PICNet
PROVINCIAL INFECTION CONTROL NETWORK OF BRITISH COLUMBIA
A program of the Provincial Health Services Authority

Vancomycin Resistant Enterococci Screening and Isolation Practices in BC Healthcare Settings: A Discussion Paper

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Document Review

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Executive Summary

There are two divergent bodies of expert opinion on Vancomycin Resistant Enterococci (VRE) control. In the past few years, several Canadian healthcare facilities have decided to reduce or discontinue screening for VRE and discontinue the use of contact precautions as a VRE control strategy, while others continue to support current guideline recommendations for VRE surveillance and the use of additional precautions. For the purposes of informing a provincial approach on the control of VRE in BC, the Ministry of Health requested that the Provincial Infection Control Network of BC (PICNet) develop an evidence-informed, risk-based discussion paper on VRE screening and isolation practices.

In September 2012, as part of the review of the provincial Antibiotic Resistant Organisms Prevention and Control Guidelines, PICNet requested the aid of the Canadian Agency for Drugs and Technologies in Health (CADTH) in performing a systematic review of the current evidence regarding screening and isolating patients with VRE and extended spectrum beta-lactamase producing organisms (ESBL). This systematic review evaluated the clinical evidence for the effectiveness of screening and isolation of patients colonized or infected with VRE and ESBL in acute and long-term care facilities. The health services impacts of these strategies were also reviewed.[1]

Following the completion of the CADTH review, the Provincial Infectious Diseases Advisory Committee of Ontario (PIDAC) undertook a further review of the literature on the control of VRE.[2] Evidence cited in the PIDAC review is also discussed in this paper.

Evidence from several studies has shown that active surveillance (screening of all high-risk patients) and other precautionary measures in hospital settings may result in reducing the spread of VRE, and may decrease colonization and infections. Specific infection prevention and control strategies to increase the effectiveness of, and compliance with, the precautionary measures may be important in preventing colonization and possibly infections with VRE and other antibiotic resistant organisms (ARO), depending on the organism and setting. The acceptance of this evidence requires caution as the cited studies have methodological concerns, and were undertaken with specific, high-risk patient populations. The applicability of the findings to the broad spectrum of healthcare is limited. With the implementation of certain precautionary measures (such as isolation), consideration must be given to the possible negative effects these may have on hospitalized patients. In addition, the use of isolation may increase the use of hospital resources through increased length of hospital stay (LOS), impacts on patient flow and discharge, increased time devoted to direct patient care by healthcare workers, and increased costs from use of personal protective equipment (PPE).

In 2010, the Vancouver Island Health Authority (VIHA) instituted a policy of screening only patients admitted to designated renal and intensive care units. Patients in these units are placed on additional precautions if found to be VRE positive. Patients in other patient care areas are not placed on additional precautions unless they have diarrhea or are known to be infected. Subsequently, VIHA has also discontinued VRE screening in intensive care units. In

2012, Fraser Health Authority (FHA) adopted a policy of not screening patients for VRE, nor placing colonized patients on contact precautions. VRE positive patients with diarrhea or VRE infections are isolated. Vancouver Coastal Health (VCH) also discontinued screening patients for VRE in 2013, applying additional precautions and declaring VRE outbreaks as did Interior Health Authority. Northern Health, Provincial Health Services Authority and Providence Health Care do not currently have any plans to implement policy changes for VRE. They will continue to screen selected patients for colonization with VRE and apply additional precautions.

In 2012, four tertiary care facilities in Ontario changed their policies regarding VRE. These hospitals no longer screen patients for VRE, nor apply additional precautions for patients with VRE, nor declare VRE outbreaks. This is despite PIDAC's recommendations, based on evidence from their December 2012 literature review, to continue VRE admission screening, surveillance, and the use of additional precautions for patients identified as being either colonized or infected with VRE.[2]

In October 2012, the Community and Hospital Infection Control Association of Canada (CHICA-Canada) issued a position statement stating that any changes to practice should be motivated by a desire to improve patient care, and should only be considered in the context of an infection control program already meeting or exceeding best practices.[3]

Additionally, any such changes should be accompanied by close monitoring of VRE culture-positive healthcare-associated infections (HAI) following the changes, to assure that increasing trends in VRE infections are not occurring related to changes in policy. In the event that such new policies are found to worsen patient outcomes, facilities should be prepared to reinstate VRE screening and isolating of patients that are found to be VRE positive. It is also highly recommended that those facilities that choose to change their strategy should communicate their experiences to other members of the infection control community for future policy making. PICNet fully endorses this position statement.

Following the initial preparation of this discussion paper further evidence has been published by McGill University Hospital regarding the evaluation of VRE associated morbidity following relaxation of screening and isolation precautions. They observed an immediate increase in both colonization and infection incidence. Despite the colonization increase, infection outcomes remained infrequent and stable, suggesting a finite number of patients at risk. Relaxation of VRE protocols may, in fact, not lead to increasing infection incidence in a hospital setting. A risk based approach with targeted screening and isolation, focused on the highest risk patients, can be a cost effective approach, without putting patients at risk and freeing up resources to address other emerging antibiotic resistant organisms.[4]

Public Health Ontario is currently evaluating and comparing the rates of VRE bacteremia and the impact of VRE screening strategies between those facilities who discontinued universal screening and isolation of VRE positive patients and those that continued. A preliminary report of their findings will be released later in 2014. An oral presentation at the 2014 Infection Prevention and Control Canada Conference by Dr. Gary Garber provided the following results.

In the 4 quarters (July 2011-June 2012) prior to discontinuing VRE precautions, bacteremias at the non-screening hospitals combined for 3.75 bacteremias /quarter (<1/mo). The counts remained unchanged for the next 3 quarters (July 2012-March 2013); but has increased to 9 bacteremias/quarter (3/mo) in the last 3 quarters (April 2013-Dec 2013). Reported bacteremia counts at hospitals continuing VRE precautions have not changed over the same period. Although VRE bacteremia has increased, the rates are still low and the clinical relevance of this increase requires further review. The plan is to collect data on the clinical factors associated with VRE bacteremia to determine the at-risk population and to identify the feasibility of a targeted screening and isolation policy.[5]

At this time, there is insufficient evidence to support a recommendation to continue or discontinue control measures for VRE. PICNet recommends that trends in VRE bacteremia identified in laboratories across British Columbia since changes in policy first took place be closely examined to determine if there have been any increases that may be related to VRE policy changes and what the impact may be on patient outcomes. Any further recommendations for changes in policy should be based upon those findings.

Introduction

In the past few years, several Canadian healthcare facilities have decided to reduce or stop screening for Vancomycin Resistant Enterococci (VRE) as well as the use of contact precautions as a VRE control strategy, while others continue to support current guideline recommendations for VRE surveillance and the use of additional precautions. These represent two divergent bodies of expert opinion on VRE control.

In 2012, four tertiary care facilities in Ontario changed their practices relating to VRE surveillance. These changes included the cessation of the following: screening patients for VRE on admission, the use of additional precautions for VRE, and declaring VRE outbreaks. As a result of this change, The Provincial Infectious Diseases Advisory Committee of Ontario (PIDAC) undertook a further review of the literature on the control of VRE up to December 2012. Based on the evidence reviewed, PIDAC continues to recommend VRE admission screening, surveillance, and the use of additional precautions for patients identified as being either colonized or infected with VRE as per their 2012 guidelines[6].

PIDAC's recommendations were based on relevant citations and expert opinions, and were not specific to any particular healthcare setting. However, some of these specific recommendations remain controversial, with some Canadian hospitals discontinuing screening for VRE colonization or isolating patients with VRE based on the argument that the increased resources required for containment are not commensurate with the increased patient risk from VRE.[7, 8]

Several of BC's health authorities have chosen to take a risk managed approach to the use of additional precautions with VRE positive patients. The rationale for this approach employed by VIHA, FHA, and VCH is discussed.

For the purposes of informing a provincial approach on the control of VRE in BC, the Ministry of Health requested that the Provincial Infection Control Network of BC (PICNet) develop an evidence-informed, risk-based discussion paper on VRE screening and isolation practices.

As part of the review of the provincial *Antibiotic Resistant Organisms Prevention and Control Guidelines*, PICNet requested the aid of the Canadian Agency for Drugs and Technologies in Health (CADTH) in performing a systematic review of the current evidence. The objective of this systematic review was to evaluate the clinical evidence for the effectiveness of screening and isolation of patients colonized or infected with VRE and other ARO (i.e., Extended Spectrum Beta-Lactamase producing organisms) in acute and long-term care facilities.

For the purposes of this discussion paper, excerpts were taken from the CADTH review that pertained specifically to VRE. Evidence cited in the PIDAC review is also discussed in this paper. This paper was originally submitted to the Ministry of Health in April 2013. Subsequent to that time some newer information has emerged regarding findings in different parts of the country

that have looked at the effects of relaxing VRE screening and precautions. The results of those investigations have been added to this revised version.

Background

Bacterial resistance to antibiotics is an increasing problem in Canada and worldwide.[9-12] Vancomycin-resistant Enterococci (VRE) are strains of *Enterococcus faecium* or *Enterococcus faecalis* that contain genes conferring resistance to vancomycin.[13, 14] The presence and growth of VRE organisms (colonization) in the gastrointestinal tract can act as a source of infection for the carrier, and a reservoir for the transmission of VRE to other persons.[15] In a cohort of patients admitted to an acute rehabilitation hospital, who did not have a history of antibacterial-resistant infections, admission swabs were positive for Methicillin-resistant *Staphylococcus aureus* (MRSA) and/or VRE in 16% of the population.[16] Results from the Canadian Nosocomial Infection Surveillance Program (CNISP) showed that from 1999 to 2005, the rate of VRE colonization and VRE infection increased from 0.37 to 1.32 cases and from 0.02 to 0.05 cases respectively per 1,000 patients admitted to hospital.[17] More recent rates reported by CNISP from 2007 to 2011 showed the rate of VRE colonization and VRE infections increased from 2.4 to 7.8 and from 0.08 to 0.51 cases respectively per 1000 patients admitted to hospital.[8]

Among patients with enterococcal bloodstream infections, bacteria that were resistant to vancomycin were shown in two meta-analyses to be directly associated with increased mortality compared with bacteria that were susceptible to vancomycin.[18-20] It is noteworthy that the meta-analyses were systematic reviews of cohort studies, most of which had inadequate sample size, and were conducted before the availability of newer antimicrobials against VRE. However, three more recent studies in bone marrow transplant patients treated with newer antimicrobials showed poor outcomes in treating VRE.[21-23] It must be noted that these studies were conducted among seriously immunocompromised individuals, and as such, it is difficult to extrapolate these finding to the vast majority of patients who are not bone marrow transplant patients.

Prevention and control measures for VRE include a screening process to identify colonized patients, and isolation of the carriers. Hospital infection prevention and control strategies and guidelines for AROs have been developed in several Canadian jurisdictions,[6, 24-26] and these include non-specific control measures such as the appropriate use of antimicrobials like vancomycin, and implementing an antimicrobial stewardship program that promotes the appropriate selection, dose, route, and duration of antimicrobial therapy. The non-specific guidelines also include performing environmental cleaning, implementing bundled practices to prevent procedure-associated infections (e.g. surgical site infections) and device-associated infections (e.g. central line-associated bloodstream infections), and educating hospital staff concerning procedures such as hand washing with an antiseptic agent. Organism-specific guidance includes routine screening for VRE and contact precautions for patients colonized or

infected with VRE. The relative contribution of specific versus non-specific measures is unknown, especially as compliance with screening and implementation of additional precautions is unknown, and would be expected to vary between institutions. The success of such measures may also be affected by the prevalence of ARO within the facility and/or the community. The prevalence of VRE in the community is currently unknown.

Infections and colonizations caused by AROs such as VRE have been shown to increase the use of hospital resources in some settings due to extended hospital stays, laboratory tests, physician consultations, and the cost of infection prevention and control measures to prevent the further spread of these pathogens.[27] However, both morbidity caused by infection and screening and control strategies contribute to this increased resource use. Additionally, AROs are commonly detected in the intensive care unit (ICU) where antimicrobial selection pressure is higher, and exposure to broad-spectrum antimicrobials is more common. The healthcare impact of antimicrobial resistance cannot be limited to the hospital perspective, as significant portions of clinical care are provided in other facilities and the community.[28]

A Risk Management Approach to the Use of Additional Precautions for VRE in BC Health Authorities

The burden of VRE among Canadian acute-care hospitals remains low, yet infection rates have been rapidly increasing since 2008 with regional variation. From the limited international data that are available, the increasing VRE infection trends observed in Canada, both regionally and over time, coincide with increasing trends reported by several European countries and the United States.[6] It should be noted, that current surveillance methodology used within the health authorities may monitor only the incidence cases of VRE when the patients are identified at the first time of a positive laboratory specimen for either colonizations or infections with VRE. If a colonized patient was to subsequently develop an infection, using the currently methodology, this infection may not be included leading to under-reporting the actual number of VRE infections. Therefore, the reported rate of VRE may not accurately reflect the burden of infections caused by VRE. In some health authorities all VRE isolates identified in the laboratory are followed up to determine if an infection is present, while others follow up only on isolates identified from sterile body sites.

The original impetus for applying additional precautions for patients with VRE arose from the concern that the resistance gene for vancomycin might be transferred to MRSA. This would result in virtually no antibiotics available to treat infections with extremely resistant and clinically important organism. However, 18 years of experience has shown that this phenomenon rarely occurs — and we now have new drugs in our arsenal to treat these infections. Efforts could therefore be redirected to treating VRE cases with a risk-managed approach. The savings could be re-directed to sustaining programs to address deficiencies such as antibiotic stewardship, environmental clutter, and inadequate equipment cleaning that may be the underlying reasons for the rise in VRE rates and the inability to further decrease *C.*

difficile cases. Several of BC's health authorities have chosen to take a risk managed approach to the use of additional precautions with VRE positive patients.

Vancouver Coastal Health

VCH proposed that it was not currently managing VRE patients and costs as efficiently as possible. In 2010-2011, VCH had approximately 17,000 routine surveillance admissions screens for VRE, and spent $5.6 million to prevent 37 new VRE infections (6% of its VRE isolates), of which 13 were serious in nature. While VRE rates reflect the systemic flaws in environmental cleaning, once an established cleaning program was in place, VCH stepped back on isolation protocols with low risk cases.

A risk managed approach to VRE was implemented to sustain the initiative. This approach entailed:

- Stopping routine admission screening except for (a) patients at higher risk for an infection (Bone Marrow Transplant [BMT], Solid Organ Transplant [SOT], Dialysis and Intensive Care Unit patients) and (b) those most at risk of transmission of VRE (patients with diarrhea and/or patients with both *Clostridium difficile* and VRE)
- Applying additional precautions only for those (a) with VRE in the above-mentioned high-risk populations for infection and (b) patients with VRE and diarrhea most at risk of transmitting VRE and/or acquiring an infection
- Removal of the majority of electronically flagged VRE patients
- Prevalence screening only for ICU, BMT and SOT wards continue; no cost recovery
- Screening of *C. difficile* stools for VRE continue for years 3 and 4; no cost recovery

This approach will eliminate 17,000 routine admission VRE screens and 55% of management and isolation costs, including personal protective equipment use, cohorting and blocking of single rooms, patient transfers and bed moves, double room cleaning, increased nursing time, and use of more expensive disinfectants. By changing VRE management, VCH expects a cost avoidance of approximately $3 million annually. These savings will be invested in an environmental program and an antibiotic stewardship program as part of an overall plan to reduce the environmental pressure for VRE.

This approach has not been recommended in any guidelines to date; however, a refocused VRE management strategy and reallocation of money saved to address the root causes of transmission can help provide a strong and sustainable infrastructure to reduce HAIs.

Fraser Health Authority

In 2012, FHA changed their policies regarding screening and isolation of VRE positive patients. The reasons for the changes include:

- VRE control measures were a significant drain on isolation resources, contributed to isolation fatigue among healthcare provided, and added to congestion problems.
- Resources were taken that were needed for other pathogens, including *C. difficile.*
- Evidence that control measures were not effective: prevalence of colonization continued to increase, but the number of infections remained low.

- Initial fear of gene transfer between VRE and other AROs had not materialized in a significant way.
- An external review done by Dr. Michael Gardam recommended that FHA consider revisiting its VRE control policies as other BC health authorities have done, given considerable effort being spent on controlling VRE, which may lead to isolation fatigue and make it harder to control *C. difficile* by using up precious isolation resources such as single rooms.

In addition, FHA wanted to highlight its VRE surveillance plan in place since the policy change. Every positive VRE clinical specimen is evaluated for colonization or infection status and included in their surveillance system. In the past, FHA only captured incidence of VRE and all new VRE positive specimens found in blood cultures. They are now documenting every positive VRE case. FHA has implemented a 30-day follow up of each VRE infection for consideration of whether the case is alive or dead within 30 days, whether they are discharged or remain in hospital, and if they remain is it related to VRE. Exposure to Linezolid in the past 30 days is also noted. For every VRE infection that has a death occur within 30 days, a thorough chart review is conducted by a consultant with clinical expertise in order to evaluate if the death was associated with the VRE infection; the purpose is to ensure that no harm occurs as a result of the VRE policy changes. VRE surveillance reports are provided to the FHA Infection Prevention and Control Committee, Quality Performance Committee, and Health Authority Medical Advisory Committee.

Vancouver Island Health Authority

Between 2008 and 2009, the Vancouver Island Health Authority declared 16 outbreaks in acute care: 13 for VRE and three for *C. difficile*. Of the VRE outbreaks, most were due to colonization and declared on the basis of aggressive roommate screening and point prevalence screening. This resulted in substantial inconvenience to patients, disruption of clinical activity, adverse media coverage, and prompted one internal and one external review. As a result, Infection Prevention and Control became one of VIHA's highest priorities. Evidence-based practice algorithms and risk management strategies were introduced as all of their policies and protocols were overhauled. Since this time, VIHA has changed its approach from a rules-based approach in infection prevention and control to one which is risk-based, focusing attention on identifying and managing risk situations. Instead of the type of organism driving use of precautions, the presence of symptoms and patient safety is utilized in decision making.

VIHA had a comprehensive screening tool administered to every patient admitted to an acute care facility, which included obtaining swabs for VRE on any person who has been hospitalized for more than 48 hours in the previous year. This created a huge workload for the laboratory and pressure to complete the results in a timely manner to avoid transmission from colonized patients before they were subsequently isolated. Any VRE colonized patient would be placed on contact precautions in a private room or cohorted, whether they were symptomatic with diarrhea or not. Over time these patients created gridlock, equipment shortage of such items as isolation carts and commodes, excessive patient bed moves to accommodate increasing

numbers of newly identified colonized patients, and most importantly, a discouraged nursing staff who were experiencing "isolation fatigue". Yet despite an increasing number of "pseudo-outbreaks," a greater number of clinical cases were not observed.

In 2009-2010, Infection Prevention and Control at VIHA was funded in a Strategic Wide Initiative (SWI) to study its surveillance policies for MRSA and VRE. They developed and tested a bundle of changes in practice in a supportive environment. The recommended changes to practice included discontinuing VRE surveillance swabs on admitted patients, discontinuing contact precautions for colonized patients with VRE, and deflagging all previous positive VRE patients in the electronic health record. In 2010-2011, VIHA continued screening high risk patients including all patients admitted to ICU and renal units. During that year, VRE screening on stools from patients admitted for *C. difficile* was discontinued. It was observed that patients with diarrhea can co-transmit *C. difficile* and VRE, but higher VRE infection rates were not observed in these individuals. VIHA has since discontinued VRE screening in their ICU population.

The estimated cost avoidance of performing VRE screening based on the surveillance tool, including supplies and labor costs associated with maintaining precautions was approximately $1.2 million. These funds have been redirected into the Antimicrobial Stewardship Program. VIHA documented that focusing on *C. difficile* has contributed to the steady decrease in those rates in the region, as evidenced in the PICNet *C. difficile* reports. At VIHA's three largest acute care facilities between fiscal years 2008-2009 and 2011-2012, the number of VRE infections declined steadily from 32 in 2008-2009 to nine in 2011-2012. The rate per 10,000 patient days declined from 0.8 to 0.2. The decline was mostly due to a reduction in VRE infections recorded at the Royal Jubilee Hospital. The number of cases at Nanaimo Regional hospital increased between 2010-2011 and 2011-2012. The VRE infection rate jumped from 0.1 to 0.5 per 10,000 patient days. However, random variation cannot be ruled out as a possible explanation (95% CI 0.0-0.7 and 0.2-0.7), nor the possibility that increases are due to more active surveillance during the 2011-2012 fiscal year. VIHA continues to collect statistics on VRE infected patients and thoroughly reviews cases and trends and is committed to being proactive in VRE management.

Providence Health Care

At Providence Health Care (PHC), an economic evaluation of VRE was conducted to determine the attributable cost and extended length of stay of VRE (for both infected and colonized patients) at St. Paul's Hospital. It was found that the total attributable cost per VRE-positive patient was $17,949, and the average extended length of stay was 13.8 days. Based on this analysis PHC concluded that the attributable cost and length of stay of VRE was considerable.[29] PHC has decided not to change their policy for VRE screening and isolation.

Active surveillance testing for VRE occurs via rectal screening, and is done universally for admissions to the clinical teaching units (CTU) and intensive care units (ICU). There are also weekly VRE rectal screens in the ICU. For units other than ICU and CTU, targeted screening is physician-initiated, based on a standard risk assessment form. For all incident PHC-associated VRE cases, current roommates are screened to rule out transmission.

Provincial Health Services Authority

In the past few years, BC Children's and Women's hospitals have been targeting their VRE screening to high risk patients only. PHSA does not plan to change their VRE screening practices in the near future.

Interior Health Authority

Interior Health Authority stopped universal admission screening for VRE as of December 1, 2013. Their management of VRE-infected patients has not changed. Patients with VRE infections are entered into the ARO alert system and are put on contact precautions.

There were several reasons for the discontinuation. From a clinical standpoint, the majority of VRE-colonized cases did not develop VRE infection, and cases of VRE infection were and are very infrequent. From the management perspective, the practice of placing patients who have been identified as a case of VRE colonization on contact precautions each time they are admitted to hospital was an inefficient use of resources and a burden on patients and healthcare providers.

Northern Health Authority

Northern Health Authority does not plan to change their approach to VRE management at this time. They will continue to screen targeted patients for VRE and apply additional precautions for those patients found to be colonized or infected.

Literature Review

The objective of the CADTH project was to review the clinical evidence for screening and isolation strategies for VRE. The health services impact of these strategies was also discussed. The following questions were used by CADTH in their systematic review of the literature.

Research Questions

1. What is the clinical evidence on the effectiveness of selective versus universal versus no screening of patients (adult and pediatric) for VRE and ESBL?
2. What is the clinical evidence on the effectiveness of patient isolation for VRE and ESBL?
3. What is the clinical evidence on the impact of isolation on the patient?
4. What is the health services impact of screening and isolating patients known to be carrying VRE or ESBL?

Literature Search Strategy

The literature search performed by CADTH involved an information specialist using a peer-reviewed search strategy. Published literature was identified by searching the following bibliographic databases: MEDLINE with in-process records and daily updates through Ovid; Embase through Ovid; The Cochrane Library (2012, Issue 3) through Wiley; and PubMed. The search strategy consisted of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were VRE and ESBL, screening, isolation, and decolonization.

Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCTs), and non-randomized studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published after January 1, 2002. Regular alerts were established to update the search until the publication of the final report. Conference abstracts were excluded from the search results. Grey literature was identified using Google and other Internet search engines to search for additional web-based materials. The detailed CADTH review is available at http://www.cadth.ca/media/pdf/htis/sept-2012/RE0028_VREReport_e.pdf.

Summary of Findings

The following summary of findings that pertained specifically to VRE was provided by CADTH in their systematic review in response to the research questions submitted by PICNet.

VRE Screening

What is the clinical evidence on the effectiveness of selective versus universal versus no screening of patients (adult and pediatric) for VRE?

A retrospective cohort study published in 2003 compared the effects of active surveillance (screening) versus no active surveillance (no screening) of patients at risk for VRE infection, between two tertiary care hospitals (total 290 patients), during a six-year period.[30] Active surveillance included weekly rectal swabs from all patients for three consecutive weeks in high-risk units such as the hematology-oncology, transplant, and ICU wards. When VRE were detected, staff from the microbiology department immediately called the nursing unit to indicate that the patient needed contact isolation. VRE isolates were also subjected to molecular typing for strain type identification. The analysis showed that when corrected for patient days, the hospital without an active surveillance program had 2.1-fold more cases (17.1 patients per 100,000 versus 8.2 patients per 100,000) of VRE bacteremia than did the hospital with an active surveillance program. The majority of isolates were clonally related in the hospital without active surveillance, while the population of VRE was more polyclonal in the hospital with the active surveillance program. The presence of polyclonal strains of VRE suggests less horizontal spread throughout the hospital, or less patient-to-patient transmission, while the majority of isolates being clonally related suggests greater patient-to-patient transmission. The authors concluded that routine active surveillance of patients in VRE high-risk units may result in lower bacteremia rates and a more polyclonal VRE population, though differences between the two settings, such as housekeeping practices, hand hygiene, or skill of staff, may contribute to observed effects. Again, it must be noted that the population studied were in high-risk settings. It is not known if these findings can be applied to the general patient population.

VRE Isolation

What is the clinical evidence on the effectiveness of patient isolation for VRE?

Multiple studies have shown that VRE control measures can be effective in endemic settings.[18, 30-35] A prospective cohort study published in 2007 examined the effectiveness of different infection prevention and control strategies in the reduction of VRE transmission in a 1,250-bed tertiary care hospital.[36] The comparative strategies consisted of contact precautions (weekly rectal cultures from index patients and roommates, and environmental cultures performed before and after terminal cleaning); strict isolation (patients with positive cultures for VRE were isolated in private rooms) plus contact precautions; and strict isolation plus modified contact precautions (rectal cultures from index patients only; environmental cultures performed only after terminal disinfection). Findings showed that the incidence rate for VRE rectal colonization was highest in the contact precautions only period (1.45 cases per 10,000 patient-days). The strict isolation plus modified contact precautions period had a similar incidence rate (0.88 cases per 10,000 patient-days) to the strict isolation plus contact precautions period (0.75 cases per 10,000 patient-days). The authors concluded that strict isolation of affected patients together with contact precautions reduced the transmission of VRE. Infection rates associated with VRE rectal colonization in these populations were not described.

A prospective cohort study published in 2004 examined the effects of strict contact isolation on control of VRE spread in a 2,000-bed teaching hospital.[37] After identifying that a patient was colonized or infected with VRE, the patient was put on strict contact isolation. Healthcare workers were asked to wear gowns, gloves, and masks before entering the room of patients infected or colonized with VRE. Devices such as thermometers, stethoscopes, and sphygmomanometers were dedicated to infected or colonized patients. Upon discharge of an infected or colonized patient, the bed, bedside equipment, and environment were disinfected. Surveillance cultures of rectal swabs or stool, wounds, or any infected sites of the index patient's roommate were performed to determine VRE status. Screening of patients in neighbouring rooms was also performed. After 2.5 years, VRE precautions were relaxed and no more surveillance was performed. Details of how precautions were relaxed were not provided in the article. Results showed that hospital-acquired infection rates remained stable during the precautions implementation period, but increased during the no-precautions period. Molecular typing of isolates in the period where strict contact isolation precautions were enforced revealed more types of VRE (i.e., VRE isolates were more polyclonal) than in the period during which precautions were relaxed. The authors concluded that implementation of precautions guidelines is important in controlling the spread of VRE. The findings of this study need to be interpreted with caution. While the authors state that the definition of infection was based on the US Centers for Disease Control criteria, the type or severity of the described infections was not provided.

Patient Impact

What is the clinical evidence on the impact of isolation on the patient?

Numerous studies on the use of additional precautions have highlighted the potential for a negative effect on quality of patient care and quality of life, such as depression, anxiety, loneliness, and other psychological problems related to isolation.[38-43] These studies need to be interpreted with caution, as it is unclear if baseline characteristics of the study groups were adjusted for comparison.

A retrospective cohort study published in 2011 examined the effect of contact precautions on depression or anxiety in more than 36,000 patients admitted to a tertiary care hospital.[40] Patients were placed on contact precautions (no detail provided on specific contact precautions, but patients were given a private room when available) when their medical record indicated the presence of ARO or when they were positive upon screening for MRSA, VRE, or ESBL. The incidence of depression, using the *International Classification of Diseases, ninth revision, Clinical Modification*, was compared between the contact precaution group and the non-contact precaution group. In the non-ICU population, patients on contact precautions were 40% more likely than those not on contact precautions to be diagnosed with depression (odds ratio [OR] 1.5, 95% confidence interval [CI], 1.2 to 1.6). In the ICU population, there was no relationship found between contact precautions and depression or anxiety. The authors concluded that there was an association between contact precautions and depression in patients hospitalized with ARO infections, except for ICU patients.

A prospective cohort study published in 2003 examined the impact of isolation on anxiety and depression in 27 patients hospitalized for colonization or infection with either MSRA or VRE.[43] The control group comprised 24 patients admitted to the hospital for the treatment of infection, but who did not require isolation. The difference of Hamilton Depression Rating Scale (HAM-D) or Hamilton Anxiety Rating Scale (HAM-A) scores at baseline and one or two-week follow-up in the isolation group was compared with the difference of scores in the control group (time-by-group interaction or changeover time between groups). Findings showed that after one week of hospitalization, patients in the isolation group experienced an increase in HAM-D and HAM-A scores, while both scores were lower for patients in the control group. Time-by-group interaction analyses showed that differences between the intervention and control groups were statistically significant. The authors suggested that isolation may increase levels of anxiety and depression in hospitalized patients.

In a study at two large North American teaching hospitals, Sunnybrook Health Sciences Centre and Women's College Hospital (both in Toronto), and Brigham and Women's Hospital in Boston,[38] patients isolated due to MRSA colonization or infection were two times more likely to experience adverse events compared with a non-isolated control group ($P < 0.001$).The difference reflected preventable adverse events that were mainly caused by supportive care failures. As well, more isolated patients expressed dissatisfaction than control patients ($P < 0.001$), particularly regarding treatment, access to staff, and communication.

However, recent studies have noted that patients on contact precautions did not perceive a negative impact on their care and often perceived additional precautions as an improvement in their care.[44, 45] Some patients valued the privacy and solitude afforded by contact precautions and the quietness and privacy of single rooms.[42]

Following the initial preparation of this discussion paper further evidence has been published by McGill University Hospital regarding the evaluation of VRE associated morbidity following relaxation of screening and isolation precautions. They observed an immediate increase in both colonization and infection incidence. Despite the colonization increase, infection outcomes remained infrequent and stable, suggesting a finite number of patients at risk. Relaxation of VRE protocols may, in fact, not lead to increasing infection incidence in a hospital setting. A risk based approach with targeted screening and isolation, focused on the highest risk patients, can be a cost effective approach, without putting patients at risk and freeing up resources to address other emerging antibiotic resistant organisms. (add reference for Miller paper).

Public Health Ontario is currently evaluating and comparing the rates of VRE bacteremia and the impact of VRE screening strategies between those facilities who discontinued universal screening and isolation of VRE positive patients and those that continued. A preliminary report of their findings will be released later in 2014. An oral presentation at the 2014 Infection Prevention and Control Canada Conference by Dr. Gary Garber provided the following results. In the 4 quarters (July 2011-June 2012) prior to discontinuing VRE precautions, bacteremias at the non-screening hospitals combined for 3.75 bacteremias /quarter (<1/mo). The counts

remained unchanged for the next 3 quarters (July 2012-March 2013); but has increased to 9 bacteremias/quarter (3/mo) in the last 3 quarters (April 2013-Dec 2013). Reported bacteremia counts at hospitals continuing VRE precautions have not changed over the same period. Although VRE bacteremia has increased, the rates are still low and the clinical relevance of this increase requires serious review. The plan is to collect data on the clinical factors associated with VRE bacteremia to determine the at-risk population and to identify the feasibility of a targeted screening and isolation policy.

Health Services Impact

What is the health services impact of screening and isolating patients known to be carrying VRE?

Several studies have specifically examined the impact of VRE on patient length of stay, but studies looking at the health services impact of VRE beyond length of stay are lacking.

Length of hospital stay

Multiple studies have found that duration of hospitalization is increased with VRE bacteremia and colonization.[46-49] In one study, bacteremia with VRE was shown to increase length of stay by 18 days compared to VSE bacteremia.[47] In another study, It was demonstrated that patients with nosocomial VRE bacteremia had prolonged hospitalization (17 days) and increased intensive care stays (12 days) when compared to matched control with the same severity of illness.[48]

In one retrospective cohort study[49], the mean number of days between inclusion into the cohort and discharge from hospital was 15.1 (range 1 to 107 days) for VRE cases (patients with a clinical isolate positive for VRE) versus 8.5 days (range 1 to 116 days) for the control cases. It was estimated that being a VRE case was associated with an average adjusted increase of 6.2 days in LOS. In addition, VRE cases were associated with a significantly higher likelihood for ICU admission after inclusion in the cohort (adjusted RR 3.47, $P < 0.001$) and a higher rate of being discharged to long-term care (RR 2.01, $P = 0.001$), thus increasing the use of resources and extending it beyond the period of hospitalization. In this study, no isolation practices were reported for colonized or infected patients. These results should be interpreted with caution as patients that acquire VRE during their hospitalization tend to be sicker and more likely to have multiple comorbidities, and thus likely to have a longer LOS.

Limitations

Due to the limited number of studies identified, it is difficult to draw definitive conclusions regarding the impact of screening and isolating patients known to be carrying VRE. In addition, all of the studies were observational studies from single institutions, which may limit the generalizability of the results. The specific populations in the studies may not be representative of all hospitals. Observational studies may also be prone to bias and confounding, as researchers can bias both the design of a study or data collection. The retrospective nature of these studies may also be prone to bias and confounding as both outcomes and exposures have already been established at the time of participant selection.

Discussion

Evidence from a limited number of observational studies showed that active surveillance with weekly rectal swabs from all patients in high-risk hospital units may be associated with lower VRE bacteremia rates compared with no surveillance strategy. Isolates in a hospital with an active surveillance program showed a population of VRE that was more polyclonal, suggesting that active surveillance and infection prevention and control measures help to prevent horizontal transmission of the infection. The implementation of guidelines to ensure strict isolation and contact precautions in hospitals was shown to be important in controlling the spread of VRE colonization. It has not been established, though, that using isolation leads to a decreased number of VRE infections in the general patient population. Contact precautions and isolation, however, may have a negative psychological impact on patients, with increased rates of depression and anxiety. The isolation process in itself may also inadvertently predispose patients to medical errors and adverse events.

To maximize the effectiveness of infection prevention and control — in addition to specific control measures such as patient screening and isolation procedures — non-specific measures such as antimicrobial stewardship programs, hand hygiene programs, and environmental cleaning need to be implemented in hospital settings. Surveillance data in an acute tertiary care hospital found that the rates of healthcare-associated infections were highest in the ICUs and lowest in the wards.[50] A Canadian tertiary care hospital found that the number of roommates to which a patient was exposed was directly associated with the risk of acquiring nosocomial MRSA and VRE infections.[51] These findings can have implications for the staff deployment and design of acute care hospitals. Decision-makers in several hospitals are choosing to discontinue screening and isolation for VRE infections because they find that VRE infections are relatively rare compared to infections with sensitive enterococci or other AROs; new drugs are available to treat infections; and there is a need to free up organizational capacity to address more pathogenic organisms.[7]

The robustness of the evidence on the effects of precaution measures on the detection and transmission of VRE is limited. A systematic review in 2006 of the literature on the use of barrier precautions, patient isolation, and surveillance cultures[52] showed that the evidence generally supports the use of these measures to prevent the transmission of ARO; however, the lack of RCTs decreased the robustness of the findings. The ability to conduct RCTs is limited due to ethical considerations. High-quality evidence, supported by adequately powered multicentre cohort studies with robust analyses to minimize potential biases, is needed to confirm the findings. A review of guidelines and literature in 2006 on the evidence of infection prevention and control strategies for MRSA and VRE[53] concluded that active surveillance and contact precautions have been effective in the reduction of MRSA and VRE transmission in some settings, but infection prevention and control measures as currently implemented failed to prevent the spread of MRSA and VRE in most hospitals. Long intervals of patient follow-up to determine transmission rates can provide a reliable calculation of the mean rates; on the other hand, this long time period may allow seasonal effects to influence the results, and care practices may have changed. In trials where the transmission rates were compared between

different hospitals, the organisms were detected in each hospital at different times. A direct comparison during the same time would have given a more accurate analysis. Some trials focused on multiple organisms, such as the inclusion of populations carrying either VRE or MRSA, making the conclusion on the effect of precautionary measures on a specific type of bacteria difficult. For psychological outcomes such as depression and anxiety, observational studies that identified a predetermined group of high-risk patients on isolation tended to be studies of association, not of causality.

With regard to the impacts on health services of screening, and of isolating patients infected or colonized with VRE, a limited number of retrospective cohort studies showed that the infected patients have longer LOS than an appropriately matched cohort of uninfected control patients.[49]

Evidence from a limited number of observational studies showed that active surveillance, patient isolation, and other precautionary measures such as staff reassignment to high-risk units, or increased compliance with hand hygiene in hospital settings, may result in reducing the spread of VRE. Implementation of precautionary measures needs to take into consideration the negative effects that isolation may have on hospitalized patients and the impact on patient flow and the unavailability of single rooms for other types of isolation. These findings on the effectiveness of infection prevention strategies for VRE should be interpreted with caution given the scarcity of evidence and the noted limitations of the included studies. Evidence from a limited number of observational studies suggested that both infection prevention and control measures and patients infected or colonized with VRE use more hospital resources due to increased LOS, increased usage of hospital beds, increased healthcare worker staffing, and the need for precautions to prevent the spread of infection. The relative contributions of infection control measures versus the effect of infection or illness itself to resource use were not clear. A balance between a potential reduction in infection risk and increased resource use is an important consideration when implementing control strategies. The cost-effectiveness of infection prevention and control measures was not considered in this review.

In Canada, there are variable practices among hospitals in implementing infection prevention and control measures for VRE. Infection prevention and control measures should take into consideration the setting, epidemiology, virulence factors, mode of transmission, and degree of transmissibility of various pathogens, as well as the robustness of non-specific control measures such as hand hygiene and environmental cleaning. Treatment options and strategies for prevention and control may differ among pathogenic organisms, and depend on the availability of local resources.

A survey sent to infection prevention and control programs in all Canadian acute care hospitals with 80 or more beds[54] found that a significant increase in the number of full-time infection prevention and control professionals (ICPs) has not translated into improvement of ARO control. Also, as part of the Canadian Nosocomial Infection Surveillance Program, a 2003 survey of Canadian tertiary care hospitals[55] found that greater than 96% and greater than 89% of Canadian teaching hospitals conducted admission screening for MRSA and VRE respectively.

Direct and efficient communication between different teams is also a factor, as shown in another survey of Canadian acute care hospitals[54], in which VRE infections were found to be less likely to occur if infection prevention and control staff frequently contacted physicians or nurses for reports of new infections. In addition, findings such as the association between a higher rate of infection and a greater number of roommates, and increased risk of infection in certain types of hospital unit as compared with others, can have implications for staff deployment and design of acute care hospitals. Finally, increased access and communication with staff for isolated patients may help to decrease the rates of preventable medical errors and increase patient satisfaction.

The Community and Hospital Infection Control Association of Canada (CHICA-Canada) issued a position statement stating that any changes to practice should be motivated by a desire to improve patient care, and should only be considered in the context of an infection control programme already meeting or exceeding best practices.[3] PICNet fully endorses this position statement.

For those healthcare facilities or health authorities that are considering a change in VRE control strategy, the following approach is recommended:

- epidemiologic investigation and risk assessment for any VRE infection specific to their facility including:
  - setting
  - epidemiology
  - compliance with non-specific control measures such as hand hygiene and environmental cleaning best practices
  - treatment options
  - strategies for prevention and control
  - availability of local resources
- consultation with staff and client groups including high risk wards/clinics
- consultation with health authority risk management and bioethics departments
- consultation with patient relations (e.g. Patient Voices Network) and public affairs
- consideration of legal consultation and review of existing practice guidelines and evidence-based studies
- discussion with external stakeholders, including the health authority
- an enhanced communication strategy, including communication between health authorities and facilities to ensure all stakeholders are made aware of the changes in policy.

Further, CHICA-Canada recommends that any savings incurred from decreased screening and contact precautions should be re-invested in the following activities (as determined by the risk assessment above):

- environmental cleaning;
- quality promotion and assessment of environmental cleaning and application of routine practices and additional precautions;
- hand hygiene;

- antimicrobial stewardship;
- monitoring of healthcare-associated infections.

Additionally, any such changes should be accompanied by close monitoring of VRE culture-positive HAIs following the changes, to assure that undue harm is not incurred as a result of any changes in policy. In the event that harm is found, facilities should be prepared to initiate screening for VRE and the use of additional precautions for patients found to be VRE positive. It is also highly recommended that those facilities that choose to change their strategy should communicate their experiences to other members of the infection control community for future policy making.

In 2010, the Vancouver Island Health Authority instituted a policy of not implementing additional precautions for patients known to be colonized with VRE unless they are receiving care in the renal unit in acute care at Nanaimo Regional and Royal Jubilee Hospitals. In 2012, Fraser Health Authority adopted a policy of not screening patients for VRE, nor placing them on contact precautions if colonized. Patients with VRE infections and risk factors for transmission are isolated. In 2013, Vancouver Coastal Health discontinued screening patients for VRE, applying additional precautions and declaring VRE outbreaks as did Interior Health Authority. Providence Health Care, Provincial Health Services Authority and Northern Health Authority do not currently have any plans to implement policy changes for VRE. They will continue to screen patients for colonization with VRE and apply additional precautions. These health authorities may detect an increase in VRE incidence if they receive VRE positive patients from other health authorities who have discontinued screening and the use of contact precautions.

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Although VRE bacteremia has increased, the rates are still low and the clinical relevance of this increase requires serious review. The plan is to collect data on the clinical factors associated with VRE bacteremia to determine the at-risk population and to identify the feasibility of a targeted screening and isolation policy.[5]

At this time, there is insufficient evidence to support a recommendation to continue or discontinue control measures for VRE. PICNet recommends that trends in VRE bacteremia identified in laboratories across British Columbia since changes in policy first took place be closely examined to determine if there have been any increases that may be related to VRE policy changes and what the impact may be on patient outcomes. Any further recommendations for changes in policy should be based upon those findings.

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