milestones, NSW residents, 2008–2009

Milestone	Missing dates		Invalid entries[a]	
	n	(%)	*n*	(%)
Specimen collection date	0	0.0	0	0.0
Salmonella spp. identified at primary laboratory	41	1.7	6	0.2
Salmonella spp. result received by PHU	405	16.5	32	1.3
Specimen received by reference laboratory	0	0	17	0.7
Salmonella serovar identification	133	5.4	12	0.5
Salmonella serovar result received[b]	17	0.7	1	0.0
MLVA result received[b]	33	1.3	1	0.0
Phage type result received[b]	88	3.6	1	0.0

MLVA: multilocus variable repeat analysis; PHU: Public Health Unit.
[a]Data determined to be impossible values and excluded from analysis.
[b]Reference laboratory results are emailed to NSW Health, with subsequent dissemination to the relevant PHU.
Source: Notifiable Conditions Information Management System (SAPHaRI), NSW Ministry of Health.

Results

Timeliness

The timeliness of all STm milestones, determined by the median interval in days, with the exception of receipt of phage typing, remained relatively consistent over time (Table 1). MLVA notification occurred 23 days earlier than phage typing in 2008 (*p* < 0.001) and 44 days earlier in 2009 (*p* < 0.001). The median time interval for MLVA notifications decreased significantly from 23 days in 2008 to 21 days in 2009 (2 days' decrease, *p* < 0.001).

Data completeness

Missing or invalid data were infrequent for most milestones, with a few notable exceptions (Table 2). The receipt of the initial *Salmonella* spp. report at PHU level was missing in 16.5% of cases and invalid in 1.3% of cases. Serovar identification date was missing in 5.4% of cases.

Sub-typing was not recorded for a small number of STm cases, including 17 serovar, 33 MLVA and 88 phage type results.

Anomalies in sequential notification

Given the consecutive nature of STm typing, milestone notification for MLVA and phage typing are expected to occur after serovar availability. Time interval analysis indicated this was not always the case. Serovar and MLVA typing results were received simultaneously in 1% of cases in 2008 and 6% of cases in 2009.

Discussion

Regular evaluation of public health surveillance is important to confirm system utility and efficiency.[6] To our knowledge, this is the first report of MLVA timeliness in

the context of a population level STm surveillance system. MLVA results were available significantly earlier than phage typing results over the 2 years of this review. The availability of NSW MLVA results in 2008 (median 23 days) and 2009 (median 21 days) was also fast in comparison to phage typing in a similar timeliness study conducted in Ireland (median 25 days).[9] Notably, median time to MLVA availability was shorter in 2009 than in 2008. This reduction during the third year of routine MLVA typing may be driven by increased efficiency as key players become accustomed to the MLVA process.

MLVA and phage typing notification was absent for a small number of cases. It is unclear whether typing was available but not reported or if typing was not conducted. One possible explanation is informed cessation of sub-typing when cases are epidemiologically linked to a known outbreak. However, as NDD data entry capabilities did not include case or outbreak linking during the study period, we cannot assess the impact of outbreak resolution on missing results.

Occasionally, laboratories did not notify sub-typing results at the earliest opportunity, as indicated by simultaneous or non-sequential notification of serovar, MLVA or phage typing results. While electronic notification via email is undoubtedly faster than postal mail, human errors in data collation and transmission between organisations are challenging to eliminate. Missing dates and notification sequence anomalies indicated notification lapses by primary laboratories. These data quality issues impact the day-to-day operational processes of outbreak identification, investigation and control. However, due to the complex nature of NDD data entry and extraction from NCIMS, further exploration of this issue was not possible.

Resourcing impacts the time interval from specimen collection to result availability. Phage typing is particularly affected as two reference laboratories (IMVS and MDU) service all Australian states. Phage type result timeliness may also be impacted by isolate 'batching', where isolate dispatch to the reference laboratory is delayed until a sufficient number of isolates are collated. Batching may have become more commonplace in NSW after the introduction of routine MLVA and an accompanying reduction in urgency for phage typing results. A previous study identified *Salmonella* spp. identification as the 'bottle neck' in the surveillance system,[7] yet we found that the majority of *Salmonella* spp. identification occurred within 3 days. Also, the time interval from specimen collection to *Salmonella* spp. PHU notification was similar to a previous international timeliness study.[9] Nonetheless, the additional median 4- (2008) or 3- (2009) day time interval from *Salmonella* spp. identification to PHU receipt provides an opportunity to reduce notification delays.

In 2010, the NDD was replaced with NCIMS, an updated data capture system with enhanced foodborne disease surveillance capacities. NCIMS capabilities include date stamping (identifying the date and time of data entry), outbreak case linking, and recording MLVA and phage typing results. NCIMS performance enhancements are expected to improve outbreak identification, establish historical sub-typing data banks, and advance future surveillance system evaluations through superior data quality. Indeed, capacity for real-time electronic importation of notifications directly into NCIMS (electronic laboratory reporting (ELR)) has been partially realised. In 2013, ELR was implemented by four laboratories conducting a substantial proportion of *Salmonella* spp. identification. The elimination of transmission delay and human error inherent in multiple data entry points may have already reduced time from *Salmonella* spp. identification to PHU receipt. However, an efficient data extraction method, to facilitate future timeliness and data quality evaluations, has not yet been developed.

Further opportunities to improve timeliness and data completeness include:

1. Dissemination of ELR across all laboratories, thereby reducing duplication of data entry and expediting data delivery.
2. Development of NCIMS capability for efficient data extraction and reporting relevant to future data completeness and timeliness evaluations. This would enable evaluation of NCIMS capacity to enhance the NSW STm surveillance system.

Limitations

Interpretation of our findings requires consideration of data limitations, including the use of secondary data collated for operational purposes. NDD data entry and NCIMS data extraction capabilities, surveillance system reliance on manual data entry at multiple laboratories and PHUs, and manual result dispatch from laboratories to health services, impacted data quality. To minimise this bias, staff scrutinised each record to assess data for exclusion as necessary.

Conclusion

Given the importance of rapid typing in outbreak responses and the endemic presence of STm in NSW, timely receipt of STm sub-typing is of public health importance. From a timeliness perspective, MLVA offers a favourable STm sub-typing option in NSW. Further, this project identified additional opportunities to enhance the STm surveillance system and improve enteric outbreak detection and control.

Acknowledgments

References

1. Kardamandis K, Heilbronn C, Munnoch S, McWeeny C, Stephens N. NSW 2009 OzFoodNet Annual Report. Available at: http://www.health.nsw.gov.au/Infectious/diseases/Documents/ofn_annual_report_2009.pdf (Cited 14 April 2014).

2. OzFoodNet Working Group. Monitoring the incidence and causes of diseases potentially transmitted by food in Australia: Annual report of the OzFoodNet Network, 2009. *Commun Dis Intell* 2010; 34: 396–426.

3. Lindstedt BA, Vardund T, Aas L, Kapperud G. Multiple-locus variable-number tandem-repeats analysis of *Salmonella* enterica subsp. enterica serovar Typhimurium using PCR multiplexing and multicolor capillary electrophoresis. *J Microbiol Methods* 2004; 59: 163–72. doi:10.1016/j.mimet.2004.06.014

4. Wang Q, Chiew R, Howard P, Gilbert G. *Salmonella* typing in New South Wales: current methods and application of improved epidemiological tools. *N S W Public Health Bull* 2008; 19: 24–8. doi:10.1071/NB07036

5. Sintchenko V, Wang Q, Howard P, Ha CW, Kardamanidis K, Musto J et al. Improving resolution of public health surveillance for human *Salmonella* enterica serovar Typhimurium infection: 3 years of prospective multiple-locus variable-number tandem-repeat analysis (MLVA). *BMC Infect Dis* 2012; 12: 78. doi:10.1186/1471-2334-12-78

6. CDC; the Guidelines Working Group. Updated Guidelines for Evaluating Public Health Surveillance Systems. *MMWR* 2001; 50: 1–35.

7. Takahashi T, Koehler J, Swenson P, Duchin J. Evaluation of a public health *Salmonella* surveillance system in King County, Washington. *Am J Infect Control* 2004; 32: 7–11. doi:10.1016/j.ajic.2003.06.003

8. Communicable Diseases Surveillance and Control Unit. NSW Notifiable Diseases Database Manual. 6th ed. Sydney: NSW Department of Health; 2002.

9. Nicolay N, Garvey P, Delappe N, Cormican M, McKeown P. Completeness and timeliness of *Salmonella* notifications in Ireland in 2008: a cross sectional study. *BMC Public Health* 2010; 10: 568. doi:10.1186/1471-2458-10-568