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Research paper

An outbreak of *vanA* vancomycin-resistant *Enterococcus faecium* in a hospital with endemic *vanB* VRE☆

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Infection control

Abstract *Background:* In Australia, *vanB* vancomycin-resistant *Enterococcus faecium* (VREfm) has been endemic for over 20 years, but *vanA* VREfm isolates have rarely been reported.
Methods: This outbreak report describes an outbreak of *vanA* VREfm in the intensive care unit (ICU) and cardiothoracic surgery (CTS) wards of a Melbourne hospital in 2015–2016. After the cluster was initially identified in the ICU ward, an active screening programme was implemented. VRE isolates were typed using *in silico* multi-locus sequence typing. In addition, to screening, enhanced environmental cleaning, chlorhexidine gluconate body washes, and standardisation of the surgical antibiotic prophylaxis regimen were implemented to control the outbreak.
Results: There were 83 new isolates of *vanA* VREfm recovered from patients in the ICU (n = 31) and CTS (n = 52) wards. Screening identified 78 (94%) of cases. Three patients required treatment for clinical infection with *vanA* VREfm during the outbreak. The outbreak was polyclonal with 5 different multilocus sequence types carrying the *vanA* gene (ST17, ST80, ST203, ST252 and ST1421) detected from a subset of isolates (N = 43). The ST17 isolates all carried both the *vanA* and *vanB* gene. The intervention bundle resulted in control of the outbreak after 10 months.

☆ Data statement: Raw data was collected during clinical care of patients and thus will remain confidential and not be shared.

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Conclusion: Geographically, *vanA* VREfm has previously been uncommon in the region and this outbreak represents a change in local epidemiology. Few VRE outbreaks have been reported in CTS patients. The infection control responses controlled the outbreak within 10-months and may help guide future management of outbreaks.

Highlights

- A polyclonal outbreak of *vanA* VRE in a hospital with endemic *vanB* VRE.
- Previously only a few outbreaks of VRE cardiothoracic surgery patients reported.
- First outbreak description during rising detection of *vanA* VRE across Australia.
- Surveillance identified the majority (94%) of cases during the outbreak.
- The infection control response was associated with outbreak control in 10-months.

Introduction

Vancomycin-resistant *Enterococcus faecium* (VREfm) is an important nosocomial pathogen in Australia and globally [1—3]. In most parts of Australia, *vanB* VREfm has previously been the most frequently isolated genotype [1,4]. This is in contrast to other parts of the world where *vanA* VREfm has been more common [2,3]. In recent years, there has been an increase in the number of *vanA* VREfm isolates in Australia from nationwide surveillance reports [1,5—7]. Nevertheless, there have been no reports of acute outbreaks of *vanA* VREfm during this period.

Successful infection control responses to acute outbreaks of VREfm are multifactorial [8—10]. Various studies have identified a number of control measures that may be particularly important. These include isolation measures to prevent patient-to-patient transmission, active screening to identify colonised individuals, efforts to improve hand hygiene (HH), education, improved environmental cleaning, chlorhexidine gluconate body washing and restricted usage of certain antibiotics [8—17].

We report an outbreak of *vanA* VREfm occurring on the intensive care unit (ICU) and cardiothoracic surgery (CTS) wards at The Royal Melbourne Hospital (RMH), Victoria, Australia between 1st August 2015 and 31st May 2016. The objectives of this study are to describe: (i) an outbreak of *vanA* VREfm including *in silico* MLST results and (ii) the strategies used to control the outbreak.

Methods

Design, setting, population and definitions

RMH is a ~570 bed teaching hospital and tertiary referral centre in Melbourne with a number of specialist services, including a CTS department and mixed medical and surgical ICU, which treats substantial numbers of trauma, immunocompromised and CTS patients. There is a dedicated infection prevention service in place. *VanB* VREfm has been endemic in the hospital for many years. Table 1 outlines in more detail the setting, population and case definitions for the outbreak.

Infection control response

The outbreak was formally recognised in September 2015, which led to a series of infection control and other interventions (see Table 1) and the establishment of a multidisciplinary outbreak team, consisting of representatives from the hospital executive, infection prevention, microbiology, ICU, CTS and environmental services, who met regularly to discuss, monitor and implement interventions for controlling the outbreak.

Prior to the outbreak, the VRE screening program consisted of screening room contacts of patients with positive VRE clinical specimens. VRE screening of all patients was introduced to the ICU and CTS wards in September 2015. Patients were screened with a rectal or groin swab on admission, discharge and twice weekly. Rectal swabs were preferred for detection of VRE. Groin swabs were utilised for patients that were unable to or refused a rectal swab.

Confirmed VRE cases were cared for with contact precautions (CP) i.e. disposable long-sleeved gown and gloves, which was standard practise prior to the onset of the outbreak. With the implementation of screening, patients from the ICU and CTS wards were cared for with empirical CP until screening results were known. Daily 4% chlorhexidine gluconate body washes were implemented for all patients on the CTS ward on the 5th November 2015. Due to logistical limitations, chlorhexidine gluconate body washes were unable to be implemented in the ICU during the outbreak.

HH audits were conducted regularly before the start of the outbreak and this continued throughout the outbreak. Ward staff on CTS and ICU who were accredited as Hand Hygiene Auditors with Hand Hygiene Australia undertook the audits. Hand hygiene audits were conducted according to the methodology of Hand Hygiene Australia [18]. Feedback was supplied in real time to ward staff about compliance levels and technique.

In September 2015, with the onset of the outbreak, several environmental cleaning changes were made in the

Table 1 Summary of clinical setting, population and infection control measures during the outbreak.

Setting:
Cardiothoracic Surgery (CTS) ward and Intensive Care Unit (ICU) in a ~570 bed tertiary public hospital.
CTS ward had a total of 20 beds; 8 High Dependency Unit beds, 2 single-person isolation rooms and 10 twin-share rooms.
ICU had a total of 24 beds; 18 separated by curtains with 6 single-person isolation rooms all with 1:1 nursing.
Presence of a dedicated Infection Control team staffed with a specialist infection control physician and infection control nurses.
Dates: 1st August 2015—31st May 2016
Population characteristics:
Mixed (medical and surgical) ICU with over 200 admissions per year.
CTS unit provides elective and emergency services for advanced cardiac and thoracic surgical care including; coronary bypass, cardiac valve repair and replacement, aortic procedures, correction of congenital abnormalities in adults, management of thoracic trauma and management of lung and oesophageal tumours.
Acute outbreak of *vanA* VREfm (N = 83) in a setting of hospital wide endemic *vanB* VREfm.
Major infection control changes during the study:

2015	September	VRE screening commenced in ICU (2/9/2015) and CTS (20/9/2015)
		Formation of a multidisciplinary VRE outbreak team.
		New cleaning policy and procedure along with implementation.
		Education for staff around cleaning procedure and cleaning products.
		Increased HH audits for ICU.
		Fluorescent marking audits for adequacy of cleaning in ICU.
		Education and feedback for staff around cleaning.
	October	CTS ward incorporated into VRE outbreak team meetings.
		Addition of CTS ward to more comprehensive cleaning procedure, fluorescent marking cleaning audits and increased HH audits.
	November	Daily CHG body washes commenced on CTS ward.
		Restricted Ward access to CTS.
		Education for visitors to CTS ward.
		Audit of CTS antibiotic prophylaxis
2016	January	CTS ward repairs followed by deep clean and UV-C light treatment of rooms.
		Changes to recommended CTS antibiotic prophylaxis.
		Implementation of GeneXpert for microbiology sample testing and analysis
	April	Screening on ICU changed to on admission screening only.
	May	Screening on CTS ward ceased.

VRE screening policy:
Prior to September 2015: Screening was performed on patients staying in the same room (contacts) as a patient with positive clinical isolate of VRE.
Early September 2015: Addition of screening of all ICU patients on admission, twice weekly and on discharge unless screened in the previous 48 h.
Late September 2015: Additional screening changed to include all ICU and CTS ward patients on admission, once weekly and on discharge unless screened in the previous 48 h.
Late October 2015: Additional screening changed to screening of all ICU and CTS ward patients on admission, twice weekly and on discharge unless screened in the previous 48 h.
April 2016: Screening changed on ICU to on admission only. Continued as previous on CTS ward.
May 2016: Screening on CTS ward ceased, on admission screening continued in the ICU.
All screening for colonization performed with a rectal swab or in some circumstances a groin swab was used.
VRE isolation policy:
Prior to September 2015: Confirmed VRE cases cared for with contact precautions (CP) ie disposable long-sleeved gown and gloves.
September 2015: Confirmed cases cared for with CP. All patients transferred to the wards from the ICU to be cared for using CP at the bedside until screening result known to be negative.
Late September 2015: Same policy as described above applied to CTS ward patients.
Isolation rooms were available on both wards but were not used explicitly for VRE patients.
CTS antibiotic prophylaxis recommendations:
No standardised recommendations prior to January 2016. Recommendations implemented 4th January 2016; Cephazolin to be used as standard prophylaxis for 24 h post-coronary artery by-pass graft and surgery and 48 h post-heart valve surgery. Vancomycin to be administered prophylactically only for patients with inpatient stay prior to surgery or known to be carrying methicillin-resistant *Staphylococcus aureus* (MRSA). Ceftriaxone to be ceased for prophylactic use.
Feedback: Number of new vanA VRE cases by ward and possibility of transmission event along with number patients screened by ward. Results of hand hygiene and environmental cleaning audits were also relayed back to relevant staff.

Table 1 (*continued*)

Definition new *vanA* VREfm case during the outbreak: Patients with a screening, urine or clinical culture positive for VREfm carrying the *vanA* gene during their admission.

Definition probable transmission event: Cases with a confirmed negative screening result prior to returning a screening, urine or clinical culture positive for VREfm carrying the *vanA* gene in the same admission period to a particular ward. *Example*: patient stays on the CTS ward from the 5th November to 10th November and has a negative screening result on the 6th November, before returning a positive result on the 9th November, was considered a "probable transmission event" on the CTS ward.

Note. CP = contact precautions; CTS = cardiothoracic surgery; HH = hand hygiene; ICU = intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; VRE = vancomycin-resistant enterococci; VREfm = vancomycin-resistant *Enterococcus faecium*.

outbreak wards. The cleaning product was changed from a quaternary ammonium compound disinfectant and detergent wipe to a hydrogen peroxide/peracetic acid and detergent disposable wipe, according to hospital cleaning procedure for outbreaks. This product had been selected previously based on microbiological properties and practical considerations for cleaning. Multiple other changes introduced included education and credentialing of environmental staff, cessation of use of agency cleaning staff, development of master charts which included pictorial lists of items to be cleaned and also delineation of which craft group cleaned which items, increased supervision, accountability of cleaners.

Cleaning performance audits were performed using fluorescent marking in ICU, the CTS ward and CTS operating theatres and were initiated in September 2015. Infection Prevention fluorescent marked and reviewed the high touch elements or surfaces in patient bedspace, bathroom and CTS operating theatres (see Appendix A for elements audited). In order for an element to be counted as a pass, the fluorescent marker needed to be removed from that whole element. For regular daily cleans a target of 80% of elements marked was set. For discharge cleans and operating theatre cleans, a target of 100% was set. Education and feedback of audit results were provided for clinical assistants (CA), cleaners and nursing staff.

In early October 2015, after recognition that the outbreak was also occurring on the CTS ward, a decision was made to restrict the number of boarder patients (those not under the care of CTS but staying on the CTS ward) and later non-essential staff in an attempt to control spread to other wards.

In November 2015, an audit of antimicrobial prophylaxis used for CTS surgery was conducted. The audit identified nine different regimens (varying combinations and durations of cephazolin, ceftriaxone, vancomycin and flucloxacillin) were in use and practises were not standardised or necessarily in line with national guidelines [19]. On the 4th January 2016, a standard antibiotic prophylaxis regimen was recommended: cephazolin for all patients or vancomycin for use in patients with a beta-lactam allergy or vancomycin and cephazolin for those at risk of or known to be colonised with methicillin-resistant *Staphylococcus aureus* (MRSA). Duration of post-operative antibiotic was also curtailed at 24 h for coronary artery bypass graft (CABG) surgery and 48 h for valve surgery. These recommendations are more in-line with current Australian antibiotic prophylaxis guidelines for CTS [19].

Between the 4th and 18th January 2016, the regular Christmas/New Year reduction in CTS surgery allowed for repairs of the CTS ward which included replacement of damaged environmental objects and painting. Following repairs a deep clean of CTS ward rooms and ultraviolet (UV)-C light treatment was conducted. The aim of these interventions was to reduce environmental sources of *vanA* VREfm.

Microbiology

VRE surveillance swabs were processed by inoculation of VRE Chromagar (Biomerieux, Marcy-L'Etoile, France), which were incubated in ambient air for 48 h at 35 °C, according to manufacturer instructions. Suspicious colonies were identified as enterococci by MALDITOF (Bruker) mass spectrometry and first positive isolates had Vitek 2 (Biomerieux, Marcy-L'Etoile, France) antimicrobial susceptibility testing to confirm vancomycin resistance. VRE clinical isolates were also identified by MALDITOF, with Vitek-2 susceptibility testing to confirm vancomycin resistance. During the outbreak, the *van* genotype was determined with the Xpert vanA/B (Cepheid, Sunnyvale, USA) molecular assay.

Supplemental antimicrobial susceptibility testing for all isolates included daptomycin and teicoplanin Etests (Biomerieux, Marcy-L'Etoile, France). The daptomycin Etest strips contains additional calcium (40 μg/ml) along the gradient of the strip. Etest strips were applied to Mueller-Hinton agar (Oxoid, ThermoFisher Scientific, Australia) inoculated with a lawn culture of 0.5 McFarland suspension of the test organism. Plates were incubated in ambient air for 16–20 h at 35 °C prior to determination of MICs. Susceptibility was interpreted using CLSI breakpoints [20].

VREfm isolates were referred for *in silico* multi-locus sequence typing. Genomic DNA was extracted with the JANUS Automated Workstation using the Chemagic Viral DNA/RNA kit (PerkinElmer). Unique dual indexed libraries were prepared using the Nextera XT DNA sample prep kit (Illumina). Libraries were sequenced on the Illumina NextSeq 500 with 150-cycle paired end chemistry as recommended by the manufacturer. *In silico* multi-locus sequence typing (MLST) was performed using mlst v2.10 (http://github.com/tseemann/mlst).

Data collection & statistical analysis

Cases of new *vanA* VREfm isolates and their relevant demographic, clinical and microbiological details were identified retrospectively by extracting data from the infection

control software, ICNet (Baxter International, USA). Data collected included age, gender, dates of hospital admission and discharge dates of admission and discharge to CTS ward, ICU and other hospital wards where relevant; and, dates, types and results of microbiological tests (as described above). For patients with clinical isolates positive for *vanA* VREfm medical records were reviewed to determine what treatment they received (if any).

Categorical variables are reported as frequencies and percentages. Continuous variables are expressed as medians and interquartile ranges (IQR). Discrete variables are expressed as means and standard deviations (SD).

All statistical analyses were performed using R (version 3.4.4.) or Microsoft Excel (version 15.36).

Results

Fig. 1 provides a timeline of the outbreak and infection control response and Table 2 summarises demographic, clinical and microbiological details of *vanA* VREfm cases by ward.

Outbreak epidemiology

Between the 1st August 2015 and 31st May 2016, there were 804 and 1543 patients admitted to the CTS ward and ICU, respectively. During this same period, 521 (65%) CTS patients and 1183 (77%) ICU patients were screened for VRE. The average number of screens per patient was three. In total, there were 83 new cases of VREfm isolates carrying the *vanA* gene detected. Cases had a median length of hospital stay of 14 days (IQR: 9—25 days). Screening detected 94% (78/83) of cases; the remainder were detected from samples taken on clinical indication. Three patients received treatment for *vanA* VREfm infection. Two patients who had only stayed in the ICU developed bacteraemia; one was treated with linezolid and the other daptomycin. Both bacteraemia patients were initially detected to be carrying *vanA* VREfm from a tracheal aspirate (Table 2). One patient who only stayed on the CTS ward was treated for a urinary tract infection with linezolid. There was an increase in newly detected sporadic *vanA* VREfm isolates from clinical samples throughout the hospital during this period.

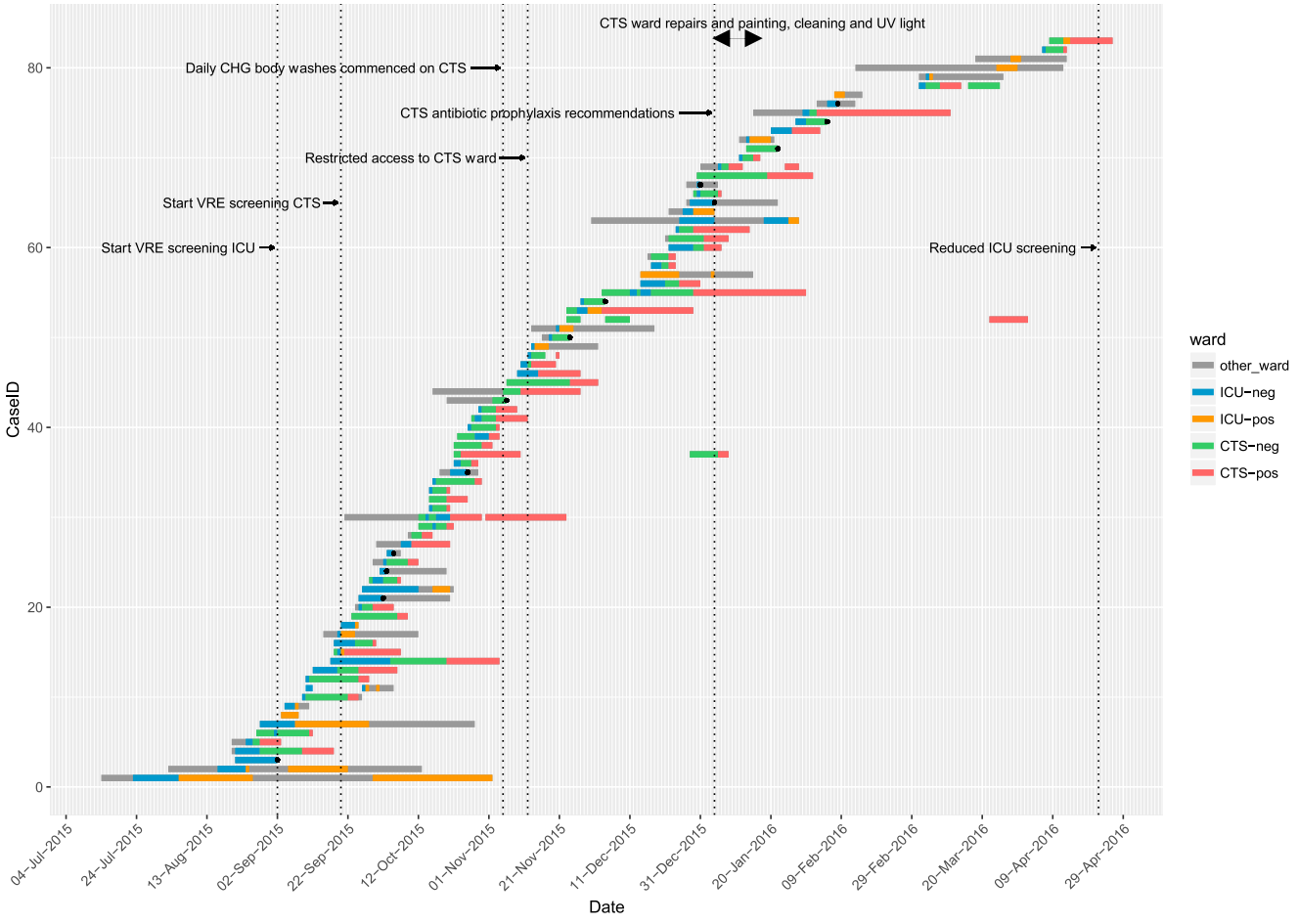

Figure 1 Timeline of the outbreak: Length of stay on CTS, ICU and other hospital wards for cases and implementation of key infection control measures. CTS-pos and ICU-pos = stay on ward with any positive vanA VREfm isolate; CTS-neg and ICU-neg = stay on ward when negative for vanA VREfm or status not yet known (assumed negative); other_ward = stay on any other ward in hospital excluding ICU and CTS and regardless of vanA VREfm status. Black dots represent vanA VREfm acquisitions detected on discharge screening to other_ward or from hospital. Note. CHG = Chlorhexidine gluconate; CTS = cardiothoracic surgery; ICU = intensive care unit; VRE = vancomycin-resistant enterococci; VREfm = vancomycin-resistant *Enterococcus faecium*.

Table 2 Summary of demographic, clinical and microbiological characteristics of vanA VREfm cases.

Variable		Ward *vanA* VREfm isolated		
		CTS	ICU	Total, n (%)
Sex, n (%)	Male	37 (70)	18 (58)	55 (66)
	Female	15 (30)	13 (42)	28 (34)
Age, n (%), (years)	20–39	7 (13)	2 (6)	9 (11)
	40–59	12 (23)	13 (42)	25 (30)
	60–79	27 (52)	13 (42)	40 (48)
	≥80	6 (12)	3 (10)	9 (11)
Specimen type, first positive specimen, n (%)	clinical[a]	0 (0)	2 (10)	2 (2)
	urine	2 (4)	1 (3)	3 (4)
	screening	50 (96)	28 (90)	78 (94)
Days to first *vanA* VREfm isolate, median (IQR)		8 (5–13)	6 (3–10.5)	8 (5–11.8)

Note. Data were not collected on patients with isolates harbouring the *vanB* gene alone and are not included in the analysis of this study.
CTS = cardiothoracic surgery; ICU = intensive care unit; n = frequency; VREfm = vancomycin-resistant *Enterococcus faecium*.
[a] Clinical specimens were both tracheal aspirates that initially detected vanA VREfm.

Fig. 2a shows the epidemic curve of new *vanA* VREfm cases that occurred in the ICU. The first case identified in the ICU was a patient with *vanA* VREfm bacteraemia who had an underlying haematological malignancy. In the ICU, there were 31 new cases of *vanA* VREfm during the outbreak and 11 (35%) of these were considered to be probable transmission events. Control of the outbreak on ICU was considered to be achieved on the 20th April 2016 after no

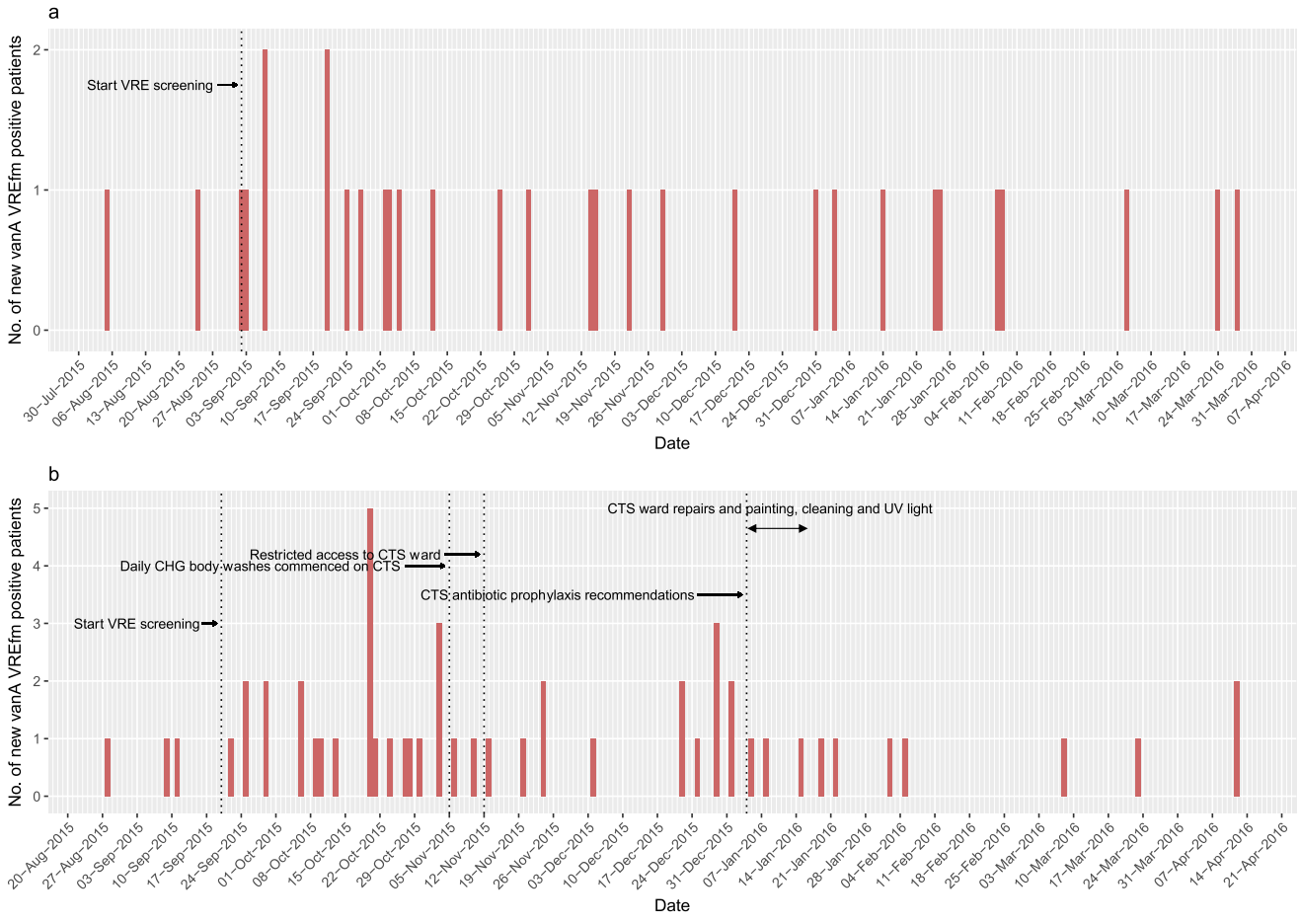

Figure 2 Epidemiological curves of new vanA VREfm cases on ICU (a) and CTS ward (b) over the course of the outbreak. Timing of some key interventions applied specifically to each ward are indicated. Note. CHG = Chlorhexidine gluconate; CTS = cardiothoracic surgery; ICU = intensive care unit; VRE = vancomycin-resistant enterococci; VREfm = vancomycin-resistant *Enterococcus faecium*.

new positive results for 4 weeks, and no probable transmission event attributable to ICU in 10 weeks. Screening of patients on admission to ICU was continued to detect any new cases transferred to the ICU.

Fig. 2b shows the epidemic curve of new *vanA* VREfm cases that occurred on the CTS ward. The first case was a screening isolate identified on 28th August 2015. The patient had previously stayed in the ICU, but had not been screened for VRE during their ICU admission as it pre-dated the widespread implementation of VRE screening. This patient was screened for VRE due to contact with another patient with a known clinical specimen of *vanA* VREfm whilst staying in the ICU. Over the course of the outbreak, a total of 52 new cases of *vanA* VREfm were detected on the CTS ward and 4 patients were transferred from the ICU known to be carrying *vanA* VREfm. In total, there were 35 probable transmission events that occurred on the CTS ward (Table 1 for definition).

During the outbreak three separate batches of isolates were referred to an external reference laboratory for *in silico* MLST. The three batches consisted of isolates from September, October and December 2015, and January 2016. In total 43 isolates from ICU and CTS patients were referred for analysis. Table 3 summarises the MLST of isolates encountered and the ward on which they were isolated. Five different MLSTs carrying the *vanA* gene were identified (ST17, ST80, ST203, ST252 and ST1421) from this subset of total isolates during the outbreak.

Infection control interventions

The infection prevention service was notified of six new *vanA* VREfm isolates from patients in August 2015, five of whom had stayed in the ICU prior to returning a positive swab. Given this link, VRE screening was commenced in the ICU on the 2nd September 2015. Subsequent screening initiated on the CTS ward identified four *vanA* VREfm isolates during September.

The results of HH audits conducted throughout the outbreak demonstrated that percentage HH compliance on the ICU was consistently below the benchmark of 80% with the exception of audits conducted in December 2015 and May 2016. The overall percentage compliance did not fall below 60% on ICU during the outbreak. In contrast percentage HH compliance on the CTS ward was mostly at or above the benchmark of 80% for the duration of the outbreak. Compliance fell below 80% during October 2015 and January 2016 on the CTS ward.

Table 3 MLST type encountered during the outbreak by ward.

MLST	van gene	ICU	CTS	Total
ST17	A/B	1	7	8
ST80	A	1		1
ST203	A	6	5	11
ST252	A	1		1
ST1421	A	6	16	22

Note. CTS = cardiothoracic surgery, ICU = intensive care unit, MLST = multi-locus sequence type.

Aggregate data of fluorescent cleaning audits indicates that on average most cleans were below the benchmarks of 80% for daily general cleaning and 100% for discharge cleans and operating theatre cleans. There was a general trend of improvement in percentage of elements cleaned over the course of the outbreak.

No evaluation of compliance with recommended changes to CTS antibiotic prophylaxis or the use of chlorhexidine gluconate body washes was conducted. Anecdotally, the antibiotic and body wash recommendations were largely followed.

Control of the outbreak on ICU was considered to be achieved on the 20th April 2016 after no new positive results for 4 weeks, and no probable transmission event attributable to ICU in 10 weeks. Screening of patients on admission to ICU has been continued till the present date December 2018, to detect any new cases transferred to the ICU. Control of the outbreak on the CTS ward was declared on the 20th May 2016 after five weeks of no new positive cases.

Discussion

This outbreak description of *vanA* VREfm was unique for several reasons. Geographically, isolates of *vanA* VREfm have previously been uncommon in our hospital and Australian hospitals generally [4,8,21–23]. Prior to and throughout the outbreak, *vanB* VREfm was endemic in our hospital and many Victorian hospitals [4,24]. However, since 2013 there has been a dramatic rise in *vanA* VREfm isolates in Victoria and nationally [1,25]. In some parts of Australia, it is now more common than *vanB* VREfm [1]. The most recent published data indicate that *vanA* VREfm makes up 17.8% of all VREfm isolates [26]. *VanB* VRE still makes up the majority of isolates in the state (78.5%) [26]. The remainder of isolates in Victoria are made up of isolates carrying both the *vanA* and *vanB* gene and those carrying neither gene. Outbreaks predominantly affecting CTS patients have been documented in the literature. However, it appears they are less common than other well-described at-risk populations such as ICU, haematological malignancy and transplant patients [27–30].

Overall, the outbreak lasted 10 months, and our study demonstrated control of the acute outbreak with a multifaceted response. The overall clinical impact of the outbreak was low, with only three cases requiring treatment for infection, although two of these cases were bloodstream infections. Our study supports the importance of screening for detecting the reservoir of VRE in acute hospital outbreaks, with 94% of cases initially detected with screening [13]. Furthermore, the utilisation of discharge screening in this outbreak detected 13 new *vanA* VREfm isolates on discharge from the ICU and CTS ward, with 9 of these cases being discharges to another hospital ward. Discharge screening ensures new cases can be appropriately managed when being transferred from high to low prevalence wards and may be important in preventing dissemination of VRE throughout the hospital. The overall screening rates were 77% of ICU patients and 65% of CTS patients admitted during the study period. A significant proportion of the unscreened patients is likely accounted

for in the delay between the start of study period and the implementation of screening on these wards. However, some patients may have been missed for screening for other reasons during the outbreak. The important implication is that not all *vanA* VREfm cases may have been captured in this description.

Early infection control measures implemented focused on improving HH, environmental cleaning and use of CP to prevent cross-transmission. These interventions were not associated with control of the outbreak. However, the environmental cleaning measures implemented (change of product, education and auditing feedback to cleaners) and HH measures (education and auditing feedback) in our outbreak have been shown to be effective when implemented in some studies [15,16]. The lack of response may have been due to sub-optimal cleaning and HH compliance observed early in this outbreak.

The subsequent interventions introduced, including daily chlorhexidine gluconate body washes for patients on the CTS ward, restricted access to CTS ward, antibiotic stewardship with recommended changes to CTS prophylaxis, and deep ward clean plus UV-C light treatment, in addition to continued efforts to improve HH and environmental cleaning measures were associated with control of the outbreak 10 months after its recognition. We did not audit antibiotic usage for CTS prophylaxis after implementation of the new recommendations, nor did we monitor whether patients received body washes, hence we cannot be certain of the contribution these interventions had to the control of the outbreak. Other studies have suggested that they may be effective [11,17]. Some antibiotics have been identified as key drivers of acquiring VRE in hospitalised patients, including vancomycin and ceftriaxone - both in use for CTS prophylaxis during the outbreak [31–33]. The recommended changes to prophylaxis instigated by the AMS to restrict the use of vancomycin and for the cessation of ceftriaxone usage are in keeping with current Australian guidelines [19].

New isolates of *vanA* VREfm were first detected on ICU and later began to be isolated on CTS ward. There is a clear epidemiological link between the CTS ward and ICU, as all patients undergoing coronary artery bypass or valve surgery have short stays in ICU post-operatively before being transferred to the CTS ward for ongoing care. It appears *vanA* VREfm likely spread from ICU to CTS, although our results do not definitively establish this link and it is possible they may have arisen independently and simultaneously. There were 35 probable transmission events on the CTS ward. CTS patients as a whole represented the greatest population of patients that acquired *vanA* VREfm during the outbreak (56/83, 67.5%). The reason why CTS patients were at greater risk during this outbreak is not clear. Our data indicate that both HH and environmental cleaning were more consistently at or above the required standard on the CTS ward compared to the ICU during the outbreak (Fig. 2). VREfm has a propensity to survive in the surrounding hospital environment from where it can be transmitted to patients [15,34]. It is possible that despite increased cleaning, there were environmental reservoirs of VREfm that were only able to be successfully removed with the deep ward clean and UV-C-light treatment implemented late in the outbreak [16,35]. However, screening for environmental sources of VREfm in the ICU or CTS ward was not undertaken during the outbreak to support this hypothesis. Alternatively, or in addition, CTS patients may have been predisposed through clinical factors such as antibiotic usage, invasive medical device usage, underlying disease or type of surgery undertaken.

In silico multi-locus sequence typing was performed on 43 (52%) of the 83 *vanA* VREfm outbreak isolates. The outbreak was polyclonal with 5 different sequence types harbouring the *vanA* gene detected. The predominant MLST encountered from these isolates was a recently designated MLST ST1421 (51%) which lacks the *pstS* gene, followed by ST203 (26%). A recent one-month cross-sectional study of VRE isolates across all hospitals in Victoria that coincided with this outbreak demonstrated that the most common *vanA* VREfm MLSTs encountered were ST1421, ST203 and ST80 [26]. ST80 was uncommon amongst our isolates ($n = 1$). Furthermore, 19% of our isolates were a relatively unique *vanA* and *vanB*-carrying ST17. Most isolates of ST17 in Victoria and around Australia have been *vanB* genotype or isolates harbouring either gene [1,26]. In general, isolates carrying both the *vanA* and *vanB* gene have been rare in Australia [1].

The origin of these *vanA* isolates in our hospital has not been elucidated in this study. One hypothesis is the introduction of a single sequence type harbouring a plasmid carrying the *vanA* gene that has subsequently been passed to other sequence types present in our hospital, which is in keeping with the epidemiology of an acute outbreak as described here. Another hypothesis is that our hospital has multiple introductions of *vanA*-harbouring sequence types. The results of recent studies looking at *vanA* VREfm in Victoria and throughout Australia indicate that the recent increase in the detection of *vanA* VREfm is more likely due to the introduction of multiple *vanA*-harbouring clones [26,36]. It is possible that both mechanisms may have been driving the increase in *vanA* VREfm isolates in our hospital. Without more detailed phylogenetic analysis and a better understanding of the molecular epidemiology of VREfm in our hospital prior to the outbreak, we cannot draw any definitive conclusions about the underlying mechanism driving this *vanA* VREfm outbreak.

This study has several limitations. The molecular epidemiology of our VREfm outbreak is incomplete as not all isolates were referred for WGS. In addition, we did not re-analyse the isolates that were sent during the outbreak and conduct phylogenetic analysis to determine relatedness of isolates. Thus, we only report here the MLSTs of isolates sent. We cannot be certain about the exact distribution or representation of MLSTs in our hospital during the outbreak nor how closely these isolates are related to one another. Furthermore, our study is unable to provide insights into how and when these *vanA* MLSTs were introduced into our hospital. Understanding their origin would help guide the prevention of future outbreaks. The majority of isolates in this study were detected through screening; thus, the epidemiology and control measures described are more relevant to colonisation than infection. However, as VREfm colonisation nearly always precedes infection, the prevention and control of colonisation amongst hospitalised patients can reduce rates VREfm infection [37]. This report of an acute polyclonal outbreak

of *vanA* VREfm reflects changing epidemiology of VRE in Victoria and our hospital. The infection control strategies described here may help to guide future strategies for preventing and controlling outbreaks of *vanA* VREfm.

Ethics

This study was conducted as a quality assurance (QA) project. All data utilised are collected as part of routine clinical care. Patient consent was not sort for this project as it fulfilled the National Health and Medical Research Council (NH&MRC) criteria for QA. The Melbourne Health, Office of Research approved this project and the gathering of patient information.

Authorship statement

AH contributed to the design of the study, conducted the acquisition, analysis and interpretation of data, drafted and revised the paper; SB contributed the analysis and interpretation of data, drafted and revised the paper; SS contributed to the conception and design of the study, analysis and interpretation of data and revised the paper; CM contributed to the conception and design of the study, analysis and interpretation of data and revised the paper.

Conflict of interest

None to declare.

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Provenance and peer review

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.idh.2018.12.002.

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