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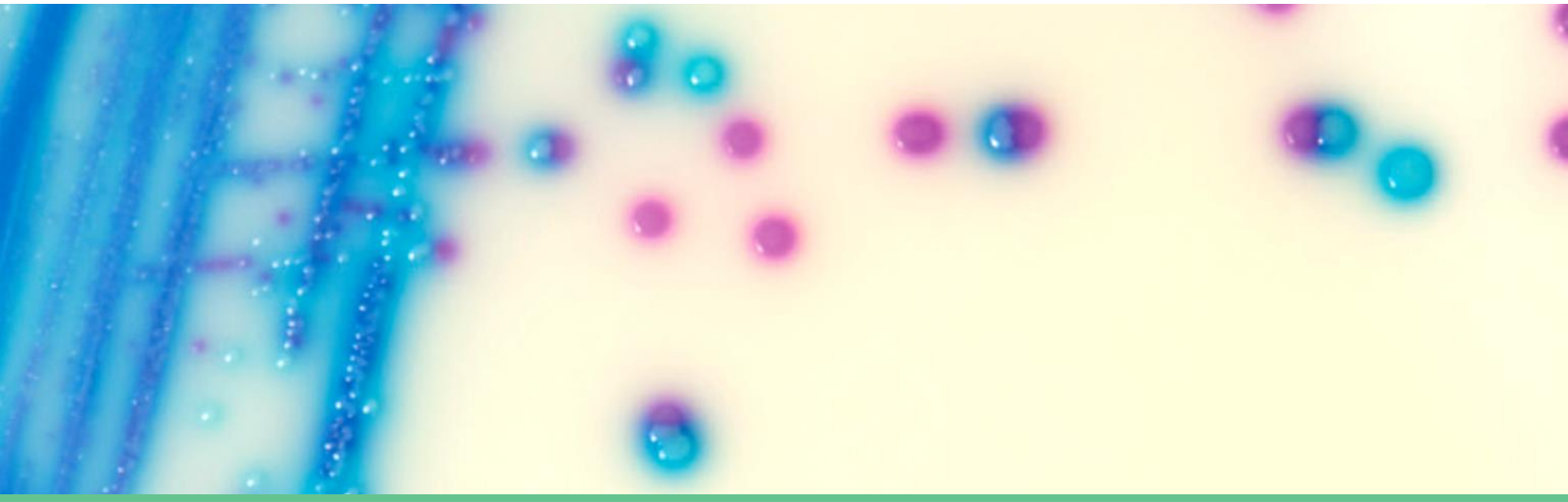

Evidence Review and Revised Recommendations for the Control of Vancomycin-Resistant Enterococci in All Ontario Health Care Facilities

March 2019

PIDAC | Provincial Infectious Diseases Advisory Committee

Infection Prevention and Control

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Colonies of vancomycin-resistant enterococci (pink) on a chromogenic media.

About PIDAC-IPC

The Provincial Infectious Diseases Advisory Committee on Infection Prevention and Control (PIDAC-IPC) is a multidisciplinary scientific advisory body that provides evidence-based advice to Public Health Ontario (PHO) regarding multiple aspects of infectious disease identification, prevention and control.

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Disclaimer

This document was developed by the Provincial Infectious Diseases Advisory Committee on Infection Prevention and Control (PIDAC-IPC). PIDAC-IPC is a multidisciplinary scientific advisory body that provides evidence-based advice to Public Health Ontario (PHO) regarding multiple aspects of infectious disease identification, prevention and control. PIDAC-IPC's work is guided by the best available evidence at the time of publication and updated as required. Best practice documents and tools produced by PIDAC-IPC reflect consensus positions on what the committee deems prudent practice and are made available as a resource to public health and health care providers.

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Abbreviations

Can $	Canadian dollars
CI	confidence interval
ICU	intensive care unit
OR	odds ratio
P	significance value
MRSA	methicillin-resistant *Staphylococcus aureus*
PHO	Public Health Ontario
PIDAC	Provincial Infectious Diseases Advisory Committee
US	United States
VRE	vancomycin-resistant enterococci or vancomycin-resistant enterococcal
VRSA	vancomycin-resistant *Staphylococcus aureus*
VSE	vancomycin-sensitive enterococci or vancomycin-sensitive enterococcal

Glossary of Terms

Colonization: the presence and growth of a microorganism in or on a body with growth and multiplication but without tissue invasion or cellular injury or symptoms.

Contact Precautions: used in addition to Routine Practices to reduce the risk of transmitting infectious agents via contact with an infectious person. The elements that comprise Contact Precautions include: accommodation, personal protective equipment, equipment dedication and cleaning, environmental cleaning, transport arrangements, and communication.

Contact Precautions for VRE: Contact Precautions applied to patients and residents who are colonized or infected by VRE. See PIDAC's *Annex A—Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (AROs)* for screening criteria and a description of the risk factors.

Endemic: the constant presence of a disease or infectious agent within a certain area.

Infection: the entry and multiplication of an infectious agent in the tissues of the host. Asymptomatic or subclinical infection is an infectious process running a course similar to that of clinical disease but below the threshold of clinical symptoms. Symptomatic or clinical infection is one resulting in clinical signs and symptoms (disease).

Nosocomial: arising while a patient is in a hospital or as a result of being in a hospital. Denoting a new disorder (unrelated to the patient's primary condition) associated with being in a hospital.

Point prevalence: surveillance for all existing and new cases of a condition in a health care setting on a single day.

Quality-adjusted life year: one quality-adjusted life year is equal to one year of life in perfect health. It is calculated by estimating the years of life remaining for a person following a particular intervention and weighting each year with a quality-of-life score (on a 0 to 1 scale), which is often measured in terms of the person's ability to carry out the activities of daily life, and freedom from pain and mental disturbance.[1]

Reservoir: an animate or inanimate source where microorganisms can survive and multiply (e.g., water, food, people).

Risk-factor–based screening for VRE: see Screening for VRE on admission.

Screening: a process to identify clients, patients, and residents at risk for being colonized with antibiotic-resistant organisms and, if risk factors are identified, obtaining appropriate specimens.

Screening for VRE on admission: a process to identify clients, patients, and residents at risk of being colonized with VRE at the time of admission, and to obtain appropriate specimens if risk factors are identified. (See PIDAC's *Annex A—Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (AROs)* for screening criteria and a description of the risk factors.) Screening for VRE on admission is NOT analogous to Universal screening for VRE.

Universal screening for VRE: a process of obtaining specimens to test for VRE colonization for all patients or residents admitted to a health care facility regardless of the presence or absence of risk factors.

Preamble

In 2012, the Provincial Infectious Diseases Advisory Committee on Infection Prevention and Control (PIDAC) published an evidence review for best practices for vancomycin-resistant enterococci (VRE) control. As evidence on the control of VRE expanded in scope and in depth, PIDAC undertook a re-assessment of the evidence, which is summarized in this document. Albeit with limitations, the Provincial Infectious Diseases Advisory Committee on Infection Prevention and Control (PIDAC) found that existing evidence suggests the following:

- Risk-factor–based screening on admission and Contact Precautions for VRE used by hospitals are effective at reducing VRE transmission.
- VRE control is more effective when all facilities within a region, including long-term care homes, use this approach.

> **These findings reinforce PIDAC's best practice recommendation that all acute care and chronic care hospitals and long-term care homes continue to perform risk-factor–based screening on admission and Contact Precautions for VRE.**

(An Executive Summary of this document is also available from the PHO website.)

Background

Enterococcal infections are a significant problem in the health care setting.[2-5] Vancomycin-resistant enterococci (VRE) are particularly difficult to treat[6-8] as they are usually resistant to both ampicillin and vancomycin, and treatment options for serious infections are limited to newer antibiotic agents such as linezolid and daptomycin.[9-12] For this reason, the US Centers for Disease Control and Prevention (CDC) have identified VRE as a "serious threat" to human health on par with drug-resistant tuberculosis and MRSA, and estimate that VRE results in 20,000 infections and 1,300 deaths annually in the US.[13]

Patients, residents and clients can be colonized or infected with VRE.[10,14-18] Treatment is only required for infected individuals. However, as a proportion of patients, residents, and clients colonized with VRE will develop VRE infection,[19-21] preventing the transmission of VRE from patient, resident, or client to patient, resident, and client will reduce the overall number of VRE infections and VRE-associated morbidity and mortality.

When caring for patients, residents and clients, the Provincial Infectious Diseases Advisory Committee (PIDAC) recommends a number of practices that can reduce the transmission of VRE including: the use of Routine Practices, environmental cleaning and disinfection, disinfection and sterilization of medical equipment, and antimicrobial stewardship.[22]

In addition, PIDAC recommends that all health care facilities implement specific surveillance, screening and control measures aimed at preventing the spread of VRE.[23] These measures can be found in PIDAC's *Annex A—Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (ARO). Annexed to Routine Practices and Additional Precautions in All Health Care Settings*.

In brief, the additional VRE control measures recommended include:[23]

- at the time of admission to facility, identifying patients and residents colonized or infected by VRE through:
    - screening all patients and residents on admission for VRE risk factors.
    - performing surveillance cultures (i.e., rectal swab or stool culture) on admission for patients and residents with VRE risk factors.
- placing patients and residents colonized or infected with VRE on Contact Precautions*.

* For the purposes of this document, other VRE control strategies applied to patients and residents colonized by VRE, as recommended in *Annex A—Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (ARO). Annexed to Routine Practices and Additional Precautions in All Health Care Settings*, such as enhanced environmental cleaning and disinfection, will be considered as part of Contact Precautions.

In 2012, four Ontario hospital corporations discontinued screening on admission and Contact Precautions for VRE.[24] In response, PIDAC reviewed the evidence in 2012 and PIDAC and PHO continued to recommend risk-factor–based screening for VRE on admission.[24] In addition, PHO undertook a five year program of research on VRE that included:

- an Ontario-wide cohort study comparing the change in incidence rate of VRE bacteremia at facilities that have discontinued screening for VRE on admission as compared to facilities that have continued screening (the PHO VRE cohort study).[25]
- a case series of VRE bacteremia to determine the patient-level characteristics, microbiological features and outcomes of patients with VRE bacteremia in Ontario.[26]
- a case-control study of VRE bacteremia to determine risk factors for VRE bacteremia and VRE-associated mortality.[27]
- a systematic review of the mortality difference for patients with VRE (vs. VSE**) bacteremia.[28]
- a systematic review of the cost-effectiveness of screening for VRE on admission.[29]
- an analysis of cost-effectiveness of screening for VRE on admission using Ontario-specific data.[30]

** vancomycin-sensitive enterococci

As the PHO VRE program of research was nearing completion, PHO had asked PIDAC to review the evidence for VRE control, which now includes PHO generated evidence obtained directly from the Ontario health care setting, as well as more up-to-date literature reviews. This document is a summary of PIDAC's review of the evidence for screening for VRE on admission, incorporating findings of PHO's VRE research. Based on this evidence, revised recommendations on VRE control are provided.

Approach to the Development of Revised VRE Guidance

The primary question addressed by PIDAC in this document is:

> **Should Ontario hospitals and long-term care homes screen admitted patients and residents for VRE, and place patients and residents who test positive for VRE (colonized or infected) on Contact Precautions?**

PIDAC considered the following questions to be of critical importance in making evidence-based recommendations:

1. Does VRE screening at the time of admission to hospitals or long-term care homes, followed by the use of Contact Precautions for patients and residents colonized or infected by VRE, reduce VRE incidence and prevalence when compared with no VRE screening?
   - 1a. Is effectiveness increased if a consistent regional or provincial approach to VRE control is used?
   - 1b. Do screening on admission and Contact Precautions for VRE applied in long-term care homes reduce the incidence of VRE transmission and VRE infection in regional acute care facilities?
2. What are the harms associated with an increased incidence of VRE colonization or infection?
3. What are the harms of VRE control measures?
4. Is the use of screening on admission and Contact Precautions for VRE cost-effective?

Of these questions, question 1 is the most important, a priori, in that the relevance of the other questions is limited if screening on admission and Contact Precautions for VRE are not effective.

In addressing these questions, PIDAC relied on three sources of information:

- PIDAC's document on VRE control measures:
  - *Annex A—Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (AROs)*, updated in 2012. And
  - *Review of Literature for Evidence - Based Best Practices for VRE* Control (PIDAC's prior VRE literature review from 2012).
- PHO literature search for relevant evidence published since the previous PIDAC literature review.
- results of PHO's five-year VRE program of research.

Based on our evidence review, PIDAC has developed revised recommendations for VRE control.

Section One:

Evidence Assessment

1. Effectiveness of Screening on Admission and Contact Precautions for VRE

Question 1:

Does VRE screening at the time of admission to hospitals or long-term care homes, followed by the use of Contact Precautions for patients and residents colonized or infected by VRE, reduce VRE incidence and prevalence when compared with no VRE screening?

1.1 Background to Question 1

PIDAC has recommended risk-factor–based screening for VRE on admission and Contact Precautions for VRE since 2009 (see Preamble), and screening on admission and Contact Precautions for VRE remain the standard of care in Ontario, with 79% of health care facilities following these recommendations as of 2015.[31] It is also the standard of care in seven of ten Canadian provinces and all Canadian territories.[32]

Risk-factor–based screening on admission and Contact Precautions for VRE were initially implemented for VRE control based on empiric evidence of effectiveness (see below) as well as indirect evidence that, without admissions screening, the majority of individuals colonized by VRE will not be identified by routine clinical cultures[33-39] and the presence of unidentified VRE cases is associated with subsequent VRE transmission.[35,40-42]

In the review below, we focused on investigating whether screening on admission and Contact Precautions for VRE are effective. Evidence was divided into three categories: 1) studies evaluating VRE screening as an outbreak control measure (see 1.2.1.1 Outbreak Studies; 2) studies evaluating screening on admission and Contact Precautions for VRE in the endemic (non-outbreak) setting (see 1.2.1.2 Quasi-Experimental Studies; and 3) studies evaluating the impact of discontinuing screening on admission and Contact Precautions for VRE (see 1.2.1.3 Randomized Controlled Trials).

1.2 Evidence Review for Question 1

1.2.1 STUDIES OF IMPLEMENTATION OF VRE SCREENING

Studies are categorized by their quality into outbreak studies, quasi-experimental studies and randomized controlled trials.

1.2.1.1 Outbreak Studies

Studies have assessed the impact of VRE screening as an outbreak control measure.[40,42-53] In most cases, VRE screening was effective in controlling the outbreak when combined with other outbreak control measures. However, only limited conclusions can be drawn from outbreak studies as they are uncontrolled and at high risk of bias due to the potential for confounding, regression to the mean, and the necessary use of co-interventions. Thus, these studies provide some evidence that VRE screening

and VRE Contact Precautions can reduce the transmission of VRE within health care facilities during outbreaks, but limited indirect evidence that VRE screening and VRE Contact Precautions can reduce VRE transmission outside the context of an outbreak.

1.2.1.2 Quasi-Experimental Studies

Studies have evaluated the impact of VRE screening in the endemic (i.e., non-outbreak) setting using quasi-experimental methods.[33,47,54-56]

A prospective, multicentred, uncontrolled pretest-posttest study by Ostrowsky et al. evaluated the impact of VRE admissions screening and Contact Precautions at 32 regional acute care and long-term care facilities in the US.[55] All 32 facilities conducted a VRE point-prevalence study when VRE was identified in the region. Screening on admission and Contact Precautions for VRE were implemented at all facilities, and point-prevalence studies were repeated annually. VRE prevalence fell from 2.2% at baseline to 1.4% after one year and 0.4% after two years, with reductions seen at both acute care and long-term care facilities.[55] Although this study is quasi-experimental, the result is impressive given that the natural history of antibiotic-resistant organism prevalence, once introduced into a region, is typically to increase in prevalence over time.

A similar study by Matsushima et al. was conducted in the Kyoto region of Japan following their first identified hospital VRE outbreak.[47] A VRE control program that included screening for VRE on admission, Contact Precautions for VRE and improved hand hygiene was recommended for a region including 177 hospitals of which 116 participated in the evaluation of the program. Regional VRE prevalence peaked at 1.2% of patients one year after program implementation and then declined over 4 years to less than 0.2% of patients.[47]

The only controlled study identified by Price et al. evaluated the incidence of VRE bacteremia at two similar hospitals in the same region in the US.[54] One hospital implemented screening on admission for VRE as well as weekly VRE screening combined with Contact Precautions for VRE, and the other hospital did not. While the nonscreening hospital had twice as many VRE bacteremias as the screening hospital,[54] their baseline VRE bacteremia rate was also higher, the time periods studies at both facilities varied slightly, and comparison of the two hospitals may not be appropriate.

An uncontrolled quasi-experimental study by Siddiqui et al. used a repeated treatment design to evaluate the impact of implementing active VRE screening in two intensive care units (ICU) in the US on overall hospital VRE incidence, measured using clinical cultures.[56] VRE incidence per 10,000 patient-days went from 5.8 (baseline, 7 months) to 3.8 (active surveillance, 11 months) to 11.4 (no surveillance, 15 months) to 7.7 (active surveillance).[56] VRE control measures other than screening cultures were unchanged. Use of a removed and repeated study design can reduce some of the bias inherent in quasi-experimental studies.[57]

The final quasi-experimental study by Calfee et al. was a retrospective, uncontrolled pretest-posttest study (in the US) in which implementation of VRE screening was associated with a reduction in VRE transmission and a stabilization in VRE prevalence.[33]

This body of evidence is limited by the quasi-experimental study design used. Lack of randomization and lack of an appropriate control group lead to the potential for bias. In addition, these studies have other

threats to their validity including: limited data points before and after the intervention, the presence of co-interventions, and the failure to measure or adjust for known confounders (e.g., hand hygiene.)

Within the context of their limitations, these studies provide direct evidence that screening on admission and Contact Precautions for VRE can reduce VRE incidence in hospitals in the endemic setting.

1.2.1.3 Randomized Controlled Trials

We identified one randomized trial of screening for VRE on admission,[58] one randomized trial comparing two methods of screening for VRE on admission,[59] and one randomized controlled trial of universal barrier precautions.[60]

The cluster randomized controlled trial by Huskins et al. compared active VRE (and MRSA) surveillance cultures performed within 48 hours of admission to ICU with usual practice at 18 ICUs in the US over a 6-month period.[58] Intervention ICUs screened admitted patients for VRE and MRSA, and used gloves for all clinical care until screening results were available, after which Contact Precautions were used for patients who tested positive for VRE or MRSA, and Routine Practices for patients who tested negative for VRE and MRSA. Control ICUs followed their usual procedures which included Contact Precautions. Surveillance cultures for VRE and MRSA were performed weekly and within 2 days before or after ICU discharge. Only patients admitted for at least 3 days were included.[58]

The study found no difference in MRSA and VRE transmission (primary outcome) or in VRE transmission (secondary outcome) in the intervention and control ICUs.[58] Patients admitted for less than 3 days and patients from whom screening cultures were missed at the time of ICU discharge were not included in the study; as a result only 38% of ICU patients were included.[58] Mean length of stay was less than 5 days and mean length of stay for included patients was 8 days,[61] patients exposed to VRE may not have had sufficient time for VRE to become detectable by rectal swab prior to the collection of their ICU discharge swab; this could have resulted in most transmission events being missed, biasing the results significantly towards the null hypothesis. The turnaround time for screening culture results was long (swab performed within 48 hours of ICU admission, followed by 5-day turnaround time for result).[58] Thus, patients who tested positive for VRE in intervention ICU spent more time in "universal gloving" precautions than they did in VRE Contact Precautions. During the intervention, the proportion of patient-days spent in Contact Precautions remained stable at approximately 36% in the control ICU, and increased from 35% to 50% in the intervention ICU. Patient-days in "universal gloving" rose from 0% to 43% in the intervention arm only.[61] Compliance with hand hygiene, universal gloving, and Contact Precautions was incomplete.[58]

The strength of this study[58] is its cluster randomized design. Limitations include the short length of stay that may have led to significant numbers of VRE transmission events being missed, the limited compliance with control measures, the number of excluded patients, and the prolonged turnaround time for the results of screening tests. Performing VRE screening at ICU, rather than at hospital, admission means that this study does not directly address the issue of hospital-wide screening on admission for VRE as it is performed in Ontario.

The cluster randomized study by Derde et al. compared conventional versus rapid microbiologic testing strategies for VRE admission swabs at 13 European hospitals.[59] The study included a quasi-experimental component that compared VRE transmission at baseline, with a nonrandomized initial intervention phase

at all hospitals that included chlorhexidine bathing and improved hand hygiene. This second phase was then followed by randomization to either rapid or conventional screening for VRE on admission.

The study[59] did not identify a reduction in VRE transmission related to rapid (compared to conventional) screening. It did not compare screening with no screening for VRE on admission. In a post hoc analysis no difference in VRE transmission was found during the phase when intervention and control hospitals used one of two VRE screening strategies as compared to the prior intervention phase involving enhanced hand hygiene and chlorhexidine bathing. This was not a controlled or randomized comparison and the hospitals followed their standard practice at baseline, which may already have included screening for VRE on admission.

The third cluster randomized controlled trial by Mody et al. compared a multimodal intervention (antibiotic-resistant organism surveillance cultures, Contact Precautions without isolation for residents, staff education on infection prevention, and hand hygiene) with usual care at 12 nursing homes in the US over three years.[60] Only residents with feeding tubes or urinary catheters were included, and "barrier precautions" were used for all of these residents regardless of antibiotic-resistant organism colonization status. A reduced prevalence density of antibiotic-resistant organisms, and a nonsignificant trend towards reduced VRE prevalence, were identified.[60] The study was underpowered to detect a reduction in VRE prevalence.

As residents were not isolated, and barrier precautions were used for all included residents in both the control and intervention facilities, this study did not assess admission VRE screening and Contact Precautions.[60]

Only the cluster randomized controlled trial by Huskins et al. addressed the issue of screening for VRE on admission in a randomized fashion.[58] In this study, screening for VRE at the time of ICU admission was not effective at limiting VRE transmission within the ICU. The other two studies by Derde et al.[59] and Mody et al.[60] provide no direct evidence on screening on admission and Contact Precautions for VRE. The study by Derde et al.[59] also does not provide quasi-experimental evidence on the effectiveness of screening for VRE on admission as the baseline VRE screening practices of the participating facilities are not described.

1.2.2 QUASI-EXPERIMENTAL STUDIES WHERE VRE SCREENING AND VRE CONTACT PRECAUTIONS WERE DISCONTINUED

In addition to the PHO VRE cohort study,[25] PHO identified ten studies[62-71] that evaluated the impact of stopping VRE control measures.

1.2.2.1 Discontinued Screening on Admission and Contact Precautions for VRE

Four studies evaluated the impact of discontinuing both active VRE (and MRSA) screening and Contact Precautions.[25,62-64]

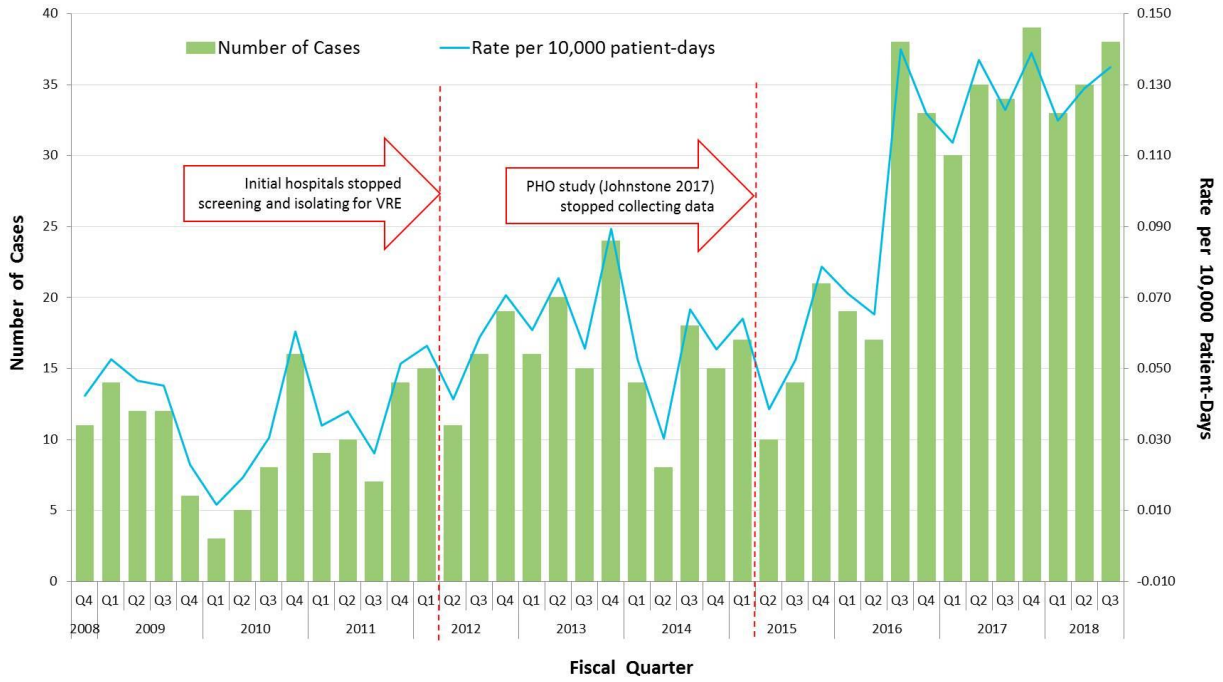
The largest study was the PHO VRE cohort study, a prospective, province-wide controlled time series analysis conducted for all 219 Ontario hospitals.[25] The study used time series analysis to compare the incidence of VRE bacteremia between hospitals that discontinued screening on admission and Contact Precautions for VRE and those that did not. Data were collected over a 3.5-year baseline period (where all hospitals screened for VRE on admission) and a 3-year post-intervention period divided into 26 quarters.

Hospitals that discontinued screening for VRE on admission at any time from June 2012 onward (when the initial nine hospitals stopped screening) were included in the "ceased VRE screening" cohort.[25]

Over 6.5 years, 395 VRE bacteremias were identified. Most (N=156, 71%) hospitals had no VRE bacteremias over 6.5 years, and 73% of all VRE bacteremias occurred in teaching hospitals. Hospitals with no VRE bacteremia over the study period were excluded from the analysis, leaving 63 hospitals in the study. Of these 63, 13 discontinued active VRE screening during the study period.[25]

The overall rate of VRE bacteremia was 1.04 per 100,000 patient-days. This rate increased 12.5% per year, from 0.93 per 100,000 patient-days in the first quarter of the study period to 1.48 per 100,000 patient-days in the last quarter, a 50% increase. In the time series analysis, there was a statistically significant 25% per year increase in the rate of increase of VRE bacteremia (i.e., the slope) in the nonscreening hospitals following discontinuation of screening. In the hospitals that continued to screen, there was a nonsignificant 20% per year decrease in the rate of increase of VRE bacteremia over the same time period (although the overall incidence of VRE bacteremia increased in both screening and nonscreening hospitals). In sensitivity analyses, the results were unchanged when the analysis was restricted only to teaching hospitals, and when the analysis was restricted to VRE bacteremias attributable to the facility. Sensitivity analyses incorporating 3- to 6-month effect lag times accentuated the increase in slope in the "ceased screening" cohort. Data from Health Quality Ontario public reporting of VRE bacteremia show that the incidence of VRE bacteremia in Ontario has continued to increase at an accelerating rate since the PHO study was completed (see Figure 1), but no formal analysis comparing screening and nonscreening hospitals has been performed since data collection for the PHO study stopped in June, 2015.[72,73]

Figure 1: VRE Bacteremia Cases and Rates by Fiscal Year and Quarter[73]



Of the other three studies, one study by Lemieux et al. was performed in four Ontario hospitals (2,200 beds) that discontinued screening on admission and Contact Precautions for VRE.[63] The incidence of VRE infection and VRE bacteremia was evaluated for 24 months before and 18 months after discontinuing

VRE control measures. VRE infection and bacteremia did not show a statistically significant increase over this time period (between July 1, 2010 and December 31, 2013).[63] This study provides no independent evidence as the same four hospitals were included in the PHO study described above, but the PHO study had a control arm and longer baseline and a longer follow-up period.

Another study by Martin et al. compared the incidence of VRE clinical cultures for 12 months (facility one) and 6 months (facility two) before and 12 months after stopping active surveillance of high-risk patients and Contact Precautions at two hospitals (805 beds) in the US.[64] No change in VRE incidence was observed over the follow-up period.[64]

A third study by Almyroudis et al. evaluated the incidence of VRE bacteremia for 36 months before and 36 months after discontinuation of active surveillance and Contact Precautions at a 125-bed hospital in the US.[62] Rates of VRE bacteremia did not increase over this time period.[62]

With the exception of the PHO study, these studies have the same limitations as the quasi-experimental, pretest-posttest studies described in 1.2.1.2 Quasi-Experimental Studies and are at high risk of bias due to the lack of a control group and the potential for confounding and co-intervention. Additionally, these studies were underpowered to detect an increase in VRE bacteremia or infection rates, particularly given the limited number of facilities evaluated and the limited follow-up period (12 to 36 months).

The PHO study,[25] although also quasi-experimental, has several strengths compared to the other quasi-experimental studies of discontinuing VRE precautions, including the large sample size (encompassing all hospitals in a province), a longer follow-up period than most other studies, the presence of a control group, the use of time series analysis rather than simple before-after comparison, and the consistency of the findings across sensitivity analyses. Additionally, as this study was conducted in Ontario, it provides an assessment of the impact of removing VRE control measures as they are applied in Ontario.

1.2.2.2 Modified or Reduced Screening on Admission and Contact Precautions for VRE

Three studies evaluated the impact of reducing or modifying screening for VRE on admission while continuing Contact Precautions for VRE.[65-67]

The first study by Bryce et al. compared the incidence of VRE bacteremia at a 728-bed hospital in Canada, for 6 years prior to reducing screening for VRE on admission to 25 months after reducing screening.[65] Screening for VRE on admission for all hospitalized patients was modified to screening on admission for VRE for high-risk units only. Enhanced environmental cleaning and antibiotic stewardship programs were intentionally initiated at the time of reducing VRE screening. No change in the incidence of VRE bacteremia was observed.[65]

The second study by Popiel et al. compared hospital-wide screening for VRE on admission, Contact Precautions for VRE or cohorting, and staff cohorting for VRE over 10 years with a program of limited screening, and no use of cohorting or dedicated staff (but continued Contact Precautions) at a 637-bed hospital in Canada.[66] Following relaxation but not complete removal of VRE control measures, the incidence of VRE colonization, VRE infection and VRE bacteremia rose rapidly. Subsequently, the incidence of VRE bacteremia and infection (but not colonization) appeared to plateau over the 34-month follow-up period.[66]

The third study by Bodily et al. compared VRE-positive clinical cultures for 18 months before and 18 months after discontinuation of "reflex VRE testing" at a 1,250-bed hospital in the US.[67] Reflex testing involved testing patients for VRE colonization whenever testing for *C. difficile* infection was ordered. A 71% increase in VRE clinical cultures was detected.[67] In a follow-up study, re-institution of reflex testing resulted in a reduction in VRE-positive cultures back to baseline levels.[74]

These studies have the same limitations as the previous quasi-experimental studies, and the two studies evaluating VRE bacteremia incidence at a single centre[65,66] were both underpowered. Results were mixed, with one study showing no impact of reduced VRE control measures,[65] a second study showing an immediate but possibly limited expansion in VRE infection and bacteremia,[66] and a third study in which VRE control measures had to be re-implemented due to increasing infection rates.[67,74]

1.2.2.3 Discontinuation of Contact Precautions at Facilities With No Baseline Active Surveillance

Four studies evaluated the impact of discontinuing VRE Contact Precautions at facilities that did not perform active screening for VRE on admission.[68-71]

One study by Bardossy et al. compared rates for VRE catheter-associated urinary tract infection and VRE central line-associated bloodstream infection for 12 months before and 12 months after discontinuation of VRE (and MRSA) Contact Precautions at a 800-bed hospital in the US.[71] No statistically significant change was seen.[71] The second study by Gandra et al. conducted an interrupted time series analysis comparing the incidence of VRE infection and colonization over a 12-month period before and 12 months after discontinuing VRE Contact Precautions at a 779-bed hospital in the US.[69] Screening on admission was not performed hospital-wide but only for patients admitted to ICU. An immediate increase in VRE colonization and infection was observed after Contact Precautions were removed. Rates declined thereafter, and although they remained above baseline for the entire study period, this difference was not statistically significant.[69] The third study by Rupp et al. compared the incidence of VRE bacteremia at a 689-bed hospital in the US for 12 months before and 12 months after discontinuation of VRE Contact Precautions.[70] No significant change in VRE bacteremia was identified.[70] Finally, VRE device-related infections were compared by Edmond et al. at a 865-bed hospital in the US for 15 months before and 15 months after discontinuation of VRE (and MRSA) Contact Precautions.[68] No statistically significant difference in VRE device-related infections was identified.[68]

These studies have the same limitations as the other quasi-experimental, pretest-posttest studies discussed above. Additionally, as the hospitals involved in these studies did not conduct screening for VRE on admission at baseline, these studies provided no direct information on the potential impact of discontinuing screening for VRE on admission.

1.3 Evidence Summary

Risk-factor–based screening for VRE on admission in Ontario was implemented based on:

- concerns about the impact of VRE (see 2. Harms Associated with Colonization or Infection).

- consistent data from quasi-experimental and observational studies suggesting that screening on admission and Contact Precautions for VRE are effective VRE control measures.[33,34,40,41,43,54,55,75,76]

In recent years, additional evidence has emerged with respect to the effectiveness of screening on admission and Contact Precautions for VRE.[33,54-56,58-60] Evidence from a single randomized controlled trial failed to detect a benefit to screening applied at the time of ICU admission.[58,61] With respect to VRE screening at hospital admission, several studies evaluated the impact of discontinuing screening for VRE on admission or limiting screening to high-risk patient populations.[25,62-71,74] The results of these studies were mixed and most were underpowered. The most robust study was the PHO study—a province-wide, controlled, interrupted time series analysis of all Ontario hospitals with a 3-year follow-up period that demonstrated an accelerating rate of increase of VRE bacteremia at Ontario hospitals that discontinued screening for VRE on admission, while the rate of increase remained stable at hospitals that continued screening.[25] Furthermore, although the per-hospital incidence of VRE bacteremia was low in this study, VRE bacteremia incidence has continued to increase in an accelerating manner since the PHO study stopped collecting data in June 2015.[72,73]

Taken together, the evidence for risk-factor–based screening on admission and Contact Precautions for VRE—as these measures are applied in Ontario—is stronger now than when these recommendations were first made.

1.4 Conclusion

Risk-factor–based screening on admission and Contact Precautions for VRE are the standard of care in Ontario. The best current evidence suggests that screening for VRE at the time of hospital admission can reduce or limit the rate of increase of VRE bacteremia,[33,55,56] and that discontinuation of screening on admission and Contact Precautions for VRE will result in an increase in VRE colonization, VRE infection and VRE bacteremia.[25,66,67,73,74]

Question 1a:

Is effectiveness increased if a consistent regional or provincial approach to VRE control is used?

1.5 Background to Question 1a

As discussed in 1.2 Evidence Review for Question 1 and 2. Harms Associated with Colonization or Infection, the distribution of harm related to VRE infection and bacteremia is highly skewed to high-risk patient populations (i.e., those at high risk of infectious complications of VRE) and high-risk facilities (i.e., facilities that care for patients at high risk of infectious complications of VRE).

The goal of VRE control measures at low-risk facilities is to reduce the number of patients colonized by VRE in order to protect patients at a high-risk facility to which patients from low-risk facilities are transferred.

There is evidence that VRE colonization can spread rapidly between acute care and long-term care facilities, and that low-risk facilities such as long-term care homes can act as a reservoir for VRE.[40,55,77-82]

PIDAC evaluated evidence that a regional approach to VRE control (i.e., use of similar VRE control measures at all hospitals in a region) is superior to VRE control measures applied at only a subset of facilities. More specifically, if one examines the incidence of VRE colonization and infection at hospital A (which screens on admission and uses Contact Precautions for VRE), is VRE control improved if all other facilities in the region are also screening for VRE as compared to the scenario where other regional facilities are not screening for VRE on admission?

1.6 Evidence Review for Question 1a

No evidence directly addressing this issue was described. The study by Ostrowsky et al.[55] and Matsushima et al.[47] discussed in 1.2.1.2 Quasi-Experimental Studies demonstrated the effectiveness of a regional approach to VRE control. However, neither study evaluated the differential effect on a given facility when other facilities in the region began screening, as all facilities started in concert.

One modelling study by Lee et al. evaluated this issue.[83] The study analyzed patient transfer data at 29 hospitals in Orange County, California and demonstrated that increasing VRE colonization at one facility would negatively impact VRE control at the other facilities; and use of effective VRE controls at all facilities would result in a large benefit for VRE control.[83] When changes in the effectiveness of VRE control measures were implemented in the model, it often took years for facilities to reach a new steady state, depending on the degree to which different facilities transfer patients directly or indirectly to each other. This suggests that the impact of initiating or discontinuing VRE control measures may require many years to evaluate fully.[83]

1.7 Conclusions to Question 1a

The results of one study suggest that VRE incidence can be reduced in an entire region when all acute care and long-term care facilities use screening on admission and Contact Precautions for VRE.[55] Additionally, based on a mathematical modelling study, increased VRE colonization at one or more hospitals will negatively impact VRE control at other hospitals.[83]

Question 1b:

Do screening on admission and Contact Precautions for VRE applied in long-term care homes reduce the incidence of VRE transmission and VRE infection in regional acute care hospitals?

1.8 Background for Question 1b

Patients frequently move back and forth between acute care and long-term care settings. Transmission of VRE from acute care to long-term care settings has been clearly documented and long-term care homes can then act as a reservoir, or potentially an amplifier, of VRE transmission.

The prevalence of VRE colonization varies widely in long-term care homes. In a survey by El Emam et al. of all 612 long-term care homes in Ontario in 2011, VRE prevalence was reported to be 0.56 per 100 residents but varied widely by region.[15] Prevalence is much higher in US long-term care homes, often ranging from 5% to 18%, with some facilities reporting that 50% of residents are colonized by VRE.[84-86] These extremely high rates were attributed to a combination of person-to-person transmission and resident movement between facilities.[86] In one US study by Elizaga et al. in an urban medical centre, admissions from 20 different long-term care homes were tested for VRE colonization upon admission to a tertiary care hospital and 45% of residents tested positive for VRE; among those who tested negative for VRE at admission, 33% acquired VRE during their hospitalization.[87] A study by Bryce et al. using whole genome sequencing found that VRE strains colonizing long-term care home residents and causing nosocomial bacteremia in hospital were often highly related.[65]

Thus, it appears that VRE can be spread within networks of interconnected acute care and long-term care facilities, and long-term care homes can act as a reservoir for VRE infection in acute care facilities.[78,85,88,89] Screening on admission and Contact Precautions for VRE in long-term care homes may contribute to the control of VRE in acute care facilities through the following mechanisms:

1. As in acute care, screening on admission and Contact Precautions for VRE could reduce VRE transmission within a long-term care home. When long-term care home residents require hospital admission, having fewer residents colonized by VRE will reduce transmission in the acute care hospital by reducing colonization pressure (a significant risk factor for VRE transmission).[81,82]

2. When acute care patients are transferred (back) to long-term care homes, screening for VRE on admission that identifies VRE colonization in residents who previously tested negative will indicate nosocomial transmission in the acute care setting; communication of these results can assist the acute care facility in recognizing VRE transmission events and outbreaks.

3. By reducing transmission of VRE in long-term care homes, the risk of VRE infection among long-term care home residents will be reduced when they are subsequently admitted to high-risk facilities (e.g., teaching hospitals, ICU, oncology centres or wards) or when they develop risk factors for infection by VRE (e.g., central lines, neutropenia, malignancy, transplant patients).

4. By indirectly reducing VRE colonization burden in acute care facilities, VRE infections in hospitalized patients never admitted to a long-term care home would also be reduced.

1.9 Evidence Review for Question 1b

Although there are some studies demonstrating the effectiveness of screening for VRE on admission to long-term care homes to control VRE outbreaks or epidemic VRE,[90,91] very little evidence directly addressing the impact of screening on admission and Contact Precautions for VRE in long-term care homes on VRE prevalence in acute care facilities was identified. As discussed above, Ostrowsky et al. demonstrated the effectiveness of a regional program to control VRE that involved implementation of screening on admission and Contact Precautions for VRE in all acute care and long-term care facilities within a region.[55] However, the impact of screening for VRE on admission within long-term care homes could not be independently assessed. The mathematic modelling study described in 1.6 Evidence Review for Question 1a suggests that increasing VRE prevalence in any interconnected facility will ultimately impact the incidence of VRE colonization and infection at other facilities within a network.[83]

1.10 Conclusion

Long-term care homes and acute care facilities share a patient population. VRE can spread between both areas and result in an increased reservoir for VRE. It is likely that controlling the transmission of VRE at long-term care homes, and reducing the prevalence of VRE, will reduce VRE colonization pressure, VRE transmission and VRE infection at acute care hospitals but there is limited direct evidence to support this assertion.

2. Harms Associated with Colonization or Infection

Question 2:

What are the harms associated with an increased incidence of VRE colonization or infection?

2.1 Background

The direct harms potentially associated with VRE infection include increased morbidity, mortality and length of stay.[28,92-95] Assuming that screening on admission and Contact Precautions for VRE are efficacious at preventing VRE transmission and resultant VRE colonization (see 1. Effectiveness of Screening on Admission and Contact Precautions), the potential harms of not using these control measures depend upon:

- the incidence of VRE infection among patients with VRE colonization.
- whether VRE infection increases morbidity, mortality of length of stay relative to VSE infection.

Additional harms include the potential for increased use of second line antibiotics (i.e., linezolid, daptomycin) as empiric and definitive therapy in regions where VRE colonization or infection become increasingly common, fostering the emergence of resistance to these agents.[96-103] Finally, an increased prevalence of VRE colonization could result in the transmission of vancomycin resistance genes to *Staphylococcus aureus*,[104-112] an event that is exceedingly rare (14 cases reported in US as of 2015[13,113]) but is associated with concomitant colonization by VRE and MRSA. These risks were not formally assessed in a systematic review.

2.2 Evidence Review

A proportion of patients colonized by VRE will go on to develop VRE infection.[18-21,33,80,95,114] The risk of VRE infection among patients colonized by VRE depends on the patient population, the definition of VRE infection and the period of follow-up.[18,95] Incidence is low in long-term care home residents,[18,115] higher in acute care hospitals and ICU patients, and highest in patients with cancer, bone marrow, or solid organ transplantation.[18,92-94,116-123] One study in hospitalized patients found that 4% of patients colonized with VRE developed bacteremia[114] while the incidence ranged from 13% to 29% in cancer patients and 4% to 29% in transplant patients.[19,95] Among transplant patients, the risk appeared to be lower in renal transplant at 4% but over 20% in studies of bone marrow or liver transplant patients.[81,92,93,95,124]

In bone marrow transplant patients, VRE colonization is associated with increased mortality even when newer agents were used for treatment.[92-94,125]

Two systematic reviews compared mortality associated with VRE versus VSE bacteremia.[116,126] A 2003 review by Salgado et al. demonstrated an unadjusted relative risk of death associated with VRE (vs. VSE) bacteremia of 2.57 (95% CI, 2.27-2.91) across 13 studies.[116] A subsequent 2005 review by

DiazGranados et al. included only studies that controlled for baseline severity of illness and used multivariate methods to assess the independent contribution of VRE (vs. VSE) bacteremia. This review identified an odds ratio of death of 2.52 (95% CI, 1.9-3.4) across 9 studies.[126]

PHO conducted an updated systematic review focusing on the studies conducted after the widespread availability of newer anti-VRE antibiotics such as daptomycin and linezolid.[28] The review found an increase in unadjusted mortality associated with VRE bacteremia (OR 1.80, 95% CI, 1.38-2.35) across 12 studies published since 1997.[28] Of these studies, five performed multivariate analyses that adjusted for in-hospital mortality risk. Two of these five identified VRE bacteremia as in independent contributor to mortality[127,128] and three did not.[129-131]

Both Salgado et al.[116] and the PHO systematic review[28] found that overall length of stay was higher for patients with VRE bacteremia. However, for length of stay after onset of bacteremia, the reviews showed differing results. Salgado et al. found that four of five studies that evaluated post-bacteremia length of stay showed an increase in VRE bacteremia.[116] The PHO review found only two studies that assessed post-bacteremia length of stay, and found no significant different in length of stay when these studies were combined.[28]

The primary limitation with all three systematic reviews[28,116,126] is that many of the included studies did not adjust for confounding factors. It is probable that patients who acquire VRE differ at baseline from patients who do not, and a substantial proportion of the increase in mortality seen may be due to the presence of confounding factors associated with VRE acquisition and mortality. Such factors could include older age, more comorbid illness,[132-134] increased severity of illness,[135] increased requirement for invasive procedures,[136,137] increased exposure to antibiotics[20,133-138] and increased duration of hospitalization prior to VRE infection.[132,136,138,139] In the PHO systematic review, those studies that attempted to adjust for confounders were less likely to show increased mortality associated with VRE.[28]

Given this limitation, there remains the potential for unmeasured and unadjusted confounders to impact the result. Increased mortality in patients with VRE bacteremia is biologically plausible and can be explained by delays in the initiation of effective empiric therapy. However, it is also clear that patients who acquire VRE are systematically different from other patients (e.g., longer length of stay prior to onset of bacteremia)[27,126] and these differences likely contribute to increased mortality. Although increased mortality was seen in the adjusted analyses included in the DiazGranados systematic review,[126] most of those studies adjusted for a limited number of confounders. In the PHO systematic review, the results were not consistent across studies that adjusted for confounders.[28]

Additional information is provided by a PHO VRE case-series that evaluated all VRE bacteremias in Ontario from 2009 to 2013.[26] In this series, the in-hospital case fatality rate was 48% (112 of 232). Comorbid conditions were present in 91% of patients and 84% had a central line at the time of diagnosis. The most frequent comorbidities included renal disease (34%), diabetes (28%), hematological malignancy (23%), other malignancies (11%) and solid or bone marrow transplantation (12%).[26]

At the time of blood culture collection, 72% of patients were on empiric antibiotic therapy but 83% were not receiving antibiotics known to be effective for the treatment of VRE.[26] Despite this, among patients who survived at least 48 hours after the identification of a VRE bacteremia, a delay in administering effective anti-VRE therapy was not associated with an increased risk of death (OR 1.0, 95% C.I. 0.29-3.1) although failure to receiving any anti-VRE treatment was associated with increased mortality (OR 2.5, 95% CI, 1-5.9, P = .04).[25]

2.3 Evidence Summary

Acquisition of VRE colonization puts patients at increased risk for VRE infection.[33,80,95,114] The risk of developing VRE bacteremia is extremely low in healthy adults and residents of long-term care homes.[95,114] The risk is moderate in hospitalized patients, particularly at teaching hospitals or in ICU,[27] and in renal transplant patients.[140] The risk is very high in patients with hematological malignancy, bone marrow transplantation or solid organ transplantation other than renal transplant.[26,93-95,117,121] The presence of neutropenia and the use of central venous catheters are also important risk factors for bacteremia.[26,95,119,124,125]

VRE bacteremia is associated with increased mortality compared to VSE bacteremia.[92-94,116,125] This association persists even if studies conducted prior to the availability of newer anti-VRE antibiotics are excluded.[28] However, it is unclear to what extent this association is causal or due to confounding or selection bias.[28] Patients with VRE bacteremia differ from patients with VSE bacteremia in several important ways, prior to the onset of bacteremia, that likely contribute to their poor outcome (i.e., selection bias).

Thus, the increased mortality that is caused by VRE is likely substantially less than the OR of 1.8 to 2.6 identified in three systematic reviews[28,116,126] but there is considerable uncertainty in this conclusion.

VRE bacteremia is associated with increased overall length of stay, but this is also due to confounding because prolonged length of stay is a risk factor for VRE acquisition. An association with post-bacteremia length of stay is less clear.[28]

Additionally, there are other potential harms associated with increasing VRE colonization rates including an increased dependence on newer anti-VRE antibiotics for empiric therapy when VRE is suspected, and an increased potential for the emergence of VRSA.[104-109,111,112]

In conclusion, VRE bacteremia is plausibly associated with increased mortality and length of stay relative to VSE bacteremia, although the evidence base is limited by the potential for confounding and selection bias, and current estimates of the effect of VRE on bacteremia on mortality are likely overestimates.

2.4 Conclusion

VRE infection is associated with increased mortality as compared to VSE although the extent of attributable mortality remains uncertain. VRE is also associated with other potential adverse consequences for patients and the health care system.

3. Harm Associated with Control Measures

Question 3:

What are the harms associated with VRE control measures?

3.1 Background

It is important to consider the potential harms of placing patients and residents in a single room in Contact Precautions when assessing the impact of screening for VRE on admission, as such screening will detect a large proportion of patients and residents colonized with VRE who would not otherwise be recognized or placed on Contact Precautions.[33-39] It is also important to consider the benefits of discontinuing placement in single rooms for all patients and residents colonized and infected by VRE, as this would substantially reduce the number of patients and residents on Contact Precautions in Ontario health care facilities.

3.2 Evidence Review

PHO conducted a literature review that focused on identifying harms associated with patient and resident isolation (i.e., placement in single room)and Contact Precautions (see A.1.3 Rapid Reviews, A.2.5 Rapid Review Three: Harms Are Associated With Contact Precautions, A.3.5 Rapid Review Three: Harms Are Associated With Contact Precautions, and A.4.5 Rapid Review Three: Harms Are Associated With Contact Precautions) This was not limited to patients and residents placed on Contact Precautions because of VRE. Two systematic and one narrative reviews were identified.[141-143]

The reviews by Morgan et al.[142] and Abad et al.[141] identified increased depression[144-149] and anxiety scores,[145-147,149-151] reduced health care provider contact,[150,152-155] and preventable harms (i.e., falls, pressure ulcers, and electrolyte imbalances)[156] associated with isolation while on Contact Precautions. No difference in patient satisfaction was observed.[152,157-159] None of these studies were randomized and most did not adjust for patient severity of illness or comorbidity.[153,155,156,160,161] As patients colonized with antibiotic-resistant organisms are systematically different from patients without antibiotic-resistant organism colonization, this likely created a bias. In one study by Gandra et al. published after these systematic reviews, the incidence of falls and pressure ulcers were higher in patients with MRSA and VRE placed on Contact Precautions than in the rest of the non-isolated patient population.[69] However, after the hospital discontinued the use of Contact Precautions for MRSA and VRE, the incidence of falls and pressure ulcers in MRSA and VRE patients did not change, and remained higher than for the general patient population.[69] This suggests that it was the patient's underlying health status that predisposed to falls rather than isolation itself.

Among several patient surveys that focused on patients on Contact Precautions,[154,158,159,161-163] one by Chittick et al. identified that 90% of patients on Contact Precautions agree that precautions are important to reduce infection transmission,[164] but across several studies a significant proportion of patients felt that they were not well informed about the indications and their nature of Contact Precautions in their own case.[150,165]

No studies identified increased mortality associated with Contact Precautions. No studies evaluated the impact of interventions intended to mitigate the harm of isolation through enhanced patient or staff education, staff training, or policies and procedures to standardize care for isolated and non-isolated patients.

3.3 Evidence Summary and Conclusion

There are a variety of important harms that are associated with single room placement in Contact Precautions (see A.4.5 Rapid Review Three: Harms Are Associated With Contact Precautions). Contact Precautions should be used only if there is an anticipated benefit with respect to decreased morbidity and mortality. However, if such a benefit is anticipated, it is likely that the benefits of reduced morbidity and mortality will outweigh the harms associated with VRE Contact Precautions. If Contact Precautions are used, health care facilities should put policies and procedures in place to ensure that patients and residents on Contact Precautions receive the same high quality care provided to patients and residents not on Contact Precautions.[141,142]

4. Cost-Effectiveness of Control Measures

Question 4:

Are VRE Control Measures Cost-Effective?

4.1 Background

Our review of the evidence suggests that screening on admission and Contact Precautions for VRE are effective at reducing VRE transmission and preventing VRE infections. Given the low incidence of VRE bacteremia in many health care facilities and patient populations,[15,25] an important ancillary question is whether these control measures are cost-effective, and in what setting.

4.2 Evidence Review

A German case-control study by Puchter et al. matched patients with VRE and VSE infections based on age, gender, duration of hospitalization prior to infection, type of infection, Charlston comorbidity index, and ICU admission.[166] Costs prior to infection onset were similar for VRE and VSE patients. After infection onset, the additional cost of a VRE infection was € 13,157 more than for a VSE infection [approximately Can $20,985 (based on Bank of Canada's exchange rate of 1 European euro to 1.5950 Canadian dollars for 2018 March)]. Differences in cost were due to increased pharmaceutical, human resource, and medical product costs. Other studies have estimated the cost of a VRE bacteremia to be between US $9,949 and US $79,000 [approximately Can $12,866 and Can $102,162 (based on Bank of Canada's exchange rate of 1 US dollar to 1.2932 Canadian dollars for 2018 March)].[167-169]

There is also a significant cost associated with screening on admission and Contact Precautions for VRE. Given these balancing costs, it is important to consider whether these control measures are also cost-effective and if so in what settings. To address this, PHO conducted a systematic review of the literature to identify cost-effectiveness studies of screening on admission and Contact Precautions for VRE.[29] Additionally, in a PHO-affiliated study, a cost-effectiveness analysis was performed focusing on a typical Ontario acute care hospital.[30]

The systematic review identified four studies that evaluated the cost-effectiveness of screening for VRE on admission.[39,65,170,171] No study compared screening on admission and Contact Precautions for VRE with no VRE control measures.

One study by Muto et al. compared VRE admission and weekly screening and VRE Contact Precautions with VRE Contact Precautions alone at two tertiary care hospitals in a region.[170] The study identified cost-savings associated with screening for VRE on admission based on an excess incidence of VRE bacteremia at the nonscreening hospital, although the nonscreening hospital had a higher VRE incidence at baseline.[170]

Three studies compared screening on admission and Contact Precautions for VRE with modified VRE screening. Bryce et al.[65] studied the impact of changing their hospital policy from screening all admissions to screening only admissions to high-risk units (i.e., transplant, burn, trauma, and intensive care units).[65] As the incidence of VRE bacteremia did not increase after limiting screening, they concluded that screening limited to high-risk units was cost-effective.[65] Lee et al.[171] concluded that VRE admission screen targeting high-risk patients (i.e., those previously admitted to hospital) was cost-effective compared to screening only renal patients, or screening high-risk patients plus reflex *C. difficile* testing on the basis that it detected 100% of patients colonized by VRE and would therefore reduce VRE infection.[171] Shadel et al.[39] conducted

a prospective observational study of screening for VRE on admission to ICU compared with reflex *C. difficile* testing.[39] Again, on the basis that screening on admission detected 91% of VRE vs. 8% from reflex testing, the authors estimated an anticipated reduction in VRE bacteremia.[39]

In addition, a PHO-affiliated cost-effectiveness analysis was conducted to evaluate the effectiveness of screening on admission and Contact Precautions for VRE.[30] Data from the PHO VRE Program of Research and from the literature were used to create a simulation model of a 20-bed medical unit at an Ontario tertiary care hospital.[30] Screening on admission plus Contact Precautions for VRE were compared to no VRE prevention strategy. The model based on 1,000 admissions per year found that implementing risk-factor–based VRE screening and Contact Precautions would cost Can $7,850 to save a quality-adjusted life year. This PHO-affiliated study was submitted for publication in a peer-review journal in February 2019.

There are limitations to all of these studies. Estimates of the effectiveness of the differing VRE control measures assessed were based on the same literature reviewed in 1. Effectiveness of Screening on Admission and Contact Precautions or were derived from before-after studies at a single facility. Not all costs were considered in any study. For example, some studies only considered the cost of VRE bacteremia, and not the cost of other VRE infections.[65,170] Additionally, all these studies were conducted at, or modelled at, moderate- to high-risk tertiary care hospitals. It is unclear if these results can be extrapolated to lower-risk community hospitals and long-term care homes where any VRE control strategy would unlikely be cost-effective at the facility level given the limited burden of infection (although it could potentially result in cost-savings at regional acute care hospitals). Additionally, no study addressed the cost-effectiveness of screening for VRE on admission at a regional, provincial or societal level.

4.3 Evidence Summary

The overall quality of these studies was limited, and the studies were heterogeneous with respect to the manner in which both cost and effectiveness were established, and in terms of the specific interventions studied. Additionally, the studies were conducted entirely in acute care hospitals and no study evaluated cost-effectiveness at a regional, provincial or societal level.

Three of four cost-effectiveness studies concluded that screening for VRE on admission is cost-effective[39,170,171] while one study found that hospital-wide screening on admission was not cost-effective compared to screening limited to high-risk units (wards that care primarily for patients at high risk of infectious complications from VRE). However, this conclusion was based on a lack of increase in VRE bacteremia rates at a single facility over a limited time period and was likely underpowered to detect a difference.[65]

In the PHO-affiliated cost-effectiveness analysis, screening for VRE on admission and Contact Precautions was associated with Can $7,850 per quality-adjusted life year gained when modelled on a prototypical Ontario tertiary care hospital.[30] In general, interventions are considered cost-effective if they cost less than US $50,000 to $100,000 per quality-adjusted life year gained,[172] suggesting that screening for VRE on admission is highly cost-effective in tertiary care hospitals.

4.4 Conclusion

The data evaluating the cost-effectiveness of screening on admission and Contact Precautions for VRE are limited. From the data available, strategies that identify a larger proportion of patients colonized by VRE at admission and strategies associated with a reduction in VRE bacteremia appear cost-effective in large acute care hospitals. There are no data on cost-effectiveness for lower-risk facilities such as smaller hospitals or long-term care homes, and no data on regional cost-effectiveness.

5. Priorities for Future Research

There are many areas where further research is needed to better inform VRE control programs in Ontario. Key priorities for future research and epidemiological study include:

- better estimates of the effectiveness of screening for VRE on admission, using a cluster randomized controlled trial or quasi-experimental methodology at reduced risk of bias (e.g., prospective controlled interrupted time series analysis, use of a stepped wedge or removed and repeated intervention design).
- better data for the impact of screening for VRE on admission in the long-term care home setting, and data on the impact of VRE control in long-term care homes on the rates of VRE colonization and infection in acute care facilities.
- higher quality cost-effectiveness and cost-utility data with studies focusing on cost-effectiveness at the provincial or regional level, cost-effectiveness in long-term care homes, and cost-effectiveness in low-risk hospitals.
- ongoing monitoring of VRE bacteremia rates in Ontario is also essential, and ongoing data on changes in the overall burden of VRE infection and the incidence of VRE infection and colonization in acute care and long-term care facilities would be valuable.

6. Overall Conclusions and Recommendations

VRE is an antibiotic-resistant organism of significant concern and is associated with increased mortality, morbidity, and health care costs. The conceptual goals of limiting VRE transmission and preventing VRE infection are not controversial. At issue is whether VRE control measures should include risk-factor–based screening on admission and Contact Precautions.

The literature demonstrates that:

- the risk of VRE transmission is higher when hospitalized patients colonized by VRE are not recognized.
- risk-factor–based screening for VRE on admission identifies the majority of patients colonized by VRE whereas reliance on clinical cultures does not.
- screening for VRE is an important element of VRE outbreak control.
- VRE control measures including risk-factor–based screening on admission and Contact Precautions for VRE (defined broadly) are effective strategies to reduce VRE transmission in the endemic setting.

Most importantly, though some single-hospital studies suggest that screening for VRE on admission can be discontinued or reduced without a short-term increase in VRE bacteremia, a prospective, controlled study that included all Ontario acute care hospitals with 3 years of follow-up demonstrated that discontinuing screening for VRE on admission as it is performed in Ontario was associated with a significant acceleration in the rate of increase in VRE bacteremia at those facilities.[25] Since the study was concluded, the overall incidence of VRE bacteremia in Ontario has continued to rise.[72,73] If screening for VRE on admission were discontinued at all Ontario health care facilities, it is likely that these rates will continue to increase, resulting in a high proportion of patients colonized by VRE in both acute care and long-term care facilities, and a much higher incidence of VRE bacteremia, and a much larger proportion of enterococcal infections secondary to VRE rather than VSE.

This review also identified that the burden of VRE bacteremia is highly concentrated in high-risk facilities (facilities that care for patients at high risk of infectious complications of VRE) and high-risk patient populations (those at high risk of infectious complications of VRE). Risk-factor–based screening for VRE on admission was also consistently identified as cost-effective in high-risk facilities, and in a study of a typical acute care hospital in Ontario, it was associated with Can $1,437 per QALY gained.[30] While there is limited evidence, it is also likely that increased VRE colonization at low-risk acute care or long-term care facilities within a region will result in increased VRE colonization in the high-risk facilities within the same region. Therefore, it appears likely that risk-factor–based screening on admission and Contact Precautions for VRE applied across all health care facilities within a region, including low-risk facilities, will help reduce VRE infection and bacteremia within high-risk facilities and high-risk patient populations in the same region. Whether this type of regional approach would be cost-effective is unknown but it is also unknown whether successful long-term VRE control is possible without taking this approach.

These conclusions are based on evidence with significant limitations. Much of the evidence is based on observational and quasi-experimental studies of varying quality. This is a common limitation of the infection prevention and control literature, and decisions can only be made based on the data available.

The evidence supporting screening for VRE on admission is both more diverse and more consistent than the evidence suggesting that screening on admission and Contact Precautions for VRE can be discontinued without increasing both VRE infections and overall health care costs.

PIDAC recommends that all acute care and chronic care hospitals and long-term care homes continue to perform risk-factor–based screening on admission and Contact Precautions for VRE.

Risk-factor–based screening on admission and Contact Precautions for VRE are described in detail in: *Annex A: Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (AROs) in All Health Care Settings*. Note that Contact Precautions for VRE include placement of patients or residents colonized or infected by VRE in a single room or cohorting with other patients or residents who have tested positive for VRE; enhanced environmental cleaning and disinfection; other suggestions for VRE control are also found in:

- *Routine Practices and Additional Precautions in All Health Care Settings*, 3rd edition. 2012
- *Annex A: Screening, Testing and Surveillance for Antibiotic-Resistant Organisms (AROs) in All Health Care Settings*. 2013
- *Best Practices for Environmental Cleaning for Prevention and Control of Infections in All Health Care Settings*, 3rd edition. 2018

Screening for VRE on admission is risk-factor–based; patients and residents with risk factors for acquiring VRE should have rectal cultures performed to detect VRE, unless they are known to have tested positive.[23] However, some facilities may consider universal VRE screening for all patients or residents if the majority of patients or residents have risk factors for acquiring VRE and the facility determines that this is a more efficient process for screening on admission.

Acute care facilities may identify patient populations where the incidence of VRE colonization is sufficiently low that screening is not required (e.g., obstetrical or mental health patients). However, this should be reassessed periodically, especially if VRE transmission or infection is recognized in that population.

These recommendations will be reviewed as new evidence emerges or the epidemiology of VRE in Ontario changes.

Section Two:

Appendices on Methodology, Evidence and References

Appendix 1: Methodology

A.1.1 Systematic Review One: VRE and VSE Bacteremia Outcomes in the Era of Effective VRE Therapy: a Systematic Review and Meta-analysis

Data from studies conducted prior to the availability of effective VRE therapies suggest that VRE bacteremia is associated with worse outcomes than VSE bacteremia. To help inform recommendations for preventing and controlling infections by VRE, PHO performed a systematic review and meta-analysis of studies comparing outcomes of patients with either VRE or VSE bacteremia, when patients with VRE bacteremia were treated with effective VRE therapy, in order to understand whether VRE bacteremia-associated outcomes are different from those of VSE bacteremia.[28]

All methods including literature searches, study selection, data collection, and quantitative analysis processes were developed a priori and were reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Intervention.[28]

Two research coordinators independently screened the titles and abstracts of all articles captured by literature searches, using the criteria in A.3.1 Systematic Review One: VRE and VSE Bacteremia Outcomes. Articles tagged for full-text review by either reviewer were reviewed in full independently by the same two research coordinators. An infection prevention and control physician was consulted to arbitrate any disagreements on study inclusion. Articles would be included in data extraction and analysis when all reviewers agreed for such inclusion.[28]

Data extraction and study quality assessment were performed independently by the same two research coordinators using an electronic template prepared beforehand. The primary and/or corresponding authors were contacted up to two times to request required information missing from the published studies. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of nonrandomized cohort or case-control studies.[28]

A.1.2 Systematic Review Two: Economic Evaluations of Vancomycin-Resistant Enterococci (VRE) Control Interventions. A Systematic Review

Preventing colonization and infection by VRE is a health care priority, yet in recent years, some Ontario health care facilities have questioned the appropriateness of maintaining costly infection prevention and control measures against VRE in the context of continually rising rates of VRE bacteremia. To inform PIDAC on its recommendations for infection prevention and control practices against VRE, PHO performed a systematic review to give an overview of cost-effectiveness, cost-benefit, and cost-utility analyses of all interventions targeting VRE control in hospital settings, and to synthesize the strengths and weaknesses of each included intervention from the perspectives of patient care safety and infection prevention and control.

All methods including literature searches, study selection and data collection were developed a priori and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were

followed.[173] Two research coordinators independently screened the titles and abstracts of all articles captured by literature searches, using the criteria in A.3.2 Systematic Review Two: Economic Evaluations of VRE Control Interventions. Articles that were not tagged for exclusion by either reviewer were reviewed in full text independently by the same two research coordinators. A scientist was consulted to arbitrate any disagreements on study inclusion. Articles would be included in data extraction and analysis when all reviewers agreed for such inclusion.

As for systematic review one, data extraction and study quality assessment were done by the same two research coordinators independently using an electronic template prepared in advance. The primary and/or corresponding authors were contacted up to two times to request required information missing from the published studies. The Newcastle-Ottawa Scale (NOS) was used to assess the quality of nonrandomized cohort or case-control studies.

A.1.3 Rapid Reviews

To inform PIDAC on its recommendations for infection prevention and control practices against VRE, PHO conducted four rapid reviews to summarize recent evidence on VRE and VRE control practices:

1. What are the long-term trends in VRE infection and colonization rates after discontinuation of screening, Contact Precautions, and isolation practices at either the local hospital or long-term care home or the regional level?

2. Do active screening and isolation programs for VRE reduce the incidence of VRE colonization and/or infection when compared to no active screening and isolation programs?

3. What patient harms are associated with Contact Precautions and/or isolation for antibiotic-resistant organisms?

4. Are there differences in rates of colonization or infection by VRE for individual vs regional VRE control practices?

The research questions in PICO (population, intervention, control and outcome) format, study selection in general, and methods of literature search were developed a priori by a group of three research coordinators and one senior research coordinator. These four persons each took on a rapid review and fine-tuned the selection criteria independently with an infection prevention and control physician. For each rapid review, articles were screened by one person independently who also performed data extraction and quality assessment.

Appendix 2: Search Strategies

A.2.1 Systematic Review One: VRE and VSE Bacteremia Outcomes

PHO Library Services assisted with the development and implementation of search strategies for electronic databases, and with the retrieval of full-text articles from the following databases: Medical Literature Analysis and Retrieval System online (MEDLINE) (see Table 1), Excerpta Medica Database (Embase) (see Table 2), Cochrane Central Register of Controlled Trials (CENTRAL) (see Table 3), Cumulative Index of Nursing and Allied Health Literature (CINAHL) (see Table 4), and ProQuest Dissertations and Theses (see Table 5).

Table 1: Systematic Review One Search Strategy for MEDLINE (1946 to February 27, 2014)

#	Searches	Results
1	(exp Enterococcus/ and (Bacteremia/ or exp Drug Resistance/ or exp Glycopeptides/ or Vancomycin/ or Vancomycin Resistance/)) or exp Enterococcus/de, ip or (Vancomycin/ and exp Drug Resistance/) or Vancomycin Resistance/	12869
2	((bacteremia adj4 vancomycin$) or (drug resistan$ adj4 enterococc$) or (glycopeptide resistan$ adj4 enterococc$) or (vancomycin$ adj4 enterococc$) or (vancomycin$ adj4 resistan$) or vancomycin-resistan$ or VRE).mp.	7273
3	"Cost of Illness"/ or Death Certificates/ or exp Epidemiologic Factors/ or exp Epidemiology/ or exp Morbidity/ or exp Mortality/ or "Outcome Assessment (Health Care)"/ or exp Risk/ or exp Treatment Outcome/	2280611
4	(attributed or attributable or (burden adj2 (illness or disease$)) or comorbid$ or death or epidemiolog$ or incidence or morbid$ or mortality or outcome$ or prevalen$).mp.	3291315
5	(1 or 2) and (3 or 4)	4387
6	limit 5 to (english language and yr="1994 -Current")	3712
7	remove duplicates from 6	3686

Table 2: Systematic Review One Search Strategy for Embase (1988 to 2014 Week 08)

#	Searches	Results
1	(exp enterococcus/ and (bacteremia/ or exp drug resistance/ or glycopeptide/ or vancomycin/)) or (vancomycin/ and drug resistance.mp.) or vancomycin resistant Enterococcus/	13803
2	((bacteremia adj4 vancomycin$) or (drug resistan$ adj4 enterococc$) or (glycopeptide resistan$ adj4 enterococc$) or (vancomycin$ adj4 enterococc$) or (vancomycin$ adj4 resistan$) or vancomycin-resistan$ or VRE).mp.	16091
3	"cost of illness"/ or death certificate/ or exp epidemiology/ or outcome assessment/ or exp risk/ or exp treatment outcome/	3433459
4	(attributed or attributable or (burden adj2 (illness or disease$)) or comorbid$ or death or epidemiolog$ or incidence or morbid$ or mortality or outcome$ or prevalen$).mp.	4132555
5	(1 or 2) and (3 or 4)	9284
6	limit 5 to (english language and exclude medline journals and yr="1994 -Current")	821
7	remove duplicates from 7	806

Table 3: Systematic Review One Search Strategy for CENTRAL (May 29, 2014)

#	Query	Limiters/Expanders	Results
S1	vancomycin OR VRE	Search modes - Boolean/Phrase	14

Table 4: Systematic Review One Search Strategy for CINAHL (1994 to February 27, 2014)

#	Query	Limiters/Expanders	Results
S6	(S1 OR S2) AND (S3 OR S4)	Limiters - Published Date: 19940101-; English Language; Exclude MEDLINE records Search modes - Boolean/Phrase	206
S5	(S1 OR S2) AND (S3 OR S4)	Search modes - Boolean/Phrase	1086
S4	(attributed OR attributable OR (burden N2 (illness OR disease*)) OR comorbid* OR death OR epidemiolog* OR incidence OR morbid* OR mortality OR outcome* OR prevalen*)	Search modes - Boolean/Phrase	810665
S3	(MH "Death Certificates") OR (MH "Epidemiology+") OR (MH "Morbidity+") OR (MH "Mortality+") OR (MH "Outcome Assessment") OR (MH "Risk Assessment") OR (MH "Treatment Outcomes+")	Search modes - Boolean/Phrase	573000
S2	((bacteremia N4 vancomycin*) OR ("drug resistan*" N4 enterococc*) OR ("glycopeptide resistan*" N4 enterococc*) OR ("vancomycin* N4 enterococc*") OR (vancomycin* N4 resistan*) OR "vancomycin-resistan*" OR VRE)	Search modes - Boolean/Phrase	1537
S1	((MH "Enterococcus+") AND ((MH "Bacteremia") OR (MH "Drug Resistance, Microbial+") OR (MH "Vancomycin") OR (MH "Vancomycin Resistance"))) OR ((MH "Vancomycin") AND (MH "Drug Resistance, Microbial+")) OR (MH "Vancomycin Resistance")	Search modes - Boolean/Phrase	1671

Table 5: Systematic Review One Search Strategy for ProQuest Dissertations & Theses (1994 to March 5, 2014)

Search statement	Results
AB,TI,SU,DISKW(((bacteremia N/4 vancomycin*) OR ("drug resistant" N/4 enterococc*) OR ("drug resistance" N/4 enterococc*) OR ("glycopeptide resistance" N/4 enterococc$) OR ("glycopeptide resistance" N/4 enterococc$) OR (vancomycin* N/4 enterococc*) OR (vancomycin* N/4 resistan*) OR "vancomycin-resistance" OR "vancomycin-resistant" OR VRE) AND (attributed OR attributable OR (burden N/2 (illness OR disease*)) OR comorbid* OR death OR epidemiolog* OR incidence OR morbid* OR mortality OR outcome* OR prevalen*))	64

In addition to the above electronic databases, websites of the following infection prevention and control authorities were scanned in January 2015 for conference abstracts, surveillance reports and recommendations:[174,175]

- Asia-Pacific Society of Infection Conrol (APSIC): no new references from website
- Association of Medical Microbiology and Infectious Disease Canada (AMMI)
  - Website: no new references
  - AMMI conference (2011, 2012, 2013, 2014): no new references
  - AMMI conference 2010 abstracts: no new references (from contacting the organization)
- Association for Professionals in Infection Control and Epidemiology (APIC):
  - Website: no new references
  - APIC conference 2012 abstracts: no new references

- APIC conference 2009, 2010, 2011 abstracts: no new references (from contacting the organization)
- APIC conference 2013: not available

- Healthcare Infection Society (HIS)
  - Website: no new references
  - HIS conference 2012: no new references (from contacting the organization)

- Infectious Disease Society of America (IDSA)
  - Website: no new references
  - ID Week 2012, 2013: no new references

- Infection Prevention and Control Canada (IPAC Canada)
  - Website: no new references
  - IPAC Canada/CHICA conference 2013: no new references
  - IPAC Canada/CHICA conference 2009, 2010, 2011 and 2012: no new references

- Infection Prevention Society (IPS)
  - Website: no new references
  - IPS conference 2010 and 2011 presentation schedule online: no new references

- International Conference on Anti-Microbial Research (ICAR) 2012 abstracts: no new references

- International Federation for Infection Control (IFIC):
  - Website: no new references
  - IFIC conference 2011, 2012 and 2013 presentations: no new references
  - IFIC conference 2009, 2010, 2011, 2012 abstracts: no new references (from contacting the organization)

- Society for Healthcare Epidemiology of America) SHEA
  - Website: no new references
  - SHEA conference 2009-2011 publications not accessible online

A.2.2 Systematic Review Two: Economic Evaluations of VRE Control Interventions

PHO Library Services assisted with the development and implementation of search strategies for electronic databases, as well as with the retrieval of full-text articles from the following databases: MEDLINE (see Table 6 and Table 7), CINAHL (see Table 8), Embase (see Table 9), CENTRAL (see Table 10), NHS Economic Evaluation Database (NHSEED) (see Table 11), and EconLit (see Table 12). A reference scan of included primary articles for additional studies for inclusion was also conducted.[173]

Table 6: Systematic Review Two Search Strategy for MEDLINE (1946 to January 2017)

#	Searches	Results	Search Type
1	Vancomycin-Resistant Enterococci/ or (exp Drug Resistance/ and (Vancomycin/ or Teicoplanin/ or Glycopeptides/)) or (exp Enterococcus/ and (Bacteremia/ or exp Drug Resistance/ or Vancomycin/ or Teicoplanin/ or Glycopeptides/)) or Vancomycin Resistance/ or (exp Enterococcus/de and (exp Drug resistance/ or Vancomycin/ or Teicoplanin/ or Glycopeptides/))	9694	Advanced

#	Searches	Results	Search Type
2	((VRE or VREfm or vancomycin-resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")).ti,ab,kw,kf.	4564	Advanced
3	(AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ti,ab,kw,kf. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,ab,kw,kf.)	6471	Advanced
4	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))).ti,ab,kw,kf.	5135	Advanced

#	Searches	Results	Search Type
5	(((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)) or (VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ti,ab,kw,kf. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,ab,kw,kf.)	5442	Advanced
6	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)).ti,ab,kw,kf. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,ab,kw,kf.)	5351	Advanced

#	Searches	Results	Search Type
7	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ti,ab,kw,kf. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,ab,kw,kf.)	6549	Advanced
8	(bacteremia adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ti,ab,kw,kf.	430	Advanced
9	exp Budgets/ or Cost allocation/ or Cost-Benefit Analysis/ or "Costs and Cost Analysis"/ or Cost control/ or cost of illness/ or Cost savings/ or direct service costs/ or Economics/ or "Economics, Nursing"/ or "Economics, Hospital"/ or "Economics, Medical"/ or "economics, pharmaceutical"/ or Efficiency, organizational/ or employer health costs/ or fees, medical/ or exp "fees and charges"/ or exp financial management/ or exp Health Care Costs/ or health care sector/ or Health Expenditures/ or hospital charges/ or hospital costs/ or investments/ or exp Models, Economic/ or exp resource allocation/ or ec.fs.	519 216	Advanced
10	(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value adj2 money)).ti,ab,kw,kf.	4 535 793	Advanced
11	(or/1-8) and (9 or 10)	2896	Advanced
12	limit 11 to english	2599	Advanced

Table 7: Systematic Review Two Search Strategy for MEDLINE (1946 to January, 2016, Week 4)

#	Searches	Results
1	(VRE or vancomycin-resist* or 'Vancomycin-Resistant Enterococcus').mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	5985
2	(surveillance or screening or monitoring).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	940 874
3	(contact-islation or patient-isolation or contact-precautions or cohorting or single-room or gown* or antimicrobial-stewardship or antibiotic-stewardship or (antibiotic and restriction) or (antibiotic and approval) or antibiotic-guideline* or (antibiotic and streamline*) or (antibiotic and cycling)).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	8787
4	2 or 3	948 440
5	1 and 4	1214
6	(((cost or costs or cost-effectiveness or cost-benefit or cost-utlity or cost-minimization or 'economics' or 'economics, hospital' or 'costs) and cost analysis') or 'cost-benefit analysis' or 'cost control' or 'health care costs' or 'direct service costs' or 'hospital costs').mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]	158 393
7	5 and 6	42

Table 8: Systematic Review Two Search Strategy for CINAHL [March 14, 2016; updated in January 2017 (results not shown)]

#	Query	Limiters/Expanders	Results
S31	S27 AND S28	Limiters - English Language; Exclude MEDLINE records Search modes - Boolean/Phrase	43
S30	S27 AND S28	Limiters - English Language Search modes - Boolean/Phrase	380
S29	S27 AND S28	Search modes - Boolean/Phrase	396
S28	S1 OR S2 OR S3 OR S4 OR S7 OR S8 OR S9 OR S10 OR S13 OR S14 OR S17 OR S18 OR S21 OR S22 OR S23	Search modes - Boolean/Phrase	1,892
S27	S24 OR S25 OR S26	Search modes - Boolean/Phrase	735 973
S26	AB(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value N2 money))	Search modes - Boolean/Phrase	505 137

#	Query	Limiters/Expanders	Results
S25	TI(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value N2 money))	Search modes - Boolean/Phrase	208 961
S24	MH "Budgets" or MH "Cost Benefit Analysis" or MH "Costs and Cost Analysis" or MH "Cost control+" or MH "economic aspects of illness" or MH "Cost savings" or MH "Economics" or MH "economics, pharmaceutical" or MH "organizational efficiency" or or MH "fees and charges+" or MH "financial management+" or MH "Health Care Costs+" or MH "health care industry" or MH "health facility charges" or MH "hospital facility costs" or MH "investments" or MH "resource allocation+" or MH "Health services purchasing" or MH "value based purchasing"	Search modes - Boolean/Phrase	148 281
S23	AB(bacteremia N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*))	Search modes - Boolean/Phrase	72
S22	TI(bacteremia N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*))	Search modes - Boolean/Phrase	38

#	Query	Limiters/Expanders	Results
S21	S19 AND S20	Search modes - Boolean/Phrase	805
S20	MH "Enterococcus+" or AB (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	2356
S19	AB(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	Search modes - Boolean/Phrase	2107
S18	TI (VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and MH "Enterococcus+" or TI(enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	1056
S17	S15 AND S16	Search modes - Boolean/Phrase	744
S16	MH "Enterococcus+" or AB (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	2356

#	Query	Limiters/Expanders	Results
S15	AB ((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 AB(drug-resistan* or resistan*))	Search modes - Boolean/Phrase	911
S14	TI((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (drug-resistan* or resistan*)) and ((MH "Enterococcus+" or TI (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	1023
S13	S11 AND S12	Search modes - Boolean/Phrase	752
S12	MH "Enterococcus+" or AB (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	2356

#	Query	Limiters/Expanders	Results
S11	AB(((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (drug-resistan* or resistan*)) or (VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*))	Search modes - Boolean/Phrase	952

#	Query	Limiters/Expanders	Results
S10	TI (((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (drug-resistan* or resistan*)) or (VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)) and ((MH "Enterococcus+" or TI (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	Search modes - Boolean/Phrase	599

#	Query	Limiters/Expanders	Results
S9	AB ((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	Search modes - Boolean/Phrase	734

#	Query	Limiters/Expanders	Results
S8	TI ((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	Search modes - Boolean/Phrase	551
S7	S5 AND S6	Search modes - Boolean/Phrase	797
S6	MH "Enterococcus+" or AB (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	Search modes - Boolean/Phrase	2356
S5	AB (AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	Search modes - Boolean/Phrase	2067

#	Query	Limiters/Expanders	Results
S4	TI (AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and (MH "Enterococcus+" or TI (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	Search modes - Boolean/Phrase	588
S3	AB((VRE or VREfm or vancomycin-resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	Search modes - Boolean/Phrase	702
S2	TI ((VRE or VREfm or vancomycin-resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	Search modes - Boolean/Phrase	533
S1	(MH "Vancomycin Resistant Enterococci") OR ((MH "Drug Resistance" or MH "Drug Resistance, Microbial") AND (MH "Vancomycin")) OR ((MH "Enterococcus+" OR MH "Enterococcus Faecium") AND (MH "Bacteremia" OR MH "Drug Resistance" OR MH "Drug Resistance, Microbial" OR MH "Vancomycin")) OR (MH "Drug Resistance, Microbial" AND MH "Vancomycin")	Search modes - Boolean/Phrase	766

Table 9: Systematic Review Two Search Strategy for Embase [March 11, 2016; updated in January 2017 (results not shown)]

#	Searches	Results
1	Vancomycin Resistant Enterococcus/ or (exp Drug Resistance/ and (Vancomycin/ or vancomycin derivative/ or Teicoplanin/ or Glycopeptide/)) or (exp Enterococcus/ and (Bacteremia/ or exp Drug Resistance/ or Vancomycin/ or vancomycin derivative/ or Teicoplanin/ or Glycopeptide/)) or (Antibiotic Resistance/ and (Vancomycin/ or vancomycin derivative/ or Teicoplanin/ or Glycopeptide/))	29861
2	((VRE or VREfm or vancomycin-resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")).ti,kw.	2676
3	((VRE or VREfm or vancomycin-resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")).ab. /freq=3	1597
4	(AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ti,kw. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,kw.)	3858

#	Searches	Results
5	(AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ab. /freq=3	10805
6	exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ab. /freq=3	37287
7	5 and 6	2222
8	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))).ti,kw.	2848

#	Searches	Results
9	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))).ab. /freq=3	1329
10	(((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)) or (VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ti,kw. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,kw.)	3391

#	Searches	Results
11	(((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)) or (VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ab. /freq=3	3215
12	exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ab. /freq=3	37 287
13	11 and 12	2713
14	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)).ti,kw. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,kw.)	3133

#	Searches	Results
15	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) adj4 (drug-resistan* or resistan*)).ab. /freq=3	1918
16	exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ab. /freq=3	37 287
17	15 and 16	1558
18	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ti,kw. and (exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ti,kw.)	4098
19	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*).ab. /freq=3	12 377
20	exp Enterococcus/ or (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium").ab. /freq=3	37 287
21	19 and 20	3614

#	Searches	Results
22	(bacteremia adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ti,kw.	252
23	(bacteremia adj4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)).ab. /freq=3	62
24	Budget/ or Cost/ or Cost Benefit Analysis/ or Cost control/ or cost effectiveness analysis/ or cost minimization analysis/ or cost of illness/ or cost utility analysis/ or economic aspect/ or exp economic evaluation/ or (economics/ and statistical model/) or exp fee/ or exp financial management/ or exp health care cost/ or health care financing/ or health economics/ or hospital charge/ or exp hospital cost/ or investment/ or medical fee/ or organizational efficiency/ or exp pharmacoeconomics/ or resource allocation/ or socioeconomics/	974 239
25	(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value adj2 money)).ti,kw.	1 049 693
26	(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value adj2 money)).ab. /freq=3	907 143
27	(1 or 2 or 3 or 4 or 7 or 8 or 9 or 10 or 13 or 14 or 17 or 18 or 21 or 22 or 23) and (24 or 25 or 26)	2954

#	Searches	Results
28	limit 27 to english	2734
29	limit 28 to embase	2658
30	remove duplicates from 29	2649

Table 10: Systematic Review Two Search Strategy for CENTRAL (January 2017)

#	Query	Results
S1	(ZU "vancomycin administration & dosage") or (ZU "vancomycin adverse effects") or (ZU "vancomycin analysis") or (ZU "vancomycin blood") or (ZU "vancomycin cerebrospinal fluid") or (ZU "vancomycin economics") or (ZU "vancomycin pharmacokinetics") or (ZU "vancomycin pharmacology") or (ZU "vancomycin resistance") or (ZU "vancomycin resistance drug effects") or (ZU "vancomycin resistance physiology") or (ZU "vancomycin therapeutic use") or (ZU "vancomycin urine") or (ZU "vancomycin/ad [administration & dosage]") or (ZU "vancomycin/administration & dosage/pharmacology") or (ZU "vancomycin/ae [adverse effects]")	338
S2	(ZU "drug resistance") or (ZU "drug resistance drug effects") or (ZU "drug resistance genetics") or (ZU "drug resistance immunology") or (ZU "drug resistance physiology") or (ZU "drug resistance, bacterial") or (ZU "drug resistance, bacterial drug effects") or (ZU "drug resistance, bacterial genetics") or (ZU "drug resistance, bacterial immunology") or (ZU "drug resistance, bacterial physiology") or (ZU "drug resistance, fungal") or (ZU "drug resistance, microbial") or (ZU "drug resistance, microbial drug effects") or (ZU "drug resistance, microbial genetics") or (ZU "drug resistance, microbial physiology") or (ZU "drug resistance, multiple") or (ZU "drug resistance, multiple drug effects") or (ZU "drug resistance, multiple genetics") or (ZU "drug resistance, multiple immunology") or (ZU "drug resistance, multiple physiology") or (ZU "drug resistance, multiple, bacterial") or (ZU "drug resistance, multiple, bacterial drug effects") or (ZU "drug resistance, multiple, bacterial genetics") or (ZU "drug resistance, multiple, bacterial physiology") or (ZU "drug resistance, multiple, viral") or (ZU "drug resistance, multiple, viral drug effects") or (ZU "drug resistance, multiple, viral genetics") or (ZU "drug resistance, multiple, viral immunology") or (ZU "drug resistance, viral") or (ZU "drug resistance, viral drug effects") or (ZU "drug resistance, viral genetics") or (ZU "drug resistance, viral immunology") or (ZU "drug resistance, viral physiology")	2518
S3	(ZU "enterococcus") or (ZU "enterococcus drug effects") or (ZU "enterococcus faecalis") or (ZU "enterococcus faecalis chemistry") or (ZU "enterococcus faecalis classification") or (ZU "enterococcus faecalis drug effects") or (ZU "enterococcus faecalis enzymology") or (ZU "enterococcus faecalis genetics") or (ZU "enterococcus faecalis growth & development") or (ZU "enterococcus faecalis immunology") or (ZU "enterococcus faecalis isolation & purification") or (ZU "enterococcus faecalis metabolism") or (ZU "enterococcus faecalis pathogenicity") or (ZU "enterococcus faecalis physiology") or (ZU "enterococcus faecalis radiation effects") or (ZU "enterococcus faecium") or (ZU "enterococcus faecium drug effects") or (ZU "enterococcus faecium growth & development") or (ZU "enterococcus faecium immunology") or (ZU "enterococcus faecium isolation & purification") or (ZU "enterococcus faecium physiology") or (ZU "enterococcus faecium/ip [isolation & purification]") or (ZU "enterococcus genetics") or (ZU "enterococcus growth & development") or (ZU "enterococcus immunology") or (ZU "enterococcus isolation & purification") or (ZU "enterococcus pathogenicity")	177
S4	S1 AND S2	22
S5	S2 AND S3	13
S6	S1 AND S3	26
S7	(((VRE or VREfm or vancomycin-resistan*)) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	59
S8	(drug-resistan* or resistan*) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	177

#	Query	Results
S9	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	62
S10	drug-resistan* or resistan* N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	3948
S11	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	909
S12	enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or gram positive bacteria OR gram-positive cocci or enterrococc* OR cocci	1030

#	Query	Results
S13	((AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*))	75
S14	S11 and S12	161
S15	S12 AND S13	64
S16	(cost* or cost adjust* or "cost-avoidance" or cost-benefit* or cost-control* or cost-effect* or cost-estimate* or "cost-minimisation" or "cost-minimization" or cost-per or cost-saving* or cost-to-charge* or cost-utili* or cost-variable* or disability adjusted life year* or disability-adjusted life year* or DALY* or disease burden or economic* or economic-evaluat* or evaluat* or expenditure* or expens* or fee or fees or financ* or fiscal or fund* or health spending or high-cost* or ICER* or "length of stay" or low-cost* or "patient bed days" or inpatient bed day* or paid or pay or payment* or pharmacoeconomic* or pharmaco-economic* or price* or pricing or quality adjusted life year* or quality-adjusted life year* or QALY* or reimburs* or resource allocat* or "resource use" or "resource-use" or resource utili* or resource-utili* or save or saving* or socioeconomic or socio-economic* or unit-cost* or valu* or "value-added" or (value N2 money))	244 614
S17	S10 AND S11	107
S18	S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S14 OR S15 OR S17	289
S19	MH "Budgets" or MH "Cost Benefit Analysis" or MH "Costs and Cost Analysis" or MH "Cost control+" or MH "economic aspects of illness" or MH "Cost savings" or MH "Economics" or MH "economics, pharmaceutical" or MH "organizational efficiency" or or MH "fees and charges+" or MH "financial management+" or MH "Health Care Costs+" or MH "health care industry" or MH "health facility charges" or MH "hospital facility costs" or MH "investments" or MH "resource allocation+" or MH "Health services purchasing" or MH "value based purchasing"	1323
S20	S16 OR S19	244 614
S21	S18 AND S20	116

Table 11: Systematic Review Two Search Strategy for NHS Economic Evaluation Database (January 2017)

#	Query	Results
S16	S1 OR S2 OR S3 OR S7 OR S8 OR S9 OR S13 OR S14 OR S15	21
S15	S10 AND S12	5
S14	S11 AND S12	9
S13	S10 AND S11	6
S12	(ZU "enterococcus") or (ZU "enterococcus classification") or (ZU "enterococcus drug effects") or (ZU "enterococcus enzymology") or (ZU "enterococcus genetics") or (ZU "enterococcus isolation & purification")	9
S11	((ZU "drug resistance") or (ZU "drug resistance drug effects") or (ZU "drug resistance physiology") or (ZU "drug resistance, bacterial") or (ZU "drug resistance, bacterial drug effects") or (ZU "drug resistance, bacterial genetics") or (ZU "drug resistance, fungal") or (ZU "drug resistance, fungal drug effects") or (ZU "drug resistance, microbial") or (ZU "drug resistance, multiple") or (ZU "drug resistance, multiple, bacterial") or (ZU "drug resistance, multiple, bacterial drug effects") or (ZU "drug resistance, multiple, viral") or (ZU "drug resistance, viral") or (ZU "drug resistance, viral drug effects") or (ZU "drug resistance, viral genetics")) or ((ZU "enterococcus") or (ZU "enterococcus classification") or (ZU "enterococcus drug effects") or (ZU "enterococcus enzymology") or (ZU "enterococcus genetics") or (ZU "enterococcus isolation & purification"))	113
S10	(ZU "vancomycin") or (ZU "vancomycin administration & dosage") or (ZU "vancomycin adverse effects") or (ZU "vancomycin blood") or (ZU "vancomycin economics") or (ZU "vancomycin pharmacokinetics") or (ZU "vancomycin pharmacology") or (ZU "vancomycin resistance") or (ZU "vancomycin therapeutic use")	58
S9	S4 AND S5	10

#	Query	Results
S8	S5 and S6	11
S7	((AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*))	10
S6	enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or gram positive bacteria OR gram-positive cocci or enterrococc* OR cocci	27
S5	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	84
S4	drug-resistan* or resistan* N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	155

#	Query	Results
S3	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	6
S2	(drug-resistan* or resistan*) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	9
S1	(((VRE or VREfm or vancomycin-resistan*)) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	7

Table 12: Systematic Review Two Search Strategy for EconLit Searched [March 14, 2016; updated in January 2017 (results not shown)]

#	Query	Results
S11	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10	47
S10	(drug-resistan* or resistan*) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"))	2
S9	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*	16

#	Query	Results
S8	((VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) and ((drug-resistan* or resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*) N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	1
S7	drug-resistan* or resistan* N4 (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")	30
S6	(VRE or VREfm or AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan* or VRE or VREfm or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	16

#	Query	Results
S5	enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium"	4
S4	(AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)	9
S3	((AB-Vancomycin or amplobac or balcorin or Diatracin or edicin or glycopeptide* or icoplax or ifavac or lyphocin or tagocid or targocid or targosid or Teichomycin or Teichomycin-A2 or Teicoplanin* or vacsol or Vamysin or vanauras or vanaurus or vancam or vancamycin or vanccostacin or vanco or vanco-cell or vanco-saar or vanco-teva or vancocid or vancocin or vancocin-cp or vancocin-hcl or vancocin-hydrochloride or vancocina or vancocina-cp or vancocine or vancoled or vancomax or vancomicina or vancomycin* or vancomycin-complex or vancomycin-hcl or vancomycin-hydrochloride or Vancomycin-ratiopharm or vancor or Vancoson or Vancox or Vanmicina or vanmycin or vanococin or varedet or AB-Vancomycin-resistan* or amplobac-resistan* or balcorin-resistan* or Diatracin-resistan* or edicin-resistan* or glycopeptide-resistan* or icoplax-resistan* or ifavac-resistan* or lyphocin-resistan* or tagocid-resistan* or targocid-resistan* or targosid-resistan* or Teichomycin-resistan* or Teichomycin-A2-resistan* or Teicoplanin*-resistan* or vacsol-resistan* or Vamysin-resistan* or vanauras-resistan* or vanaurus-resistan* or vancam-resistan* or vancamycin-resistan* or vanccostacin-resistan* or vanco-resistan* or vanco-cell-resistan* or vanco-saar-resistan* or vanco-teva-resistan* or vancocid-resistan* or vancocin-resistan* or vancocin-cp-resistan* or vancocin-hcl-resistan* or vancocin-hydrochloride-resistan* or vancocina-resistan* or vancocina-cp-resistan* or vancocine-resistan* or vancoled-resistan* or vancomax-resistan* or vancomicina-resistan* or vancomycin*-resistan* or vancomycin-complex-resistan* or vancomycin-hcl-resistan* or vancomycin-hydrochloride-resistan* or Vancomycin-ratiopharm-resistan* or vancor-resistan* or Vancoson-resistan* or Vancox-resistan* or Vanmicina-resistan* or vanmycin-resistan* or vanococin-resistan* or varedet-resistan*)) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	1
S2	(((VRE or VREfm or vancomycin-resistan*)) AND ((enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")))	1
S1	vancomycin	4

In addition to the above electronic databases, The websites of the organizations in A.3.2.1 Inclusion Criteria were searched with the following queries, using the search engine of Google.ca:

- (VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci)
- ((vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium"))

In addition, general web searches from the following sources were conducted with the following strategies:

Google:

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (cost effective|HTA|health technology assessment|evaluation|CER)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (cost effective|HTA|health technology assessment|evaluation|CER)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (cost|"cost-avoidance"|cost-benefit|cost-control|cost-effectiveness|cost-estimate)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (cost|"cost-avoidance"|cost-benefit|cost-control|cost-effectiveness|cost-estimate)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) ("cost-minimisation"|"cost-minimization"|cost-per|cost-saving|cost-to-charge|cost-utility)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") ("cost-minimisation"|"cost-minimization"|cost-per|cost-saving|cost-to-charge|cost-utility)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (cost-variable|disability adjusted life year|DALY|disease burden)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (cost-variable|disability adjusted life year|DALY|disease burden)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (economic|economic-evaluation|evaluate|expenditure)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (economic|economic-evaluation|evaluate|expenditure)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (expense|fee|fees|finance|financial|fiscal|fund)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (expense|fee|fees|finance|financial|fiscal|fund)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (funding|health spending|high-cost|ICER|"length of stay") ("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (funding|health spending|high-cost|ICER|"length of stay")

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (low-cost|"patient bed day"|"inpatient bed day"|paid)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (low-cost|"patient bed day"|"inpatient bed day"|paid)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (pay|payment|pharmacoeconomic|pharmaco-economic|price)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (pay|payment|pharmacoeconomic|pharmaco-economic|price)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (pricing|quality-adjusted life year|QALY|reimbursement|resource allocation)

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (pricing|quality-adjusted life year|QALY|reimbursement|resource allocation)

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) ("resource use"|"resource utilisation"|"resource utilization")

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium")("resource use"|"resource utilisation"|"resource utilization")

(VRE|VREfm|vancomycin resistant enterococcus|vancomycin resistant enterococci) (save|savings|socioeconomic|socio-economic|unit-cost|value|"value-added")

("vancomycin-resistant") (enterococcus|"E.faecalis"|"E.faecium"|"e faecalis"|"e faecium") (save|savings|socioeconomic|socio-economic|unit-cost|value|"value-added")

(AB-Vancomycin-resistant or amplobac-resistant or balcorin-resistant or Diatracin-resistant or edicin-resistant or glycopeptide-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(icoplax-resistant or ifavac-resistant or lyphocin-resistant or tagocid-resistant or targocid-resistant or targosid-resistant or Teichomycin-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(Teichomycin-A2-resistant or Teicoplanint-resistant or vacsol-resistant or Vamysin-resistant or vanauras-resistant or vanaurus-resistant or vancam-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(vancamycin-resistant or vanccostacin-resistant or vanco-resistant or vanco-cell-resistant or vanco-saar-resistant or vanco-teva-resistant or vancocid-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(vancocin-resistant or vancocin-cp-resistant or vancocin-hcl-resistant or vancocin-hydrochloride-resistant or vancocina-resistant or vancocina-cp-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(vancocine-resistant or vancoled-resistant or vancomax-resistant or vancomicina-resistant or vancomycint-resistant or vancomycin-complex-resistant)(enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(vancomycin-hcl-resistant or vancomycin-hydrochloride-resistant or Vancomycin-ratiopharm-resistant or vancor-resistant or Vancoson-resistant) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

(Vancox-resistant|Vanmicina-resistant|vanmycin-resistant|vanococin-resistant|varedet-resistan) (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")

EDU Domain (Google.ca):

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) domain:.edu

((vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")) domain:.edu

PDF Search (Google.ca):

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) filetype:PDF

CDC Search (Google.ca):

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci)(cost effective|HTA|health technology assessment|evaluation|CER) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")(cost effective|HTA|health technology assessment|evaluation|CER) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (cost|"cost-avoidance"|cost-benefit|cost-control|cost-effectiveness|cost-estimate) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")(cost|"cost-avoidance"|cost-benefit|cost-control|cost-effectiveness|cost-estimate) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) ("cost-minimisation"|"cost-minimization"|cost-per|cost-saving|cost-to-charge|cost-utility) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") ("cost-minimisation"|"cost-minimization"|cost-per|cost-saving|cost-to-charge|cost-utility) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (cost-variable|disability adjusted life year|DALY|disease burden) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")(cost-variable|disability adjusted life year|DALY|disease burden) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci)(economic|economic-evaluation|evaluate|expenditure) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")(economic|economic-evaluation|evaluate|expenditure) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci)((expense|fee|fees|finance|financial|fiscal|fund) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium")(expense|fee|fees|finance|financial|fiscal|fund) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci)(funding|health spending|high-cost|ICER|"length of stay")site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") (funding|health spending|high-cost|ICER|"length of stay") site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (low-cost|"patient bed day"|"inpatient bed day"|paid) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") (low-cost|"patient bed day"|"inpatient bed day"|paid) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (pay|payment|pharmacoeconomic|pharmaco-economic|price) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") (pay|payment|pharmacoeconomic|pharmaco-economic|price) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (pricing|quality-adjusted life year|QALY|reimbursement|resource allocation) site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") (pricing|quality-adjusted life year|QALY|reimbursement|resource allocation) site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) ("resource use"|"resource utilisation"|"resource utilization") site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") ("resource use"|"resource utilisation"|"resource utilization") site:cdc.gov

(VRE | VREfm | vancomycin resistant enterococcus | vancomycin resistant enterococci) (save|savings|socioeconomic|socio-economic|unit-cost|value|"value-added") site:cdc.gov

(vancomycin-resistant | "vancomycin resistant") (enterococcus | "E.faecalis" | "E.faecium" | "e faecalis" | "e faecium") (save|savings|socioeconomic|socio-economic|unit-cost|value|"value-added") site:cdc.gov

A.2.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions

PHO Library Services searched three databases for peer reviewed publications for this rapid review:

Table 13: Rapid Reviews One, Two and Four Search Strategy for MEDLINE (1946 to October 6, 2017)

#	Searches	Results
1	(exp Enterococcus/ and Vancomycin Resistance/) or Vancomycin-Resistant Enterococci/ or (((vancomycin adj3 resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")) or VRE*).ab,ti,kw.	6794
2	Population surveillance/ or Public health surveillance/ or Public health informatics/ or Disease notification/ or Pattern Recognition, Automated/ or Hospitals, Isolation/ or Patient isolation/ or Quarantine/ or Mass screening/ or multiphasic screening/ or neonatal screening/ or (((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) adj2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* adj1 shar*) or roommate* or surveill* or screen* or ((barrier or contact) adj precaution*)).ab,ti,kw.	988057
3	1 and 2	1551
4	animals/ not (humans/ and animals/)	4640441
5	3 not 4	1510
6	limit 5 to (yr="2012 -Current" and english)	504

Table 14: Rapid Reviews One, Two and Four Search Strategy for Embase (1974 to October 3, 2017)

#	Searches	Results
1	Disease surveillance/ or health survey/ or disease notification/ or automated pattern recognition/ or medical informatics/ or mass screening/ or screening/ or isolation/ or contact isolation/ or isolation facility/ or patient isolation/ or isolation hospital/ or isolation facility/ or quarantine/ or (cohorting or segregat* or containment or (room* adj1 shar*) or roommate* or ((barrier or contact) adj precaution*)).ab,ti,kw.	539831
2	vancomycin resistant enterococcus/ or vancomycin intermediate staphylococcus aureus/ or vancomycin resistant enterococcus/ or vancomycin susceptible staphylococcus aureus/	4876
3	1 and 2	531
4	limit 3 to (english language and yr="2012 -Current")	294

Table 15: Rapid Reviews One, Two and Four Search Strategy for CINAHL (up to October 6, 2017)

#	Searches	Results
S1	(MH "Enterococcus") OR (MH "Enterococcus Faecium")	1401
S2	(MH "Vancomycin Resistance")	1168
S3	S1 AND S2	412
S4	(MH "Vancomycin Resistant Enterococci")	152
S5	TI ((((vancomycin N3 resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")) or VRE*)) OR AB ((((vancomycin N3 resistan*) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium")) or VRE*))	1319
S6	S3 OR S4 OR S5	1434
S7	TI ((((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) N2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* N1 shar*) or roommate* or surveill* or screen* or ((barrier or contact) N1 precaution*))) OR AB ((((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) N2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* N1 shar*) or roommate* or surveill* or screen* or ((barrier or contact) N1 precaution*)))	150583
S8	(MH "Disease Surveillance") OR (MH "Population Surveillance") OR (MH "Medical Informatics") OR (MH "Biosurveillance") OR (MH "Patient Isolation") OR (MH "Quarantine") OR (MH "Health Screening")	56957
S9	S7 OR S8	178824
S10	S6 AND S9	488
S11	S10 Limiters - Published Date: 20120101-; English Language	175

A.2.4 Rapid Review Two: Do Active Screening and Isolation Programs Reduce Incidence of VRE Colonization and Infection

The databases searched and the search strategies for this rapid review were the same as those for A.2.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions.

A.2.5 Rapid Review Three: Harms Are Associated With Contact Precautions

PHO Library Services searched four databases for peer reviewed publications for this rapid review:

Table 16: Rapid Review Three Search Strategy for MEDLINE (1946 to October 6, 2017)

#	Searches	Results
1	Patient isolation/ or Quarantine/ or (((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) adj2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* adj1 shar*) or roommate* or ((barrier or contact) adj precaution*)).ab,ti,kw.	121353
2	"Quality of Life"/ or Stress, Psychological/ or mental health/ or anxiety/ or depression/ or patient satisfaction/ or Treatment outcome/ or Mortality/ or morbidity/ or (((mental or psychological) adj3 (impact* or health or distress or effect or stress*)) or anxiety or depressed or (depressive adj2 (episode* or state)) or depression or wellbeing or well-being or "treatment outcome*" or "quality of life" or "length of stay" or readmit* or readmission or ((death* or fatal* or mortalit* or morbidit*) adj2 (number* or rate* or statistics))).ab,ti,kw.	2066294
3	Disease Transmission, Infectious/pc or (Methicillin Resistance/ and staphylococcus aureus/) or methicillin-resistant staphylococcus aureus/ or Clostridium difficile/ or (exp Enterococcus/ and Vancomycin Resistance/) or Vancomycin-Resistant Enterococci/ or (((vancomycin adj3 (intermediate or resistan*)) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or staph*)) or VRE* or AROs or "C diff*" or "clostridium difficile*" or CDAD or ARO or AROs or MRSA or VISA or VRSA or (methicillin-resistan* adj2 staph*) or (carbapen* adj3 (Enterobacteriaceae or organism*)) or CPE or CPO or CRE or ESBL or "extended spectrum B-lactamase producing Enterobacteriaceae" or "Klebsiella pneumonia" or super bug* or superbug* or ((multi-drug-resistan* or drug-resistan* or antimicrobial-resist* or antibiotic-resistan*) adj5 (infection* or organism*))).ab,ti,kw.	91533
4	1 and 2 and 3	264
5	limit 4 to (yr="2008 -Current" and english)	171

Table 17: Rapid Review Three Search Strategy for Embase (1974 to October 3, 2017)

#	Searches	Results
1	isolation/ or contact isolation/ or isolation facility/ or patient isolation/ or isolation hospital/ or isolation facility/ or quarantine/ or (cohorting or segregat* or containment or (room* adj1 shar*) or roommate* or ((barrier or contact) adj precaution*)).ab,ti,kw.	89856
2	"quality of life"/ or psychological well-being/ or mental health/ or wellbeing/ or fear/ or anxiety/ or mood disorder/ or depression/ or anxiety disorder/ or "mixed anxiety and depression"/ or panic/ or mental stress/ or patient satisfaction/ or treatment outcome/ or clinical outcome/ or critical care outcome/ or disease free interval/ or patient-reported outcome/ or treatment failure/ or morbidity/ or mortality rate/ or hospital mortality/ or mortality/ or "length of stay"/	2690047
3	disease transmission/pc or bacterial transmission/pc or methicillin resistant Staphylococcus aureus/ or vancomycin intermediate staphylococcus aureus/ or vancomycin resistant enterococcus/ or vancomycin susceptible staphylococcus aureus/ or peptoclostridium difficile/ or (AROs or "C diff*" or "clostridium difficile*" or CDAD or ARO or AROs or (carbapen* adj3 (Enterobacteriaceae or organism*)) or CPE or CPO or CRE or ESBL or "extended spectrum B-lactamase producing Enterobacteriaceae" or "Klebsiella pneumonia" or super bug* or superbug* or ((multi-drug-resistan* or drug-resistan* or antimicrobial-resist* or antibiotic-resistan*) adj5 (infection* or organism*))).ab,ti,kw.	116025
4	1 and 2 and 3	252
5	limit 4 to (english language and yr="2008 -Current")	217

Table 18: Rapid Review Three Search Strategy for PsycINFO (1806 to October Week 1, 2017)

#	Searches	Results
1	Social isolation/ or Patient seclusion/ or (((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) adj2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* adj1 shar*) or roommate* or ((barrier or contact) adj precaution*)).ab,ti,id.	23391
2	"depression (emotion)"/ or major depression/ or sadness/ or separation reactions/ or anxiety/ or anxiety disorders/ or fear/ or generalized anxiety disorder/ or panic/ or panic attack/ or stress/ or mortality rate/ or "quality of life"/ or well being/ or treatment outcomes/ or "remission (disorders)"/ or "side effects (treatment)"/ or treatment duration/ or treatment termination/ or (((mental or psychological) adj3 (impact* or health or distress or effect or stress*)) or anxiety or depressed or (depressive adj2 (episode* or state)) or depression or wellbeing or well-being or "treatment outcome*" or "quality of life" or "length of stay" or readmit* or readmission or ((death* or fatal* or mortalit* or morbidit*) adj2 (number* or rate* or statistics))).ab,ti,id.	691814
3	infectious disorders/ or exp bacterial disorders/ or Treatment resistant disorders/ or (((vancomycin adj3 (intermediate or resistan*)) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or staph*)) or VRE* or AROs or "C diff*" or "clostridium difficile*" or CDAD or ARO or AROs or MRSA or VISA or VRSA or (methicillin-resistan* adj2 staph*) or (carbapen* adj3 (Enterobacteriaceae or organism*)) or CPE or CPO or CRE or ESBL or "extended spectrum B-lactamase producing Enterobacteriaceae" or "Klebsiella pneumonia" or super bug* or superbug* or ((multi-drug-resistan* or drug-resistan* or antimicrobial-resist* or antibiotic-resistan*) adj5 (infection* or organism*))).ab,ti,id.	13017
4	1 and 2 and 3	32
5	limit 4 to (english language and yr="2008 -Current")	19

Table 19: Rapid Review Three Search Strategy for CINAHL (up to October 6, 2017)

#	Searches	Results
S1	(MH "Disease Transmission/PC") OR (MH "Clostridium Difficile") OR (MH "Methicillin-Resistant Staphylococcus Aureus") OR ((MH "Staphylococcus Aureus") AND (MH "Methicillin Resistance")) OR (MH "Vancomycin Resistant Enterococci") OR ((MH "Vancomycin Resistance") AND ((MH "Enterococcus") OR (MH "Enterococcus Faecium")))	9314
S2	TI ((((vancomycin N3 (intermediate or resistan*)) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or staph*)) or VRE* or AROs or "C diff*" or "clostridium difficile*" or CDAD or ARO or AROs or MRSA or VISA or VRSA or (methicillin-resistan* N2 staph*) or (carbapen* N3 (Enterobacteriaceae or organism*)) or CPE or CPO or CRE or ESBL or "extended spectrum B-lactamase producing Enterobacteriaceae" or "Klebsiella pneumonia" or super bug* or superbug* or ((multi-drug-resistan* or drug-resistan* or antimicrobial-resist* or antibiotic-resistan*) N5 (infection* or organism*)))) OR AB ((((vancomycin N3 (intermediate or resistan*)) and (enterococc* or "E.faecalis" or "E.faecium" or "e faecalis" or "e faecium" or staph*)) or VRE* or AROs or "C diff*" or "clostridium difficile*" or CDAD or ARO or AROs or MRSA or VISA or VRSA or (methicillin-resistan* N2 staph*) or (carbapen* N3 (Enterobacteriaceae or organism*)) or CPE or CPO or CRE or ESBL or "extended spectrum B-lactamase producing Enterobacteriaceae" or "Klebsiella pneumonia" or super bug* or superbug* or ((multi-drug-resistan* or drug-resistan* or antimicrobial-resist* or antibiotic-resistan*) N5 (infection* or organism*))))	15553
S3	S1 OR S2	18832
S4	(MH "Quarantine") OR (MH "Patient Isolation")	2442
S5	TI ((((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) N2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* N1 shar*) or roommate* or ((barrier or contact) N1 precaution*))) OR AB ((((contact or home or hospital* or patient* or precaution* or resident* or room* or unit* or ward*) N2 isolat*) or cohorting or quarantin* or segregat* or containment or (room* N1 shar*) or roommate* or ((barrier or contact) N1 precaution*)))	12417
S6	S4 OR S5	14001
S7	(MH "Quality of Life") OR (MH "Stress, Psychological") OR (MH "Mental Health") OR (MH "Anxiety") OR (MH "Depression") OR (MH "Patient Satisfaction") OR (MH "Treatment Outcomes+") OR (MH "Mortality") OR (MH "Hospital Mortality") OR (MH "Morbidity")	500261

#	Searches	Results
S8	TI ((((mental or psychological) N3 (impact* or health or distress or effect or stress*)) or anxiety or depressed or (depressive N2 (episode* or state)) or depression or wellbeing or well-being or "treatment outcome*" or "quality of life" or "length of stay" or readmit* or readmission or ((death* or fatal* or mortalit* or morbidit*) N2 (number* or rate* or statistics)))) OR AB ((((mental or psychological) N3 (impact* or health or distress or effect or stress*)) or anxiety or depressed or (depressive N2 (episode* or state)) or depression or wellbeing or well-being or "treatment outcome*" or "quality of life" or "length of stay" or readmit* or readmission or ((death* or fatal* or mortalit* or morbidit*) N2 (number* or rate* or statistics))))	325 908
S9	S7 OR S8	679 507
S10	S3 AND S6 AND S9	161
S11	S10 Limiters - Published Date: 20080101-; English Language	122

A.2.6 Rapid Review Four: Individual vs Regional VRE Control Practices

The databases searched and the search strategies for this rapid review were the same as those for A.2.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions.

Appendix 3: Criteria for Literature Inclusion and Exclusion

A.3.1 Systematic Review One: VRE and VSE Bacteremia Outcomes

The following criteria were developed a priori for selecting studies for data extraction for this systematic review:

A.3.1.1 INCLUSION CRITERIA

- study populations: patients within hospital settings, including hospitals: acute teaching, community health centres, and tertiary care[175]
- interventions: cases of VRE bacteremia, which is defined as a laboratory-confirmed bloodstream infection with VRE strains *E. faecium* or *E. faecalis* (that have a minimum inhibitory concentration to vancomycin of ≥ 32 mcg/mL, and contain *vanA* or *vanB* resistance genes), or a VRE bacteremia as defined within the primary study of interest. A glycopeptide-resistant enterococci (GRE) bacteremia will be synonymous to a VRE bacteremia.[175]
- comparisons: cases of VSE bacteremia[175]
- outcomes:
    - primary outcome: all-cause in-hospital mortality[28]
    - Secondary outcomes: bacteremia-attributable mortality, total hospital length of stay, total ICU length of stay, post-VRE– or VSE bacteremia diagnosis hospital length of stay, post-VRE– or VSE bacteremia diagnosis ICU length of stay. If a composite of the outcomes listed earlier is reported, that composite will also be taken into account.[28]
- study types: randomized controlled trials, observational studies (i.e., cohort studies, case-control studies, cross-sectional studies, and ecologic studies). The reference lists of all relevant reviews, letters to the editor, case-series, case reports, and commentaries captured by the title and abstract scan will be reviewed to identify additional primary research studies that meet the inclusion criteria.[175]
    - Grey literature will be scanned for conference abstracts, surveillance and recommendation from various infection prevention and control authorities:[174,175]
        - Association of Medical Microbiology and Infectious Disease Canada (AMMI)
        - Association for Professionals in Infection Control and Epidemiology (APIC)
        - Asia-Pacific Society of Infection Control (APSIC)
        - International Conference on Anti-Microbial Research (ICAR)
        - Infectious Disease Society of America (IDSA)
        - International Federation for Infection Control (IFIC)
        - Infection Prevention and Control Canada (IPAC Canada)
        - Infection Prevention Society (IPS)
        - Healthcare Infection Society (HIS)
        - Society for Healthcare Epidemiology of America) SHEA

- publication range: primary research articles matching the above criteria, published in English between January 1997 and February 2014. Articles published after January 1997 that include data collected prior to 1997 will be excluded.[175]
    - This time frame is meant to capture the advent of effective treatment for VRE bacteremias (quinupristin-dalfopristin, linezolid, daptomycin, tigecycline, teicoplanin and telavancin), including compassionate use and study. Penicillin, ampicillin, amikacin, streptomycin, chloramphenicol, doxycycline, rifampin, imipenem-cilastatin, and nitrofurantoin were not considered effective treatments for VRE.[28,175]
    - Studies analyzing data collected between January 1997 and January 2000 were excluded if the antibiotics used for the treatment of VRE bacteremia patients were not reported or could not be obtained by contacting study authors.[28]
    - Studies conducted after January 2000 were assumed to have administered effective VRE treatment(s) and will be included.[28]

A.3.1.2 EXCLUSION CRITERIA

- not in English
- published before January 1997
- narrative reviews, case series, case reports, commentaries
- not meeting criteria in A.3.1.1 Inclusion Criteria

A.3.2 Systematic Review Two: Economic Evaluations of VRE Control Interventions

The following criteria were developed a priori for selecting studies for data extraction for this systematic review:

A.3.2.1 INCLUSION CRITERIA

- study types: full economic evaluations (cost-effectiveness analysis, cost-utility analysis, cost-benefit analysis) based on primary study data. Full economic evaluations are defined as the comparative analysis of alternative course of action in terms of both costs (resource use) and consequences (outcomes, effects).[176]
- articles: peer-reviewed primary literature and primary study data reported within Letters to Editor; reviews will be scanned for references.
- study populations: any individuals seeking health care services in hospital settings (e.g., tertiary care hospitals, acute teaching hospitals, community health centres, community hospitals.)
- interventions: any intervention intended or found to control the transmission of VRE among study populations. VRE control interventions included traditionally recommended VRE control practices, routine infection prevention and control practices, and any interventions proposed as alternatives to traditionally recommended VRE control practices.

- comparisons: studies must contain a comparator for the reported VRE control intervention, and can be the absence of the said intervention (e.g., historical control data), an alternative intervention, routine infection prevention and control practices, or standard patient car.
- outcomes measures: full economic analysis outcomes, i.e., cost-effectiveness, cost-benefit, or cost-utility analyses. Costs related to intervention resources, costs related to benefit/gain post intervention (e.g., colonizations or infections prevented, life years, quality adjusted life years, length of stay) must be explicitly compared and reported.
- date of publication: articles published after January 1985 (since the first isolation of VRE),[177] and conference publications in the five years prior to this systematic review.
- published in English
- grey literature sources to capture relevant research in progress and primary literature not captured by the database search:
    - International sources:
      International Consortium for Prevention and Infection Control (ICPIC), International Congress on Infectious Diseases (ICID), Congress of the International Federation of Infection Control (IFIC), International Union of Microbiological Societies (IUMS) (Bacteriology, Virology and Mycology), International Health Economics Association (iHEA), International Society for Pharmacoeconomics and Outcomes Research (ISPOR), Society for Medical Decision Making (SMDM), Health Technology Assessment International (HTAi)
    - North American sources:
      US-based organizations: Agency for Healthcare Research and Quality, American Industrial Hygiene Association, American Society for Healthcare Risk Management (ASHRM), Association for Professionals in Infection Control and Epidemiology (APIC), American Society for Microbiology (ASM), Infectious Diseases Society of America (IDSA), Society for Healthcare Epidemiology of America (SHEA), Healthcare Infection Control Practices Advisory Committee (HICPAC)
      Canada-based organizations: Association of Medical Microbiology and Infectious Disease Canada (AMMI/Can), Canadian Association for Clinical Microbiology and Infectious Diseases (CACMID), Infection Prevention and Control (IPAC) Canada (formerly CHICA), Canadian Association for Drugs and Technologies in Health (CADTH), Ontario Health Technology Advisory Committee (OHTAC), Provincial Infectious Disease Advisory Committee (PIDAC)—The Ontario Public Health Convention (TOPHC) infection prevention and control content, Health Quality Ontario (HQO), Infection Prevention and Control Canada (IPAC Canada), Institute of Health Economics (IHE/Canada), Canadian Association of Health Services and Policy (CAHSPR)
    - Asian sources:
      International Congress of the Asia Pacific Society of Infection Control (APSIC), Hong Kong Infection Control Nurses' Association (HKICNA), National Evidence-based healthcare Collaborating Agency, KOREA
    - Australian and New Zealand sources:
      Australian Infection Control Association (AICA), Australian College for Infection

Prevention and Control (ACIPC), Australasian Society for Infectious Diseases (ASID), The Australian Society for Microbiology, Australian Health Economics Society (AHES), Medical Services Advisory Committee (MASC), Health Policy Advisory Committee on Technology (HealthPACT), New Zealand National Health Committee (NHC), New Zealand Health Technology Assessment (NZHTA)

- European sources:
  European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), European Health Economics Association (EuHEA), UK Health Tec, European Committee on Infection Control (EUCIC), Healthcare Infection Society (HIS/UK), Infection Prevention Society (IPS/UK), National Institute for Healthcare Excellence (NICE/UK), National Institute for Health Research (NIHR/UK), Health Information and Quality Authority (HIQA/Ireland), Belgian Federal Health Care Knowledge Centre (KCE/Belgium), Danish Centre for Health Technology Assessment (DACEHTA/Denmark), Agency for Health Technology Assessment in Poland (AHTApol), Norwegian Knowledge Centre for the Health Services (NOKC/Norway), Swedish Council on Technology Assessment in Health Care (SBU), Comité d´Evaluation et de Diffusion des Innovations Technologiques (CREDIT/France), The Netherlands Organization for Health Research and Development (ZonMw /The Netherlands)

A.3.2.2 EXCLUSION CRITERIA

- study types: opinions, commentary, and those not listed in A.3.2.1 Inclusion Criteria
- not peer-reviewed
- not published in English A search without language restrictions was also run, and the number and types of articles that would be excluded from the review due to language restrictions was assessed to gain insight in possible language bias.
- comparator data not informed by primary study or historical site data (i.e., solely derived from literature reviews or data modeling processes)
- not conducted among the study population in A.3.2.1 Inclusion Criteria
- interventions not directly related to the transmission or control of VRE, and interventions without any economic analysis.

A.3.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions

The following criteria developed a priori were used to select studies for data extraction for this rapid review:

A.3.3.1 INCLUSION CRITERIA

- study types: randomized controlled trials, cohort, cross-sectional, case-control, case series, ecological studies
- published in English from 2012 to September 2017, and prior to 2012 if not already captured in PIDAC's 2012 *Review of Literature for Evidence - Based Best Practices for VRE Control*
- no geographical restriction
- has VRE-specific outcomes (colonization rate, infection rate)
- in acute care and long-term care settings, including retirement homes, nursing homes, community care

A.3.3.2 EXCLUSION CRITERIA

- study types: systematic review and meta-analysis (but will check references)
- already captured in PIDAC's 2012 *Review of Literature for Evidence - Based Best Practices for VRE Control*
- published in languages other than English
- does not have VRE-specific outcomes

A.3.4 Rapid Review Two: Do Active Screening and Isolation Programs Reduce Incidence of VRE Colonization and Infection

Literature retrieved for this rapid review was selected for data extraction based on the same criteria as for A.3.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions.

A.3.5 Rapid Review Three: Harms Are Associated With Contact Precautions

The following criteria developed a priori were used to select studies for data extraction for this rapid review:

A.3.5.1 INCLUSION CRITERIA

- study types: randomized controlled trials, cohort, cross-sectional studies
- published in English
- addresses psychological patient outcomes of patients on Contact Precautions or under isolation precautions
- addresses health care provider behaviour or interactions with patients on Contact Precautions or under isolation precautions
- in acute care and long-term care settings, including retirement homes, nursing homes, community care

A.3.5.2 EXCLUSION CRITERIA

- study types: qualitative studies
- published in languages other than English

A.3.6 Rapid Review Four: Individual vs Regional VRE Control Practices

The following criteria developed a priori were used to select studies for data extraction for this rapid review:

A.3.6.1 INCLUSION CRITERIA

- study types: randomized controlled trials, cohort, cross-sectional, case-control, case series, ecological studies
- published in English from 2012 to September 2017, and prior to 2012 if not already captured in PIDAC's 2012 *Review of Literature for Evidence - Based Best Practices for VRE Control*
- no geographical restriction
- has VRE-specific outcomes (colonization rate, infection rate)
- in acute care and long-term care settings, including retirement homes, nursing homes, community care
- comparison between individual and regional VRE control practices are described
- outcomes for individual and regional VRE control practices are described

A.3.6.2 EXCLUSION CRITERIA

- study types: systematic review and meta-analysis (but will check references)
- already captured in PIDAC's 2012 *Review of Literature for Evidence - Based Best Practices for VRE Control*
- published in languages other than English
- does not have VRE-specific outcomes
- no specific outcomes on individual vs regional VRE control practices

Appendix 4: Evidence Tables

A.4.1 Systematic Review One: VRE and VSE Bacteremia Outcomes

Table 20: Study Design of Articles for Systematic Review One[174]

Study Design	Author	Study Period	Location	Pt. Population	Sample Size: VRE	Sample Size: VSE
Cohort	Bar et al.[129]	Nov 2000 to Dec 2002	Richmond, USA	Adult	17	33
Cohort	Bilington et al.[130]	2000 to 2008[A]	Calgary, Canada	Mixed	27	640
Cohort	Butler et al.[167]	Jan 2002 to Dec 2003	St. Louis, USA	Adult, non-surgical, > 2 days LOS	94	182
Cohort	Cheah et al.[127]	Jan 2002 to Mar 2010	Victoria, Australia	Adult, > 2 days LOS	116	116
Cohort	Cho et al.[128]	July 2009 to Dec 2011	Seoul, Korea	Adult, neutropenia post CHEMO or SCT	24	67
Cohort	da Silva et al.[178]	Sep 1998 to Dec 2008	Sao Jose do Rio Preto, Brazil	Mixed	30[C]	273[C]
Cohort	Haas et al.[179]	2001 to 2006	Philadelphia, USA	Pediatrics	39	300
Cohort	Marschall et al.[131]	Jan 2006 to Dec 206	St. Louis, USA	Adult, CVC-associated bacteremia	67	39
Cohort	Mikulska et al.[180]	2004 to 2011[A]	Genoa, Italy	Adult, allogeneic HSCT	9	58
Cohort	Mohr et al.[181]	Jan 2000 to Dec 2009	58 sites, USA	Mixed[B], dap Tx.	151	211
Cohort	Vydra et al.[182]	Jan 2004 to Dec 2008	Minneapolis, USA	Mixed, HSCT	50	43
Cohort	Yoo et al.[183]	Jan 2000 to Dec 2001	Seoul, Korea	Adult, HSCT or cytotoxic CHEMO	19[D]	8
Case-control	Peel et al.[184]	Jan 2000 to Dec 2009	Victoria, Australia	Adult	80	360

Abbreviations: Pt.= patient; LOS = length of stay; HSCT= hematopoietic stem cell transplantation; CHEMO= chemotherapy; dap Tx = daptomycin treatment; CVC = central venous catheter; SCT = stem cell transplantation

A Months not reported.
B Assumed to be mixed, unconfirmed due to demographics being reported as <30 years of age.
C Data obtained by contacting study authors.
D 8 VRE patients received VRE therapies and included in the review.

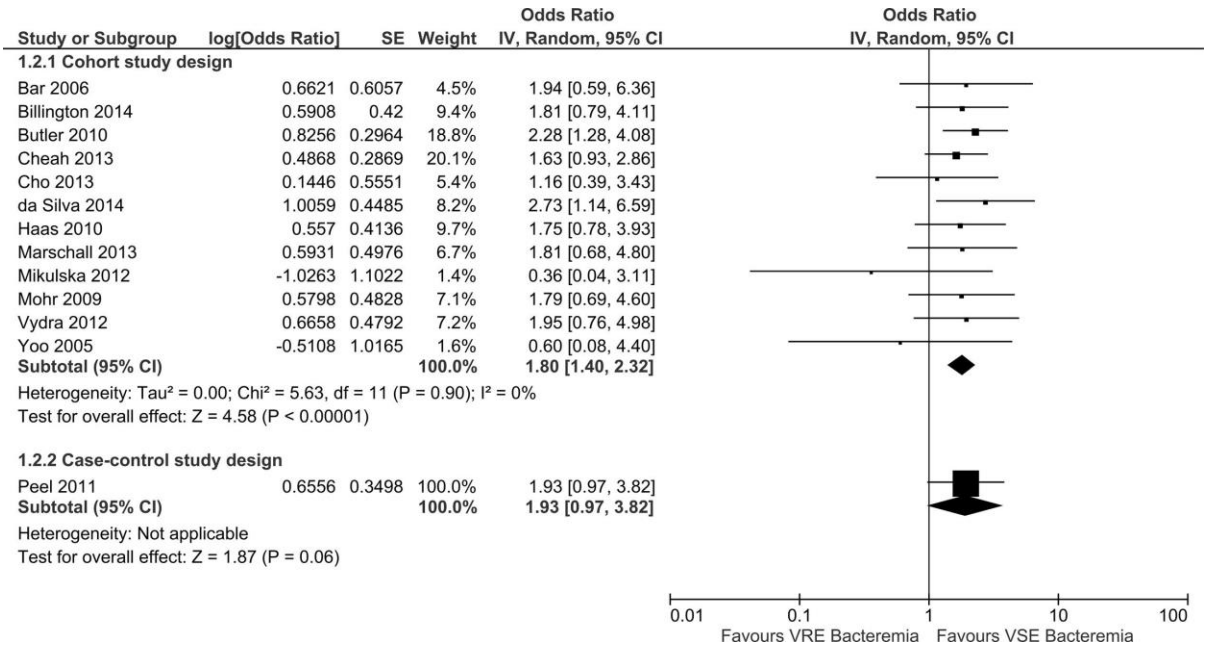
Table 21: Assessment of Study Quality for Systematic Review One Based on the Newcastle-Ottawa Scale Star System[174]

Author	Selection	Comparability[A]	Outcome/Exposure	Total Stars
Bar et al.[129]	****		***	7
Bilington et al.[130]	****		***	7
Butler et al.[167]	****		***	7
Cheah et al.[127]	****	**	***	9
Cho et al.[128]	***	**	***	8
da Silva et al.[178]	****		***	7
Haas et al.[179]	***		***	6
Marschall et al.[131]	***		***	6
Mikulska et al.[180]	**		**	4
Mohr et al.[181]	****		***	7
Vydra et al.[182]	***		***	6
Yoo et al.[183]	***		***	6
Peel et al.[184]	***		***	6

The Newcastle-Ottawa Scale was used to establish quality of evidence within nonrandomized cohort or case control studies, via a 9-star system; a study awarded a greater number of stars is considered to be of higher methodological study quality.[185]

A Illness severity and comorbid conditions were selected as the most important factors when assessing comparability.

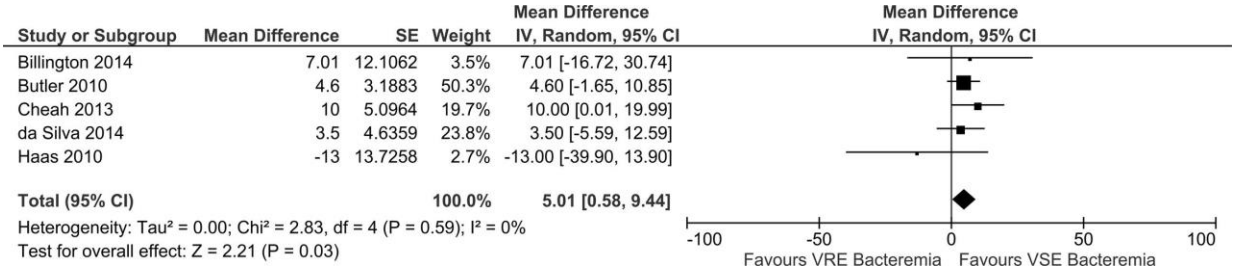
Figure 2: VRE and VSE Bacteremia Unadjusted In-Hospital Mortality Risk by Study Design[28]



Results of included studies for VRE and VSE bacteremia unadjusted in-hospital mortality risk stratified by study design.

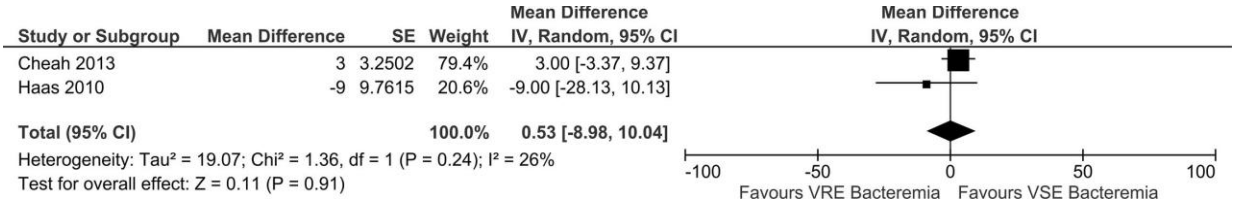
Abbreviations: 95% CI = 95% confidence interval; SE = standard error; IV = random, inverse variance random effects method.

Figure 3: VRE and VSE Bacteremia Total Hospital Length of Stay Mean Difference[28]



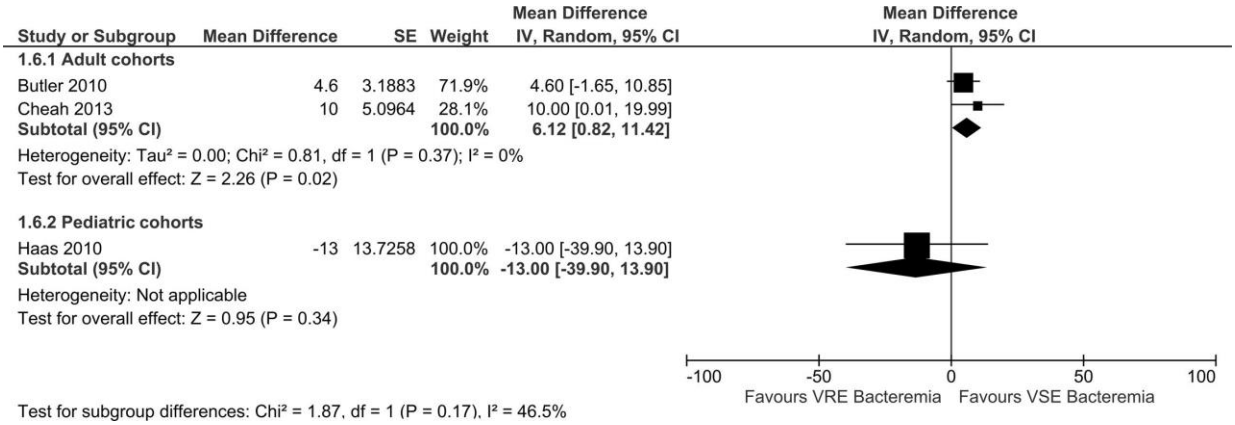
Results of studies reporting on VRE and VSE bacteremia total hospital LOS.
Abbreviations: 95% CI = 95% confidence interval; SE = standard error; IV= random, inverse variance random effects method.

Figure 4: VRE and VSE Post-Bacteremia Total Hospital Length of Stay Mean Difference[28]



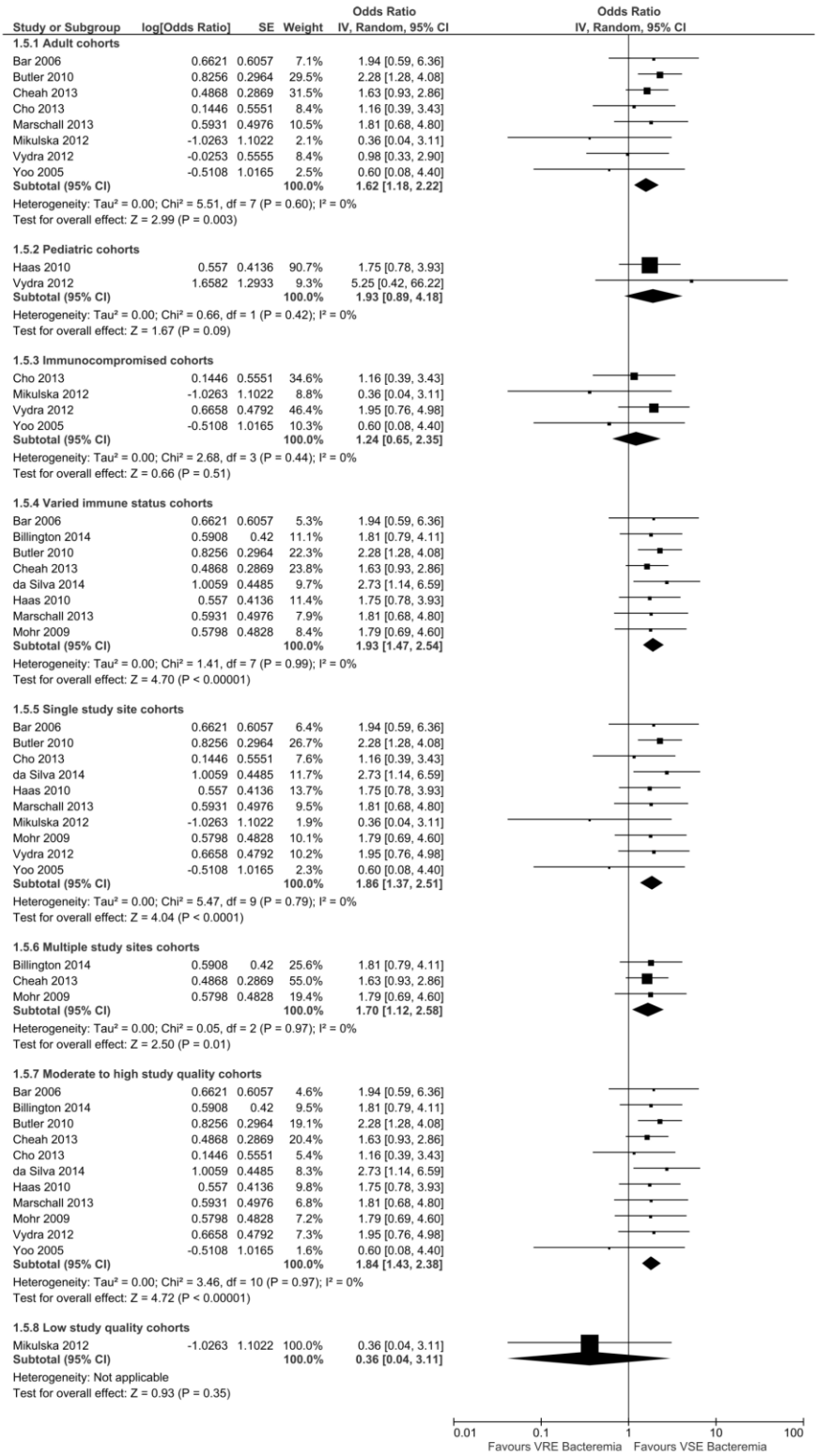
Results of studies reporting on VRE and VSE post-bacteremia hospital LOS.
Abbreviations: 95% CI= 95% confidence interval; SE = standard error; IV= random, inverse variance random effects method.

Figure 5: Subgroup Analysis of VRE and VSE Bacteremia Hospital Length of Stay by Age, for Each Included Cohort Study Reporting These Data[28]



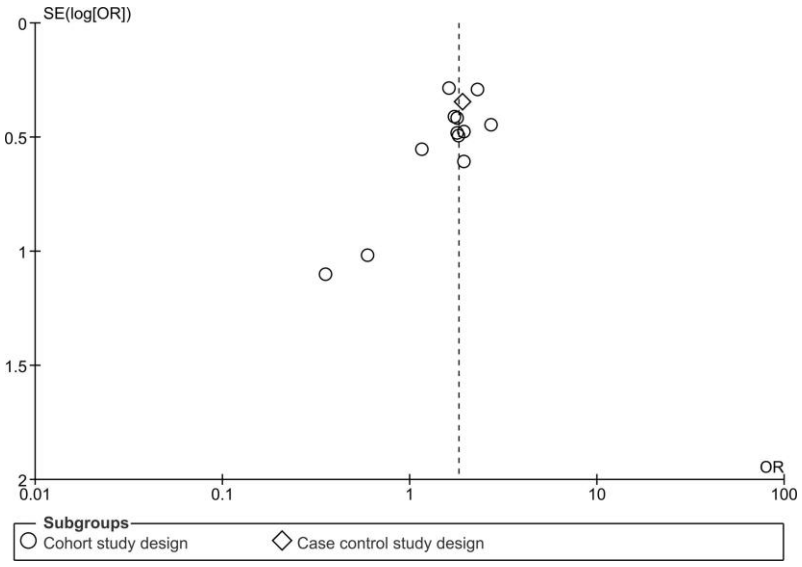
Abbreviations: 95% CI = 95% confidence interval; SE = standard error; IV= random, inverse variance random effects method.

Figure 6: Subgroup Analysis of VRE and VSE Bacteremia Unadjusted In-Hospital Mortality Risk by Age, Immune Status, Study Site(s), and Study Quality, for Each Included Cohort Study Reporting These Data[28]



Abbreviations: 95% CI = 95% confidence interval; SE = standard error; IV = random, inverse variance random effects method.

Figure 7: Asymmetrical Funnel Plot of VRE and VSE Bacteremia In-Hospital Mortality Effect Estimates of All Included Studies[28]



A.4.2 Systematic Review Two: Economic Evaluations of VRE Control Interventions

The studies selected and data extracted for systematic review two are summarized in Table 22 below.

Table 22: Study Design and Results of Studies for Systematic Review Two

Author	Study Time Frame (m/d/yy)	Setting and Location	VRE Control Intervention(s)	Comparison	Trial- or Model-based	Sensitivity Analysis Performed	Cost-Effectiveness of VRE Control Practices
Bodily et al.[67]	1/1/09-12/31/11	Entire hosp. US: Saint Louis, MO	Reflex testing	Discontinuation of reflex testing	Trial-based	No	Reflex testing cost-effective
Bryce et al.[65]	4/1/07-3/31/15	Entire hosp. Canada: Vancouver, BC	Screening/isolation	Discontinuation of screening/isolation, replaced with general EC and AMS programs	Trial-based	No	Not cost-effective (EC and AMS strategies more cost-effective)
Everett et al.[186]	1/1/09-6/30/11	Entire hosp. US: Riverside, CA	Comprehensive EC intervention	Period before the intervention (different practices)	Trial-based	No, but used the low estimate for costs (also presented the high estimate)	Cost-effective
Hendrix et al.[187]	6/1/96-8/31/96	Entire hosp. US: Baltimore, MD	Several alternative surv. strategies (e.g. admission + twice weekly, or only on admission)	Alternative surv. strategies were compared to each other	Trial-based	No	Admission + twice weekly rectal screening most cost-effective

Author	Study Time Frame (m/d/yy)	Setting and Location	VRE Control Intervention(s)	Comparison	Trial- or Model-based	Sensitivity Analysis Performed	Cost-Effectiveness of VRE Control Practices
Lee et al.[171]	n/a (informed by 2001 data)	Entire hosp. US: Chicago, IL	Current surv. strategy (screening of high-risk areas, transfers)	2 alternative surv. strategies (current strategy + either renal pts or pts with prior hospitalizations)	Model-based	For several parameters	Current strategy + screening pts with previous hospitalizations most cost-effective
Martin et al.[64]	7/1/13-6/30/15	2 entire hosps. US: California	CP, CHG bathing in ICUs	Discontinuation of CP for VRE/MRSA, expansion of CHG bathing to all units	Trial-based	No	Not cost-effective (CHG more cost-effective)
Montecalvo et al.[188]	11/1/93-6/30/95	Entire hosp. US: Westchester, NY	15-component infection control strategy, including active surv./isolation, AMS, hand hygiene, glove/gown use, and more	Active surv., contact isolation	Trial-based	For several parameters	Cost-effective
Morgan et al.[189]	8/30/07-10/30/09	Med. & surg. acute care units in 1 hosp. US: Baltimore, MD	Targeted active surv.	Universal active surv.	Trial-based	No	Targeted active surv. more cost-effective
Muto et al.[170]	1/1/95-12/31/96	Entire hosp. US: Virginia	Active surv., contact isolation	No active surv. or contact isolation	Trial-based	No	Cost-effective
Mutters et al.[190]	6/1/12-12/31/14	Entire hosp. Germany: Heidelberg	Active surv., isolation	Hypothetical scenario with no surv.	Trial-based	For transmission rate of MDROs	Cost-effective
Puzniak et al.[191]	7/1/97-12/31/99	19-bed MICU US: Saint Louis, MO	Gowns combined with isolation precautions	Discontinuation of gown use for pts in isolation precautions	Trial-based	For several parameters	Cost-effective if 7 cases of colonization are avoided
Shadel et al.[39]	2/1/97-12/31/99	19-bed MICU US: Saint Louis, MO	CAS	LAS	Trial-based	For several parameters	CAS cost-effective vs. LAS

Abbreviations: AMS=antimicrobial stewardship; CAS = clinical active surveillance; CHG=chlorhexidine gluconate; CP = Contact Precautions; EC=environmental cleaning; hosp(s). = hospital; ICU=intensive care unit; LAS = Laboratory-based active surveillance; med. = medical; MICU=medical intensive care unit; MRSA=methicillin-resistant *Staphylococcus aureus*; pt(s.) = patient(s); SICU=surgical intensive care unit; surg. = surgical; surv. = surveillance; VRE=vancomycin-resistant enterococci

A.4.3 Rapid Review One: Trends in VRE Infection and Colonization Rates After Discontinuation of Screening, Contact Precautions

The studies selected and data extracted for rapid review one are summarized in Table 23 and Table 24 below.

Table 23: Study Design of Articles for Rapid Review One

Article	Setting	Duration (Pre-intervention; Intervention)	Pre-intervention practices	Intervention period practices
Bardossy et al.[71]	800-bed hospital (Michigan)	12 m; 12 m	No act. surv.; C/isolation	no act. surv. nor C/isolation
Gandra et al.[69]	779-bed hospital (Massachusetts)	12 m; 12 m	Act. surv. in ICU; C/isolation	C/isolation discontinued; act. surv. continued
Martin et al.[64]	540-bed and 265-bed hospitals (California)	12/6 m (hospitals A/B); 12 m	Screening (high-risk pts); C/isolation	C/isolation discontinued
Rupp et al.[70]	689-bed hospital (Nebraska)	12 m; 12 m	No act. surv.; C/isolation	C/isolation discontinued except for pts with uncontained secretions
Edmond et al.[68]	865-bed hospital (Virginia)	15 m; 15 m	C/isolation for all pts with MDRO; no active screening	C/isolation discontinued (VRE and MRSA)
Bodily et al.; Munigala et al.[67,74]	1,250-bed hospital (Missouri)	18 m; 18 m, then 36 m	Reflex testing*; C/isolation	no reflex testing*; C/isolation reflex testing* resumed in Munigala et al.
Lemieux et al.[63]	2200-bed hospital (Ontario)	24 m; 18 m	Either universal or targeted surv. for VRE; C/isolation	all aspects of VRE control program discontinued
Bryce et al.[65]	728-bed hospital (British Columbia)	~6 y; 25 m	Act. surv. (hospital-wide); C/isolation	targeted act. surv. (only high-risk units); C/isolation
Almyroudis et al.[62]	125-bed hospital (New York)	36 m; 36 m	Act. surv.; C/isolation	no act. surv. nor C/isolation
Popiel et al.[66]	637-bed hospital (Québec)	~ 10 y; 36 m	Act. surv.; C/isolation; dedicated VRE cohort unit and staff	targeted screening; C/isolation; no more dedicated unit/staff

* reflex testing: any stool submitted to the laboratory for *Clostridium difficile* toxin testing from an inpatient was also tested for VRE, using selective media.
Abbreviations: act. surv. = active surveillance; C = Contact Precautions; ICU = intensive care unit; m = month; MDRO = multidrug-resistant organisms; pt(s) = patient(s); surv. = surveillance; y = year

Table 24: Results of Studies for Rapid Review One

Article	Relevant Outcomes Measured	Results of Discontinuation	Co-interventions/Confounders
Bardossy et al.[71]	VRE: CAUTIs, CLABSIs (measured SSIs, but not VRE-associated in either period)	↓ VRE CAUTI rates (not SS), equivalent CLABSI rates	Several potential confounders measured (e.g., HH compliance, ICU pt-to-nurse staffing levels)
Gandra et al.[69]	VRE infections and colonizations	Immediate ↑ in VRE rate, reverted to pre-intervention rate by end of 12 m	Not mentioned
Martin et al.[64]	VRE laboratory-identified clinical culture rates	Rate-ratio favoured C/isolation discontinuation (not SS)	Trained volunteers observed HH and PPE
Rupp et al.[70]	Hospital-onset VRE bacteremia	No SS difference in rate of hospital-onset VRE bacteremia	Tracked HH and EC; chlorhexidine bathing
Edmond et al.[68]	Device-related HAIs	No change in the rates of VRE device-associated infections	Not SS
Bodily et al.; Munigala et al.[67,74]	VRE-positive blood or urine cultures. HAI if > 48 hours after admission	Discontinuation: VRE rates ↑ by 71%; resumption: VRE rates ↓ to pre-discontinuation levels	No additional interventions targeting VRE
Lemieux et al.[63]	VRE infections/bacteremias	↑ in VRE infections and bacteremias in malignant hematology, ↓ in solid organ transplant	Some changes in antibiotic usage trends
Bryce et al.[65]	VRE bacteremia	Incidence rates stable	EC and AMS programs started around the time of intervention
Almyroudis et al.[62]	VRE bacteremia	Incidence rates stable	Not SS
Popiel et al.[66]	VRE infection and colonization	Dramatic ↑ in VRE colonizations and infections, eventually reaching a steady state	Not mentioned

Abbreviations: AMS = antimicrobial stewardship; C = Contact Precautions; CAUTI = catheter-associated urinary tract infection; CLABSI = central line-associated bloodstream infection; EC = environmental cleaning; HAI = health care-associated infections; HH = hand hygiene; ICU = intensive care unit; m = month; PPE = personal protective equipment; pt = patient; SS = statistically significant; SSI = surgical site infection

A.4.4 Rapid Review Two: Do Active Screening and Isolation Programs Reduce Incidence of VRE Colonization and Infection

The studies selected and data extracted for rapid review one are summarized in Table 25 and Table 26 below.

Table 25: Study Design of Articles for Rapid Review Two (with relevance to VRE)

Author	Design	Setting and Population	Duration	Intervention	Outcomes Measured
Derde[59]	ITS/C-RCT	Europe 13 adult ICUs; 8 countries Pts admitted to ICU ≥ 3 days, having ≥ 1 nasal, rectal or wound swab Phase 1: 1,962 pts Phase 2: 1,926 pts Phase 3: rapid screening—2,351 pts (7 hosp), conventional screening—2,280 pts (6 hosp)	May 2008-Apr 2011 Phase 1: 6-month baseline Phase 2: 6-month ITS study optimizing HH and universal daily body wash with chlorhexidine Phase 3: 12-15–month CRCT	Phases 1 and 2: Barrier precautious according to local isolation protocol. ICU personnel unaware of pts colonization status due to 2-month delay in surveillance culture results. Unclear whether screening on admission was performed. Phase 3: 1. Active surveillance within 2 days of ICU admission, then twice per week for 3 weeks, then weekly for pts staying at ICU ≥ 3 days; results released immediately. 2. CP for carriers identified. 3. Continuing from phase 2: HH improvement program from the WHO's 5 moments and universal daily body wash with chlorhexidine.	Primary outcome: incidence of VRE acquisition in ICU. Secondary outcomes: incidence density of ICU-acquired VRE colonization and bacteremia, compliance with HH, ICU and hospital LOS, 28-day mortality.
Mody[60]	C-RCT	Michigan, USA 12 NH with a mean of 137 beds each 418 residents: 203 (intervention), 215 (control)	May 2010-Apr 2013	Randomization was done on NH level. Only residents with feeding tubes or urinary catheters or both for ≥72 hours were included. Intervention group: 1. Pre-emptive barrier precautions. 2. Active surveillance for MDROs colonization at baseline, day 15, and monthly for up to 1 year, regardless of prior colonization status, with monthly data feedback to NH. 3. NH staff education on IPAC and HH Standard precautions and transmission-based precautions as needed for residents residing in intervention NHs but not enrolled in study. Control group: 1. Standard precautions and transmission-based precautions as needed based on NH policy. 2. Passive surveillance, cultures collected at baseline, day 15, and monthly for up to 1 year, used only for outcome measurements with no data feedback to NHs. 3. Staff education provided as needed.	Primary outcomes: overall MDRO prevalence density in residents with indwelling devices. Secondary outcome: 1. Number of residents with new acquisitions of MDRO. 2. Incidence of device-associated infections.

Author	Design	Setting and Population	Duration	Intervention	Outcomes Measured
Huskins et al.[58]	C-RCT	USA 19 adult ICUs (MICU, SICU and MSICU) enrolled; 1 withdrawn after randomization (surveillance cultures missing.) Only pts with a LOS ≥ 3 days were included—3,488 pts: 2,132 (intervention), 1,356 control) Excluded from study: No surveillance culture or positive surveillance or clinical culture within 2 days of ICU admission.	1. Baseline Period (Apr-Nov 2005) 2. Randomization and implementation (Dec 2005-Feb 2006) 3. Intervention (Mar-Aug 2006)	Aggregate report on HCPs' use of standard precautions provided to all ICUs before (1:1) randomization with stratifications based on ICU type and baseline incidence of MRSA or VRE colonization or infection. Intervention group: 1. Stool or perianal swabs for VRE within 2 days of admission, weekly, and within 2 days before or after discharge from ICU. 2. Training in the intervention. 3. Signage on doors. 4. Universal glove use until results of screening culture for VRE on admission were available (except for those already known to be colonized or infected with VRE). CP for duration of ICU stay for pts who tested positive clinically or in surveillance cultures. 5. Aggregate report HCPs' use of universal gloving during first month of the intervention period provided to ICUs. Control group: isolation precautions (CP) for pts with VRE colonization or infection identified through existing hosp procedures. Surveillance culture results not provided to ICU.	Primary outcome: incidence of VRE colonization or infection (colonization not distinguished from infection.) Secondary outcomes: incidences of VRE colonization or infection calculated separately for: - percentage of ICU pt-days - percentage of HCP contacts gloves during and HH before or after pt contact - percentage of HCP contacts with gloves during and HH after pt contact

Abbreviations: C-RCT = clustered randomized controlled trial; CP = Contact Precautions; HCP = health care provider; HH = hand hygiene; hosp. = hospital(s); IPAC = infection prevention and control; ICU = intensive care unit; ITS = interrupted time series; LOS = length of stay; MDRO = multidrug-resistant organism; MICU = medical intensive care unit; MSICU = medical surgical intensive care unit; MRSA = methicillin-resistant *Staphylococcus aureus*; NH = nursing home; pt(s) = patient(s); QE = quasi-experimental; SICU = surgical intensive car`e unit; VRE = vancomycin-resistant enterococci

Table 26: Results of Studies for Rapid Review Two (with relevance to VRE)

Author	Summary	Limitations	Results and Effect Measured*
Derde et al.[59]	ITS: reduced ARO transmission (primarily through their impact on MRSA). C-RCT: did not identify a reduction in ARO transmission with rapid, as compared to conventional, screening. Neither the ITS nor C-RCT compared screening to no screening for VRE on admission. Provides no evidence to indicate whether screening for VRE on admission is effective or not.	Co-intervention effect assessed in phase 2. Covariants include potential confounding factors (sex, age, month, invasive devices, nurse-to-pt staffing ratio, location before ICU admission, reason for admission, APACHE/SAPS, hospital, and number of days-at-risk for acquisition). No introduction of any intervention during the study that might affect the outcomes.	VRE colonization on ICU admission (all phases): 384 (4.7%) of 8,243. No evidence of step changes in acquisition or trends in either phases 2 and 3, or between each screening group. (P > .05). Total number of ICU-acquired first VRE bacteremia recorded during the trial was 9—too low for statistical analysis.
Mody et al.[60]	418 residents included. Reduced ARO prevalence density identified—NSS change in VRE acquisition identified but study was underpowered to detect reduction in VRE prevalence. Because residents were not isolated and barrier precautions were applied to all residents, this study was a comparison of universal barrier precautions and enhanced HH, and provides no direct evidence relevant to the use of screening for VRE on admission to hospitals or long-term care homes. It was therefore excluded from further consideration.	Participant-level baseline colonization with specific MDRO, age, sex, race, and LOS before enrollment, and NH quality ratings were adjusted as covariates.	NSS difference between intervention and control group in VRE prevalence after adjusting for clusters and covariants. Adjusted rate ratio, geometric mean: 1.20 (95% CI, 0.82-1.75). NSS difference in new VRE acquisition rates between intervention and control group with cluster- and covariate-adjusted hazard ratio: 0.85 (95% CI, 0.45-1.60); P = .61.
Huskins et al.[58]	Mean LOS: 4-5 days for all pts, 8 days for pts included in study. Overall, 51% of intervention unit pt-days and 38% of control unit pt-days required CP; 41% of pt-days in intervention unit required universal gloving. Mean time from collection of screening specimen to reporting: 5.2 days (SD = 1.4). Incomplete compliance with universal gloving and CP. No difference in VRE acquisition in intervention vs. control ICU overall. Provides moderate evidence that VRE screening (and CP) at time of ICU admission does not impact VRE transmission in the ICU setting, and indirect evidence on the efficacy of VRE screening at hospital admission.	Unmasked C-RCT. Confounders not significant. This study differs in multiple ways from how screening for VRE on admission is performed in Ontario as screening was performed at the ICU rather than the facility level. Only 1/3 of ICU pts were included, with most exclusions due to LOS ≤ 2 days; 10%-15% of the included pts did not have a repeat VRE swab performed within 2 days of ICU discharge. These factors, as well as the relatively short length of the study, mean that significant VRE transmission, and changes in VRE incidence over time, could have been missed.	NSS difference in mean (±SE) ICU-level incidence of VRE colonization or infection per 1000 pt-days at risk after adjusting for baseline incidence (38.9±5.6 and 33.4±6.3 in the intervention and control groups, respectively; P = .53). No significant association between incidence of VRE colonization or infection with % ICU pt-days on which pts with VRE colonization or infection were assigned to CP or % HCP contacts when HCPs wore gloves during and performed HH after pt contact (P > .05).

Abbreviations: APACHE = acute physiology and chronic health evaluation; ARO = antibiotic-resistant organism; CP = Contact Precautions; C-RCT = clustered randomized controlled trial; HH = hand hygiene; ICU = intensive care unit; IPAC = infection prevention and control; ITS = interrupted time series; LOS =

length of stay; NH = nursing home; NSS = not statistically significant; pt(s) = patient(s); SAPS = simplified acute physiology score; SE = standard error; VRE = vancomycin-resistant enterococci

A.4.5 Rapid Review Three: Harms Are Associated With Contact Precautions

Two systematic reviews on the topic were identified in the literature search; data from those reviews were extracted to inform this document and summarized in Table 27 and Table 28 below.

Table 27: Study Design of Articles for Rapid Review Three

Author	Design	Setting and Population	No. of Patients cases/controls	Isolation Type	Outcomes Measured and Methodology
Catalano et al.[146]	Cohort	ID/isolation unit; med. unit Adults	27 pts. with VRE or MRSA on AP matched with 24 pts. with infections not in isolation	C	Anxiety and depression (Hamilton Anxiety Rating Scale)
Chittick et al.[164]	Qualitative descriptive	Med., surg. and rehab. units Adults	249 pts. on C and 70 caregivers	C	Pt. and caregiver understanding and satisfaction with the use of C (survey)
Cohen et al.[159]	Cohort	Med. unit Children	24 pts. with HAI and 41 pts. not on AP	C, A, D	Quality of care (Pediatric Family Satisfaction Questionnaire Time spent in direct pt care (observation)
Rees et al.[148]	Evaluation	Inpt. and rehab.	21 consecutive pts. on AP	C	Pt. mood, satisfaction, quality of care (interviews)
Day et al.[144]	Cohort	Tertiary care hospital Adults	ICU pts.: 1644 on C (reasons not specified) and 5854 not on C Non-ICU pts.: 3138 on C (reasons not specified) and 25 426 not on C	C	Anxiety and depression (administrative, pharmacy and laboratory data review for ICD-9 code)
Evans et al.[154]	Cohort	SICU and surg. unit Adults	48 pts. with HAI and 48 matched pts. not in isolation	C, D	Questionnaire Time spent in direct pt care (observation)
Gammon et al.[162]	Cohort	3 hospitals Adults	20 pts. with mixed infections in C and 20 pts. not in isolation, in unit ≥ 7 days	C	Anxiety and depression (Hospital Anxiety and Depression Scale) Questionnaire Self-esteem (Self-Esteem Scale)
Gasink et al.[158]	Cross-sectional survey	Med. and surg. units Adults	43 pts. with mixed infections and 43 pts. not in isolation, in unit ≥ 3 days	C	Pt. care satisfaction (HCAHPS)
Guilley-Lerondeau et al.[150]	Cohort	5 med. and surg. Units in a hospital	30 pts. in isolation matched with 60 pts. not in isolation	Not specified	Pt. satisfaction (qualitative scale) Anxiety (Spielberger scale)

Author	Design	Setting and Population	No. of Patients cases/controls	Isolation Type	Outcomes Measured and Methodology
Kennedy and Hamilton[163]	Cohort	Spinal cord rehab. Med. unit and MICU Adults	16 pts. with MRSA	C	Anxiety (State Anxiety Inventory, Profile of Mood States) Depression (Beck Depression Inventory, Profile of Mood States)
Kirkland and Weinstein[155]	Cohort	MICU Adults	29 pts. with MDRO and 88 pts. not in isolation	C	Frequency of pt encounters (observation)
Klein et al.[160]	RCT	PICU Children	32 pts. with unspecified infections and 38 pts. randomized to standard care	C	Delivery of care
Livorsi et al.[157]	Cohort	Hospital	70 pts. with MRSA in isolation and 139 pts. not in isolation	C	Anxiety, depression and delirium (chart review for ICD-9 codes) Pt satisfaction (HCAHPS)
Mehrotra et al.[152]	Cohort	Med. and surg. units	238 pts. on C; 290 pts. not on C	C	Pt satisfaction (interviews, HCAHPS)
Pacheco and Spyropoulos [165]	Qualitative descriptive	University-affiliated teaching hospital: med. geriatrics, cardiac, stroke units)	5 pts. isolated for CDI and 5 family members	C	Isolation experience (semi-structured interviews)
Davies and Rees[192]	Cohort	Rehab. unit Adults	21 pts. with mixed infections	C, A	Anxiety and depression (Hospital Anxiety and Depression Scale)
Saint et al.[153]	Cohort	Med. unit in 2 hospitals Adults	139 pts. (31 of whom on AP with unspecified infections)	C	Time spent in direct pt care (observation)
Soon et al.[145]	Cohort	Hospital	20 pts. in isolation for MDRO and 20 pts. not in isolation	C	Anxiety and depression
Stelfox et al.[156]	Cohort	Med. and CHF pts. in 2 hospitals	Med pts.: 78 in isolation for MRSA and 156 not in isolation CHF pts: 72 in isolation and 144 not in isolation	C	Quality of medical care (chart review)
Tarzi et al.[147]	Cohort	Rehab. Adults > 65 years old	22 pts. (MRSA colonization or infection) matched with 20 pts. (no MRSA colonization or infection)	C	Depression (Geriatric Depression Scale)
Wilkins et al.[151]	Cohort	ID unit Adults	41 pts. with unspecified infections	C	Psychoneurotic pathology (Crown-Crisp Experimental Index)

Abbreviations: A = airborne isolation; AP = Additional Precautions; C = Contact Precautions; cardio = cardiology; CDI = *Clostridium difficile* infection; CHF = congestive heart failure; D = Droplet Precautions; HCAHPS = Hospital Consumer Assessment of Healthcare Providers and Systems; HAI = health care-

associated infection; ID = infectious disease; inpt. = inpatient; MDRO = multidrug-resistant organism; med. = medical; MICU = medical intensive care unit; PICU = pediatric intensive care unit; pt.(s) = patient(s); RCT = randomized controlled trial; rehab. = rehabilitation unit; SARS = severe acute respiratory syndrome; SICU = surgical intensive care unit; surg. = surgical

Table 28: Results of Studies for Rapid Review Three

Author	Anxiety	Depression	HCP Interactions	Pt Satisfaction	Pt Knowledge of C	Adverse Events
Catalano et al.[146]	NS	Pos. assoc.; ↑over time	NS	NS	NS	NS
Chittick et al.[164]	NS	NS	NS	80% pts. happy with C process	90% pts. agree C prevents infection transmission	NS
Cohen et al.[159]	NS	NS	No SSD (physician attendance)	No SSD	NS	NS
Davies and Rees[192]	NS	Pos. assoc.	NS	NS	NS	NS
Day[144]	No SSD	Pos. assoc.	NS	NS	NS	NS
Evans et al.[154]	NS	NS	Neg. assoc. (HCP visit frequency or duration)	NS	NS	NS
Gammon et al.[162]	Pos. assoc.	Pos. assoc.	NS	NS	NS	NS
Gasink et al.[158]	NS	NS	NS	No SSD	NS	NS
Guilley-Lerondeau et al.[150]	Pos. assoc.	NS	Neg. assoc. (pt. perception of HCP)	Neg. assoc.	<80% pts. knowledgeable of MDRO status and isolation 67% pts. not satisfied with information quality	NS
Kennedy and Hamilton[163]	No SSD	No SSD	NS	NS	NS	NS
Kirkland and Weinstein[155]	NS	NS	Neg. assoc. (HCP visit frequency); no SSD (HCP visit duration)	NS	NS	NS
Klein et al.[160]	NS	NS	No SSD (HCP interaction)	NS	NS	NS
Livorsi et al.[157]	NS	NS	NS	No SSD	NS	NS

Author	Anxiety	Depression	HCP Interactions	Pt Satisfaction	Pt Knowledge of C	Adverse Events
Mehrotra et al.[152]	NS	NS	104 (20%) of 528 pts. perceived concerns with care (poor coordination of care, *P* = .02); lack of respect for pt. needs and preferences (*P* = .001), OR = 2.05; 95% CI, 1.31-3.21; *P* < .01	No SSD in HCAHPS scores for 88 pts.: OR = 1.79; 95% CI, 0.64-5.00; *P* = .27	NS	NS
Pacheco and Spyropoulos[165]	NS	NS	NS	NS	Variability in pts.' understanding of infection transmission, illness trajectory, and pt. report lack of consistency with information provided	NS
Saint et al.[153]	NS	NS	No SSD in physician visits; neg. assoc. (attending physician visits)	NS	NS	NS
Soon et al.[145]	Pos. assoc.	Pos. assoc.	NS	NS	NS	NS
Stelfox et al.[156]	NS	NS	Isolated pts had less documented care	Isolated pts. expressed greater dissatisfaction with their treatment	NS	Isolated pts. experienced more preventable adverse events
Tarzi et al.[147]	Pos. assoc.	Pos. assoc.	NS	NS	NS	NS
Wilkins[151]	Pos. assoc.	NS	NS	NS	NS	

Abbreviations: C = Contact Precautions; HCAHPS = Hospital Consumer Assessment of Healthcare Providers and Systems; HCP = health care providers; MDRO = multidrug-resistant organism; neg. assoc. = negative association; NS = not studied; pos. assoc. = positive association; pt.(s) = patient(s); SSD = statistically significant difference

Overall comments on the quality of the studies selected for data extraction:

(i) Studies that report on psychological patient outcomes are often based on survey or questionnaire. Also, respondents' participation in these studies varied and was often low, leading to issues with selection bias and questionable generalizability of study findings.

(ii) Although patients on Contact Precautions were infected or colonized with antibiotic-resistant organisms, most studies on patient outcomes did not adjust for underlying illness severity. Therefore, the impacts of patient illness on the reported psychological outcomes and health care provider behaviours did not consider effect modification due to illness severity.

(iii) Based on the qualitative evidence on the topic we noted some patients did not like Contact Precautions as they felt alone and lacking in human interactions. However, sometime patients with antibiotic-resistant organisms were restricted to wards and multiple-patient rooms. Many studies did not specifically consider how the patients were housed and if they were roomed with other patients when on placed on Contact Precautions.

(iv) Similarly based on the qualitative evidence, there seemed to be a connection between patient knowledge of infection transmission and Contact Precautions and satisfaction with their care. Most studies did not directly assess patient knowledge of Contact Precautions and the impacts of patient knowledge on reported outcomes.

A.4.6 Rapid Review Four: Individual vs Regional VRE Control Practices

No articles met the inclusion criteria following full text review.

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