Discontinuation of Vancomycin Resistant Enterococcus (VRE) Screening and Isolation Practices: A Province-Wide Multi-Hospital Quasi-Experimental Study of VRE Positive Blood Culture Rates in Ontario, Canada, January 2009-June 2015

Jennie Johnstone, MD, PhD[1-4]; Michelle Policarpio, MSc[1]; Freda Lam, MPH[1]; Kwaku Adomako, MSc[1]; Chatura Prematunge, MSc[1]; Emily Nadolny, MA, MPH[1]; Ye Li, PhD[1,4]; Kevin Brown, PhD[1,4]; Elaine Kerr, ART, BA[5]; Gary Garber, MD[1,3,6]

[1]Public Health Ontario, Toronto, ON, Canada

[2]St. Joseph's Health Center, Toronto, ON, Canada

[3]Department of Medicine, University of Toronto, Toronto, ON, Canada

[4]Dalla Lana School of Public Health, University of Toronto, Toronto, ON, Canada

[5]Institute for Quality Management in Healthcare, Toronto, ON, Canada

[6]Department of Medicine, University of Ottawa, Ottawa, ON, Canada

Corresponding Author:
Jennie Johnstone, MD, PhD
Infection Prevention and Control Physician Scientist
Public Health Ontario
480 University Avenue, Suite 300
Toronto ON M5G 1V2
Telephone number: +1 647 260 7205
Fax: +1 647 260 7600
Email: jennie.johnstone@oahpp.ca

Counts:
Abstract: 277 words
Main Text: ~2750 words
References: 37
Tables: 2
Figures: 2

Funding Statement: There are no sources of funding to declare.

Conflict of Interest: All authors report no conflicts of interest.

ABSTRACT

Objectives: To determine whether discontinuation of hospital VRE screening and isolation practices are associated with change in rates of VRE-positive blood cultures.

Methods: Ontario hospitals are mandated to report VRE bacteremias. Using this publically reported dataset, all validated VRE-positive blood cultures between January 2009-June 2015 were included. Beginning in June 2012, some hospitals ceased screening and isolating patients with VRE. Hospitals were stratified into a ceased-screening cohort and a screening cohort. Applying a quasi-experimental study design, Poisson regression over time was used to assess changes in VRE-positive blood culture rates before and after the practice change in the ceased-screening cohort. The screening cohort was used as a comparison group. Rates were adjusted for hospital type and clustering within hospital site using generalized estimating equations.

Results: The overall rate of VRE-positive blood cultures increased during the study period from 0.93 to 1.48 per 100,000 patient days ($p<0.0001$). In ceased-screening hospitals (n=13), there was initially a 10% annual relative decrease in VRE positive blood cultures; once screening was discontinued there was a 12% annual relative increase in rate (adjusted $p=0.04$). In screening hospitals (n=50), the annual rate of rise was not significantly different before June 2012 versus after (31% versus 6% annual relative increase in rate, adjusted $p=0.24$).

Conclusion: Rates of VRE-positive blood cultures are increasing in Ontario. In hospitals that ceased VRE screening and isolation, there was a significant increase in the rate of rise of VRE-positive blood cultures but not in hospitals that continued to screen and isolate for VRE.

INTRODUCTION

Vancomycin resistant enterococcus (VRE) is an important nosocomial pathogen [1]. Since its emergence in the 1980s [2, 3], rates of VRE colonization and infection have risen dramatically in hospitals worldwide [4-8]. Patients with VRE bacteremia are thought to have worse outcomes than patients with vancomycin susceptible enterococcus (VSE) bacteremia, including increased mortality and length of hospital stay [9]. Preventing healthcare-associated VRE infections is therefore a patient safety priority in many jurisdictions [10-13].

In an effort to minimize the spread of antimicrobial resistance within hospitals, it is widely recommended to emphasize hand hygiene, environmental cleaning and antimicrobial stewardship (including control of vancomycin use) [14-18]. Additional infection control interventions including active screening programs for patients thought to be at increased risk for VRE colonization and the placement of patients colonized or infected with VRE on contact precautions have generated controversy due to the lack of robust evidence [19, 20]. Active screening programs increase the detection of VRE colonized patients and reduce the initiation time of contact precautions [21]. However the efficacy of contact precautions for the prevention of antimicrobial resistant organism spread including VRE has been questioned in two randomized controlled trials [22, 23] and studies investigating the impact of discontinuation of VRE screening and isolation practices have been conflicting [24-27]. VRE infection control practices in Canadian institutions are increasingly heterogeneous, and there is no clear consensus on approach [28-30].

In Ontario, Canada, prior to June 2012, all in-patient hospitals maintained active screening programs for the detection of VRE colonization in patients thought to be at increased risk [14] and patients colonized or infected with VRE were placed in a private room on contact

precautions [14]. In June 2012, some hospitals discontinued these VRE screening and isolation practices. The objective of this study was to examine the rates of VRE positive blood cultures in Ontario between January 2009 and June 2015, and to determine whether discontinuation of hospital VRE screening and isolation practices were associated with a change in rates of VRE positive blood cultures.

METHODS

Study Setting

All 219 Ontario hospitals with inpatients were eligible to be included in the study. Hospitals were classified as acute teaching, large community, small community and complex continuing care and rehabilitation hospitals [31, 32]. Since January 2009, Ontario hospitals have been mandated to report VRE bacteremia cases to the Ontario Ministry of Health and Long-Term Care (MOHLTC) on a monthly basis via the Self-Reporting Initiative. These indicators are then publicly reported online via Health Quality Ontario (HQO) on a quarterly basis [10].

VRE Positive Blood Culture Case Definition

We used the MOHLTC's case definition for a VRE bacteremia which is summarized as follows [33]: "A case is a patient identified with a laboratory confirmed bloodstream infection with VRE. A blood stream infection is a single positive blood culture for VRE. VRE are strains of *Enterococcus faecium* or *Enterococcus faecalis* that have a minimum inhibitory concentration (MIC) to vancomycin of ≥ 32 mcg/ml. They contain the *vanA* or *vanB* resistance genes. A subsequent VRE bacteraemia in the same patient is to be considered a new episode, and counted as such, if the original infection had been successfully treated with clinical resolution and more

than six weeks have elapsed since the completion of the antimicrobial treatment of the original bacteraemia."

Hospital facilities that reported at least one VRE positive blood culture between January 1, 2009 and June 30, 2015 (inclusive) were included in the study. When reporting a VRE positive blood culture case, hospital facilities are required to indicate if the case is attributable to the reporting facility itself, another healthcare facility or if the attribution is unknown, as per MOHLTC definitions [33].

Dataset Validation

Study investigators used the publicly reported Health Quality Ontario VRE Patient Safety Reporting data as the data source for this study. To minimize any potential false positive cases in the dataset, study investigators contacted Infection Control Practitioners at each hospital site after each reporting quarter to confirm the reported VRE positive blood culture met the case definition. To quantify validated case count accuracy, the hospital-verified VRE positive blood culture case counts were compared to the number of VRE positive blood cultures reported by hospital laboratories on quarterly surveys issued by the Institute for Quality Management in Healthcare (IQMH), during the same study period.

VRE Screening and Isolation Practice

Prior to June 2012, all hospitals in Ontario had active VRE screening and isolation programs whereby patients at risk were screened for VRE [14]. Patients at increased risk for VRE infection were defined as: 1) those who have previously been colonized or infected with VRE, 2) those who have spent time in a healthcare facility outside of Canada in the last 12

months, 3) those who have been admitted to, or who have spent more than 12 continuous hours as a client/patient/resident in any healthcare facility in the past 12 months, 4) those transferred between healthcare facilities (e.g., between hospitals or between a long-term care facility and a hospital), 5) those who have recently been exposed to a unit/area of a healthcare facility with a VRE outbreak and 6) any other high-risk client/patient/resident populations as identified by infection control (e.g., internal transfers, such as admission to an intensive care unit) or Public Health [14]. Any patient colonized or infected with VRE is to be placed on contact precautions, ideally in a private room [14].

After June 2012, some hospitals discontinued their active VRE screening program and no longer isolated patients colonized or infected with VRE. To identify hospital VRE screening and isolation infection control practices, an annual survey in 2013, 2014 and 2015 was conducted. The short survey was sent to the Infection Control Practitioners at each hospital site across the province. Respondents were asked if 1) their hospital site is screening patients for VRE (yes/no) and 2) if their hospital site is isolating VRE positive patients (yes/no). If the hospital site responded 'no' to either question, they were requested to record the date of practice change.

Ethics

The study received Research Ethics Board approval at Public Health Ontario prior to its commencement.

Statistical Analysis

The study period consisted of 26 reporting quarters (time variable) between January 1, 2009 and June 30, 2015. All data were reported as the number of VRE positive blood cultures

divided by patient days per quarter. First, Poisson regression analysis over time was used to assess whether there was an overall change in incidence of VRE positive blood cultures during the study period.

Next, the cohort was stratified into two groups; 1) a ceased-screening cohort defined as hospitals that discontinued VRE screening and isolation practices at some point within the study period and 2) a screening cohort used as a comparison group, which included hospitals that continued to screen and isolate patients for VRE throughout the study period. For the ceased-screening hospital cohort, the intervention date was defined as the calendar quarter in which the hospital stopped screening and isolating for VRE. For the screening hospital cohort, the intervention date was defined as June 2012 and fell under quarter 15 in the sequence.

The mean VRE positive blood culture rates were compared pre- and post- discontinuation date of VRE screening and isolation in the ceased-screening cohort, and pre- and post- June 2012 in the screening cohort. Poisson regression stratified by VRE control strategy was used to determine whether the rate of rise of VRE positive blood culture incidences over time was different before and after the change in screening practice. For both the ceased-screening and the screening cohort the change in level and trend was examined by fitting an interaction between the intervention and time in the Poisson model (level and slope change model, as per Bernal et al [34]). Based on this model, we assessed the change in the rate of rise of VRE positive blood cultures. The number of cases was used as an outcome while the number of patient days was used as an offset parameter. The model was adjusted for hospital type (acute teaching versus community hospitals) and clustering within hospital site was accounted for using a generalized estimating equation (GEE) with the independence covariance structure.

A sensitivity analysis was performed to account for lagged intervention effects. For these analyses, follow-up time 3 and 6 months post-intervention were excluded. We hypothesized that the 3 and 6 month post intervention exclusion should magnify any differences seen in the full analysis in the ceased-screening cohort, and should have no effect in the screening cohort. A two-tailed p-value of <0.05 was deemed as significant. SAS (version 9.3, North Carolina, United States) was used to analyze data.

RESULTS

In total, there were 523 VRE positive blood cultures publically reported by hospitals during the study period. After contacting hospitals, 128/523 (24%) were erroneously reported, leaving 395 VRE positive blood cultures as our final study sample. This number was comparable to the number of VRE positive blood cultures reported to IQMH (n=362).

The 395 VRE positive blood cultures were reported by 63/219 (29%) hospitals. All 63 hospitals responded to the VRE screening and isolation survey each year (100% response rate). In total, 13 hospitals discontinued VRE screening and isolation at some point during the study period and 50 hospitals continued to screen and isolate patients colonized or infected with VRE. Most VRE positive blood cultures occurred in acute teaching hospitals (73%), and most (79%) were attributed to the reporting facility.

The overall rate of VRE positive blood cultures during the study period was 1.04 per 100,000 patient days; the rate increased from 0.93 per 100,000 patient days in the first reporting quarter to 1.48 per 100,000 patient days in the last reporting quarter. The increase over time was statistically significant, increasing by 3% per quarter (95% CI 1.5% to 4.3%, p<0.0001)(Figure 1).

In the ceased-screening cohort, the mean rate of VRE positive blood cultures before VRE screening and isolation was discontinued was 1.16 per 100,000 patient days and this increased to 2.81 per 100,000 patient days after VRE screening and isolation was discontinued (percent change 63.3% [95% CI 23.2% to 116.5%], p=0.0006). In the screening cohort, the mean rate of VRE positive blood cultures before June 2012 was 0.49 per 100,000 patient days, and this increased to 0.89 per 100,000 patient days after June 2012 (percent change 74.4% [95% CI 31.3% to 131.6%] p=0.0001).

In the ceased-screening cohort, in unadjusted analysis, before discontinuation of VRE screening there was a 20% annual relative decrease in VRE positive blood cultures; however, once screening was discontinued there was a 9% relative annual increase (slope change p=0.03). Similarly, in adjusted analyses, there was a 10% annual relative decrease in VRE positive blood cultures prior to discontinuing screening and once screening was discontinued there was a 12% annual relative increase in rate (slope change p=0.04)(Figure 2). In the comparison screening group, in unadjusted analysis, before June 2012, the relative annual rate of rise was 31% versus a 6% annual relative increase in rate after June 2012 (slope change p=0.16). In adjusted analysis, the results were essentially the same; before June 2012, the relative annual rate of rise was 31% versus a 6% annual relative increase in rate after June 2012 (slope change p=0.24)(Figure 2). The results of the sensitivity analysis were similar to the main analysis (Table 2).

INTERPRETATION

The main findings of this study are as follows: 1) in Ontario hospitals, rates of VRE positive blood cultures have almost doubled since reporting began in January 2009; 2) VRE positive blood culture rates have increased in hospitals that ceased VRE screening and isolation

practices and hospitals that continued to screen and isolate for VRE; 3) discontinuation of VRE screening and isolation of those colonized or infected with VRE was associated with an increased rate of rise of VRE positive blood cultures, however this change in rate of rise was not observed in hospitals that continued to perform VRE screening and isolation.

Our finding, that discontinuation of active screening and isolation of patients with VRE is associated with an increased rate of rise of VRE positive blood cultures, is consistent with a prior observational study that suggests that active screening programs for VRE colonization and isolation for those affected is associated with reduced VRE bacteremia rates [24]. Price et al reported VRE bloodstream infections of 17.1/100,000 days in a hospital without active screening for VRE, in comparison to 8.2/100,000 patient days at the hospital with VRE screening. Active VRE screening programs have also demonstrated reduction in VRE bloodstream infection among high risk patients (i.e., those with malignancy or requiring critical care) in outbreak settings [26, 36].

In contrast, our results are not consistent with a recent study that found that discontinuation of active VRE screening programs and contact precautions for those affected did not appear to prevent VRE bacteremia in patients with hematologic malignancies and stem cell transplant in a single center setting over a 6 year period [27]; these authors found that after discontinuing active VRE surveillance and contact precautions, the rate of VRE bacteremia remained stable (2.32/1,000 patient days before versus 1.87/1,000 patient days after, $p>0.05$). However, all patients in this study were admitted to single bed rooms with private bathroom and thus the results may not be generalizable to more traditional hospital settings where patients are admitted to multi-patient rooms and shared bathrooms. There have also been two cluster randomized controlled trials investigating the efficacy of screening and isolating patients for

antimicrobial resistant organisms in the ICU setting [22, 23]. Results of these trials question the use of contact precautions for the prevention of antibiotic resistant organism transmission in the ICU setting; however whether these results are generalizable outside the ICU setting [22, 23] is unknown.

Although our study had many strengths including comprehensive data collection from multiple provincial centers over a 6-year time period, several limitations require consideration. First, we did not have data on potential confounders such as changes in hand hygiene adherence, environmental services activities, and antibiotic use which may have explained the increased rate of rise of VRE positive blood cultures in the period after VRE screening and isolation was discontinued. However, we included a comparison cohort and would have expected changes in these potential confounders to apply to this group as well. Second, this study was a quasi-experimental design and not a randomized controlled trial and is therefore susceptible to biases inherent to this type of design, including the potential for regression to the mean as an explanation for the results. To help mitigate this potential bias, our sensitivity analyses which incorporated lag effects amplified the results in the ceased-screening cohort but reduced the differences in the screening cohort, increasing the confidence of our results. Third, we did not have patient level clinical data, and the clinical consequences of having a VRE positive blood culture were unknown. We chose to use the term VRE positive blood culture, rather than VRE bacteremia because of this limitation. Last, misclassification bias remains a possibility; however, we sought to minimize this by validating each reported positive case with individual hospitals, and verifying case count accuracy with a separate dataset.

Our main finding, that there is an associated increased rate of rise of VRE positive blood cultures when screening and isolation for VRE is discontinued, adds to the literature of the

potential benefits of VRE screening and isolation practices outside of outbreak settings, and is generalizable to a wide variety of in-patient hospital settings, extending beyond ICUs or single room settings. Whether there is still need to prevent VRE transmission given the availability of effective anti-VRE therapy has been debated; however the best available evidence suggests that patients with VRE positive blood cultures have an associated increased risk of death and prolonged length of stay when compared to patients with VSE positive blood cultures [9]. In addition, a recent paper suggests that a delay in effective antimicrobial therapy may be associated with increased risk of death [36]. Thus, knowledge of VRE colonization may theoretically help reduce delays of effective antimicrobial therapy, which in lieu may have important implications for patient safety and prevention. Any infection control intervention must balance costs of screening and contact precautions against costs associated with infection. The few studies that have evaluated the economic impact of VRE screening and isolation have shown that it is cost effective, although the studies were generally from single centers and specific high risk populations [35, 37]. Future research should better characterize the costs and benefits of VRE screening and isolation practices.

In summary, rates of VRE positive blood cultures are increasing in Ontario hospitals. Hospitals aiming to minimize the rising rate of VRE positive blood cultures should consider active VRE screening and isolation programs.

ACKNOWLEDGEMENTS

We would like to acknowledge the following for their contributions on this project: Christine Flemming at IQMH (formerly QMP–LS) for support with the validation of VRE positive clinical isolates; Dr. Giulio Didiodato for his review of the original study design; Cathy Egan for her unwavering support for the project; hospital-based Infection Prevention and Control Practitioners who helped validate data; and to the Ministry of Health and Long-Term Care and Health Quality Ontario for their valued partnership and support to this research project.

REFERENCES

1. Murray B. Vancomycin resistant enterococcal infections. N Engl J Med 2000; 342 : 710-721.
2. Leclercq R, Derlot E, Duval J, et al. Plasmid-mediated resistance to vancomycin and teicoplanin in Enterococcus faecium. N Engl J Med 1988; 319 :157-61.
3. Uttley A, Collins C, Naidoo J, et al. Vancomycin-resistant enterococci. Lancet 1988; 1 : 57-8.
4. Public Health Agency of Canada. Vancomycin-resistant enterococci infectionsin Canadian acute-care hospitals : Surveillance Report January 1, 1999 to December 31, 2011. Centre for Communicable-Diseases and Infection Control, Public Health Agency of Canada, 2013.
5. Adam H, DeCorby M, Rennie R, et al. Prevalence of antimicrobials resistant pathogens from blood cultures from Canadian hospitals: results of the CANWARD 2007-2009 study. Diagn Microbiol Infect Dis 2011; 69: 307-313.
6. Bourdon N, Fines-Guyon M, Thiolet J, et al. Changing trends in vancomycin-resistant enterococci in French hospitals, 2001-08. J Antimicrob Chemother 2011; 66 : 713-721.
7. Gastmeier P, Schroder C, Behnke M, et al. Dramatic increase in vancomyin-resistant enterococci in Germany. J Anticrob Chermother 2014; 69 : 1660-1664.
8. Centers for Disease Control and Prevention. National Nosocomial Infections Surveillance (NNIS) System Report, data summary from January 1992 through June 2004, issued October 2004. Am J Infect Control 2004; 32 : 470-85.

9. Prematunge C, MacDougall, Johnstone J, et al. VRE and VSE bacteremia outcomes in the era of effective VRE therapy: A systematic review and meta-analysis. Infect Control Hosp Epidemiol 2015; 37(1): 26-35.
10. Health Quality Ontario. Patient Safety Individual Hospital Results – Introduction [internet]. Health Quality Ontario (HQO); 2016. [cited 2016 July 12]. Available from: http://ww w.hqontario.ca/portals/0/Modals/pr/patient-safety/en/individual/index-en.html
11. Canadian Institute for Health Information. Key Projects on Patient Safety [internet]. Canadian Institute for Health Information (CIHI); 2016. [cited 2016 July 12]. Available from: https://www.cihi.ca/en/health-system-performance/quality-of-care-and-outcomes/patient-safety/key-projects-on-patient-safety
12. Canadian Patient Safety Institute. Vancomycin-resistant Enterococci (VRE) [internet]. Canadian Patient Safety Institute (CPSI); 2016. [cited 2016 July 12]. Available from: http://www.patientsafetyinstitute.ca/en/Topic/Pages/Vancomycin-resistant-Enterococci-(VRE).aspx
13. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013 [internet]. CDC; 2013. [cited 2016 July 13]. Available from: http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf#page=5
14. Ontario Agency for Health Protection and Promotion, Provincial Infectious Diseases Advisory Committee. Annex A – Screening, testing and surveillance for antibiotic-resistant organisms (AROs). Annexed to: Routine Practices and Additional Precautions in All Health Care Settings. Toronto, ON: Queen's Printer for Ontario; 2013.

15. Weiner LM, Fridkin SK, Aponte-Torres Z, et al. Vital Signs: Preventing Antibiotic-Resistant Infections in Hospitals — United States, 2014. MMWR Morb Mortal Wkly Rep 2016;65:235–241.

16. Cookson B, Macrae M, Barrett S, et al. Guidelines for the control of glycopeptide-resistant enterococci in hospitals. J Hosp Infect 2006; 62 : 6-21.

17. Nicolle LE. Infection Control Programmes to Control Antimicrobial Resistance. Geneva, Switzerland: World Health Organization; 2001.

18. Muto C, Jernigan J, Ostrowsky B, et al. SHEA guideline for preventing nosocomial transmission of multidrug-resistant strains of Staphylococcus aureus and Enterococcus. Infect Control Hosp Epidemiol 2003;24:362-386.

19. Ho C, Lau A, Cimon K, et al. Screening, Isolation, and Decolonization Strategies for Vancomycin-Resistant Enterococci or Extended Spectrum Beta-Lactamase Producing Organisms: A Systematic Review of the Clinical Evidence and Health Services Impact. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2012 (Rapid Response Report: Systematic Review).

20. Talbot T. Two studies feed the debate on active surveillance for methicillin-resistant Staphylococcus aureus and vancomycin resistant enterococci carriage: to screen or not to screen? J Infect Dis 2007; 195: 314-317.

21. Huang S, Rifas-Shiman S, Pottinger J, et al. Improving the assessment of vancomycin-resistant enterococci by routine screening. J Infect Dis 2007; 195 : 339-346.

22. Huskins W, Huckabee C, O'Grady N, et al. Intervention to reduce transmission of resistant bacteria in intensive care. N Engl J Med 2011; 364(15) : 1407-1418.

23. Derde L, Cooper B, Goossens H, et al. Interventions to reduce colonisation and transmission of antimicrobial-resistant bacteria in intensive care units : an interrupted time series study and cluster randomised trial. Lancet 2014; 14 : 31-39.

24. Price C, Paule S, Noskin G, et al. Active surveillance reduces the incidence of vancomycin-resistant enterococcal bacteremia. Clin Infect Dis 2003; 37 : 921-928.

25. Perencevich E, Fisman D, Lipsitch M, et al. Projected benefits of active surveillance for vancomycin-resistant enterococci in intensive care units. Clin Infect Dis 2004; 38 : 1108-1115.

26. Hachem R, Graviss L, Hanna H, et al. Impact of surveillance for vancomycin resistant enterococci on controlling a bloodstream outbreak among patients with hematologic malignancy. Infect Control Hosp Epidemiol 2004; 25 : 391-394.

27. Almyroudis N, Osawa R, Samonis G, et al. Discontinuation of systematic surveillance and contact precautions for vancomycin-resistant enterococcus (VRE) and its impact on the incidence of VRE faecium bacteremia in patients with hematologic malignancies. Infect Control Hosp Epidemiol 2016; 1-6.

28. Nadolny E, Prematunge C, Policarpio M, et al. Vancomycin Resistant Enterococcus (VRE) Screening and Isolation Practices (SIP) Scan: Hospital based Infection Control Policy in Ontario (2012-2015). Poster presented at: Wisdom Begins with Wonder: IPAC Canada 2016 Annual Conference. 2016 May 15-17; Niagara Falls, ON.

29. Position Statement – VRE screening and contact precautions [internet]. CHICA-Canada; 2012 [updated June 29, 2012; cited October 2, 2014. Available from: http://www.ipac-canada.org/pdf/VRE_position_statement%20%5b4%5d.pdf.

30. Marrie T. Consensus statement on Canadian consensus development conference on surveillance and screening for antimicrobial resistant organisms. Institute of Health Economics Consensus Statement 2014; 6 : 1-19.

31. Ontario Hospital Association (OHA). Hospital Report Mental Health 2007. OHA; 2007. [cited 2016 July 13]. Available from: http://www.oha.com/KnowledgeCentre/Library/HospitalReports/Documents/Hospital%20Reports%202007/Mental%20Health.pdf

32. Canadian Institute of Health Information (CIHI). Hospital Report Acute Care 2007. CIHI; 2007. [cited 2016 July 13]. Available from: https://secure.cihi.ca/free_products/OHA_Acute07_EN_final_secure.pdf

33. Ministry of Health and Long Term Care (MOHLTC). Vancomycin resistant enterococcus (VRE bacteremia) infection rate – Resource for Indicator Standards (RIS) [internet]. MOHLTC; 2012. [cited 2016 July 13] Available from: http://www.health.gov.on.ca/en/pro/programs/ris/docs/vancomycin_resistant_enterococcus_infection_rate_en.pdf

34. Bernal JL, Cummins S, Gasparrini A. Interrupted time series regression for the evaluation of public health interventions: a tutorial. Int J Epidemiol 2016: 1-8.

35. Montecalvo M, Jarvis W, Uman J, et al. Costs and savings associated with infection control measures that reduced transmission of vancomycin-resistant enterococci in an endemic setting. Infect Control Hosp Epidemiol 2001; 22 : 437-442.

36. Zasowski E, Claeys K, Lagnf A et al. Time is of the essence: the Impact of delayed antibiotic therapy on patient outcomes in hospital-onset Enterococcal bloodstream infections. Clin Infect Dis 2016; 62(10):1242-50.

37. Muto C, Giannetta E, Durbin L, Simonton B, Farr B. Cost-effectiveness of perirectal surveillance cultures for controlling vancomycin-resistant enterococci. Infect Control Hosp Epidemiol 2002; 23 : 429-435.

Table 1: VRE positive blood culture cases in Ontario between January 2009 and June 2015, overall and stratified by VRE screening and isolation practices.

	Total n=395 n (%)	Ceased Screening n=194 n (%)	Screening n=201 n (%)
Hospital type			
Acute teaching	287 (73%)	187 (65%)	100 (35%)
Large Community	100 (25%)	6 (6%)	94 (94%)
Small Community	8 (2%)	1 (13%)	7 (87%)
Case Attribution			
Reporting Facility	309 (78%)	154 (79%)	155 (77%)
Other Facility	26 (7%)	7 (4%)	19 (10%)
Unknown	60 (15%)	33 (17%)	27 (13%)
Year			
2009	52 (13%)	34 (17%)	18 (9%)
2010	31 (8%)	18 (9%)	13 (7%)
2011	48 (12%)	23 (12%)	25 (12%)
2012	68 (17%)	25 (13%)	43 (21%)
2013	73 (19%)	39 (20%)	34 (17%)
2014	82 (21%)	36 (19%)	46 (23%)
2015	41 (10%)	19 (10%)	22 (11%)

Table 2 : Annual relative change of VRE rates before and after discontinuation of VRE screening and isolation practices (in ceased-screening cohort) and June 2012 (in screening cohort) in unadjusted and adjusted analysis with no lag time, 3 month lag time and 6 month lag time post intervention incorporated into the analyses.

	Before	After	Slope Change P-value	Before	After	Slope Change P-value
	Unadjusted Annual Relative Change			Adjusted Annual Relative Change		
Non-screening						
No lag	20% decrease	9% increase	0.03	10% decrease	12% increase	0.04
3 month lag		20% increase	0.004		24% increase	0.01
6 month lag		35% increase	0.0004		39% increase	0.001
Screening						
No lag	32% increase	6% increase	0.16	31% increase	6% increase	0.24
3 month lag		23% increase	0.67		23% increase	0.72
6 month lag		52% increase	0.39		52% increase	0.42

Figure 1: VRE positive blood culture rates in Ontario January 2009 – June 2015.

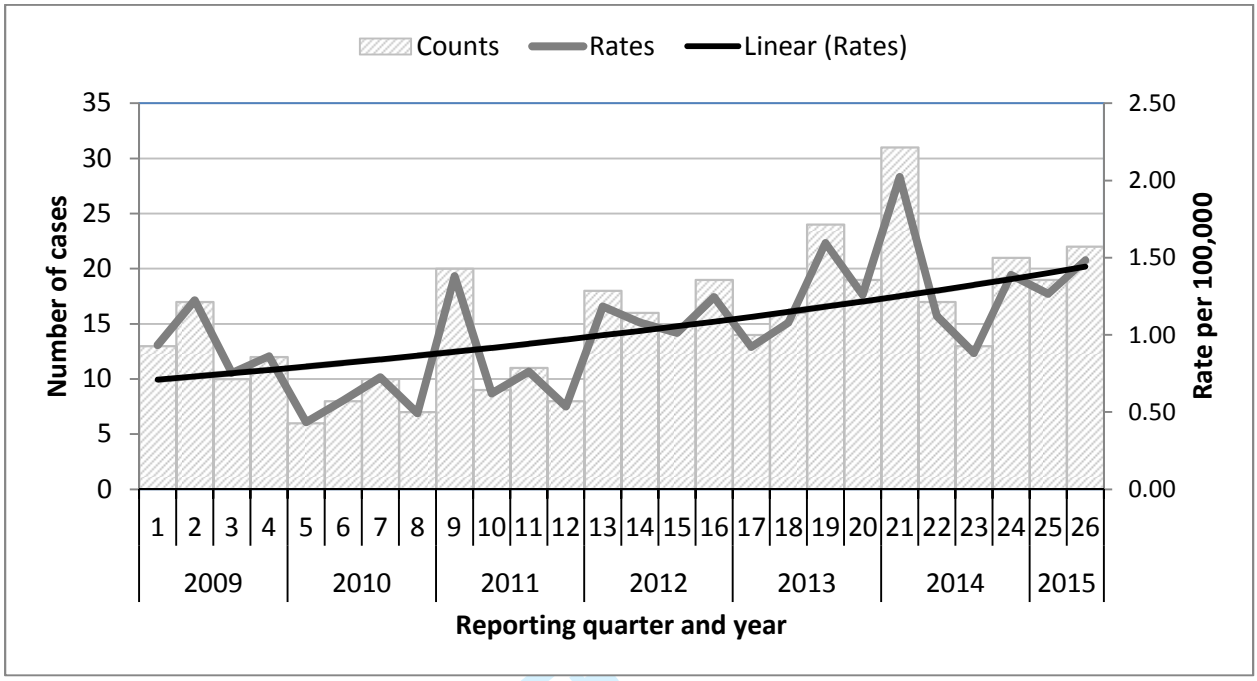

Figure 2: VRE positive blood culture rates in Ontario between January 2009 - June 2015, stratified by hospitals that ceased VRE screening and isolation practices within the study period versus hospitals that continued VRE screening and isolation practices within the study period. Dotted lines represent observed rates and solid lines represent the model-based rates. Nine hospitals changed their screening and isolation practices in reporting quarter 15, 1 hospital in quarter 25, and 3 in quarter 26.