

Mastering Resistant Bacteria using Whole Genome Sequencing

Integrating innovation in to patient care to provide greater understanding of antibiotic resistance and infection transmission at a molecular level

Ms Trish Hurst¹, Mrs Michelle Doidge¹, Dr Krispin Hajkowicz^{1,3}, Dr Patrick Harris^{2,6,7}, Dr Brian Forde⁹, Mr Haakon Bergh², Dr Amy Jennison⁴, Ms Leah Roberts⁹, Dr Tony Allworth^{1,3,8}, Professor Graeme Nimmo^{2,5}, Associate Professor Scott Beatson⁹, Professor David Paterson⁶

¹Royal Brisbane And Women’s Hospital, Herston, QLD, Australia, ²Pathology Queensland, Herston, QLD, Australia, ³The University of Queensland, School of Medicine, St Lucia, QLD, Australia
⁴Public Health Microbiology, Forensic and Scientific Services, Queensland Department of Health, Coopers Plains, QLD, Australia, ⁵School of Medicine, Griffith University, Nathan, QLD, Australia
⁶Faculty of Medicine, University of Queensland Centre for Clinical Research (UQCCR), Herston, QLD, Australia, ⁷Princess Alexandra Hospital, Woolloongabba, QLD, Australia
⁸Mater Pathology Services, South Brisbane, QLD, Australia, ⁹School of Chemistry and Molecular Biosciences, Australian Infectious Diseases Research Centre, Australian Centre for Ecogenomics, St Lucia, QLD, Australia

Introduction

The scarcity of single room accommodation coupled with the emergence of new virulent strains of Multi-resistant Organisms (MROs) poses a challenge in creating isolation room capacity.

The Royal Brisbane and Women’s Hospital (RBWH) convened a Multi-Resistant Organism Expert Working Group (MRO EWG) to provide evidence based recommendations regarding patient placement priorities and Multi-Resistant Organism (MRO) management strategies.

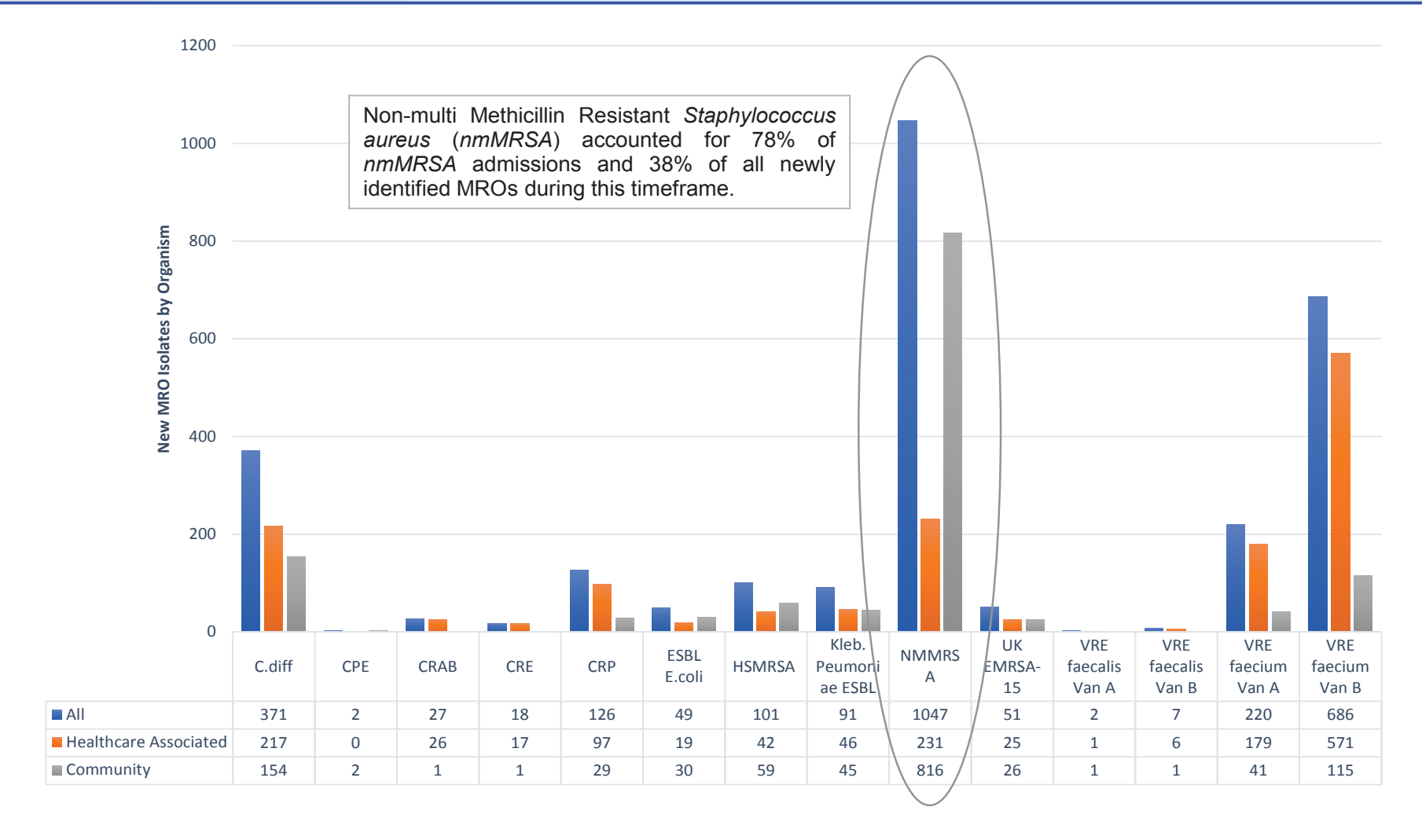
An initiative was undertaken over a 2 year period using Whole Genome Sequencing (WGS). The aim of this quality activity was to demonstrate the limited benefit of isolating patients colonised/infected with non-multiresistant Methicillin Resistant *Staphylococcus aureus* (nmMRSA) on Contact Precautions.

The RBWH in collaboration with the Queensland Genomics Health Alliance (QGHA) is utilising Whole Genome Sequencing (WGS) to look at innovative ways to Master Resistant Bacteria by providing evidence of transmission at a molecular level.

Method

- A review of 3.5 years of data was undertaken to quantify the organisational burden of MROs.
- An extensive literature review was undertaken focusing on the efficacy of Contact Precautions in preventing the spread of nmMRSA in hospital but yielded little evidence.

Figure 1 RBWH New MRO Isolates 1 Apr 2013 – 31 Oct 2016



Source: Significant Organisms Report, Multiprac™

- MRO EWG formulated the null hypothesis – “That the use of Standard Precautions is sufficient to prevent the spread of nmMRSA for patients sharing the same environment”.
- Tasked with this quality improvement activity the group conducted a simple observational activity, undertaken in two phases:

Figure 2 Implementation Timeline

Phase 1		Phase 2	
1/2/2017	31/7/2017	31/7/2017	31/7/2018
<ul style="list-style-type: none">• Routine isolation and Contact Precautions for all new nmMRSA• Screening of all contacts in patient’s shared environment		<ul style="list-style-type: none">• No isolation and Standard Precautions for all new nmMRSA• Screening of all contacts in patient’s shared environment	

- All new nmMRSA isolates were sent to Forensic Scientific Services (FSS) for WGS. WGS was performed using rapid next generation ultra high-resolution molecular typing of bacteria as an adjunct to phenotypic testing.

Results

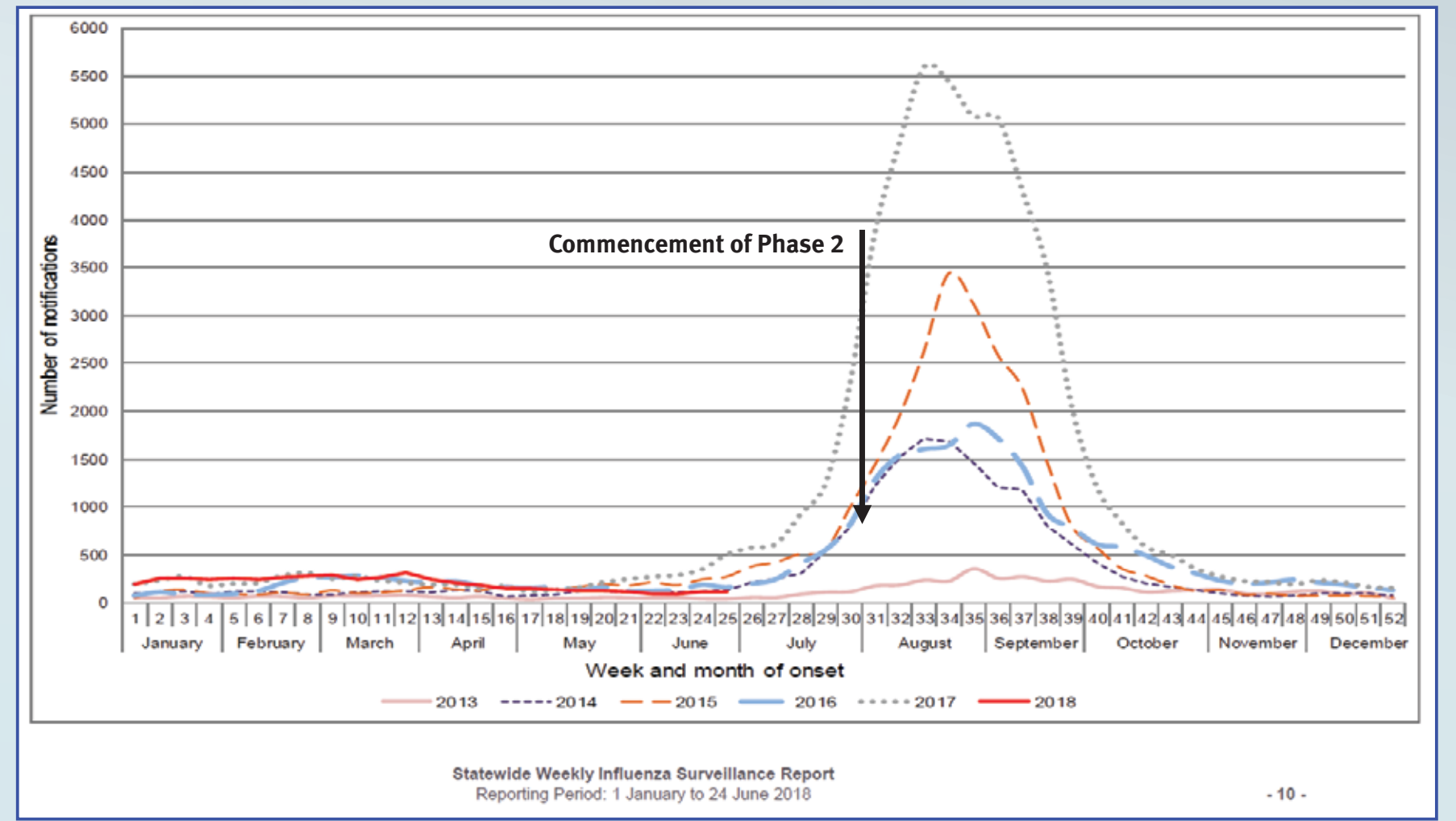
Surveillance data

- During Phase 1, 170 new cases of nmMRSA were identified and Contact Precautions were applied.
- During Phase 2, 338 new cases of nmMRSA were identified (see Fig 3). Standard Precautions were used instead of Contact Precautions for this period.

Figure 3: Breakdown of new cases by location of acquisition

Attribution	Number of Isolates Identified	
	Phase 1 - 1/2/17 to 31/7/17	Phase 2 - 1/8/17 to 31/7/18
Community	140	258
Other Healthcare Facilities	10	20
RBWH	20	60
Surveillance of contacts	71 contacts, 52 screened, 1 transmission (0.6%)	49 contacts, 20 screened, 1 transmission (0.3%)
Total	170 (34 cases/month)	338 (28 cases/month)

Figure 4: Laboratory confirmed influenza notifications in Queensland by week onset, 1 Jan 2013 to 24 Jun 2018



QGHA Data Collection Period 26th Jan 2018 - 31st Jul 2018

- 57 consecutive nmMRSA isolates sequenced that met healthcare associated acquisition criteria
- Potential clusters were identified using WGS.
- Three patients were identified with an identical genetic strain - nmMRSA ST5:
 - All 3 patients located in the same ward at the same time, in close proximity, with the same treating team.
 - Epidemiological investigation of the cases indicated two out of three patients (a married couple) were admitted together post motor vehicle accident and presumably sharing their microbes prior to admission.
 - The third case may have been attributed to poor hand hygiene compliance in the ward which was 56% for the month. This accounted for 1.8% (n=1/57) of cases.

Conclusion

Throughout this quality activity one probable case of transmission of nmMRSA were discovered. This case was detected by WGS. While accounting for only 1.8% (n=1/57) of cases, this challenges the null hypothesis “That the use of Standard Precautions is sufficient to prevent the spread of nmMRSA for patients sharing the same environment”. Nonetheless the remaining 98.2% of unrelated cases provides a convincing measure of assurance that the benefits of the nmMRSA intervention have outweighed the risk to patient safety.

WGS can be used to both substantiate and disprove the transmission of MROs, facilitating the re-evaluation of infection control procedures relating to the acquisition of healthcare associated infections. Hospital resources can be prioritised based on the evidence of transmission risk when reconsidering historical practices.

It is acknowledged that the results of this activity have limitations due to sample size, however there is ongoing collection and analysis of supporting evidence. New isolates of healthcare associated nmMRSA and episodes of possible transmission to contacts continues to be monitored via routine surveillance and WGS. The methodology used for this quality improvement activity will be reapplied to review the effectiveness of Contact Precautions and management of other MROs at the RBWH.

The average length of stay (LOS) for the Phase 2 cases was 12 days which equated to ≈ 4056 single room days saved.

The nmMRSA numbers during this period:

- Included only the admission associated with the positive screen.
- Excluded readmissions of these patients and,
- Excluded the LOS for patients admitted with old nmMRSA alerts.

Single room savings are therefore underestimated.

The commencement of the intervention on the 1st August coincided with the severe 2017 influenza season. During the 9 week peak, a minimum of 902 single bed days were saved due to the nmMRSA intervention, thus creating capacity to meet the single room demand for influenza isolation.

Figure 5 Multi-Resistant Organism Genome Sequencing Report generated by QGHA

Multi-Resistant Organism Genome Sequencing Report									
Date: 18/10/201									
Survey of suspected hospital-acquired methicillin-resistant <i>Staphylococcus aureus</i> (MRSA) collected at the Royal Brisbane and Women’s Hospital (RBWH)									
Executive Summary:									
<ul style="list-style-type: none">• Whole genome sequencing (WGS) of 9 multidrug resistant <i>Staphylococcus aureus</i> collected from patients in RBWH between 20/08/18 and 13/09/18.• 8/9 isolates were positive (<i>in silico</i>) for <i>mecA</i>• 1/9 isolates (M88413) were negative (<i>in silico</i>) for <i>mecA</i>• No clustering to report									
1. Isolates:									
Table 1: Sample information									
Sample ID	UKS	Lab No.	Sample date	Site	Species	MLST (ST)	SCCmec	Admission date	Ward
M88199			6/09/2018	Respiratory	<i>S. aureus</i>	1	IVa(2B)	6/09/2018	
M88413			13/09/2018	Respiratory	<i>S. aureus</i>	5	IIIa(2A)		
M88202			7/09/2018	Respiratory	<i>S. aureus</i>	6	IVa(2B)		
M87884			20/08/2018	Respiratory	<i>S. aureus</i>	97	IVa(2B)	21/08/2018	
M88200			5/09/2018	Wound / skin / soft tissue	<i>S. aureus</i>	834	IVa(2B)	2/09/2018	
M87883			20/08/2018	Respiratory	<i>S. aureus</i>	NF	IVa(2B)	18/08/2018	
M87885			21/08/2018	Respiratory	<i>S. aureus</i>	NF	IVa(2B)	16/08/2018	
M87887			22/08/2018	Respiratory	<i>S. aureus</i>	NF	Va(5C&S)	27/08/2018	
M87888			23/08/2018	Rectal swab	<i>S. aureus</i>	NF	IVa(2B)	23/08/2018	
MLST = Multi-Locus Sequence Typing; NF = Not found									
2. Cluster detection:									
This reporting period:									
<ul style="list-style-type: none">• No clustering of isolates within the RBWH• No clustering with isolates from other hospitals.									
QGHA survey period:									
<ul style="list-style-type: none">• No clustering with any previously reported isolates.									

Report and analysis prepared by: Dr Brian Forde (Lab Head: A/Prof Scott Beatson) as part of the QGHA Infectious Disease Demonstration Project (unpublished), (2018).