

Outbreaks of Vancomycin-Resistant Enterococci in Hospital Settings: A Systematic Review and Calculation of the Basic Reproductive Number

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BACKGROUND. Vancomycin-resistant enterococci (VRE) have spread worldwide.

OBJECTIVE. To systematically review VRE outbreaks and estimate the pooled basic reproductive rate (R_0) of VRE.

METHODS. Eligible studies criteria were (1) published within 10 years, (2) report outbreak details, (3) involve 1 center, (4) estimate epidemic duration, and (5) concern adults. Descriptive analysis included number of index cases, secondary cases, and screened patients; infection control measures; and definition of contact patients. R_0 was estimated by the equation $R_0 = (\ln 2) D/t_d + 1$, with D as the generation time and t_d as the doubling time.

RESULTS. Thirteen VRE outbreaks were retained from 180 articles and, among them, 10 were kept for R_0 calculation. The mean (range) number of index cases was 2.3 (1–8) and the mean (range) number of secondary cases was 15 (3–56). The mean (range) number of screened patients was 174 (32–509), with pooled VRE prevalence of 5.4% (95% CI, 4.5%–6.3%). Contact precautions were reported in 12 studies (92%), wards were closed in 7 (54%), with cohorting in 6 (46%). Two major screening policies were implemented: (1) a surveillance program in the unit or hospital (7 studies [54%]) and (2) screening of selected contact patients (6 studies [46%]). The pooled R_0 of VRE was 1.32 (interquartile range, 1.03–1.46).

CONCLUSION. We discerned considerable heterogeneity in screening policies during VRE outbreaks. Pooled R_0 was higher than 1, confirming the epidemic nature of VRE.

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After first appearing in the United Kingdom¹ and France² in 1986, vancomycin-resistant enterococci (VRE) have spread worldwide.^{3–6} Dramatic increases in VRE isolation (0% to 25.9%) have been reported over a 10-year period, from 1989 to 1999, in the United States, and this trend is continuing.⁴ According to the National Healthcare Safety Network, one-third of enterococci strains were vancomycin-resistant in 2006–2007.⁷ The European Antimicrobial Resistance Surveillance System has highlighted wide variability between European countries,⁸ with VRE proportions ranging from less than 2% (Finland, the Netherlands) to more than 20% (Ireland, Greece, Portugal). Mortality caused by bloodstream VRE infections is at least twice that occurring with susceptible strains.⁸ Moreover, the risk of horizontal *vanA* gene transfer from vancomycin-resistant *Enterococcus faecalis* to methicillin-resistant *Staphylococcus aureus* can lead to dissemination of vancomycin-resistant *S. aureus*.^{9–11}

To manage and control VRE outbreaks, several measures are usually taken simultaneously, including contact precautions,

cohorting, contact screening, active surveillance, or ward closure. The cost of such measures is significant—US \$193,469—with \$68,301 for infection control measures and \$125,168 for loss of income from spare isolation beds.¹² One of the first steps in hospital outbreak investigations is to identify the magnitude of infection spread. Because VRE outbreaks often result in digestive carriage without clinical infection, the definition of at-risk populations and screening policies during investigation of outbreaks is crucial for better control. To our knowledge, no review has analyzed different screening policies during VRE outbreaks in hospital settings.

Basic reproductive rate or R_0 , defined as the average number of secondary cases generated by 1 primary case, is a key concept in infectious disease dynamics.¹³ An epidemic can occur if R_0 is greater than 1. Few estimates of VRE R_0 have been reported, and no one has ascertained the pooled R_0 of VRE outbreaks in hospital settings.^{13,14}

We undertook a systematic review of VRE outbreaks worldwide. Our primary goal was to describe VRE outbreaks

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with particular emphasis on definition of contact patients. Our secondary objective was to estimate the pooled R_0 of VRE in hospital settings on the basis of investigation reports.

METHODS

Data Acquisition

We conducted our searches according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement.¹⁵ Published outbreak investigations were identified through the English-language Medline database. The keywords were “vancomycin-resistant enterococcus” and “outbreak.” Inclusion criteria were the following: (1) publication between January 1, 2004, and March 31, 2014; (2) studies reporting details of VRE outbreaks including number of cases, contacts, and screening policies; (3) studies involving only 1 center; (4) epidemic duration estimated; (4) total duration of the outbreak less than 6 months; and (5) only adult populations included. Studies that did not fulfill all these criteria were excluded. We considered that outbreaks lasting more than 6 months might be related to endemic situations or surveillance studies, not only to outbreaks. Then, we excluded studies with longer duration that are exposed to unpredictable confounders, loss of follow-up, and lower quality of data.

Descriptive Data

Descriptive analysis included number of index cases and secondary cases, definition of contact patients, and infection control measures. An index case was a patient, infected or colonized by confirmed positive culture of VRE, identified at time of initiation of outbreak investigation. Secondary cases were VRE-positive patients, infected or colonized, identified during the course of the outbreak. Screened cases were all patients who had at least 1 screening test to detect VRE carriage during the total duration of the outbreak. VRE prevalence was calculated for the whole outbreak on the basis of results of active screening cultures. Summary statistics were described as number and proportions of qualitative variables, with mean (SD) or median (interquartile range) of quantitative variables. Pooled VRE prevalence was estimated by the inverse variance method with Metaprop in Stata, version 10.0 (StataCorp), and heterogeneity was quantified by I^2 measurement. I^2 test permits the quantification of the heterogeneity between studies in meta-analysis. I^2 describes the percentage of total variation across studies caused by heterogeneity rather than chance. A value of 0% indicates no observed heterogeneity, and larger values indicate increasing heterogeneity.

R_0 Calculation

The pooled R_0 of VRE was ascertained according to the method developed by Anderson et al.¹⁶ Outbreaks lasting less than 6 months were selectively included in this analysis; indeed, longer studies might be related to endemic situations, not to outbreaks. R_0 can be estimated by fitting an exponential growth equation

because the chain of transmission events within an epidemic is expanding if each index case, on average, generates more than 1 secondary case. In epidemics of a directly transmitted respiratory or gastrointestinal pathogen, during early growth in a totally susceptible population, doubling time (t_d) is related to R_0 magnitude by the simple equation $t_d = (\ln 2) D / (R_0 - 1)$, where D is the average duration of latency plus infectious periods in days.¹⁶ D , also known as the generation time or serial interval, denotes the average time taken for a secondary case to be infected by a primary case.

For each VRE outbreak included, we calculated t_d with epidemic duration and number of index and secondary cases. D was figured through a literature search. It was 5 days during the investigation of an outbreak in Cook County Hospital in the United States in 1995.¹⁷ We calculated R_0 in each study according to the mathematical formula $R_0 = (\ln 2) D / t_d + 1$, and we estimated pooled R_0 by applying it to the estimation of weighting by population proportions in every outbreak. Each R_0 estimation for a particular study was weighted according to its size, and pooled R_0 was the sum of the different R_0 weighted according to study size.

RESULTS

Review

The initial Medline search identified 180 articles (Figure 1); 150 were excluded because they did not concern VRE or VRE outbreaks, involved several centers, or did not report details of

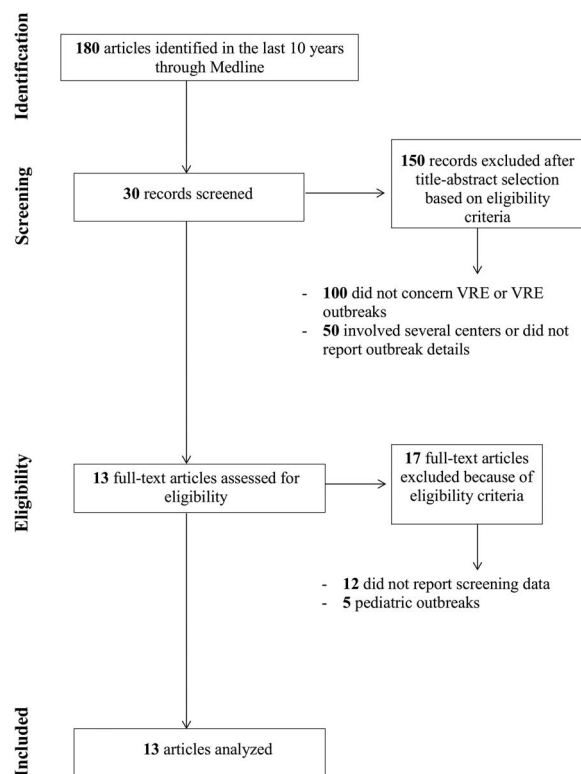


FIGURE 1. Flow chart of studies reporting vancomycin-resistant enterococci outbreaks.

outbreaks in the title and/or abstract. Another 17 articles were excluded because they did not contain screening data or entailed pediatric outbreaks. Finally, 13 VRE outbreaks were retained for descriptive analysis. Among them, 10 studies were included for R_0 calculation (epidemic duration <6 months).^{12,18–26}

Epidemiological Features of Outbreaks

In our search, we found 8 descriptive studies, 3 case-control studies, 1 descriptive study with economic impacts, and 1 outbreak investigation with prospective surveillance. Among the 13 studies, 8 took place in Europe (5 in France, 1 in Belgium, 1 in the Netherlands, 1 in Italy), 3 in Asia (2 in China and 1 in Singapore), and 2 in the Americas (1 in Canada and 1 in Brazil).

Contact precautions (isolation room and hand hygiene with gown and glove use) were implemented in 12 studies (92%), wards were closed or transfers and admissions restricted in 7 (54%), cases and contacts (dedicated medical and nursing staff) were cohorted in 6 (46%), environmental samples were taken in 4 (31%), antimicrobial policies were applied in 3 (23%), and readmission entailed an automatic alert in 1 (8%).

Two studies (15%) reported outbreak costs. Infection control costs plus loss of income from spare isolation beds were calculated: they ranged from US \$222,244 to \$268,343 per outbreak, with a mean of \$17,096 to \$29,816 per infected or colonized patient.

Description of Contact Patients

The number of screened patients ranged from 32 to 509, with a mean (SD) of 174 (134). The number of secondary cases ranged from 3 to 56, according to the number of index cases

(Table 1), with a mean (SD) of 15 (14) per outbreak. The prevalence of digestive VRE carriage in contact patients ranged from 1.6% to 21.9% (Figure 2). Pooled VRE prevalence was 5.4% (95% CI, 4.5%–6.3%), with significant heterogeneity between outbreaks ($I^2 = 86.8\%$). Table 1 describes the characteristics of each VRE outbreak.

Two major screening policies were implemented: (1) a surveillance program in the unit or hospital (7 studies [54%]) and (2) screening of selected contact patients (6 studies [46%]) (Table 2). Contact patient policies may entail patient hospitalization (in the same sector or care by the same staff) at the same time as index patients^{12,21,23–25} or secondary cases.¹⁸ Screening could even continue after index patient discharge.²¹ Surveillance programs generally consist of rectal swab samples from all patients during or 24 h after admission in the unit, then weekly.^{19,20,23,26–29}

R_0 Estimation

In the studies selected, we observed t_d of 3.5 to 180 days with a median (interquartile range) of 14.5 (7.8–84.4). The average duration of latency plus infectious periods (D) was considered as median time to VRE acquisition after admission, on the basis of observational data in outbreak setting,¹⁷ that applied the duration of 5 days for R_0 calculation. R_0 ranged from 1.02 to 1.99 in the studies selected,^{12,18–26} and the pooled R_0 , found after weighting by population proportions in every outbreak, was 1.32 (interquartile range, 1.03–1.46) (Figure 3). R_0 tended to increase with time (Spearman rank order correlation: $R = 0.46$, $P = .11$). Pooled R_0 was 1.27 (interquartile range, 1.02–1.46) in the studies that implemented surveillance; it was 1.41 (range, 1.02–2.0) in studies where selected contact patients were screened.

TABLE 1. Characteristics of 13 Studies Reporting Vancomycin-Resistant Enterococci (VRE) Outbreaks

Study	Duration of epidemic (case findings) in months	Specialty	Number of index cases	Number of screened patients	Number of secondary cases	VRE prevalence, % ^a
Marcadé et al ¹⁸	0.5	Hematology unit	1	56	7	12.5
Escaut et al ¹²	1.5	Liver transplantation unit	1	294	12	4.0
Liu et al ¹⁹	5	Intensive care unit	8	70	15	21.4
Tuon et al ²⁰	1	Renal transplant unit	1	32	7	21.9
Brossier et al ²¹	3	Geriatric unit	1	48	8	16.7
Servais et al ²²	0.75	Nephrology unit	1	138	13	9.4
Cheng et al ²³	1	Neurosurgical unit	1	192	3	1.6
Al-Mohri et al ²⁷	NA ^b	Cardiovascular surgery unit	1	114	14	12.3
Deplano et al ²⁸	9	Hematology unit	2	307	11	3.6
Chlebicki et al ²⁴	6	Hematology ward and intensive care units	2	136	4	2.9
Mascini et al ²⁵	2	Several specialties	2	183	27	14.8
Peta et al ²⁹	16	Intensive care unit	2	509	56	11.0
Naas et al ²⁶	5	Nephrology and internal medicine wards	7	180	20	11.1

^aNumber of secondary cases/number of screened patients.

^bNot available.

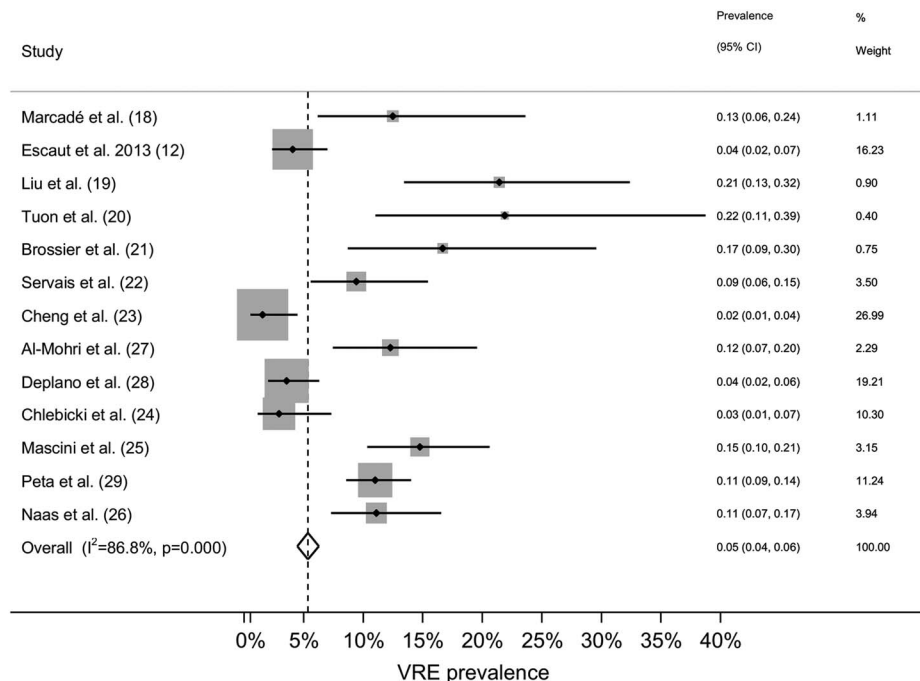


FIGURE 2. Pooled reporting of vancomycin-resistant enterococci prevalence: 13 studies, N = 2,259 patients. The numeral after an author’s name is the reference.

TABLE 2. Definitions of Contact Patients in Reported Vancomycin-Resistant Enterococci (VRE) Outbreaks in 13 Studies

Study	Definition of contact patients	Screening frequency	Screening policy
18	Patients whose hospital stay overlapped with the stay of a patient with VRE in the same unit	No frequency reported	Contact patients
12	Patients present in the same sector or tended by the same staff as the index patient	No frequency reported	Contact patients
19	All patients admitted	Weekly for all patients who stayed more than 24 h	Unit surveillance
20	All patients admitted in the unit	Weekly	Unit surveillance
21	Patients hospitalized in the same ward at the same time as the index case	Weekly from initial detection of the index case until 2 months after detection of the last VRE case	Contact patients
22	No definition	No frequency reported	Contact patients
23	All patients discharged or transferred to hospitals during the investigation period	No frequency reported	Unit surveillance
27	Patients in the affected unit	Weekly	Unit surveillance
28	All patients in the hematology unit	Weekly	Unit surveillance
24	Remaining inpatients	Daily	Contact patients
25	All patients still hospitalized who might have had contact with the 2 presumed index patients	Weekly	Contact patients
29	All patients within 24 h of admission	On a weekly basis if patients underwent prolonged ICU stay	Unit surveillance
26	All patients hospitalized in the ward and all newly admitted patients	Weekly	Unit surveillance

NOTE. ICU, intensive care unit.

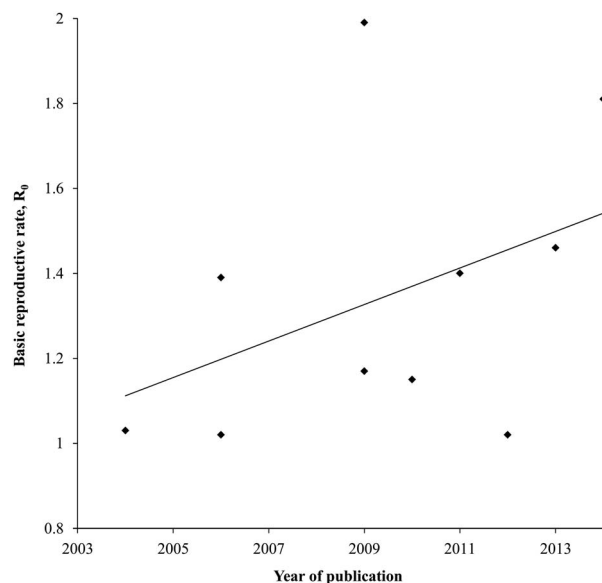


FIGURE 3. Basic reproductive rates of vancomycin-resistant outbreaks over time. $N = 13$ studies. R_0 was calculated according to the following formula: $R_0 = (\ln 2) D/t_d + 1$, where t_d is the doubling time and D is the average duration of latency plus infectious periods in days. The linear trend is shown (Spearman rank order correlation: $R = 0.46$, $P = .11$).

DISCUSSION

Our objectives were to review reports of VRE outbreaks, with particular emphasis on the definition of contact patients, and estimate the pooled R_0 in hospital settings. We discerned wide heterogeneity in the definition of contact patients, with screening based on several definitions of hospital-wide programs. The pooled R_0 of VRE outbreaks was 1.32 (interquartile range, 1.03–1.46).

To estimate the spread of outbreaks and the implementation of control measures, it is important to identify, as soon as possible, how many patients are contacts and potentially colonized secondarily. The cost of such screening programs, with repeated rectal swabs and completed with other control measures, is not negligible. Therefore, it seems appropriate to maximize detection capacity by focusing on selected patient groups. However, no standard definitions of exposed/contact patients were proposed in the reported articles, which led to considerable heterogeneity in VRE screening policies worldwide and did not facilitate comparisons.

In 2013, in France, the High Council of Public Health published a report on preventing the spread of highly resistant bacteria where a clear screening policy was defined.³⁰ Contact patients were those who were attended to by the same staff at the same time as VRE patients. In the United States, screening policies are different. The Hospital Infection Control Practices Advisory Committee recommends obtaining stool cultures or rectal swab samples from roommates of patients newly found to be infected or colonized by VRE and additional screening of patients on the ward at the discretion of infection control

staff.³¹ The optimal timing and extent of screening procedures in Canadian guidelines remain unclear.³¹

Significant heterogeneity of VRE prevalence was observed in contact patients with a pooled rate of 5.4% (95% CI, 4.5%–6.3%) in screened individuals. This heterogeneity may be partially explained by screening policies, by different baseline prevalences of VRE carriage in endemic or nonendemic countries, and by the implementation of infection control measures.

Pooled R_0 was higher than 1, confirming the epidemic nature of VRE. Austin et al¹³ found that the estimated R_0 of VRE, during a study at Cook County Hospital in Chicago, was approximately 3 to 4 without infection control but only 0.7 when infection control measures were included. Our estimate was lower than the R_0 of VRE without infection control measures, meaning pooled R_0 was an mean estimate of the reproductive number during the entire outbreak course. Lowden et al¹⁴ tested a new model showing that the estimate of $R_0 = 0.751$, in the baseline scenario, could be reduced by 28.6% by implementing a hospital policy that simultaneously allocates maximum resources to both preventive care of VRE colonization and treatment of VRE infections. Interestingly, we have seen an increased R_0 trend in recent reports, which could be related to detection bias or to greater difficulties in controlling outbreaks in recent times.

Main limitations include possible publication bias of large VRE outbreaks with insufficient information on latency period because of the asymptomatic nature of VRE carriage that was based on a single study¹⁷; however, we did not discern a more precise and reliable description of this parameter in the literature. Moreover, because the number of articles was limited, we were unable to quantify which factors were associated with better outbreak control. Thus, R_0 was calculated for the entire outbreak period, which included time before and after the implementation of control measures. Indeed, estimates of the reproductive rates are dependent on the ability to detect all secondary cases. For colonization or infection with multi-resistant organisms, screening procedures are crucial because they are the only chance to detect secondary cases in nearly all instances. Thus, the choice of the population to be screened directly influences the sensitivity of the detection of secondary cases and consequently the estimates of the reproductive R_0 .

In conclusion, VRE outbreaks frequently occur in hospital settings. Large heterogeneity in the definition of contact precautions can be problematic because it can evoke delays in identifying the magnitude of VRE cross-transmission. Future study might assess the impact of different infection control measures on the reproductive rate of VRE.

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REFERENCES

- Uttley AH, Collins CH, Naidoo J, George RC. Vancomycin-resistant enterococci. *Lancet* 1988;1:57–58.
- Leclercq R, Derlot E, Duval J, Courvalin P. Plasmid-mediated resistance to vancomycin and teicoplanin in *Enterococcus faecium*. *N Engl J Med* 1988;319:157–161.
- Werner G, Coque TM, Hammerum AM, et al. Emergence and spread of vancomycin resistance among enterococci in Europe. *Euro Surveill* 2008;13. pii:19046.
- Deshpande LM, Fritsche TR, Moet GJ, Biedenbach DJ, Jones RN. Antimicrobial resistance and molecular epidemiology of vancomycin-resistant enterococci from North America and Europe: a report from the SENTRY antimicrobial surveillance program. *Diagn Microbiol Infect Dis* 2007;58:163–170.
- Willems RJJ, Top J, van Santen M, et al. Global spread of vancomycin-resistant *Enterococcus faecium* from distinct nosocomial genetic complex. *Emerg Infect Dis* 2005;11:821–828.
- Molton JS, Tambyah PA, Ang BSP, Ling ML, Fisher DA. The global spread of healthcare-associated multidrug-resistant bacteria: a perspective from Asia. *Clin Infect Dis* 2013;56:1310–1318.
- Hidron AI, Edwards JR, Patel J, et al. NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. *Infect Control Hosp Epidemiol* 2008;29:996–1011.
- Orsi GB, Ciorba V. Vancomycin resistant enterococci healthcare-associated infections. *Ann Ig Med Prev E Comunità* 2013;25:485–492.
- Friães A, Resina C, Manuel V, Lito L, Ramirez M, Melo-Cristino J. Epidemiological survey of the first case of vancomycin-resistant *Staphylococcus aureus* infection in Europe. *Epidemiol Infect* 2015;143:745–748.
- Limbago BM, Kallen AJ, Zhu W, Eggers P, McDougal LK, Albrecht VS. Report of the 13th vancomycin-resistant *Staphylococcus aureus* isolate from the United States. *J Clin Microbiol* 2014;52:998–1002.
- Moravvej Z, Estaji F, Askari E, Solhjoui K, Naderi Nasab M, Saadat S. Update on the global number of vancomycin-resistant *Staphylococcus aureus* (VRSA) strains. *Int J Antimicrob Agents* 2013;42:370–371.
- Escaut L, Bouam S, Frank-Soltysiak M, et al. Eradication of an outbreak of vancomycin-resistant *Enterococcus* (VRE): the cost of a failure in the systematic screening. *Antimicrob Resist Infect Control* 2013;2:18.
- Austin DJ, Bonten MJ, Weinstein RA, Slaughter S, Anderson RM. Vancomycin-resistant enterococci in intensive-care hospital settings: transmission dynamics, persistence, and the impact of infection control programs. *Proc Natl Acad Sci U S A* 1999;96:6908–6913.
- Lowden J, Miller Neilan R, Yahdi M. Optimal control of vancomycin-resistant enterococci using preventive care and treatment of infections. *Math Biosci* 2014;249:8–17.
- Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLOS Med* 2009;6:e1000097.
- Anderson RM, Fraser C, Ghani AC, et al. Epidemiology, transmission dynamics and control of SARS: the 2002–2003 epidemic. *Philos Trans R Soc Lond B Biol Sci* 2004;359:1091–1105.
- Bonten MJ, Hayden MK, Nathan C, et al. Epidemiology of colonisation of patients and environment with vancomycin-resistant enterococci. *Lancet* 1996;348:1615–1619.
- Marcadé G, Micol JB, Jacquier H, et al. Outbreak in a haematology unit involving an unusual strain of glycopeptide-resistant *Enterococcus faecium* carrying both vanA and vanB genes. *J Antimicrob Chemother* 2014;69:500–505.
- Liu Y, Cao B, Gu L, Liu K, Feng Z. Successful control of vancomycin-resistant *Enterococcus faecium* nosocomial outbreak in a teaching hospital in China. *Am J Infect Control* 2012;40:568–571.
- Tuon FF, Pentead-Filho SR, Camilotti J, van der Heijden IM, Costa SF. Outbreak of vancomycin-resistant *Enterococcus* in a renal transplant unit. *Braz J Infect Dis* 2011;15:403–405.
- Brossier F, Lefrançois S, Paute J, et al. Decolonisation for early control of an outbreak of vancomycin-resistant *Enterococcus faecium* in a geriatric rehabilitation care facility. *J Hosp Infect* 2010;76:368–369.
- Servais A, Mercadal L, Brossier F, et al. Rapid curbing of a vancomycin-resistant *Enterococcus faecium* outbreak in a nephrology department. *Clin J Am Soc Nephrol* 2009;4:1559–1564.
- Cheng VC, Chan JF, Tai JW, et al. Successful control of vancomycin-resistant *Enterococcus faecium* outbreak in a neurosurgical unit at non-endemic region. *Emerg Health Threats J* 2009;2:e9.
- Chlebicki MP, Ling ML, Koh TH, et al. First outbreak of colonization and infection with vancomycin-resistant *Enterococcus faecium* in a tertiary care hospital in Singapore. *Infect Control Hosp Epidemiol* 2006;27:991–993.
- Mascini EM, Troelstra A, Beitsma M, et al. Genotyping and preemptive isolation to control an outbreak of vancomycin-resistant *Enterococcus faecium*. *Clin Infect Dis* 2006;42:739–746.
- Naas T, Fortineau N, Snanoudj R, Spicq C, Durrbach A, Nordmann P. First nosocomial outbreak of vancomycin-resistant *Enterococcus faecium* expressing a VanD-like phenotype associated with a vanA genotype. *J Clin Microbiol* 2005;43:3642–3649.
- Al-Mohri HA, Tadros MA, Louie L, Vearncombe M, Simor AE. Utility of direct, real-time PCR in the management of a nosocomial outbreak of vancomycin-resistant *Enterococcus faecium* (vanB genotype). *Eur J Clin Microbiol Infect Dis* 2008;27:321–322.
- Deplano A, Denis O, Nonhoff C, et al. Outbreak of hospital-adapted clonal complex-17 vancomycin-resistant *Enterococcus faecium* strain in a haematology unit: role of rapid typing for early control. *J Antimicrob Chemother* 2007;60:849–854.
- Peta M, Carretto E, Barbarini D, et al. Outbreak of vancomycin-resistant *Enterococcus* spp. in an Italian general intensive care unit. *Clin Microbiol Infect* 2006;12:163–169.
- Prévention de la transmission croisée des “Bactéries Hautement Résistantes aux antibiotiques émergentes.” Haut Conseil de la Santé Publique website. <http://www.hcsp.fr/Explore.cgi/avisrapportsdomaine?clefr=372>. Published 2013. Accessed August 25, 2014.
- Recommendations for preventing the spread of vancomycin resistance: recommendations of the Hospital Infection Control Practices Advisory Committee (HICPAC). *Am J Infect Control* 1995;23:87–94.