

Incidence of Vancomycin Resistant Enterococci (VRE) colonization in adult hematopoietic stem cell transplant (HSCT) patients after discontinuation of isolation precautions.

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Table of Contents

Abstract.....	3
Background and Significance	4
Purpose.....	6
Review of Current Evidence	7
Introduction.....	7
Screening.....	8
Isolation Precautions	8
Infection Control Measures.....	9
Incidence of VRE.....	10
Implications.....	11
Discussion	11
Theoretical Model	11
Methods.....	12
Design	12
Translational Framework	13
Setting	13
Sample.....	13
Data Collection	14
Data Analysis	15
Results.....	15
Discussion	17
Limitations	18
Relevance and Recommendations for Clinical Practice	18
Conclusion	19
References:.....	20

Abstract

Background: Vancomycin-resistant enterococcus (VRE) is a leading cause of hospital acquired infection and a major cause of bacteremia among hematopoietic stem cell transplant (HSCT) patients. To prevent the transmission of VRE colonization, many institutions employ contact isolation precautions including gown and glove for contact with patients that are VRE colonized. This practice is based on guidelines from the Centers for Disease Control and Prevention (CDC) which are outdated and do not reflect recent studies that demonstrate no adverse effects of discontinuation of contact isolation on the incidence of VRE colonization.

Purpose: To determine if there was significant change in the incidence of VRE colonization after institutional practice change that temporarily suspended routine contact isolation precautions for VRE colonized patients.

Methods: The incidence of VRE colonization was measured retrospectively in Adult HSCT patients during two different 3-month time periods; the first during active use of contact isolation and the second after discontinuation of contact isolation.

Results: The incidence of VRE colonization remained stable after discontinuation of contact isolation precautions of VRE colonized patients.

Conclusion: Discontinuation of contact isolation precautions in VRE colonized patients did not appear to increase the incidence of VRE colonization in adult HSCT patients. The project site continues to practice without contact isolation for VRE colonized patients.

Key Words: ‘Vancomycin-resistant enterococci’, ‘contact isolation’, ‘adults’, ‘hematopoietic stem cell transplant or bone marrow transplant’, ‘personal protective equipment’, ‘COVID-19’, ‘personal protective equipment’, and ‘shortage’

Background and Significance

Vancomycin-Resistant *Enterococcus* (VRE) is a leading cause of hospital-acquired infections that pose a clinically significant risk to hematopoietic stem cell transplant (HSCT) patients (O'Driscoll & Crank, 2015). Enterococci are bacteria that can become resistant to the antibiotic Vancomycin and are commonly found in the gastrointestinal tract (GI) and the skin (Centers for Disease Control and Prevention, 2019a). Not only are these bacteria a major pathogen worldwide (O'Driscoll & Crank, 2015) but they have emerged as one of the most common causes of bloodstream infections (Diaz Granados et al., 2005). Studies estimate VRE bacteremia rates 10-34% in post-HSCT patients with an associated mortality rate ranging from 40-100% (Benamu & Deresinski, 2018). In 2017, the Centers for Disease Control and Prevention (CDC) estimated \$539 million in healthcare cost associated with VRE and over 54,000 cases of VRE in the United States (CDCb, 2019).

Transmission of VRE can be via indirect or direct contact through contaminated surfaces, equipment, and healthcare workers (Anderson et al., 2019). Patients that carry VRE but do not have active infections or show symptoms of infection are colonized (Anderson et al., 2019). Colonization of VRE is identified through cultures obtained from perirectal or rectal swabs or stool cultures (Anderson et al., 2019). Not all patients who are colonized with VRE become infected with VRE (CDCa, 2019). Patients that are infected with VRE have positive blood cultures and can exhibit clinical symptoms such as fevers and pain (Anderson et al., 2019). Risk factors associated with VRE colonization include recent hospitalizations, indwelling medical devices, prolonged antibiotic usage, and patients that are acutely ill or immunocompromised (Anderson et al., 2019). Both VRE colonization and infection are associated with increased

hospital length of stay, healthcare associated cost, hospital expenditure and an increased risk of morbidity and mortality (Butler et al., 2010).

In HSCT patients, VRE is a leading cause of bloodstream infection and bacteremia (Kamboj et al., 2010). Patients undergoing HSCT are at an increased risk for the development of VRE colonization and bacteremia due to alterations in GI tracts, prolonged neutropenia or immunosuppression, previous antibiotic exposure, multiple or prolonged hospital stays, and indwelling devices such as central venous access devices (Benamu & Deresinski, 2018). Adverse outcomes associated with VRE infections in HSCT patients include increased mortality, multi-organ failure, severe graft versus host disease and leukemia relapse (Benamu & Deresinski, 2018).

Currently, limited guidelines and data for routine surveillance and isolation of VRE in healthcare facilities exist. Routine surveillance screening and contact isolation for VRE colonized patients vary among healthcare facilities and HSCT transplant centers (Muto et al., 2003). Contact isolation with gown and gloves has been utilized to reduce the transmission of VRE colonization among patients (CDC, 1995). The most recent guidelines for routine screening and isolation of VRE in healthcare facilities published by the CDC in 1995 recommend implementation of contact isolation precautions with gown, gloves, and hand hygiene in VRE colonized patients to prevent patient-to-patient transmission of VRE (CDC, 1995). In 2000, the CDC reported that continuous isolation of VRE colonized and infected patients was controversial and stated that no formal recommendations could be provided (CDC, 2000). However, the CDC recommended contact precautions for patients with VRE until the discontinuation of antibiotics (CDC, 2000). Infectious complication prevention guidelines released by The American Society for Transplantation and Cellular Therapy (ASTCT) in 2009 also recommend contact precautions

including gowns and gloves for patients colonized or infected with VRE (Tombly et al., 2009). Despite these recommendations from CDC and ASTCT, numerous studies have emerged questioning the need for routine surveillance screening and isolation among high-risk patient populations including HSCT patients.

In March 2020, the outbreak of Coronavirus Disease 2019 (COVID-19) resulted in a shortage of personal protective equipment (PPE) in healthcare facilities (Thomasian et al., 2020). Based on CDC recommendations, some healthcare facilities suspended contact isolation in VRE colonized patients to conserve PPE. On March 19, 2020, a large, tertiary academic institution in the southeast temporarily suspended routine contact isolation for VRE colonized patients based on these CDC recommendations. Per institutional standard of care, all patients admitted to the HSCT service were screened on admission and weekly for VRE colonization via rectal swab. Prior to March 2020, institutional policy required all patients that were VRE colonized be placed on contact precautions (gown and gloves). Prophylactic anti-microbials were administered per standard institutional protocol in neutropenic patients. Standard hand hygiene precautions continued throughout the project.

As the COVID-19 pandemic resolves, the temporary suspension of routine contact isolation remains under question. This project retrospectively evaluated the incidence of VRE colonization that occurred on adult HSCT patients admitted to the adult HSCT unit before and after this temporary practice change to determine if sufficient data exists to support a permanent practice change eliminating contact isolation precautions for VRE colonized patients.

Purpose

The purpose of this quality improvement (QI) project was to determine if there was significant change in the incidence of VRE colonization after institutional practice change that

temporarily suspended routine contact isolation precautions for VRE colonized patients. This project evaluated the incidence of colonization prior to practice change and post practice change.

Review of Current Evidence

Introduction

A literature search was conducted to establish the relationship of contact isolation in VRE colonized patients to the incidence VRE colonized patients. An initial query of database searches was performed in Pub Med, JSTOR, and CINAHL using keyword search phrases of ‘Vancomycin-resistant enterococci’, ‘contact isolation’, ‘adults’, ‘hematopoietic stem cell transplant or bone marrow transplant’, and ‘personal protective equipment’. Inclusion criteria included articles written in English, adults, and in-patient hospital units. Initial search included articles between 2015-2020 with little yield therefore the search was expanded to 2003-2021 with a total of 18 studies found. Next, a separate search was conducted in the same databases to determine the impact of COVID-19 on PPE supplies. Search terms included ‘COVID-19’, ‘personal protective equipment’, and ‘shortage’. Also included in the search were relevant guidelines with a direct correlation to VRE screening and isolation. In total, 19 articles and one guideline from the CDC were included. Common themes identified from the review of literature include variation in practices regarding screening and isolation precautions, utility of other infection control measure, VRE incidence and implications for practice.

Current guidelines and recommendations aimed to reduce the incidence of VRE colonization and infection are lacking. The most recent recommendations and guidelines were reported by the CDC in 1995 and supported the implementation of contact isolation with personal protective equipment (PPE). However little data supports the evidence that the

implementation of contact precautions prevent VRE infections (Morgan et al., 2014) and current routine surveillance and screening also vary among healthcare facilities (Muto et al., 2003). The emergence of Coronavirus Disease 2019 (COVID-19) resulted in a shortage of PPE. In response to this shortage, healthcare institutions have conserved PPE or eliminated of routine isolation for various pathogens such as VRE (Thomasian et al., 2020).

Screening

Screening for VRE colonization differs among various institutions. In several studies, routine screening was implemented via stool cultures perianal or rectal cultures (Almyroudis et al., 2016; Bardossy et al., 2017; Calderwood et al., 2008; Ford et al., 2016; Ford et al., 2017; Gedik et al., 2014; Hachem et al., 2004; MacAllister et al., 2018). Screening practices also varied among institutions with some surveillance screening performed on admission (Ford et al., 2016; Hachem et al., 2004; Calderwood et al., 2008), weekly on Mondays (Almyroudis et al., 2016; Ford et al., 2017) or frequency not defined (Gedik et al., 2014; Bardossy et al., 2017). Others did not have an active surveillance protocol practice implemented during their study (Satlin et al. 2014; Rupp et al., 2017). One study suggested that routine screening and isolation of asymptomatic patients is associated with an increased financial burden when compared to the cost of treating a VRE infection (Ulu-Kilic et al., 2016). Routine screening for VRE varied amongst institutions due to limited and outdated guidelines to establish routine VRE screening.

Isolation Precautions

Contact isolation for VRE colonized patients also varied among hospitals and transplant centers worldwide. Institutions that routinely screened for VRE on admission and weekly also placed VRE colonized patients on contact isolation precautions (Almyroudis et al., 2016; Bardossy et al., 2017; Calderwood et al., 2008; De Angelis et al., 2014; Ford et al., 2016;

Ford et al., 2017; Hachem et al., 2004; MacAllister et al., 2018). Contrarily, Martin et al. (2016) did not routinely screen patients for VRE but patients with active disease or positive surveillance cultures were placed on contact precautions prior to policy change eliminating contact precautions. Gedik et al. (2014) reported a deviation from standard contact isolation precautions as noted by gloves when entering the room and the use of gloves and gown only when in contact with bodily fluids. Almyroudis et al. (2016), Bardossy et al. (2017), and Rupp et al. (2017) evaluated the incidence of VRE after elimination of contact isolation for colonized patients. Data and results from these studies do not support current guidelines and recommendations for implementation of contact precautions in VRE colonized and patients with bacteremia.

Infection Control Measures

While the aim of this project was not specifically evaluating other infection control measures currently utilized in practice, most of these articles discussed other infection control measures that were implemented. Several studies not only evaluated the incidence of VRE in relation to contact isolation but in relation to other specified infection control measures as well. Infection control measures that were in current practice or implemented during the studies include environmental cultures of high touch areas (Ford et al., 2016), routine hand hygiene, patients housed in single bed private rooms (Almyroudis et al., 2016; Calderwood et al., 2008; Ford et al., 2017; MacAllister et al., 2018; Satlin et al., 2014), co-horting of patients with VRE colonization (Gedik et al., 2014) use of Chlorhexidine gluconate (CHG) bathing (Almyroudis et al., 2016; MacAllister et al., 2018; Rupp et al., 2017), prophylactic antibiotics in neutropenic patients (Almyroudis et al., 2016), and terminal cleaning of colonized rooms (Almyroudis et al., 2016; MacAllister et al., 2018). Martin et al. (2016) retrospectively reviewed culture rates after implementing the use of CHG bathing whereas Bardossy et al. (2017) utilized only standard

precautions after discontinuation of routine contact precautions for VRE. It is noted that hand hygiene audits were performed by both Bardossy et al. (2017) and Rupp et al. (2017). Hachem et al. (2004) implemented no other infection control measures apart from contact isolation. Almyroudis et al. (2016) introduced CHG bathing two years after the study discontinued routine surveillance screening and contact isolation for patients. Daily CHG bathing had no effect on the incidence on VRE infection (Almyroudis et al., 2016).

Incidence of VRE

Data is conflicting regarding the incidence of VRE colonization in relation to the routine practice of contact precautions for VRE colonized patients as several studies did not measure the incidence of VRE colonization. Hachem et al. (2014) demonstrated a decrease in VRE colonization related to use of contact isolation. Ford et al. (2016) found that colonization was linearly linked to the overall length of hospital stay whereas Calderwood et al. (2008) demonstrated 28.1% of patients that previously screened negative on admission were later found to be VRE colonized during their hospital stay.

In contrast, there were several studies that specifically evaluated the impact of discontinuation of contact isolation precautions on the incidence of VRE infection. Almyroudis et al. (2016), Bardossy et al. (2017), Martin et al. (2016), and Rupp et al. (2017) all reported no increased rates of VRE infections following the discontinuation of contact precautions. In a systematic review by De Angelis et al. (2014), several studies reviewed also demonstrated that contact precautions did not significantly reduce the rate of VRE infections. Many studies evaluated other infection control measures as previously highlighted such as co-horting which demonstrated an increased VRE incidence (Gedik et al., 2014) whereas CHG baths and Ultra-violet light terminal disinfection resulted in no significant change (MacAllister et al., 2018).

Implications

Implications for routine contact isolation in VRE colonized patients varied amongst studies. While several studies did not specifically measure VRE incidence in direct correlation to routine contact isolation, some still provided insight and recommendations favoring contact isolation. Ford et al. (2016) alluded that adherence to isolation guidelines to decrease VRE colonization rates and Hachem et al. (2004) supported both routine stool surveillance and contact isolation for VRE colonized patients. Studies that evaluated incidence of VRE infections after discontinuation of contact isolation supported this practice in VRE colonized patients (Bardossy et al., 2017; Martin et al., 2016; Rupp et al., 2017). Routine contact isolation can also have negative effects on patient care and patient outcomes as isolation can be associated with delayed patient care, lower patient satisfaction and increased falls (Morgan et al., 2014) and poses several financial considerations (Mac et al. (2019).

Discussion

Many institutional practices for the screening and isolation of VRE colonized patients are based on CDC guidelines. However, these guidelines are outdated and lack clear guidance regarding recommendations for isolation of VRE colonized patients. In response to COVID-19 and the national shortage of PPE, routine isolation of VRE colonized patients was temporarily discontinued in the setting of this project. Given the risk associated with VRE infections, specifically in hematologic malignancy patients, review of this change in isolation practice was warranted.

Theoretical Model

Roger's Diffusion of Innovation Theory provided an approach to promote the adoption of new ideas within a system or organization. This behavioral theory evaluates the steps and

processes of how innovation or ideas are received, disseminated, and shared within a system (Mohammadi et al., 2018). Knowledge is the first step proposed by this theory in which the diffusion of innovation or proposed practice change is not supported or adopted due to uncertainty or lack of information (Mohammadi et al., 2018). The goal of this project was to promote a practice change by demonstrating sufficient clinical data to support the new innovation. This theory is applicable when a new innovation or a practice change is introduced with the intent to gain interest from key stakeholders who will in turn promote, support, and disseminate the data collected and proposed practice change within the institution (Mohammadi et al., 2018). The goal of this project was to provide sufficient data to key stakeholders such as physicians and advance practice providers who would in turn adopt this practice and disseminate it throughout the larger healthcare system.

Methods

Design

This quantitative retrospective chart review was aimed to determine if sufficient data exists to either support or negate an organizational practice change that occurred in March 2020 that temporarily suspended contact isolation precautions for VRE colonized patients due to PPE shortages in the setting of the COVID-19 pandemic. Data was collected through an electronic medical record (EMR) retrospective chart review of adults over 18 years of age admitted to the adult HSCT unit. This review consisted of a 3-month period prior to the temporary practice change of suspended contact isolation precautions for VRE colonized patients and for a 3-month period post practice change. The convenience sample accessed through the EMR consisted of adult autologous and allogeneic HSCT patients from Hematologic Malignancy and Cellular Therapy Division of a large, tertiary academic institution.

Translational Framework

The Iowa model for Evidence Based Practice (EBP) guided the dissemination of this project and has been widely used in both academic settings and healthcare institutions (Brown, 2014). The Iowa model aligned with this project as it not only promotes a step-by-step approach to a problem or knowledge trigger but supported an organizational practice change as well (Brown, 2014). This project accomplished the three main decision points of the Iowa Model as outlined by Gawlinksi and Rutledge (2008) with the intent to determine if sufficient data existed to support a permanent practice change of discontinuation of contact isolation precautions for VRE colonized patients. Gawlinski and Rutledge (2008) identified these key decision points as an institutional need to focus on this problem, determining if there is sufficient research, and if a practice change was based appropriate. This project was supported and aligned with both institutional and unit priorities.

Setting

This project was implemented at a 957-bed, tertiary academic hospital located in the southeast. The Adult HSCT unit contains 16 beds and cares for patients undergoing autologous and allogeneic stem cell transplantation for hematologic malignancies and non-malignant hematologic diagnoses such as scleroderma, sickle cell and germ cell tumor patients. The average daily patient census from July 2019 through December 2020 was 11.95 patients. All patient rooms are single bed private rooms with private bathrooms.

Sample

A total of 269 patient encounters were included in this review. A 3-month period was chosen pre and post practice change resulting in a total of 109 pre-practice change and 162 post-practice change VRE polymerase chain reaction (PCR) samples tested on the inpatient HSCT

unit. Sample size was determined after obtaining the patient census pre and post practice change to establish equivocal sample sizes pre and post practice change. Inclusion criteria included adult patients over 18 years of age, admitted to the inpatient HSCT unit and service with a hematologic malignancy diagnosis and non-malignant hematologic with indications for HSCT for pre-transplant chemotherapy conditioning, and monitoring following HSCT. Exclusion criteria included patients that are under 18 years of age, not admitted to the Adult HCST service, and those that have a history of previous positive VRE PCR.

Data Collection

A representative from the Infection Prevention department at the project site provided data from the HSCT unit that was obtained from the Performance Services database. Data was focused on patients admitted to the HSCT service between March 2019-March 2021 for the following: age at time of admission, sex, underlying hematologic malignancy diagnosis, VRE PCR testing results including admission and weekly basis. An additional chart review was conducted on encounters with a positive VRE PCR to determine if there was a previous documented history of VRE colonization. Testing and results of VRE PCR were tracked for the entire duration of patient's hospitalization.

De-identified data was entered into an Excel spreadsheet and stored on a secure, password-protected platform (Box), which was only accessed by the student. Data was collected in 3-month intervals pre-practice change (6/1-8/31/2019) and post practice change (6/1-8/31/2020). Data was not reproduced and only accessible via hospital server. After completion of project, data was deleted. Informed consent from patients was not needed for this project.

The student, Director of Nursing Research and Evidence Based Practice for the institution, Adult Bone Marrow Transplant and Hematology Malignancy Clinical Nurse

Specialist, and Infection Prevention Department personnel facilitated data collection for this project. Institutional Review Board (IRB) approval was obtained from both the university and healthcare institution.

Data Analysis

Inferential statistics (Chi square test) were used to summarize the effect of contact isolation on the rate of VRE colonization in HSCT patients. The incidence of VRE colonization before March 2020 compared to the incidence of VRE colonization after practice change implemented on March 19, 2020 was determined. Independent variables included age, sex, and hematologic malignancy diagnosis. Data was analyzed to assess for the statistical correlation of VRE colonized patients and the use of contact isolation precautions. De-identified data was imported into SPSS statistical software program. The statistical analysis was performed using SPSS software.

Results

A total of 269 patient encounters qualified for this chart review. There were 109 pre- and 162 post-practice change VRE PCR samples reviewed on the inpatient HSCT unit during the two 3-month periods: Active VRE contact isolation precautions and cessation of VRE contact isolation precautions. Two patient encounters were excluded as they previously tested positive for VRE colonization prior to hospital admission. The patient populations were similar between the two study periods based on median age, gender and hematologic malignancy diagnosis as described in Table 1.

Table 1*Demographics*

	Contact precautions	No contact precautions
Patients (N)	109	160
Median age, (range)	54, (25-77)	58, (23-74)
Males, n (%)	62, (57%)	87, (54%)
Females, n (%)	47, (43%)	73, (46%)
Underlying Hematologic Malignancy, N (%)		
ALL/AML	19, (17.4%)	44, (27.5%)
CML/MDS/MPN	19, (17.4%)	41, (25.63%)
HL/NHL/CLL	26, (24)	19, (11.9%)
Plasma Cell Malignancy ^a	39, (35.7%)	41, (25.63%)
Other ^b	6, (5.58%)	15, (9.38)

Note: ALL, Acute Lymphoblastic leukemia; AML, Acute Myeloid Leukemia; CML, Chronic Myeloid Leukemia; MDS, Myelodysplastic Syndrome; MPN, Myeloproliferative neoplasm; HL, Hodgkin Lymphoma; NHL, Non-Hodgkin Lymphoma; CLL: chronic lymphocytic leukemia

^aPlasma Cell Malignancy include Amyloidosis, Multiple Myeloma

^bOther include NK cell lymphoblastic, Langerhan's histiocytosis, Scleroderma, Sickle Cell Disease

Chi-square tests were used to assess for statistical associations between the use of contact isolation precautions and VRE colonization rates. In total, there were six cases of VRE colonization reported, four cases with active VRE contact isolation precautions and two after cessation of VRE contact isolation precautions. Within this sample, Chi square tests revealed a statistically insignificant association between VRE colonization rates in HSCT patient pre and post practice change. Fisher's Exact test revealed a P value of .226. $P < 0.5$ was considered statistically significant.

Discussion

In HSCT patients, VRE is a leading cause of hospital acquired infections and bacteremia (Benamu & Deresinski, 2018). These infections can lead to significant clinical complications including death for patients undergoing HSCT (Benamu & Deresinski, 2018). Historically, contact isolation precautions have been utilized in healthcare settings to reduce transmission of VRE. However, contact precautions also pose a risk for adverse effects such as medication errors, falls, and pressure injuries (Karki et al., 2013).

Prevention strategies are vital to the reduction and elimination of healthcare-associated infections such as VRE (Benamu & Deresinski, 2018). Contact isolation has been the predominant practice for VRE colonized patients to reduce transmission rates, however, newer literature questions the efficacy and associated adverse effects of contact isolation precautions (Benamu & Deresinski, 2018). Although guidelines from both the CDC and ASTCT support routine contact isolation for VRE colonized patients, infection control measures and prevention practices vary across HSCT centers (Benamu & Deresinski, 2018).

The Iowa model was utilized in development of this project as it supports the translation of research into best clinical practice. Due to PPE shortages in the setting of COVID-19, the

Iowa model supported the idea to evaluate current guidelines and data for the routine contact isolation for VRE colonized patients. Guided by this model, it was determined that current guidelines were insufficient and a practice change eliminating contact isolation precautions in VRE colonized patients were evaluated. While results of this project are not statistically significant, they were clinically significant to support further inquiry into this practice change.

Limitations

Several limitations of this project were identified. The population evaluated was limited to adult patients undergoing bone marrow transplantation admitted to the HSCT unit. This excluded adult HSCT patients admitted to other units and those treated as an outpatient for the duration of their transplant. This project was only conducted at single site which limited the sample size. The sample size of 269 limits the validity of the project. This project was also conducted over a limited time frame which could also contribute to a smaller sample size. The results derived from this project are constrained due to these limitations, however, it further supports the need for continued data regarding screening and isolation for VRE.

Relevance and Recommendations for Clinical Practice

Advanced practice providers (APP) including nurse practitioners, physician assistants, and clinical nurse specialist play a vital role in the translation of research into clinical practice. As the need for medical providers continues to increase, the role and utility of APP's is increasing. Change is constant in healthcare and APPs have a responsibility to be at the forefront of change. As the initial or primary provider for patients, APPs often identify and conduct quality improvement (QI) initiatives from their experiences. They play an active role in organizational QI efforts by supporting best practice through the implementation of protocols, education of staff, adherence to guidelines, and leading patients to engagement efforts aimed at

quality improvement (Boucher et al., 2015). Evaluating practice change related to the need to conserve PPE is an example of this type of QI initiative. As leaders in healthcare and lifelong learners, APPs are catalyst for change to enhance clinical outcomes, patient satisfaction and organizational growth (Boucher et al., 2015).

Conclusion

Patients undergoing HSCT are at high risk for VRE colonization, bacteremia, and mortality (Benamu & Deresinski, 2018). Guidelines and recommendations for contact isolation precautions for infection control are obsolete with more recent data necessitating updated guidelines for practice. This project demonstrated that discontinuation of contact isolation precautions in VRE colonized patients did not significantly increase the incidence of VRE colonization in adult HSCT patients. These findings are clinically significant despite statistical analysis as the routine use of contact isolation has negative implications for patient care. Contact precautions should be used judiciously due to associated risk for falls, delays in patient care and decreased patient satisfaction (Morgan et al., 2014). This data demonstrates that more research is needed to support a change in practice guidelines.

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