

Table A: Population and Effectiveness Data Resource of the Reviewed Economic Evaluations

Reference Author/Year	Country	Population	Effectiveness Data Resource
Buendía et al.(40) 2024	Colombia	A mathematical model VAP patients with MRSA, age 18+ This study using published data to build this mathematical model, not human participants were directly involved in the study.	Kato et al. 2007 (A recent meta-analysis of seven randomized controlled trials (RCTs) involving 1239 patients and eight retrospective cohort or case–control studies (CSs) involving 6125 patients)
Grau et al.(38) 2005	Spain	VAP patients in ICU (4 subgroups including: All patients with VAP, Patients with VAP with a gram-positive agent, Patients with VAP with gram-positive Staphylococcus aureus, the MRSA VAP (44 cases treated with LIN and 47 cases treated with VAN). The Cases in this study were based on the results of a study conducted by Kollef et al. who retrospectively evaluated data of two prospective, randomized and double-blind clinical trials (Wunderink 2003 & Rubinstein 2001)	In this study effectiveness were based on the results of a study conducted by Kollef et al who retrospectively evaluated data of two prospective, randomized and double-blind clinical trials: Of the 1,030 cases of nosocomial pneumonia included in two clinical trials on which this study was based, 544 (52.8%) were VAP. In 282 (51.8%) cases, the treatment was carried out with LIN and in 262 (48.2%) with VAN. Of the cases treated with LIN, in 134 cases (47.5%) Gram-positive pathogens were identified, 110 of which were SA and 44 MRSA, while in those receiving VAN, 130 cases with Gram-positive pathogens (49.6%) were identified, of which 111 were SA and 47 MRSA. No differences were seen in the main characteristics of the patients treated with LIN or VAN, including sex (man, 66.3% vs 65%), age (>65 years, 51.1% vs 44.7%), severity degree (APACHE II >20, 22.7% vs 21.5%), or need for AV (AV >7 days, 28.0% vs 31.3%).
Machado et al.(4) 2005	Brazil	A mathematical model patient with VAP MRSA in ICU (44 cases treated with LIN and 47 cases treated with VAN). The Cases in this study were based on the results of a study conducted by Kollef et al. who retrospectively evaluated data of two prospective, randomized and double-blind clinical trials (Wunderink 2003 & Rubinstein 2001)	In this study effectiveness and duration of antibiotic therapy in patients with VAP-MRSA were based on the results of a study conducted by Kollef et al. who retrospectively evaluated data of two prospective, randomized and double-blind studies in 134 sites, involving 1,019 patients with nosocomial pneumonia, including 160 with identified MRSA and 91 with VAP MRSA.
Lin et al.(20) 2016	Taiwan	In this study HAP patients with MRSA are simulated	The analysis was based on the results of the ZEPHYR trial 2012 and the probabilities of clinical events were obtained directly from the clinical trial
Collins et al.(34) 2015	USA	A hypothetical cohort of adult HAP patients (Suspected MRSA)	Inpatient costs, long term survival, and health-utility information obtained from the results of Shorr 2004 and clinical variables such as mortality and adverse events obtained from results reported in the intent-to-treat (ITT) population in the ZEPHYR trial 2012
Tan et al.(39) 2014	China	The model was based on the hypothetical HAP patients with MRSA in 4 cities in China (Beijing, Guangzhou, Nanjing, Xi'an)	Clinical and resource use parameters used in this study were identified from the ZEPHYR trial 2012 and its subsequent post hoc published analysis (Solem 2012) while the local resource use and cost data were provided through review of local published literature and surveys with local clinicians who were experienced in managing MRSA confirmed.
Patel et al.(35) 2014	USA	In this study no patients were enrolled specifically and the hypothetical model population was based on two studies data (Solem 2012 and Niederman 2014: HAP patients with MRSA, age 18+, mean age 62 years, 69% white, 66% male, 75% mechanically ventilated, 87% had at least 1 day in the ICU and 63% were from the United States) and similar to the population included in a phase IV, prospective, double-blind, controlled, multicenter, international clinical trial (ZEPHYR trial 2012)	Data on length of hospital stay, inpatient and outpatient resource use and associated costs, and drug costs were obtained by analyses of the clinical trials and published literatures (ZEPHYR trial 2012, Solem 2012, Niederman 2012)
Patel et al.(37) 2014	Germany	This economic model used only previously published data to simulate a hypothetical patient pathway and no patients were enrolled specifically for this study and the model population was assumed to be hospitalized patients 18+ with confirmed MRSA NP and similar to clinical characteristics as patients in a prospective, controlled, multicenter Phase IV clinical trial (ZEPHYR trial 2012)	Data on hospital length of stay, inpatient and outpatient resource use, and associated costs and drug costs were obtained from analyses of the clinical trials and published literatures (ZEPHYR trial 2012, Solem 2012, Niederman 2012)
De Cock et al.(36) 2009	Germany	HAP patients (Suspected/Proven MRSA) In this study no patients were enrolled specifically and the model was based on simulation.	Clinical data were obtained from a retrospective analysis (Wunderink 2003) of two prospective, randomized, double-blind clinical trials in patients with NP (Rubinstein 2001 & Wunderink 2003)
Mullins et al.(21) 2006	USA	HAP patients with MRSA, age 16+ Hospital Claims: N= 1812 (M=800, F=1010, Age>65y =66.6%) The Cases in this study were based on the results of a study conducted by Wunderink 2003 who retrospectively evaluated data of two prospective, randomized, double-blind controlled trials in patients with NP (Rubinstein 2001 & Wunderink 2003)	Rates of commonly observed NP outcomes and measures of clinical effectiveness were derived from a pooled analysis of clinical-trial data (Wunderink 2003) that included 160 patients with MRSA (LIN: N=75 (M=44, F=31, Age>65y =66.7% and VAN: N=85 (M=48, F=37, Age>65y =72.9%) from 2 prospective, randomized, double-blind, controlled trials.

Summary of Effectiveness Data of the Reviewed Economic Evaluations

Reference	Outcome Criterion	Sensitivity Analysis Performed	Final findings																																
Buendía (40) 2024 (Colombia)	Clinical Cure Rate	- One-way SA, - Probabilistic SA (10,000 Monte Carlo Simulations)	Linezolid is the dominant treatment compared to vancomycin with a \$517 lower cost and a 10% incremental benefit. 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. <table><tr><td></td><td>Clinical Cure Rate[®]</td><td>Mortality Rate[®]</td><td>Nephrotoxicity[®]</td><td>Cost of renal failure[®]</td><td>Thrombocytopenia[®]</td><td>Cost of thrombocytopenia[®]</td></tr><tr><td>Linezolid</td><td>53 %</td><td>5 %</td><td>8 %</td><td rowspan="2">\$2461</td><td>16 %</td><td rowspan="2">\$46</td></tr><tr><td>Vancomycin</td><td>43 %</td><td>4 %</td><td>18 %</td><td>13 %</td></tr></table> The baseline results of the study were "robust to changes in all assumptions and parameters."		Clinical Cure Rate [®]	Mortality Rate [®]	Nephrotoxicity [®]	Cost of renal failure [®]	Thrombocytopenia [®]	Cost of thrombocytopenia [®]	Linezolid	53 %	5 %	8 %	\$2461	16 %	\$46	Vancomycin	43 %	4 %	18 %	13 %													
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Grau (38) 2005 (Spain)	- Clinical Cure Rate - QALY - LYS	- Univariate SA - Scenario Analysis (8 scenarios)	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 LYS with LIN = 2.175 The additional QALY with LIN = 1.805 <table><tr><td></td><td>Clinical Cure Rate[®] (CI95%)</td><td>Survival Rate[®] (CI95%)</td><td>Days of ICU stay (95%CI)[®]</td></tr><tr><td>Linezolid</td><td>62.2 %</td><td>84.1 %</td><td>11.2 (Days)</td></tr><tr><td>Vancomycin</td><td>21.2 %</td><td>61.7 %</td><td>11.4 (Days)</td></tr></table> The results were stable under sensitivity analysis.		Clinical Cure Rate [®] (CI95%)	Survival Rate [®] (CI95%)	Days of ICU stay (95%CI) [®]	Linezolid	62.2 %	84.1 %	11.2 (Days)	Vancomycin	21.2 %	61.7 %	11.4 (Days)																				
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Machado (4) 2005 (Brazil)	Death or Survival	NR	Despite its higher drug cost, linezolid has a lower overall cost per recovered patient, making it more cost-effective than vancomycin. <table><tr><td></td><td>Effectiveness[®] (Clinical Cure Rate)</td><td>Invested amount per cured patient</td></tr><tr><td>Linezolid</td><td>62.2%</td><td>R\$ 7,764.72</td></tr><tr><td>Brand-name Vancomycin</td><td>21.2%</td><td>R\$ 13,231.65</td></tr><tr><td>Generic Vancomycin</td><td>21.2%</td><td>R\$ 11,277.59</td></tr></table>		Effectiveness [®] (Clinical Cure Rate)	Invested amount per cured patient	Linezolid	62.2%	R\$ 7,764.72	Brand-name Vancomycin	21.2%	R\$ 13,231.65	Generic Vancomycin	21.2%	R\$ 11,277.59																				
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Lin (20) 2016 (Taiwan)	Clinical Cure Rate	One-way SA (5%, 10%, 20% changes)	The total cost of linezolid treatment per patient is \$376 more than vancomycin, and the treatment rate with linezolid is also higher than vancomycin. 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. <table><tr><td></td><td>Clinical Cure Rate[®]</td><td>Nephrotoxicity[®]</td><td>Thrombocytopenia[®]</td><td>The Aggregate Adverse Event Rates[®]</td><td>Total lengths of Hospital Stay[®] (d)</td><td>No. of ICU stays[®] (d)</td><td>No. of general ward stays[®] (d)</td></tr><tr><td>Linezolid</td><td>57.6 %</td><td>3.69 %</td><td>1.34 %</td><td>13.40 %</td><td>17.2</td><td>10.1</td><td>7.1</td></tr><tr><td>Vancomycin</td><td>46.6 %</td><td>7.33 %</td><td>2.21 %</td><td>19.76 %</td><td>18.1</td><td>10.6</td><td>7.5</td></tr></table>		Clinical Cure Rate [®]	Nephrotoxicity [®]	Thrombocytopenia [®]	The Aggregate Adverse Event Rates [®]	Total lengths of Hospital Stay [®] (d)	No. of ICU stays [®] (d)	No. of general ward stays [®] (d)	Linezolid	57.6 %	3.69 %	1.34 %	13.40 %	17.2	10.1	7.1	Vancomycin	46.6 %	7.33 %	2.21 %	19.76 %	18.1	10.6	7.5								
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Collins (34) 2015 (USA)	QALY	- Univariate SA - Probabilistic SA (10,000 Monte Carlo Simulation) - Threshold Analysis	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 and ICER Per life saved=\$68,615 and in the mITT population, linezolid was dominated both ICER Per QALY and ICER Per life saved. However, at a 60-day time horizon, in the mITT population and assuming the same mortality rate between drugs, vancomycin prevails. <table><tr><td></td><td colspan="3">ITT</td><td colspan="3">mITT</td><td rowspan="2">Cost of Nephrotoxicity[®]</td><td rowspan="2">Cost of Thrombocytopenia[®]</td></tr><tr><td></td><td>Survival Rate[®]</td><td>Nephrotoxicity[®]</td><td>Thrombocytopenia[®]</td><td>Survival Rate[®]</td><td>Nephrotoxicity[®]</td><td>Thrombocytopenia[®]</td></tr><tr><td>Linezolid</td><td>84.3 %</td><td>3.7 %</td><td>1.3 %</td><td>71.9 %</td><td>8.4 %</td><td>16.3 %</td><td rowspan="2">\$14,386</td><td rowspan="2">\$17,860</td></tr><tr><td>Vancomycin</td><td>83 %</td><td>7.3 %</td><td>2.2 %</td><td>73.7 %</td><td>18.2 %</td><td>13.2 %</td></tr></table>		ITT			mITT			Cost of Nephrotoxicity [®]	Cost of Thrombocytopenia [®]		Survival Rate [®]	Nephrotoxicity [®]	Thrombocytopenia [®]	Survival Rate [®]	Nephrotoxicity [®]	Thrombocytopenia [®]	Linezolid	84.3 %	3.7 %	1.3 %	71.9 %	8.4 %	16.3 %	\$14,386	\$17,860	Vancomycin	83 %	7.3 %	2.2 %	73.7 %	18.2 %	13.2 %
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Tan (39) 2014 (China)	Clinical Cure Rate	Scenario Analysis (8 scenarios)	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 <table><tr><th></th><th>Clinical Cure Rate[®] (CI 95%)</th><th>Proportion of successfully treated patients</th><th>Survival Rate[®]</th><th>Mortality Rate[®]</th><th>Rates of adverse events leading to treatment Discontinuation[®]</th><th>Rates of treatment failure leading to treatment Discontinuation[®]</th><th>Nephrotox icity[®]</th><th>Thrombocyt openia[®]</th><th>Total lengths of Hospital Stay[®] (d)</th><th>No. of ICU stays[®] (d)</th><th>No. of general ward stays[®] (d)</th></tr><tr><td>Linezolid</td><td>54.8 %</td><td>62.9 %</td><td>72.8 %</td><td>27.2 %</td><td>1.78 %</td><td>15.32 %</td><td>4.02 %</td><td>16.3 %</td><td>17.9</td><td>10.1</td><td>7.8</td></tr><tr><td>Vancomycin</td><td>44.9 %</td><td>60.2 %</td><td>72.8 %</td><td>27.2 %</td><td>3.13 %</td><td>25.68 %</td><td>15.18 %</td><td>13.2 %</td><td>18.6</td><td>10.6</td><td>8</td></tr></table> ICERs were stable under sensitivity analyses.		Clinical Cure Rate [®] (CI 95%)	Proportion of successfully treated patients	Survival Rate [®]	Mortality Rate [®]	Rates of adverse events leading to treatment Discontinuation [®]	Rates of treatment failure leading to treatment Discontinuation [®]	Nephrotox icity [®]	Thrombocyt openia [®]	Total lengths of Hospital Stay [®] (d)	No. of ICU stays [®] (d)	No. of general ward stays [®] (d)	Linezolid	54.8 %	62.9 %	72.8 %	27.2 %	1.78 %	15.32 %	4.02 %	16.3 %	17.9	10.1	7.8	Vancomycin	44.9 %	60.2 %	72.8 %	27.2 %	3.13 %	25.68 %	15.18 %	13.2 %	18.6	10.6	8		
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Patel (35) 2014 (USA)	Clinical Cure Rate	- Univariate SA - Probabilistic SA (10,000 Monte Carlo Simulation) - Scenario Analysis (3 scenarios)	Linezolid is superior to vancomycin in terms of lower cost (\$824) and higher clinical response (2.7%). <table><tr><th></th><th>Clinical Cure Rate[®] (CI 95%)</th><th>Proportions of Successfully Treated Patients</th><th>Survival Rate[®]</th><th>Mortality Rate[®]</th><th>SAEs leading to discontinuation[®]</th><th>Failure leading to discontinuation</th><th>Total lengths of Hospital Stay[®] (d)</th><th>No. of ICU stays[®] (d)</th><th>No. of general ward stays[®] (d)</th></tr><tr><td>Linezolid</td><td>54.8 %</td><td>62.9 %</td><td>72.8 %</td><td>27.2 %</td><td>1.8 %</td><td>16.2</td><td>17.9</td><td>10.1</td><td>7.8</td></tr><tr><td>Vancomycin</td><td>44.9 %</td><td>60.2 %</td><td>72.8 %</td><td>27.2 %</td><td>3.1 %</td><td>24.8</td><td>18.6</td><td>10.6</td><td>8</td></tr></table> The results were stable under sensitivity analyses (at a WTP of \$0, linezolid has a 64.4% chance of being cost-effective).		Clinical Cure Rate [®] (CI 95%)	Proportions of Successfully Treated Patients	Survival Rate [®]	Mortality Rate [®]	SAEs leading to discontinuation [®]	Failure leading to discontinuation	Total lengths of Hospital Stay [®] (d)	No. of ICU stays [®] (d)	No. of general ward stays [®] (d)	Linezolid	54.8 %	62.9 %	72.8 %	27.2 %	1.8 %	16.2	17.9	10.1	7.8	Vancomycin	44.9 %	60.2 %	72.8 %	27.2 %	3.1 %	24.8	18.6	10.6	8								
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Patel (37) 2014 (Germany)	Clinical Cure Rate	- Univariate SA - Probabilistic SA (10,000 Monte Carlo Simulation) - Scenario Analysis (3 scenarios)	Linezolid is superior to vancomycin in terms of lower cost (123 euros) and higher clinical response (2.7%). <table><tr><th></th><th>Clinical Cure Rate[®] (CI 95%)</th><th>Proportions of Successfully Treated Patients</th><th>Survival Rate[®]</th><th>Mortality Rate[®]</th><th>SAEs leading to discontinuation[®]</th><th>Failure leading to discontinuation</th><th>Total lengths of Hospital Stay[®] (d)</th><th>No. of ICU stays[®] (d)</th><th>No. of general ward stays[®] (d)</th></tr><tr><td>Linezolid</td><td>54.8 %</td><td>62.9 %</td><td>72.8 %</td><td>27.2 %</td><td>1.8 %</td><td>16.2</td><td>17.9</td><td>10.1</td><td>7.8</td></tr><tr><td>Vancomycin</td><td>44.9 %</td><td>60.2 %</td><td>72.8 %</td><td>27.2 %</td><td>3.1 %</td><td>24.8</td><td>18.6</td><td>10.6</td><td>8</td></tr></table> The results were stable under sensitivity analyses (at a WTP of €0, linezolid has a 53.9% chance of being cost-effective)		Clinical Cure Rate [®] (CI 95%)	Proportions of Successfully Treated Patients	Survival Rate [®]	Mortality Rate [®]	SAEs leading to discontinuation [®]	Failure leading to discontinuation	Total lengths of Hospital Stay [®] (d)	No. of ICU stays [®] (d)	No. of general ward stays [®] (d)	Linezolid	54.8 %	62.9 %	72.8 %	27.2 %	1.8 %	16.2	17.9	10.1	7.8	Vancomycin	44.9 %	60.2 %	72.8 %	27.2 %	3.1 %	24.8	18.6	10.6	8								
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De Cock (36) 2009 (Germany)	- Clinical Cure Rate - Survival - LYG	- One-way SA - Two-way SA - Scenario Analysis (2 scenarios)	Linezolid is associated with 8.7% greater clinical improvement and 13.2% higher survival than vancomycin, and has a small additional cost (€ 420). ICER Per Life Gained = € 180 ICER Per Death Avoided = € 3,171 ICER Per Additional Cure = € 4,813 <table><tr><th></th><th>Clinical Cure Rate</th><th>Survival Rate</th><th>Mortality Rate</th><th>Life-Years Gained (2.3 Additional Years for Linezolid)</th><th>Serious adverse event rate requiring therapy switch[®]</th><th>Cost of Nephrotoxicity[®]</th><th>Cost of Thrombocytopenia[®]</th><th>Adverse Event Management Cost</th><th>Average total costs per episode of patient treatment</th><th>LOS</th></tr><tr><td>Linezolid</td><td>73.6 %</td><td>79.3 %</td><td>20.7 %</td><td>14</td><td>5.2 %</td><td rowspan="2">€3,052</td><td rowspan="2">€914</td><td>€222</td><td>€12,829</td><td>11.2</td></tr><tr><td>Vancomycin</td><td>64.9 %</td><td>66.1 %</td><td>33.9 %</td><td>11.7</td><td>6.5 %</td><td>€271</td><td>€12,409</td><td>10.8</td></tr></table> The results were stable under sensitivity analysis.		Clinical Cure Rate	Survival Rate	Mortality Rate	Life-Years Gained (2.3 Additional Years for Linezolid)	Serious adverse event rate requiring therapy switch [®]	Cost of Nephrotoxicity [®]	Cost of Thrombocytopenia [®]	Adverse Event Management Cost	Average total costs per episode of patient treatment	LOS	Linezolid	73.6 %	79.3 %	20.7 %	14	5.2 %	€3,052	€914	€222	€12,829	11.2	Vancomycin	64.9 %	66.1 %	33.9 %	11.7	6.5 %	€271	€12,409	10.8							
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Linezolid	73.6 %	79.3 %	20.7 %	14	5.2 %	€3,052	€914	€222	€12,829	11.2																															
Vancomycin	64.9 %	66.1 %	33.9 %	11.7	6.5 %			€271	€12,409	10.8																															
Mullins (21) 2006 (USA)	Survival	- Univariate SA - Multifactorial SA	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 <table><tr><th rowspan="2"></th><th rowspan="2">Mortality Rate</th><th colspan="2">Survival with bacteremia</th><th colspan="2">Survival without bacteremia</th><th colspan="2">Non-Survival with bacteremia</th><th colspan="2">Non-Survival without bacteremia</th></tr><tr><th>Probability of Outcome[®]</th><th>Expected Charge, \$</th><th>Probability of Outcome[®]</th><th>Expected Charge, \$</th><th>Probability of Outcome[®]</th><th>Expected Charge, \$</th><th>Probability of Outcome[®]</th><th>Expected Charge, \$</th></tr><tr><td>Linezolid</td><td>7.3 %</td><td>9 %</td><td>241</td><td>71 %</td><td>1802</td><td>1 %</td><td>69</td><td>19 %</td><td>638</td></tr><tr><td>Vancomycin</td><td>13.3 %</td><td>11 %</td><td>273</td><td>53 %</td><td>1350</td><td>6 %</td><td>303</td><td>31 %</td><td>1045</td></tr></table> The results were stable under sensitivity analysis.		Mortality Rate	Survival with bacteremia		Survival without bacteremia		Non-Survival with bacteremia		Non-Survival without bacteremia		Probability of Outcome [®]	Expected Charge, \$	Probability of Outcome [®]	Expected Charge, \$	Probability of Outcome [®]	Expected Charge, \$	Probability of Outcome [®]	Expected Charge, \$	Linezolid	7.3 %	9 %	241	71 %	1802	1 %	69	19 %	638	Vancomycin	13.3 %	11 %	273	53 %	1350	6 %	303	31 %	1045
	Mortality Rate	Survival with bacteremia				Survival without bacteremia		Non-Survival with bacteremia		Non-Survival without bacteremia																															
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®: These effectiveness data in the economic evaluation studies reviewed were extracted from other clinical studies.