Supplementary Material V: Summary of Results of the sensitivity analyses of the Reviewed Economic Evaluations

Reference	Outcome Criterion	Sensitivity Analysis Performed	Results of sensitivity analysis	Final findings
Buendía (37) 2024 (Colombia)	Clinical Cure Rate	One-way SA, Probabilistic SA (10,000 Monte Carlo Simulations)	The baseline results of the study were "robust to changes in all assumptions and parameters." Linezolid is more cost-effective with a probability of 0.999. NMB is always positive.	Linezolid is the dominant treatment compared to vancomycin with a $517 lower cost and a 10% incremental benefit. Clinical Cure Rate: Linezolid = 53 % vs Vancomycin =43 % The mean incremental NET BENEFIT of linezolid is US$1048 (1009-1088) CI 95%. The PSB for vancomycin is US $1036, while linezolid reduces the PSB to zero, eliminating any decision-making uncertainty.
Grau (32) 2005 (Spain)	• Clinical Cure Rate • QALY • LYS	• Univariate SA • Scenario Analysis (8 scenarios)	At baseline, linezolid provided greater cost-effectiveness and more LYS and QALYs than vancomycin, and the effectiveness values were stable even across minimum and maximum changes. In the "best case" scenario, linezolid prevailed. In the "worst case" scenario, vancomycin was dominant (more effective and less expensive) in all subgroups except MRSA.	Linezolid is dominant in the treatment of patients with VAMP, with an ICER of less than €30,000 (the Spanish acceptable threshold for new treatments is €30,000). ICER Per life year saved = € 289.51 ICER Per QALY = € 348.85 The additional QALY with LIN = 1.805 The additional LYS with LIN = 2.175 The results were stable under sensitivity analysis.
Machado (4) 2005 (Brazil)	Survival	NR	NR	Despite its higher drug cost, linezolid has a lower overall cost per recovered patient, making it more cost-effective than vancomycin. Linezolid: Clinical Cure Rate 62.2%; Invested amount per cured patient R$ 7,764.72 Brand-name Vancomycin: Clinical Cure Rate 21.2%; Invested amount per cured patient R$ 13,231.65 Generic Vancomycin: Clinical Cure Rate 21.2%; Invested amount per cured patient R$ 11,277.59
Lin (17) 2016 (Taiwan)	Clinical Cure Rate	One-way SA (5%, 10%, 20% changes)	Clinical parameters had the greatest impact on ICPC = Incremental Cost Per Cure, topped by the number of days in the intensive care unit and the rate of clinical improvement. Increasing the number of days in the intensive care unit with vancomycin reduces ICPC, making linezolid appear relatively more cost-effective. Cost components (i.e., drug costs, dose, and duration of treatment) did not have as much impact on ICPC as clinical parameters.	The total cost of linezolid treatment per patient is $376 more than vancomycin, and the treatment rate with linezolid is also higher than vancomycin. Clinical Cure Rate: Linezolid = 57.6 % vs Vancomycin = 46.6 % Incremental Cost Per Cure (ICPC) = $3421 Depending on the willingness to pay for clinical treatment, linezolid can be affordable in Taiwan. Clinical parameters (number of days in intensive care unit and rate of clinical improvement) had the greatest impact on ICPC.
Collins (33) 2015 (USA)	QALY	• Univariate SA • Probabilistic SA (10,000 Monte Carlo Simulation) • Threshold Analysis	➢ Results of univariate sensitivity analysis: The study results were sensitive to time horizon, survival rate, population, and mortality: • Time horizon: In the 60-day time horizon analysis, the incremental cost per QALY gained with linezolid increased significantly, reaching $443,662 in the ITT (intent-to-treat) population. And in the population of hospital-acquired pneumonia with confirmed MRSA, vancomycin outperformed linezolid (meaning lower cost and greater effectiveness). Also, in this 60-day analysis, the reduction in the cost of linezolid had the potential to change the results. • Survival rates: Survival rates for vancomycin or linezolid had the potential to influence outcomes, such that small changes in survival rates could change the preferred option. • Patient population: Results varied depending on whether the analysis was performed in the overall population (ITT) or the population of patients with confirmed MRSA (mITT). In patients with confirmed MRSA, vancomycin was superior to linezolid. • No mortality advantage: If no mortality difference between the two drugs were assumed, linezolid would not be significantly cost-effective, with an incremental cost per QALY of millions of dollars. • Costs and adverse event rates: In the baseline analysis, costs and adverse event rates did not affect the results. However, in certain scenarios (such as the 60-day analysis), nephrotoxicity costs and its rates could have shifted the results in favor of linezolid. ➢ Probabilistic Sensitivity Analysis Results: This analysis was performed by varying parameters in 10,000 Monte Carlo simulations and showed that linezolid would be cost-effective in 78% of cases with a payout threshold of $100,000. ➢ Results of threshold sensitivity analysis: • Threshold of $50,000 per QALY: When the model sensitivity was examined at this threshold, survival rate, linezolid cost, nephrotoxicity cost, and conversion rate to oral linezolid were found to influence the results. At this threshold, if the survival rate for linezolid or vancomycin decreased by 1.1% or increased by 1%, linezolid was no longer cost-effective, and also if the estimated lifetime survival was less than 1.5 years, linezolid was no longer cost-effective. • Threshold of $150,000 per QALY: The study also considered a variable payment threshold between $50,000 and $150,000 and reported that at this threshold linezolid was cost-effective 72.1% to 79.7% of the time.	The model was sensitive to changes in time horizon, mortality, and population. Over the lifetime time horizon, in the ITT population and assuming no difference in mortality rates between drugs, linezolid prevails with an ICER Per QALY=$6,089. However, at a 60-day time horizon, in the mITT population and assuming the same mortality rate between drugs, vancomycin prevails.
Tan (36) 2014 (China)	Clinical Cure Rate	Scenario Analysis (8 scenarios)	Based on the opinions of the expert panel, a series of scenario analyses were conducted with varying values of resource utilization and unit costs. In the most scenario analyses for Beijing, Guangzhou, and Nanjing, linezolid was found to dominate over vancomycin. • In the scenario of switching to second-line therapy (due to first-line failure or adverse events) from day 7 to day 3, the difference in total hospitalization cost between linezolid and vancomycin increased, resulting in a higher ICER. • In the "use linezolid instead of vancomycin" scenario, ICERs increased with reduced daily costs in the general and intensive care units, which offset the lower cost of linezolid (due to shorter hospital stays for patients treated with linezolid). • In the "lower cost of vancomycin CP" scenario, which resulted in a greater increase in total inpatient costs for linezolid than vancomycin, ICERs increased. The regional analysis	In four cities in China, linezolid is a cost-effective option compared to brand-name vancomycin with relatively low ICERs (less than ¥20,000 per patient improved). ICER per additional successfully treated patient: Beijing= ¥1,861 Nanjing= ¥163 Xi'an= ¥16,509 Guangzhou= Linezolid Dominated

			of Xi'an reported a similar trend due to lower hospitalization costs (reported for category A3 hospitals compared to other cities). • **Another scenario of "removing the 13% hospital profit margin from drug costs" as part of the People's Republic of China's national healthcare reform was tested for drug procurement costs of ¥400 and ¥125 for a 600 mg vial of linezolid and a 500 mg vial of vancomycin CP, respectively. In this scenario, linezolid was superior to vancomycin for Beijing, Guangzhou, and Nanjing except Xi'an, with an ICER of ¥7,810 per successfully treated patient.** **Parameters such as duration of treatment, consideration of the cost of managing side effects, and drug procurement costs create the greatest uncertainty in cost-effectiveness results.**	
Patel (35) 2014 (USA)	**Clinical Cure Rate**	• **Univariate SA** • **Probabilistic SA (10,000 Monte Carlo Simulation)** • **Scenario Analysis (3 scenarios)**	**The results of one-way sensitivity analysis showed the variables that had the greatest impact on the model results.** **The lowest ICER was approximately -$240,000 for the shortest ICU length of stay scenario with linezolid, 6.1 days (representing the prevailing scenario for linezolid),** **The highest ICER was approximately $210,000 for the highest clinical efficacy scenario of vancomycin, 52.9%.** **And the ICER approximately $160,000 was related to the shortest ICU length of stay scenario with vancomycin, 6.6 days.** **Since these ICER values can be considered higher than the acceptable willingness-to-pay (WTP) threshold, vancomycin appears to be a cost-effective option in these scenarios.** **There is no specific WTP threshold for successful treatment of a patient, hence different WTP values have been tested in the PSA cost-effectiveness acceptability curve.** **PSA showed a 64.4% chance of Linezolid being cost-effective at $0 WTP, rising to 90.8% at $120,000 WTP.**	**Linezolid is superior to vancomycin in terms of lower cost ($824) and higher clinical response (2.7%).** **The results were stable under sensitivity analyses (at a WTP of $0, linezolid has a 64.4% chance of being cost-effective).**
Patel (34) 2014 (Germany)	**Clinical Cure Rate**	• **Univariate SA** • **Probabilistic SA (10,000 Monte Carlo Simulation)** • **Scenario Analysis (3 scenarios)**	**One-way sensitivity analysis identified variables with the greatest impact on model results.** **The lowest ICER was approximately - €81,000 for the shortest ICU length of stay scenario with linezolid, 6.1 days (representing the dominant scenario for linezolid).** **The highest ICER was approximately €102,000 corresponding to the scenario with the highest clinical efficacy of vancomycin, 52.9%.** **And the ICER of approximately €65,000 corresponded to the scenario of the shortest ICU length of stay with vancomycin, 6.6 days.** **Since these ICER values can be considered higher than the acceptable willingness-to-pay (WTP) threshold, vancomycin appears to be a cost-effective option in these scenarios.** **No specific WTP threshold has been established for successful treatment of a patient, hence different WTP values were tested in the PSA cost-effectiveness acceptability curve which shows the percentage of linezolid as a cost-effective option compared to vancomycin at different WTP thresholds.** **PSA showed a 53.9% chance of Linezolid being cost-effective at €0 WTP, rising to 94.1% at €120,000 WTP.**	**Linezolid is superior to vancomycin in terms of lower cost (123 euros) and higher clinical response (2.7%).** **The results were stable under sensitivity analyses (at a WTP of €0, linezolid has a 53.9% chance of being cost-effective).**
De Cock (31) 2009 (Germany)	• **Clinical Cure Rate** • **Survival** • **LYG**	• **One-way SA** • **Two-way SA** • **Scenario Analysis (2 scenarios)**	**The incremental cost effectiveness in the base case model is most sensitive to:** • **Number of days in intensive care unit with linezolid or vancomycin (hospitalization is the main cost driver)** • **Number of days of isolation** • **Intravenous injection time** • **Length of stay of deceased patients (when death occurred during or after first-line treatment) was shown.** **However, a 25% change in these parameters did not change the overall conclusion (results were stable and ICERs changed little).** **In all scenarios, linezolid was dominant and consistent under sensitivity analyses.**	**Linezolid is associated with 8.7% greater clinical improvement and 13.2% higher survival than vancomycin, and has a small additional cost (420 euros).** **ICER Per Life Gained = € 180** **ICER Per Death Avoided = € 3,171** **ICER Per Additional Cure = € 4,813** **The results were stable under sensitivity analysis.** **Clinical Cure Rate / Survival / LYG** **Linezolid: 73.6 % / 79.3 % / 14** **Vancomycin: 64.9 % / 66.1 % / 11.7**
Mullins (18) 2006 (USA)	**Survival**	• **Univariate SA** • **Multifactorial SA**	**In all analyses performed with varying parameters (using the expected total billed hospital charges, using median allowed charges or median payments instead of median billed charges, using actual payments made to the hospital, employing the mean instead of the median daily billed hospital charges, using total median billed hospital charges from the claims data rather than imputing a median daily charge, using the acquisition cost of linezolid to its AWP ($163), varying the treatment duration, using an alternative mortality rate derived from the hospital claims data, using mortality rates derived from the adjusted multivariate logistic regression analysis of clinical-trial data) the results were stable and linezolid was the cost-effective option.** **When a break-even analysis was performed in which mortality rates were adjusted, the marginal cost-effectiveness of linezolid over vancomycin reached $50,000 per life saved only when linezolid-associated mortality was as high as 0.324 (62% increase in linezolid-related mortality rate) or when vancomycin-related mortality was as low as 0.242 (33% reduction in vancomycin-related mortality rate).** **These results suggest that linezolid may not be a cost-effective option for treating MRSA HAP except in unlikely scenarios.** **A multivariate sensitivity analysis was also performed in which several input parameters were changed simultaneously. By simultaneously changing parameters and "creating the worst case", the ICER per life saved was $34,035, still below the conventional cost-effectiveness value.**	**Linezolid is cost-neutral compared to vancomycin ($32,636 for Linezolid vs. $32,024 for Vancomycin) but provides a higher clinical response/survival rate (Survival: Linezolid=80% vs Vancomycin=63.5%).** **Given the cost-neutral finding, Linezolid's significantly higher clinical response/survival rate made it a cost-effective alternative.** **ICER per life year saved= $3,600** **The results were stable under sensitivity analysis.**

NR: Not Reported - SA: Sensitivity Analysis