

## Vancomycin-Resistant Enterococci in Patients Attending for Colonoscopy: An Estimate of Community Prevalence

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### Abstract

#### **Aims**

Ireland has the highest vancomycin-resistant *Enterococcus faecium* (VRE) bloodstream infection prevalence in Europe. Two patterns of VRE carriage are recognised. European, with widespread community prevalence and North American, where carriage is predominantly nosocomial. It is unclear which pattern is dominant in Ireland. This uncertainty limits infection control measures. This study sought to explore this issue via a cross sectional point prevalence study.

#### **Methods**

Asymptomatic community volunteers, represented by patients undergoing elective outpatient colonoscopy testing, were opportunistically screened for VRE. Demographic and risk factor data were collected via a patient survey. Rectal swabs were collected before colonoscopy and VRE was identified using the VITEK MS system.

#### **Results**

102 patients were cultured. A single patient tested positive, representing a prevalence rate of 0.98% (95% CI <0.01-5.8%). This patient demonstrated traditional risk factors, suggesting nosocomial rather than community acquisition. 94% (N=94) of patients had no knowledge of VRE, while 83% (N=83) had low levels of concern regarding hospital acquired infections.

#### **Conclusion**

There is a low incidence of VRE in the Irish community setting, in contrast to other European Countries, suggesting asymptomatic community colonization is not responsible for the high rates of VRE seen in Ireland. Wider screening or atypical infection control measures would not be supported by this data.

## Introduction

Enterococci are among the most common cause of hospital acquired infections(HAIs) and represent a significant proportion of multiple drug resistant organisms(MDROs)<sup>1</sup>. Enterococci benefit from natural resistance to several antibiotics and can rapidly acquire resistance to others. The European Antimicrobial Resistance Surveillance System(EARSS) and the World Health Organisation have listed vancomycin-resistant *Enterococcus faecium*(VRE) as a pathogen with high priority<sup>2</sup>, with VRE now ranked as the 3<sup>rd</sup>-4<sup>th</sup> most common nosocomial pathogen<sup>1,2</sup>.

EARSS data show Ireland has the highest VRE bloodstream infection prevalence in Europe(45%), the prevalence has been increasing for the past decade despite a steady decline in MRSA infections<sup>1</sup>. It has been suggested that VRE in Ireland may be spread across all inpatient populations and not confined to traditional high-risk subgroups<sup>3</sup>. It has been theorised that a high rate of asymptomatic community carriage of VRE, as seen in Europe, could be responsible for the presence of VRE outside of these traditional groups; advocating for broader screening and isolation to contain this vector of infection.

VRE first emerged in Europe in the late 1980's, and soon spread to the United States<sup>4,5</sup>. Interestingly, the initial epidemiology between the two areas was remarkably different. North American outbreaks were limited to hospitals, with spread almost exclusively attributable to health-care-associated transmission<sup>6</sup>. In contrast, the major reservoirs of VRE in Europe were asymptomatic carriers in the community setting, with a limited presence in hospital<sup>6,7</sup>. This was believed to arise from agricultural use of the glycopeptide avoparcin, which was subsequently banned by the European Union.

The first reports of VRE in Ireland were published in 1997 and 1998<sup>8,9</sup>. Initial cases were isolated to large tertiary referral hospitals in the Dublin metropolitan area, with minimal presence in the community despite extensive use of avoparcin in Ireland, suggesting a pattern of endemicity more akin to the United States than our European counterparts.

To date, estimates of true prevalence in Irish hospitals are limited. One study showed a 6% prevalence among ICU patients<sup>10</sup>, while a similar study found an incidence of 20%<sup>11</sup>. Studies in other clinical settings have found prevalence between 3-40%<sup>3,12,13</sup>.

Data regarding community prevalence are more limited. A single study showed no cases of VRE in 129 GP submitted rectal swabs<sup>12</sup>, as did a survey in the paediatric population<sup>13</sup>. Data from a Dublin hospital reported a prevalence of 1% for community samples<sup>3</sup>. Samples from a long term care facility found rates of 3%<sup>14</sup>. Given the paucity of data, there has been a consistent call for further surveillance studies on the incidence of VRE in the Irish population<sup>3,15</sup>.

Our study sought to address these concerns via a cross sectional point prevalence study to define the prevalence rate of VRE carriage amongst asymptomatic healthy volunteers in an outpatient setting and assess patient opinions regarding the impact of MDROs on their interactions with the healthcare service to further inform infection control strategy.

## Methods

Data were collected between June 2017 and June 2018 in the Mercy University Hospital, Cork. The trial was approved by the local clinical research and ethics committee.

Patients presenting to the surgical day ward for routine colonoscopy were opportunistically enrolled into the study. Patients who consented received a rectal swab for VRE after having received sedation, but before their colonoscopy was performed.

Demographic data and patient characteristics were collected, and a patient survey was completed to identify the presence of presumed risk factors for VRE colonisation, patient knowledge regarding VRE and their broader opinions regarding MDROs. All patients were provided with a study number, which was used for the interviews and processing of microbiological samples to ensure anonymity. All patient information was anonymised and stored in a separate locked cabinet on the hospital site.

The patient's rectum was swabbed using standard cotton swabs, by proceduralists blinded to the outcomes of the trial. All proceduralists were trained using a standardised collection technique. Rectal swabs were rotated against the mucosal surface 1–2 cm beyond the anal sphincter. Rectal swabs fully coated in stool were considered adequate specimens. No samples were rejected due to inadequate sampling. Samples were transferred to our microbiology laboratory for storage and inoculation.

Swabs were inoculated onto a chromogenic agar selective for VRE (BioMérieux, France) and incubated for 48 h at 37°C. This allowed the presumptive identification of the two main species involved: *E. faecium* (violet colonies) and *E. faecalis* (blue-green colonies). Full identification and susceptibility testing was performed using VITEK MS (BioMérieux, France); an automated mass spectrometry microbial identification system that uses Matrix Assisted Laser Desorption Ionization Time-of-Flight.

Data were entered into Microsoft Excel (Microsoft Corporation, Redmond) for analysis. Data were assessed for duplication and data validation tools were used to verify data integrity. Data were anonymised and originals destroyed. Only required information was stored in compliance with data protection legislation.

Categorical and continuous variables were analysed using the Fischer's exact test, Chi<sup>2</sup> Test, and Student's T test as appropriate. Confidence intervals for prevalence were calculated by the modified Wald method. P values of <0.05 were regarded as significant. All P values are 2-tailed. Statistical analysis was conducted using Prism (GraphPad, San Diego).

## Results

122 patients were enrolled during the specified study period. 20 samples were incorrectly transferred, stored, or labelled and had to be discarded. Demographic and patient questionnaire data was unavailable for two patients, leaving a total of 100 patients. A total of 102 samples were cultured, only one sample grew VRE for a total prevalence rate of 0.98% (95% CI <0.01-5.8%).

Patient survey data is displayed in (Table 1). Risk factors for the positive patient were compared to the negative population using methodology described above. As expected, given the low prevalence, statistical testing did not meaningfully contribute to analysis.

**Table 1:** Demographic Study data. (Values for demographic data gathered from study participants)

	<b>N (%)</b>	<b>VRE Positive</b>
<b><i>Mean Age of Patient</i></b>	<b>58 ±15</b>	<b>62</b>
<b><i>Gender of Patient</i></b>		
<i>Female</i>	47 (47%)	1 (100%)
<i>Male</i>	52 (52%)	
<b><i>Was the patient previously aware of VRE</i></b>		
<i>Yes</i>	5 (5%)	
<i>No</i>	94 (94%)	1 (100%)
<b><i>Level of Concern Regarding HAI</i></b>		
<i>Not At All</i>	42 (42%)	
<i>Somewhat</i>	41 (41%)	1 (100%)
<i>Greatly</i>	16 (16%)	
<b><i>Indication For Colonoscopy</i></b>		
<i>Colorectal Cancer Surveillance</i>	38 (38%)	1 (100%)
<i>Altered Bowel Habit</i>	25 (25%)	
<i>Rectal Bleeding</i>	17 (17%)	
<i>Pre-Existing Disease</i>	14 (14%)	
<i>Patient Unsure</i>	6 (6%)	
<i>Anaemia</i>	1 (1%)	
<b><i>First Colonoscopy</i></b>		
<i>Yes</i>	40 (40%)	
<i>No</i>	59 (59%)	1 (100%)
<b><i>Recent Healthcare Interactions</i></b>		
<i>No Previous Attendance</i>	33 (33%)	
<i>1-3 Attendances</i>	42 (42%)	
<i>4-11 Attendances</i>	15 (15%)	
<i>&gt;12 Attendances</i>	9 (9%)	1 (100%)

The single positive sample was from a 62-year-old female who lived independently. She was receiving a colonoscopy as part of the colorectal cancer screening service. She demonstrated multiple traditional risk factors. The patient had spent more than a month in hospital in the past three years, had attended a healthcare setting >12 times in the past year and had been hospitalised within the past fortnight. She reported >28 days of antibiotic usage within the past year and had previously required ICU admission.

Overall participant characteristics adequately represented a community sample. Previous hospital attendance was uncommon with 33% of patients reporting no previous attendances in the past year, and 42% reporting only one to three attendances. 61% reported no overnight admissions to hospital in the past three years and 92% of patients had no experience of isolation precautions at any healthcare setting. Prior antibiotic usage was uncommon with 59% of patients reporting no antibiotics in the past year and 26% reporting only a short course of <7 days. For 40% of patients this was their first colonoscopy.

Awareness of VRE was low with 95% of patients having never heard the term before. As was concern regarding HAIs; only 16% of patients felt that HAIs caused them a “great” deal of concern, while 42% felt only “somewhat” concerned.

## **Discussion**

As discussed earlier, Ireland has a significant problem with VRE. Multiple bodies at a local and national level have suggested implementation of wider screening protocols, outside of traditional high-risk groups, to identify VRE colonised patients earlier and attempt to limit transmission<sup>3,9,11-15</sup>. However, clear data to guide these decisions is lacking, and our study had hoped to provide further guidance.

In our study the low prevalence rate of 0.98% suggests VRE is predominantly a hospital-acquired organism, lacking the traditional community reservoir seen in other European countries and more closely mirrors the pattern of infection demonstrated in the United States. This is supported by other Irish studies<sup>3,12,15</sup>. Our limited sample size generates broad confidence intervals, limiting precise estimation of prevalence. However, our data remains in stark contrast to other European studies; which demonstrate high community prevalence rates, for example: Germany(12%), Belgium(28%) and rural France(11%-18%)<sup>16-19</sup>.

The low prevalence of community VRE carriage in our study suggests the benefit of routine screening, outside of traditional high-risk groups, would be limited. The single positive patient demonstrated multiple traditional risk factors and had a complex medical history suggesting nosocomial colonisation rather than asymptomatic community carriage. Given this pattern, widespread VRE carriage outside of traditional high-risk groups in the Irish community setting is unlikely.

Assessing patient focused factors, such as the acceptability of increased isolation and screening procedures, is vital when considering the feasibility of such measures. The majority of patients in this study were either “not at all (42%)” or only “somewhat (42%)” concerned with the risks of acquiring HAIs as part of their treatment course. This suggests a low level of concern among the general patient cohort. Patient preferences and desires are essential to consider when focusing on any intervention, our data suggests patients would not support a more intensive infection control screening strategy.

We must also consider the potential for harm. Other authors have shown that patients under infection control precautions are twice as likely to experience adverse events, eight times as likely to experience supportive care failure, have lower rates of satisfaction with care and suffer higher psychological distress<sup>20-23</sup>. As a result, we feel that our data would suggest that wider screening or atypical infection control measures would not be acceptable from an epidemiologic basis, or a patient focused, risk-benefit viewpoint.

A contentious point of our study would be the use of patients presenting to a surgical day ward for colonoscopy as surrogates to represent asymptomatic community carriage. It could be argued that attendance at a healthcare facility or the presence of symptoms requiring a colonoscopy would naturally give these patients a different risk factor profile. We feel that our demographic data shows these patients did not have significant prior interaction with healthcare services, and overall were representative of the general Irish community-based populace.

Additionally, previous studies have shown patient’s strong distaste for rectal swabbing<sup>24</sup>, limiting ethical access to true community volunteers. We theorised periprocedural sedation would significantly alleviate patient discomfort, improving patient tolerability and participation. No patient approached during the study period declined participation, supporting the validity of this approach.

Other potential limitations of our study include concerns over storage and transport of study samples. Rectal swabs were frozen prior to culturing for VRE. Thermal damage could explain the low frequency of VRE isolation. Other studies have shown that enterococci remain viable after freezing, suggesting this is unlikely to have caused a significant decrease in sensitivity<sup>25</sup>.

Sampling methodology may also account for the low rate of isolation. The overall sensitivity of rectal swab cultures for detection of VRE was 58% in one report<sup>24</sup>. While other methods may be superior, these swabs are widely used as a screening method in the Irish healthcare setting and many similar prevalence studies have reported similar methods. As such, it represents a true practical application of screening techniques.

The use of stimulant laxatives prior to colonoscopy may have lowered the density of VRE in the rectum, hindering detection. However, this remains a theoretical concern with limited data to support this hypothesis.

Finally, it should be acknowledged that our findings were generated in a single centre with a small sample size. As a result, our confidence intervals are large, limiting precision. Additionally, almost 5 years have passed from initial data collection to publication, it is possible that the prevalence pattern could have changed in the interim. These limitations occurred given the limited resources of our small research group.

In conclusion, these results suggest that there is a low incidence of VRE in the Irish community setting, in contrast to other European Countries. Despite widespread historical avoparcin use and an agrarian community, the epidemiology of VRE in Ireland more closely resembles that of North America than Europe. There was an almost complete absence of VRE carriage in the asymptomatic healthy population, suggesting that asymptomatic community colonization is not responsible for the high rates of VRE seen in Ireland.

The single positive case demonstrated extensive interaction with the healthcare services and did not display any atypical risk factors, suggesting that priorities for future infection control strategies should focus on screening traditional at-risk groups.

**Declaration of Conflicts of Interest:**

The authors have no conflicts of interest to declare.

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