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# Discontinuation of Reflex Testing of Stool Samples for Vancomycin-Resistant Enterococci Resulted in Increased Prevalence

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## Abstract

Discontinuation of reflex testing stool submitted for *Clostridium difficile* testing for vancomycin-resistant enterococci (VRE) led to an increase of patients with healthcare-associated VRE bacteremia and bacteriuria (2.1 versus 3.6 per 10,000 patient days; $p<0.01$ ). Cost-benefit analysis showed reflex screening and isolation of VRE reduced hospital costs.

### Keywords

Vancomycin; Clostridium difficile; enterococci; Isolation; Feces; Microbiology; Bacteremia; Bacteriuria

## Introduction

Vancomycin-resistant enterococci (VRE) cause infections that result in increased cost and hospital length of stay (1). Previous studies reported a substantial proportion of patients with *Clostridium difficile* infection who are co-colonized with VRE (2,3). Based on these data, a “reflex” testing program was initiated at our hospital in the 1990’s to limit VRE transmission. Reflex testing was defined as any stool submitted to the laboratory for *C. difficile* toxin testing from an inpatient was also tested for VRE, using selective media (VRE Agar, Remel, Lenexa, KS). Patients identified as being VRE colonized or infected by reflex testing, routine clinical cultures, or records from an outside facility, were placed on contact precautions.

In 2010, concerns were raised about the cost-benefit of reflex testing. Healthcare-associated VRE rates both within the hospital and nationally over the previous decade had been stable

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(4,5). Based on lack of clear evidence that reflex testing was affecting VRE epidemiology, it was discontinued. The purpose of this study is to examine the effect of discontinuation of this VRE reflex testing program on healthcare-associated VRE transmission.

## Methods

Barnes-Jewish Hospital is a 1,250 bed academic tertiary care hospital in Saint Louis, Missouri. There are 1,160 patient rooms, of which 741 can be semi-private. Hospital policy is to place VRE colonized or infected patients in contact precautions in a private room. Reflex testing for VRE was discontinued in July 2010. Physicians were notified of this change. Clinicians could still order stool or peri-rectal cultures for VRE testing at their discretion. No additional interventions targeting VRE were implemented at the time.

To determine the effect of discontinuing reflex testing on VRE transmission, the healthcare-associated VRE rate was evaluated from January 2009 to December 2011. All hospitalized patients with a positive urine or blood culture for VRE were identified. A healthcare-associated VRE case was defined as the first positive specimen per patient, where VRE was detected in blood or urine > 48 hours after admission. A VRE case was considered present on admission if VRE first was detected in blood or urine ≤ 48 hours after admission. VRE cases were expressed per 1,000 patient-days.

Rate trends were evaluated using interrupted time series modeling (SPSS version 18.0; IBM SPSS, Chicago, IL). Segmented regression analysis was performed to assess the effect of the discontinuing VRE reflex testing on healthcare-associated VRE rates (6). We hypothesized that there would be a delay between discontinuation of the testing and resulting change in acquisition rates, as the effect of increased colonization pressure would not be immediately seen (7). Therefore, we utilized a one-month delay for evaluating the post-discontinuation segment. Monthly VRE prevalence on hospital admission was included in the model to account for any change during the study period. Institutional review board approval was obtained from Washington University.

## Results

In the 18 months prior to discontinuation of reflex testing, 9,652 stool specimens underwent VRE testing (mean 536 per month). In the 18 months after reflex testing was stopped, 2,974 stool specimens were tested (mean 165 per month; −62% difference; $p$ <0.01). The monthly mean number of patients with a VRE-positive stool culture decreased from 136 to 45 (−67% difference; p <0.01).

There were 92 cases of healthcare-associated VRE during 433,855 patient (pt) days (0.21/1,000 pt days) in the reflex testing period, versus 159 cases in the 444,092 pt days after discontinuation (0.36/1,000 pt days) (Figure). The full regression model showed no baseline trend in healthcare-associated VRE ($p$=0.772), and no trend change after discontinuation of reflex testing ($p$=0.727). There was no significant trend in rates of VRE present on hospital admission (0.16 before versus 0.22 cases per 1,000 patient-days after discontinuation; p=0.704). There was a significant change in the y-intercept, with the

monthly healthcare-associated VRE rate increasing by 0.17 cases per 1,000 patient days ($p$=0.04) when VRE reflex testing was discontinued.

The cost-benefit analysis was completed for the first 12 months postdiscontinuation. Assuming reflex testing had been continued and the rate of healthcare-associated VRE was the same as the pre-intervention rate, we would have expected 14 fewer patients with VRE bacteremia and 26 fewer patients with bacteriuria. During the discontinuation period, the institution saved $20,920 in laboratory costs ($4 per VRE test, 5230 fewer tests). Isolation bed avoidance saved approximately $95,788 ($77 per isolation bed-day, 1,244 fewer VRE isolation days). Based on estimates in the literature (1) the cost of treating the excess VRE bacteremias was approximated at $139, 286 ($9,949/ bacteremia, 14 excess bacteremias), resulting in an excess cost of at least $22,578 per year without reflex testing.

## Conclusion

The role of routine active surveillance in the control of antimicrobial resistant organisms in hospitals remains unclear (8,9). Previous studies have demonstrated the benefit of active surveillance cultures to control VRE transmission in hospitals, however, these were generally done during an outbreak in which multiple interventions were introduced simultaneously (10,11). We found that discontinuation of reflex VRE testing of stool submitted for testing for *C. difficile* resulted in an approximately 71% increase in the endemic healthcare-associated VRE rate. Strengths of the study are no other infection prevention measures were implemented when reflex testing was stopped, and that the VRE rate was stable prior to discontinuation. We hypothesize that the discontinuation of VRE reflex testing resulted in decreased identification and isolation of patients with VRE colonization, resulting in increased VRE colonization pressure throughout the hospital, and a subsequent increased risk of VRE transmission.

The cost of laboratory testing was a consideration in the decision to discontinue the VRE reflex testing program. Microbiological cultures performed on inpatients for the purpose of screening cannot be submitted to Medicare for reimbursement. Therefore, the cost of active surveillance must be absorbed by the facility. Our cost analysis suggests that savings gained from reduced laboratory and isolation bed cost were nullified by the increased cost of treating patient VRE bacteremia.

There are limitations to this study. We used a quasi-experimental study design. Therefore, we cannot rule out the possibility that unmeasured variables, such as underlying patient characteristics, may have changed during the study period and affected our findings. The VRE rate increased when reflex testing was discontinued even after controlling the data for incoming colonization pressure (i.e., patients who had VRE detected in blood or urine within 48 hours of admission). Laboratory methods for identifying VRE from urine and blood cultures did not change during the study period. This study was done in a large academic medical facility and the results may not be generalizable to other healthcare facilities with differing endemic VRE rates. We did not determine the cost associated with the treatment of VRE infections, other than bacteremia, though we would anticipate that these would further increase the cost-benefit of reflex testing. Finally, we examined cost

from a hospital, rather than a societal perspective, though hospitals bear the direct cost of an active surveillance program.

In conclusion, we found that discontinuation of reflex testing of stool submitted to the laboratory for *C. difficile* testing for VRE resulted in a hospital-wide increase in healthcare-associated VRE and was not cost-effective. Based on these results, reflex testing was re-instituted in at our facility. Additional studies in a variety of healthcare facilities are needed to determine if this screening strategy is effective in other settings.

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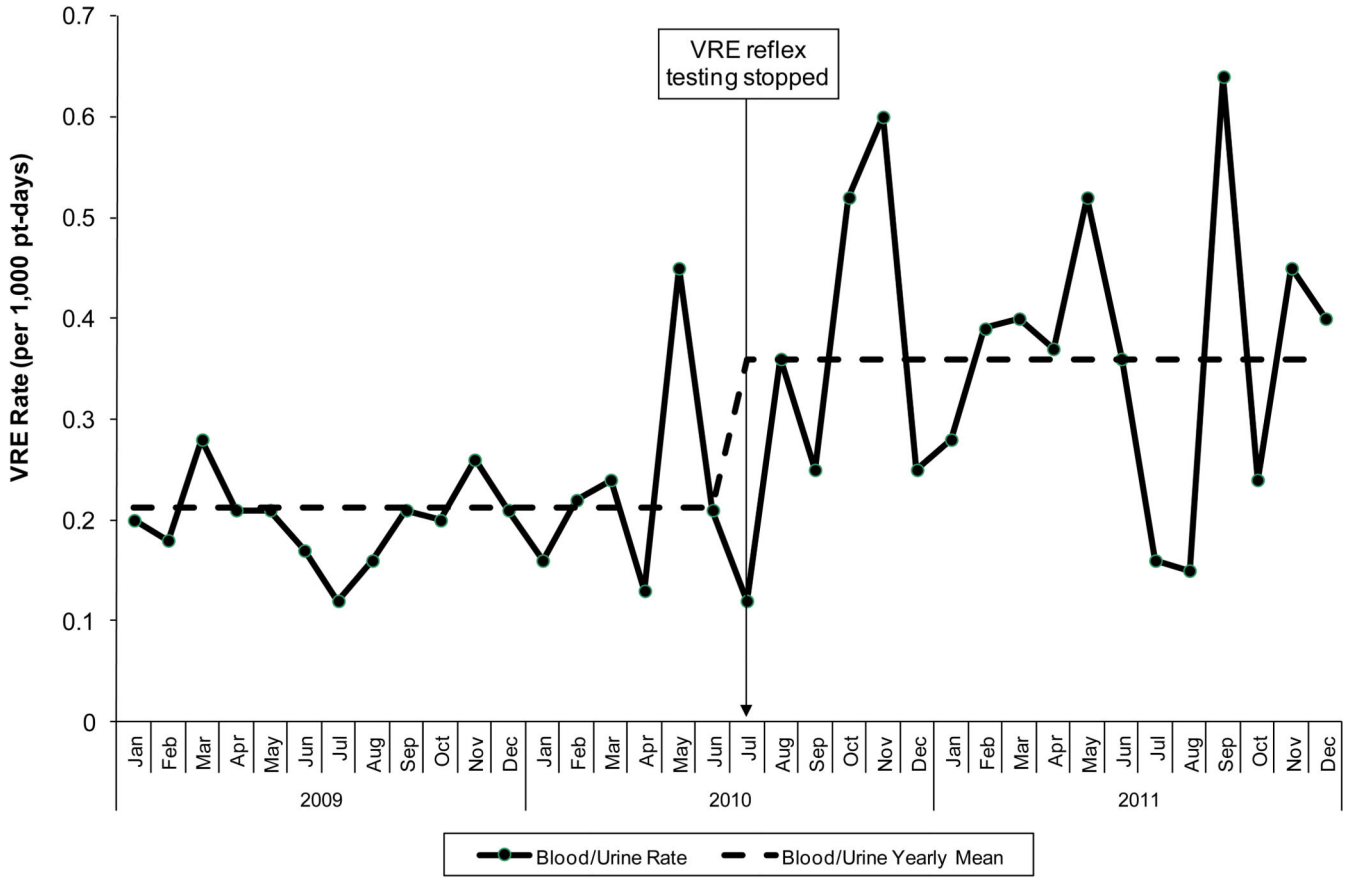


**Figure.**

Monthly incidence of healthcare-associated vancomycin resistant enterococci (VRE), January 2009 - December 2011