World Journal of Pharmaceutical Sciences
ISSN (Print): 2321-3310; ISSN (Online): 2321-3086
Available online at: https://wjpsonline.com/
Review Article

PHARMACOECONOMIC EVALUATION OF VANCOMYCIN AND TEICOPLANIN

M. Indhu Priya Dharshini[1], S.Pavith Sagar, S.Vishnu Varthan

[1]Department of pharmacy practice, PSG college of Pharmacy, Peelamedu Coimbatore 641004, Tamil Nadu.

Received: 13-08-2024 / Revised Accepted: 17-08-2024 / Published: 04-09-2024

ABSTRACT:

Teicoplanin and vancomycin are antibiotics widely prescribed for the treatment of Gram-positive bacterial infections. This review presents a pharmacoeconomic evaluation comparing the efficacy and cost-effectiveness of these two antibiotics. Clinical studies indicate that teicoplanin demonstrates superior efficacy in treating a range of Gram-positive infections, with higher cure rates and fewer adverse effects compared to vancomycin. Additionally, teicoplanin's pharmacokinetic properties allow for less frequent dosing, enhancing patient compliance and reducing hospital resource utilization. Economically, teicoplanin proves to be more cost-effective due to its lower overall treatment costs, including reduced hospitalization and monitoring expenses. These findings suggest that teicoplanin offers a more effective and economically advantageous option over vancomycin for the management of Gram-positive infections. This review underscores the importance of considering both clinical outcomes and economic factors in antibiotic selection to optimize healthcare resources and patient care.

Keyword: pharmacoeconomics, vancomycin, teicoplanin, cost-effectiveness, safety, efficacy

INTRODUCTION

Hospital infections caused on by Gram-positive bacteria are treated with the glycopeptides teicoplanin and vancomycin[1].Glycopeptide antibiotics have long been considered the standard treatment for confirmed or suspected life-threatening Gram-positive bacterial infections that are resistant to multiple antibiotics. In recent years, there has been a rise in infections caused by these bacteria, which can become resistant to penicillin and methicillin. Currently, there are only two options in the glycopeptide antibiotic class available on the market. These options differ significantly in terms of dosage, toxicity, cost, and route of administration, factors that may impact the selection between the two in specific situations[2].

The objective of this research was to assess and contrast the expenses associated with vancomycin and teicoplanin when used in the treatment of Gram-positive bacterial organisms.[3]

Background information on vancomycin vs teicoplanin:

Teicoplanin and vancomycin are equally effective in treating Gram-positive infections, both clinically and bacteriologically, according to clinical study results. Compared to teicoplanin, vancomycin has a shorter half-life and needs to be taken in many doses to maintain sufficient blood levels[4]. We determine that vancomycin has

Address for Correspondence: M. Indhu Priya Dharshini**,** Department of pharmacy practice, PSG college of Pharmacy, Peelamedu Coimbatore 641004, Tamil Nadu., **E-Mail:** Indhupriyapsg@gmail.com.

How to Cite this Article: M. Indhu Priya Dharshini. Pharmacoeconomic evaluation of vancomycin and teicoplanin. World J Pharm Sci 2024; 12(03): 9-17; https://doi.org/10.54037/WJPS.2022.100905

lower acquisition costs and is less likely to produce resistance based on the different information found in the literature. Teicoplanin is a group of five glycopeptides that are closely related to each other and have a structure that resembles vancomycin[5]. Teicoplanin binds to the final D-Ala-D-Ala sequence found in the peptides comprising the bacterial cell wall, thereby impeding the synthesis of peptidoglycan by stearically obstructing the transglycosylation process. In in vitro studies, Teicoplanin exhibited effective inhibitory effects against S. aureus, even strains that displayed resistance to methicillin[6].

The most frequent side effect of vancomycin is an anaphylactoid reaction, sometimes known as red-neck or red-man syndrome. Compared to vancomycin, dose-related nephrotoxicity, ototoxicity, and the red-neck (red-man) syndrome don't seem to be as common[7].

The costs of vancomycin and teicoplanin for the treatment of Gram-positive hospital infections. Our study's objective was to use cost minimization analysis of data collected in an observational scenario from the perspective of healthcare providers to estimate and evaluate[8].

PHARMACOKINETICS OF VANCOMYCIN AND TEICOPLANIN:

Due to its lipophilic nature, vancomycin exhibits poor absorption in the gastrointestinal tract. When administered via intramuscular route, vancomycin can cause significant discomfort, necessitating intravenous delivery as a slow infusion in 100 to 250 milliliters of 5% dextrose or normal saline, at a maximum rate of 15 mg/min. The half-life of vancomycin in individuals with normal renal function ranges from 3 to 9 hours[9].Vancomycin exhibits a variable capacity to attach to serum proteins, with a range spanning from 10% to 80%. Its primary affinity is towards albumin, although it may also interact with other proteins present in the serum. In cases where it binds to IgA, individuals with IgA myeloma may experience decreased levels of free serum concentrations, potentially leading to suboptimal therapeutic outcomes. The medication undergoes very little metabolism and is largely eliminated unaltered through glomerular filtration in the urine. Therefore, in individuals with renal impairment, it can build up to hazardous amounts. To maintain therapeutic levels and prevent toxicity, serum level monitoring and dosage adjustments are helpful. Its high tissue and cellular penetration may be explained by this. However, it is administered intravenously or intramuscularly since, like vancomycin, it is poorly absorbed orally[10].(Table.1)

Table.1.Pharmacokinetic profile of teicoplanin and vancomycin[4].

PARAMERTERS	Teicoplanin	Vancomycin
Bioavailability after i.m. injection (%)	90 (6)	Not applicable
Protein binding (%)	90 (1,39)	10-80 (32,35)
Distribution volume at steady state (l/kg)	0.84-1.17 (41)	0.5-1 (32)
Mean elimination halh-life in healthy adult (h)	156 (42,56)	6 (15)
Recommended dose (mg/kg)	6	8-10
Dose intervals (h)	24	6-12

INDICATION:

Vancomycin is suggested for the management of septicemia, infective endocarditis, skin and skin structure infections, bone infections, and lower respiratory tract infections in adult and pediatric individuals through intravenous administration[11].

Teicoplanin is known for its specific inhibition of Gram-positive organisms that secrete coagulase. It is commonly administered for the treatment of conditions such as osteoarthritis, septicemia, peritonitis, and endocarditis[12].

PATIENT AND MANAGEMENT:

There were only two intravenous medications that were suitable for treating MRSA infective endocarditis: vancomycin and teicoplanin. To identifying MRSA by blood culture analysis[13].

All patients were administered intravenous vancomycin at a dosage of 1 g every 12 hours as a component of their therapy. Monitoring of vancomycin serum levels was conducted regularly to ensure that levels remained within the target range of 18–26 ug/ml at peak and 10-15 ug/ml at trough in the serum[14].

Teicoplanin was given intravenously (IV) or directly as a single daily dose of 200 mg or 400 mg (3-6 mg/kg)[15].

Teicoplanin serum levels were not monitored. Due to its extended half-life (≈100 hours) and outstanding postantibiotic effect, teicoplanin can be administered once daily. Patients in the hospital received intravenous antibiotics for a minimum of 4-8 weeks, or until laboratory and clinical indicators of infection were stable, which were assessed at various time points during the initial 9 days of therapy for patients receiving teicoplanin as the sole treatment[16].

Analysis of plasma concentration data (peak and trough) for endocarditis and enterococci.Concentration was assessed at several points during the first nine days of treatment for patients taking teicoplanin either by itself or in combination with another medication.
Typically, patients receiving either monotherapy or combination therapy receive 5–10 mg/L[17].

TREATMENT OF TEICOPLANIN:

Teicoplanin provides a number of advantages over vancomycin, including the ability to be delivered intravenously or intramuscularly and a significantly longer elimination half-life in serum that permits once-daily administration[18].
Teicoplanin was given as a single 200 mg or 400 mg (3-6 mg/kg) i.m. or i.v. dose, with the ability for investigators to alter this amount.Researchers were free to employ teicoplanin as a stand-alone treatment or in combination with other antibiotics. A dose of up to 30 mg/kg of tecoplanin may be required to attain vancomycin-like efficacy; this is in addition to the typical suggested doses of 6 mg/kg/day for severe infections and 12 mg/kg/day for endocarditis[19].

It’s produced minor advers effect compare with vancomycin.

TREATMENT OF VANCOMYCIN:

For all patients, an intravenous vancomycin (1 g every 12 hours) treatment was initiated. Vancomycin serum levels were checked on a regular basis. Vancomycin levels at peak and serum trough were maintained at 10–15 ug/ml and 18–26 ug/ml, respectively[11].

Red-neck or red-man syndrome, also referred to as an anaphylactoid reaction, is the most common side effect associated with vancomycin. Nephrotoxicity, ototoxicity, and the red-neck (red-man) syndrome associated with vancomycin are less frequent in occurrence when the dosage is considered. [20]

EFFICACY OF VANCOMYCIN:

Vancomycin is a bactericidal antibiotic that is effective against a variety of gram-positive bacteria. As such, it is a useful treatment for endocarditis and bacteremia-related diseases. Its main therapeutic value is in the efficient management of these difficult medical problems. Vancomycin is a helpful, nontoxic antibiotic for endocarditis patients when cephalosporin or penicillin treatment is not appropriate[21].

When managing patients with an allergy to penicillin and infective endocarditis, treatment with vancomycin can be utilized either on its own or in conjunction with an aminoglycoside. In vitro studies have shown that vancomycin is effective at killing bacteria at low concentrations (~10 ~g/ml) for nearly two-thirds of the species involved. In cases where the infective endocarditis is caused by these susceptible species, vancomycin can be administered alone for a duration of one month. For infections caused by organisms with MBC values exceeding 10 ~g/ml, a combination of vancomycin and streptomycin for a two-week period is recommended. Vancomycin

is often prescribed as the primary treatment for prosthetic-valve endocarditis or as an alternative therapy for individuals with infective endocarditis who cannot take penicillin due to allergies or intolerance[17].

For enterococci, vancomycin is bacteriostatic but not bactericidal[22].

(Table.2[23])

S.NO	AUTHOR	PATIENT DEATILES	DISCUSSION	OUT COME
1	EDWARD W. HOOK, III, M.D.' WARREN D. JOHNSON, Jr., M.D. New York, New York	TOTAL NO. PATIENT:15 INCLUSION:13 EXCLUSION:2 AGE: 29 to 78 years.	Four out of the total of 15 patients did not exhibit any known underlying cardiac conditions. Among these individuals, two were diagnosed with Staphylococcus aureus endocarditis, while the remaining two were found to have culture-negative endocarditis. Furthermore, three patients were identified as having rheumatic heart disease, and eight patients were noted to have prosthetic cardiac valves. Notably, three of these patients had prosthetic cardiac valves implanted within two months prior to the onset of endocarditis. In a subset of cases, vancomycin served as the sole antibiotic treatment for five patients. Additionally, in seven other patients, the duration of vancomycin therapy matched or exceeded the duration of their alternative antibiotic treatments. Consequently, vancomycin was denoted as the primary antibiotic in these latter cases.	In the current study, 15 patients were treated with vancomycin for endocarditis caused by various bacteria such as Staph. epidermidis, Staph. aureus, diphtheroids, viridans streptococci, or enterococci. Of these, thirteen patients showed improvement, including four who solely received vancomycin, six who used vancomycin as their primary antibiotic, and three who had brief vancomycin courses. Assessing the effectiveness of vancomycin therapy was challenging in some cases due to the concurrent use of multiple antibiotics by 10 patients or successful heart valve replacement in five patients. Nevertheless, vancomycin played a significant role in the treatment of most of these patients.

(Table.3[24])

S.NO	AUTHOR	PATIIENT DEATILES	DISCUSSION	OUTCOME
1	Joseph E. Geraci and Walter R. Wilson From the Division of Infectious Diseases and Internal Medicine, Mayo Clinic and Mayo Foundation, Rochester, Minnesota	TOTAL.NO. PATIENT:55	A total of 55 cases were identified. The causative organisms in this cohort included Staphylococcus aureus (12 cases), enterococci (11 cases), viridans streptococci (14 cases), Staphylococcus epidermidis (five cases), diphtheroids (five cases), Streptococcus bovis (three cases), group B beta-hemolytic streptococci (two cases), microaerophilic streptococci (one case), and negative blood culture (two cases). These 55 individuals were treated by various healthcare providers, receiving different treatment regimens. Prior to receiving vancomycin, many had been treated with other antibiotics, and a considerable number underwent valve replacement while on therapy.	The purpose of these reports is to present the outcomes of treatment involving vancomycin, administered either as a sole medication or in conjunction with other antibiotics. Out of the 55 patients included in the study, forty-eight (87%) were successfully healed.

EFFICACY OF TEICOPLANIN:

Teicoplanin has been shown to be particularly effective in preventing endocarditis caused by both MRSA and a tolerant strain of S. oralis. Its preventive effectiveness was on comparable with that of well-known antibiotic regimens, such as ampicillin for viridans group streptococci and vancomycin for MRSA. Teicoplanin had some efficacy against a strain of E. faecium that was tolerant but did not produce b-lactamases. Its preventive effectiveness against E. faecium was still notable , and exceeded by vancomycin. For the prevention of endocarditis, teicoplanin administered as a single 400 mg intramuscular or intravenous dose should be taken into consideration as an alternative to vancomycin, particularly in the outpatient context[25].

ECONOMIC EVALUATION:

According to a pharmacoeconomic analysis, treating 100 patients with vancomycin for a mean of 10 days at a dosage of 2 g/day in 2 split doses cost $US30 251.76, with medication procurement expenses accounting for just 55% of the overall treatment cost. Fifty adverse events (of which phlebitis accounted for 91% of the events) were thought to be possible or probably connected to vancomycin, and 67% of patients had their serum drug concentration monitored. Cost-minimization studies are the basis of all published pharmacoeconomic evaluations that compare vancomycin and teicoplanin. Comparative efficacy has to be thoroughly proven since cost-minimization studies choose the therapy that will be most advantageous economically based on the assumption that the therapies under comparison are equally effective. Comparative trials on feverish neutropenic patients to date suggest that vancomycin and tecoplanin are equally effective. However, the relative efficacy of these medications has not been conclusively demonstrated due to small patient numbers in investigations of individuals with other infection types.
This section's studies were all conducted from the viewpoint of the hospital, which is the healthcare provider,

and they only assessed the direct costs of treatment. Different criteria were used in each trial for assessing organ function and serum medication levels when using these medicines[26].

A study was conducted with 124 febrile patients diagnosed with hematological malignancies to compare the effectiveness of teicoplanin and vancomycin in addition to the initial amikacin-ceftazidime regimen following documented bacteremia caused by gram-positive cocci. Both study groups had similar characteristics at the start, including age, gender, underlying hematologic conditions, and duration of neutropenia. The therapeutic success rates were 87.3% (55 out of 63 patients) for teicoplanin and 91.8% (56 out of 61 patients) for vancomycin, with no significant difference observed ($p = 0.560$). Treatment duration was around 12.2 days for teicoplanin and 11.4 days for vancomycin, showing comparable efficacy ($p = 0.216$). Interestingly, patients treated with teicoplanin had slightly longer fevers compared to those treated with vancomycin, lasting on average 4.9 days and 4.0 days, respectively ($p = 0.013$).

Among the participants, thirteen individuals encountered adverse reactions to the drugs, but there was no significant variance between the two groups. Over the course of the 8-year study, it was observed that isolated staphylococci displayed a gradual and notable decline in susceptibility to both glycopeptides. Moreover, the economic analysis conducted revealed that the supplementation of vancomycin proved to be cost-effective. The cost estimation was based on the guidelines of the Italian Health Care System, considering only expenses directly covered by the system. The analyzed cost components encompassed the cost of drugs based on hospital pharmacy prices, expenses associated with drug preparation and administration, costs linked to treatment monitoring, and expenditures related to managing adverse effects. Any costs induced by the trial were excluded from the analysis.

The average cost per patient for each drug group was calculated by dividing the total costs by the number of evaluable patients. The economic assessment pointed towards teicoplanin-containing regimens being relatively more costly compared to those incorporating vancomycin. This outcome aligns with findings from previous studies conducted in the Netherlands, which indicated a slight cost advantage for vancomycin. Additionally, a recent study abstract suggested that the higher treatment expenses associated with teicoplanin, as opposed to vancomycin, were primarily due to the acquisition costs of the drugs. However, recent comparative studies on teicoplanin and vancomycin regimens have indicated similar costs between the two options, possibly influenced by varying study methodologies.

The evaluation was specifically focused on patients with confirmed infections caused by gram-positive cocci and included costs related to the treatment of superinfections, which were observed to be more frequent in the teicoplanin group based on our experience. Consequently, our findings demonstrating an economic benefit for vancomycin-based regimens could prompt further economic analyses encompassing all relevant costs involved in treatment, including adverse events and superinfections.[27]

The direct cost of treatment was assessed by considering a variety of factors, which included the type and amount of drug used, the frequency of doses given, the monitoring procedures performed, consultation expenses, adverse events, hemodialysis procedures, and the extension of hospital follow-up time. Costs were allocated based on the actual expenses incurred by the hospital for acquiring medications and materials, the value of procedures conducted (such as administration, monitoring, and hemodialysis), and the length of hospitalization. Indirect costs, like loss of productivity during treatment, were not factored in due to the similar treatment application durations for admission and follow-up.

To ensure the reliability of the findings, a sensitivity analysis was conducted. This analysis considered the potential impact of increased personnel costs (Scenario 1) and the acquisition of teicoplanin at a price of $15.03 per vial (Scenario 2) on the results. The costs associated with these scenarios were detailed in Table 1. Furthermore, a simulation was performed to assess the value of improving the conditions of teicoplanin use. This simulation involved adjusting the model used in the study to reflect a shorter admission time for patients who could potentially reduce their stay by completing glycopeptide therapy earlier. The impact of these adjustments on the outcomes was carefully evaluated to understand the potential benefits of early discharge and transitioning to intramuscular outpatient treatment.[28]

CONCLUSION:

Teicoplanin, a glycopeptide antibiotic akin to vancomycin, is utilized for the treatment of a broad spectrum of gram-positive bacterial infections. Its efficacy has been demonstrated in various clinical settings, such as endocarditis, intravenous catheter-associated infections, and septicemia caused by different strains of bacteria. Teicoplanin, whether administered alone or in conjunction with other antibiotics, has proven effective in managing diverse gram-positive infections including septicemia, endocarditis, skin and soft tissue infections, osteomyelitis, and lower respiratory tract infections. In laboratory studies, teicoplanin exhibited superior efficacy in reducing the bacterial count of S. aureus compared to vancomycin. While both teicoplanin and vancomycin demonstrate similar clinical and bacteriological outcomes, the former is characterized by lower toxicity and greater ease of administration in severe infections. Moreover, from a cost-effectiveness standpoint, teicoplanin may be considered a favourable alternative to vancomycin.

REFERENCE:

1. Blaskovich, Mark A T et al. “Developments in Glycopeptide Antibiotics.” *ACS infectious diseases* vol. 4,5 (2018): 715-735. doi:10.1021/acsinfecdis.7b00258

2. Wood MJ. The comparative efficacy and safety of teicoplanin and vancomycin. J Antimicrob Chemother. 1996 Feb;37(2):209-22

3. Guo, Yunlei et al. “Prevalence and Therapies of Antibiotic-Resistance in *Staphylococcus aureus*.” *Frontiers in cellular and infection microbiology* vol. 10 107. 17 Mar. 2020, doi:10.3389/fcimb.2020.00107

4. Murphy S, Pinney RJ. Teicoplanin or vancomycin in the treatment of gram-positive infections? J Clin Pharm Ther. 1995 Feb;20(1):5-11. doi: 10.1111/j.1365-2710.1995.tb00619.x. PMID: 7775615.

5. Sieradzki, K et al. “Decreased susceptibilities to teicoplanin and vancomycin among coagulase-negative methicillin-resistant clinical isolates of staphylococci.” *Antimicrobial agents and chemotherapy* vol. 42,1 (1998): 100-7. doi:10.1128/AAC.42.1.100

6. Kim, Sung Joon et al. “Vancomycin derivative with damaged D-Ala-D-Ala binding cleft binds to cross-linked peptidoglycan in the cell wall of Staphylococcus aureus.” *Biochemistry* vol. 47,12 (2008): 3822-31. doi:10.1021/bi702232a

7. Rocha, Jaime Luis Lopes et al. “Uncommon vancomycin-induced side effects.” *The Brazilian journal of infectious diseases : an official publication of the Brazilian Society of Infectious Diseases* vol. 6,4 (2002): 196-200. doi:10.1590/s1413-86702002000400007

8. Portolés, A et al. “Health economics assessment study of teicoplanin versus vancomycin in Gram-positive infections.” *Revista espanola de quimioterapia : publicacion oficial de la Sociedad Espanola de Quimioterapia* vol. 19,1 (2006): 65-75.

9. De Cock, Pieter A J G et al. “Impact of vancomycin protein binding on target attainment in critically ill children: back to the drawing board?.” *The Journal of antimicrobial chemotherapy* vol. 72,3 (2017): 801-804. doi:10.1093/jac/dkw495

10. Cantú, T G et al. “Protein binding of vancomycin in a patient with immunoglobulin A myeloma.” *Antimicrobial agents and chemotherapy* vol. 34,7 (1990): 1459-61. doi:10.1128/AAC.34.7.1459

11. Estes KS, Derendorf H. Comparison of the pharmacokinetic properties of vancomycin, linezolid, tigecyclin, and daptomycin. Eur J Med Res. 2010 Nov 30;15(12):533-43. doi: 10.1186/2047-783x-15-12-533. PMID: 21163728; PMCID: PMC3352102.

12. Leport, C et al. "Evaluation of teicoplanin for treatment of endocarditis caused by gram-positive cocci in 20 patients." *Antimicrobial agents and chemotherapy* vol. 33,6 (1989): 871-6. doi:10.1128/AAC.33.6.871

13. Sacar, Mustafa et al. "Comparison of antimicrobial agents as therapy for experimental endocarditis: caused by methicillin-resistant Staphylococcus aureus." *Texas Heart Institute journal* vol. 37,4 (2010): 400-4.

14. Kovacevic, Tijana et al. "The Effect of Hypoalbuminemia on the Therapeutic Concentration and Dosage of Vancomycin in Critically Ill Septic Patients in Low-Resource Countries." *Dose-response : a publication of International Hormesis Society* vol. 17,2 1559325819850419. 20 May. 2019, doi:10.1177/1559325819850419

15. Ahn, Byung-Jin et al. "Teicoplanin dosing strategy for treatment of Staphylococcus aureus in Korean patients with neutropenic fever." *Yonsei medical journal* vol. 52,4 (2011): 616-23. doi:10.3349/ymj.2011.52.4.616

16. Ueda, Takashi et al. "Clinical efficacy and safety in patients treated with teicoplanin with a target trough concentration of 20 μg/mL using a regimen of 12 mg/kg for five doses within the initial 3 days." *BMC pharmacology & toxicology* vol. 21,1 50. 8 Jul. 2020, doi:10.1186/s40360-020-00424-3

17. Baddour, Larry M et al. "Infective Endocarditis in Adults: Diagnosis, Antimicrobial Therapy, and Management of Complications: A Scientific Statement for Healthcare Professionals From the American Heart Association." *Circulation* vol. 132,15 (2015): 1435-86. doi:10.1161/CIR.0000000000000296

18. Bibler, M R et al. "Clinical evaluation of efficacy, pharmacokinetics, and safety of teicoplanin for serious gram-positive infections." *Antimicrobial agents and chemotherapy* vol. 31,2 (1987): 207-12. doi:10.1128/AAC.31.2.207

19. Schaison, G et al. "Teicoplanin in the treatment of serious infection." *Journal of chemotherapy (Florence, Italy)* vol. 12 Suppl 5 (2000): 26-33. doi:10.1080/1120009x.2000.11782315

20. Bruniera, F R et al. "The use of vancomycin with its therapeutic and adverse effects: a review." *European review for medical and pharmacological sciences* vol. 19,4 (2015): 694-700.

21. De Oliveira, David M P et al. "Antimicrobial Resistance in ESKAPE Pathogens." *Clinical microbiology reviews* vol. 33,3 e00181-19. 13 May. 2020, doi:10.1128/CMR.00181-19

22. Hayden, M K et al. "Bactericidal activities of antibiotics against vancomycin-resistant Enterococcus faecium blood isolates and synergistic activities of combinations." *Antimicrobial agents and chemotherapy* vol. 38,6 (1994): 1225-9. doi:10.1128/AAC.38.6.1225

23. Hook EW 3rd, Johnson WD Jr. Vancomycin therapy of bacterial endocarditis. Am J Med. 1978 Sep;65(3):411-5. doi: 10.1016/0002-9343(78)90766-0. PMID: 152580.

24. Geraci JE, Wilson WR. Vancomycin therapy for infective endocarditis. Rev Infect Dis. 1981 Nov-Dec;3 suppl:S250-8. PMID: 7342289.

25. Baddour, Larry M et al. "Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America." *Circulation* vol. 111,23 (2005): e394-434. doi:10.1161/CIRCULATIONAHA.105.165564

26. Garrelts, J C et al. "A pharmacoeconomic model to evaluate antibiotic costs." *Pharmacotherapy* vol. 14,4 (1994): 438-45.

27. D'Antonio, D et al. "Addition of teicoplanin or vancomycin for the treatment of documented bacteremia due to gram-positive cocci in neutropenic patients with hematological malignancies: microbiological, clinical and economic evaluation." *Chemotherapy* vol. 50,2 (2004): 81-7. doi:10.1159/000077807

28. Portolés, A et al. "Health economics assessment study of teicoplanin versus vancomycin in Gram-positive infections." *Revista espanola de quimioterapia : publicacion oficial de la Sociedad Espanola de Quimioterapia* vol. 19,1 (2006): 65-75.