Making Informed Decisions

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CHAPTER 3

Costs of Two Vancomycin-resistant Enterococci Outbreaks in a Dutch Academic Hospital

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Abstract

Introduction: In early 2017, the University Medical Center Groningen, the Netherlands, had an outbreak of two strains of vancomycin-resistant Enterococci (VRE) which spread to various wards. In the Summer of 2018, the hospital was again hit by a VRE outbreak, which was detected and controlled early, because of aggressive screening. During these outbreaks various costs were incurred by the hospital, such as the costs of cleaning, personnel costs, laboratory costs and lost costs due to closed beds. This study aimed to quantify the costs of the 2017 and 2018 VRE outbreaks.

Methods: Using data from various sources in the hospital and interviews, we identified and quantified the costs of the two outbreaks, resulting from tests, closed beds (opportunity costs), cleaning, additional personnel, and patient isolation.

Results: The total costs associated with the 2017 outbreak were estimated at €352,070, or €8,383 per day; the total costs associated with the 2018 outbreak were estimated at €157,474 or €8,288 per day.

Discussion: The main drivers of the costs were the opportunity costs due to the reduction in admitted patients, tests, and cleaning. Although the second outbreak was considerably shorter, the costs per day were similar to the first outbreak. This paper shows that there are major investments associated with the VRE control measures. From this study, we can conclude that an outbreak of VRE can lead to considerable costs for a hospital: hitting hard and early may reduce the total costs and improve the continuity of care within the hospital.

Introduction

Enterococci are bacteria normally present in the human gastrointestinal system. Especially in healthcare settings, Enterococci resistant to certain antibiotics are transmitted, most importantly vancomycin-resistant Enterococci (VRE)[84]. The number of resistant isolates varies by country: in continental Europe low resistance generally is found in Northern and Western countries, while high resistance in found towards the East and South[85]. In the Netherlands, the prevalence of VRE is low compared to most European countries, ranging from 0 to 2% of clinical isolates[85]. VRE is mainly transmitted through contaminated surfaces and the hands of healthcare workers[86,87], hence VRE transmission can be reduced by strictly isolating patients carrying the resistant bacterium and by adhering to hygiene guidelines, such as frequent handwashing[88]. An important tool to adequately isolate VRE carrying patients concerns the screening of high-risk patients, such as patients suffering from gastrointestinal diseases or patients who have been admitted to hospitals in regions with a high prevalence of VRE.

Early in 2017, the University Medical Center Groningen (UMCG) in the Netherlands had an outbreak of VRE[89]. Due to an incidental finding from a patient that was hospitalized for about 10 days, patients that shared the same hospital room were screened. Several patients tested positive for VRE causing an extensive screening with many additional patients testing positive. Due to typing with Next Generation Sequencing (NGS) it was found that not one strain, but two strains were causing the outbreak. One of these strains was isolated first from a patient who had previously been admitted to a German hospital and was tested positive in November 2016. Despite isolation measures, the VRE strain could spread during December 2016 and the first weeks of January 2017. Due to the movements of patient to various wards and intensive care units, the VRE could spread to several locations.

Two wards with many positive patients closed completely and the patients had to be moved to a temporary ward which was only used for VRE positive or high-risk patients, for example patients who tested negative at the initial sampling but shared rooms or facilities with positive patients. A patient-stop was initiated in the UMCG, to prevent further transmission, and to ensure adequate capacity at the intensive care unit for acute care. A total of 38 patients were tested positive for VRE during this outbreak, with two separate strains. During the Summer of 2018, 27 patients tested positive in another outbreak, who could all be traced back to a single VRE-carrying patient. Again, despite isolation measures, the VRE could spread. Because of an early and aggressive screening, the outbreak was detected in an early stage and quickly controlled. To contain the spread of VRE, new patients were temporarily rejected, current patients were moved to an outbreak ward and the original ward was completely disinfected using hydrogen peroxide vapour decontamination.

During these outbreaks various costs were incurred by the hospital, such as the costs of cleaning, personnel costs, laboratory costs and lost costs due to closed beds. This research aims to quantify the costs of the 2017 and 2018 VRE outbreaks in the UMCG.

Methods

In a prior study, in which costs associated with several outbreaks in the UMCG were quantified, five main categories of costs were identified: diagnostics, closed beds, cleaning, additional personnel and patient isolation[44], these were also assessed in this study. To calculate the costs associated with each category, we estimated volumes of the various categories and multiplied them with the unit costs. To estimate the volumes of the various items, we used clinical data and data collected during interviews with representatives of various departments that were affected by the outbreaks.

The first outbreak started 10 January 2017 and ended 21 February 2017, while the second outbreak started 21 August 2018 and ended 8 September 2018. For both outbreaks, transmission occurred before the starting date; in this study only the time periods were considered where the hospital staff was aware of the outbreak.

For the analyses, the VRE-status of patients is important. For this paper, we used three categories of patients:

- VRE-positive, for patients confirmed to carry VRE, having positive results in both a polymerase chain reaction (PCR) test and a culture;
- VRE-suspect, for patients at high risk to carry VRE; and
- VRE-negative, for patients not suspected to carry VRE.

Data sources

<u>Interviews</u>

Eight interviews with representatives of relevant departments were conducted to get an overview of the relevant costs. We interviewed staff from the infection prevention unit, the microbiological and viral laboratories, the most severely affected department (the gastrointestinal unit), facility services, procurement, and business intelligence. These interviews were used to get an expert opinion on various costs, but interviewees were also requested to provide data sources where available.

<u>Data sources</u>

Various sources of clinical input data were used to assess the unit volumes used for the cost analysis. Patient movement data were used to estimate the number of times a room had to be cleaned. Cleaning staff was estimated to need one to two hours per room in which a VRE-positive patient was admitted to completely clean the room. Some patients were admitted to rooms where more than one VRE-positive patient was admitted, we therefore assumed that the cleaning time per VRE-positive patient was one hour. Patient isolation data were used to estimate the number of days VRE-positive or VRE-suspect patients were put in isolation, with the aim to prevent further spread through the hospital. Ward occupancy data were used to estimate the opportunity costs due to closed beds[90]. Laboratory data were used to estimate the volume of VRE tests performed, both patient and environmental samples.

To estimate the unit costs, Dutch reference prices[91] were used where possible, otherwise data from previously-published literature were used, table 3.1 provides an overview of the various unit costs, including references. All costs were converted to 2020 euros using the health-related consumer price index, as published by statistics Netherlands[92]. Internal cost calculations from the microbiology department were used for the unit prices of the various tests: these are the costs that are offset to the clinical departments, they include staff costs but do not reflect commercial prices as all tests were performed by the internal laboratory of the UMCG. Cleaning costs per hour were used as published in previous research[44]. For the 2018 outbreak, the affected ward was cleaned using hydrogen peroxide, which amounted to almost €35.000.

Table 3.1. Unit prices, expressed in 2020 euros

Item	Price	Reference
Ward stay (academic hospital), per day	€662.87	[91]
Intensive care unit stay, per day	€1,224.55	[91]
Contact isolation, per patient per day	€26.27	[44]
Cleaning costs (weekday), per hour	€26.52	[44]
Hourly labour costs: infection and prevention specialist	€39.28	[93]
Hourly labour costs: nurse during regular hours	€36.36	[93]
Hourly labour costs: nurse during night shifts and on Saturday	€53.45	[93]

Opportunity costs due to closed beds

During both outbreaks, there was a patient stop in the UMCG, making it likely that there was missed revenue. To estimate the missed revenue for both outbreaks, we used occupancy rates of the patient wards in the hospital, and we compared the real occupancy from the start of the outbreak up till two weeks after the outbreak with the expected occupancy. This expected occupancy was estimated using autoregressive integrated moving average (ARIMA) models[94]. For each ward, the best fitting ARIMA model was automatically determined using the Hyndman-Khandakar algorithm[95]. To estimate the opportunity costs, we used the difference between the measured occupancy and the bootstrapped 95% prediction interval of the forecast occupancy[94]. (For example, if the lower bound of the ARIMA model predicted an occupancy of 10, but only 6 patients were admitted to a ward, the difference 10 – 6 = 4 was used to calculate the opportunity costs due to closed beds.) The result was then multiplied by the ward stay costs (see table 3.1) to estimate the opportunity costs. The various fit models, including the prediction intervals and the measured values, are displayed in supplementary figures 3.1 and 3.2.

During both outbreaks, there was a transfer ward, which was established to isolate VRE-positive patients. To prevent the double counting of outbreak-related costs, we did not include the hospitalization costs of this transfer department in the analysis, as they are counted using the ARIMA models.

Cleaning and patient isolation costs

For all VRE-positive patients, we assumed one hour of cleaning for every movement through the hospital, from the moment at which the VRE infection was confirmed. For all VRE-suspect patients, we also assumed one hour of cleaning for every movement through the hospital, until they were confirmed to be VRE-negative; if this exact point of time was unknown in the patient isolation records, we assumed a period of 48 hours between the start of the suspicion of VRE and the confirmation of the VRE status, either positive or negative. Patient isolation costs were applied to all patients, for each isolation day[44].

Test costs

Test costs were calculated by multiplying the number of tests performed with the costs per test. After the 2017 outbreak, an inhouse PCR test was developed, resulting in a less expensive test used in the 2018 outbreak, compared to the 2017 outbreak, where the Cepheid GeneXpert ® was used. All positive tests were sequenced using NGS. VRE tests are performed regularly in the UMCG. To correct for the baseline level of VRE tests, we used the average daily number of VRE tests from the preceding four months and subtracted this number from the total tests during the outbreaks.

Analyses

All analyses were performed using R 4.1.0 and the package dplyr for data transformation[96,97]. For time series analyses, the fable package was used[98]. In addition to the total costs of both outbreaks, the outbreak costs per day were calculated.

Results

The total costs associated with the 2017 outbreak are estimated at €352,070, or €8,383 per day; the total costs associated with the 2018 outbreak are estimated at €157,474 or €8,288 per day. Table 3.2 summarizes the costs associated with the 2017 and 2018 outbreaks, which are graphically displayed in figure 3.1. The main driver of the costs in the 2017 outbreak are the diagnostics, followed by the opportunity costs due to closed beds. For the 2018 outbreak, the opportunity costs are the main driver, followed by the cleaning costs. A large proportion of the costs in 2018 concerns the hydrogen peroxide cleaning costs, which amounted for over a quarter of the total costs during this outbreak.

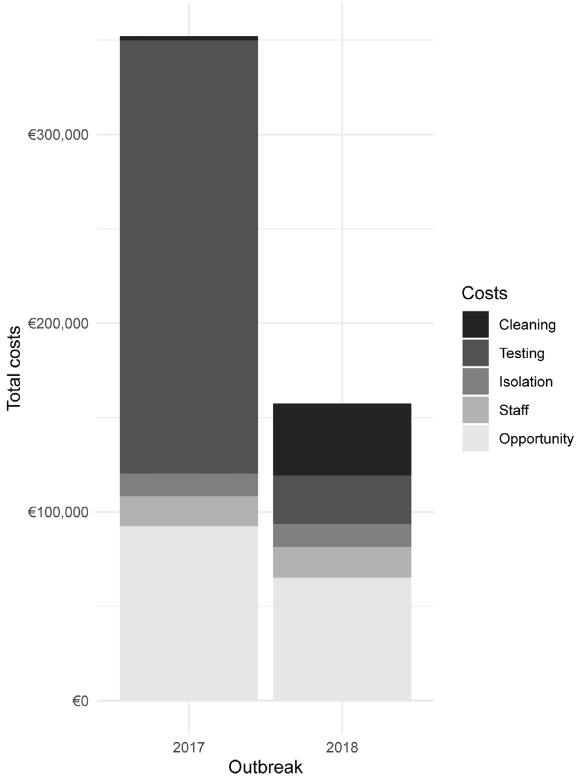

Figure 3.1. Schematic overview of costs related to VRE outbreaks in 2017 and 2018

Table 3.2. Costs associated with 2017 and 2018 VRE outbreaks, total costs and percentage of total outbreak costs

	2017		2018	
Cleaning	€2,175	1%	€38,222	24%
Testing	€229,526	65%	€25,516	16%
Isolation	€11,981	3%	€12,217	8%
Staff	€15,789	4%	€16,260	10%
Opportunity	€92,600	26%	€65,258	41%
Total	€352,070	100%	€157,474	100%

Discussion

In this study, we assessed the outbreak costs of two VRE outbreaks in the UMCG (Groningen, The Netherlands). The total costs of the 2017 outbreak were estimated at €352,070 and the total costs of the 2018 outbreak were estimated at €157,474. The main drivers of the costs were the opportunity costs, additional diagnostics, and cleaning costs. Although the second outbreak was considerably shorter, the costs per day were similar to the first outbreak.

There are few studies published on the costs associated with VRE outbreaks in hospitals. A VRE outbreak in the UMCG in 2013 was estimated to cost around €3800 per day[44], which is considerably less than the outbreaks considered in the current study. However, this outbreak was smaller, as 19 patients were involved and affected only one ward. As in the 2017 and 2018 outbreaks, the major drivers of these costs were those of diagnostics and opportunity costs due to closed beds[44]. A study in a French university hospital estimated the total costs of a VRE outbreak amongst 13 patients at €171,439 (2008 euros), where the opportunity costs were also a major driver[99]. A difference in this study with ours concerns the inclusion of costs of antibiotics, which was the second most important driver of costs. We also considered the inclusion of antibiotics, however, considering the alternative for VRE patients would be teicoplanin and the price differences between vancomycin and teicoplanin in the Netherlands are negligible, we decided to not include these as extra costs[100].

Our analysis has some limitations. It is complex to accurately estimate the opportunity costs due to closed beds, as patients are exchanged between the various wards in the hospital, and it is unknown exactly how many patients went to other hospitals during the patient stop. We tried to estimate this using various ARIMA models and considered the measured occupancy outside the 95% prediction intervals to be caused by the outbreaks. This is a conservative approach, as the prediction intervals are rather wide due to the variability in the data; hence we may underestimate the opportunity costs due to closed beds. In December 2017, the UMCG switched the computer system used to measure the ward occupancy and movements of patients through the hospital, resulting in poorly comparable data for the two periods. We trained the time series model on the four months preceding both outbreaks to make sure the data cut caused by the new system did not affect the analysis, but this prevented us from fitting more advanced predictive models.

Another limitation is related to the cleaning costs. While the cleaning procedures for patients in contact isolation are rather strict, there were no data available on increased staff expenditure and cleaning materials. Instead, an approximation was used where we counted one hour of cleaning time per isolated patient. The cleaning costs in the 2018 outbreak are higher compared to the 2017 outbreak: in the 2018 outbreak hydrogen peroxide vapour decontamination was used to ensure a rapid reopening of the ward. This was very precisely accounted for in this analysis as the invoice was available. The limitations concerning data collection raise an important opportunity to improve the registration and findability of data, as even for directly involved staff, high-quality data was difficult, and in many cases impossible to find.

This study did not consider clinical consequences of VRE-positive patients. A meta-analysis including 12 cohort studies found increased mortality for patients with a VRE bacteraemia and increased length-of-stay, compared to vancomycin susceptible Enterococci (VSE)[101]. A case-control study from a German hospital compared nosocomial infections of VRE to VSE and found significantly higher costs for VRE-infected patients, but found no statistically significant differences in the hospital length of stay and mortality[102]. A recent review of economic analyses of VRE infection prevention and control interventions included nine studies, six of which recommended the (continued) implementation of VRE control practices, while three concluded that VRE control practices were not cost-effective[103]. However, the quality of the included studies was considered to be low[103]. A cost-effectiveness analysis not included in this review, considered VRE screening and isolation in Ontario, Canada using a dynamic transmission model and concluded that this was cost-effective, albeit with considerable uncertainty[104]. Another aspect to consider is the hospital's reputation and patient opinions: patients expect their health to be improved when hospitalized, they should not fear contagion with resistant bacteria[105]. Hospitals with high rates of resistant organisms or frequent outbreaks may suffer from a loss in reputation[106] and, eventually, patient trust.

Currently, the incidence of VRE is low in the Netherlands[85] and the stringent VRE control measures may have played a role in that. This paper shows that there are major investments associated with the VRE control measures. However, the containment of VRE may result in lower healthcare costs overall due to a shorter length-of-stay and decreased mortality. Estimations from previous research show that annually there are around 16,000 VRE infections in Europe, causing over 1,000 deaths, but that the burden of VRE-related morbidity and mortality in the Netherlands is very low[11]. However, for such a study, it is important to consider that VRE rates are likely to rise if these measures are not implemented, negatively affecting patient outcomes.

From this study, we can conclude that an outbreak of VRE can lead to considerable costs for a hospital. Although no outbreak will be the same, hitting hard and early can reduce the total costs and improve the continuity of care within the hospital.

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