

Linezolid cSSTI Economic Model

Economic Modeling to Compare Linezolid and Vancomycin for the Treatment of Methicillin-Resistant *Staphylococcus Aureus* (MRSA) Related Complicated Skin and Skin Structure Infections (cSSSI): A Quebec Healthcare System Perspective

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OUTLINE

■ Background/ Introduction

■ Pharmacoeconomic Model

- ◆ Overview

- ◆ Structure

- ◆ Inputs (clinical, resource, costs)

- ◆ Assumptions

- ◆ Results (Base Case, Sensitivity Analyses)

- ◆ Limitations

■ Summary and Conclusions

Background - Epidemiology

Disease Prevalence

SSSI:

36% of all MRSA-related infections

MRSA Infections:
8.18 cases per 1,000 admissions (2007)

Quebec Population

Disease Burden

- Treatment of cSSSI often requires hospitalization and intravenous (IV) antibiotics, resulting in **high treatment costs**
- direct medical costs estimated at **\$129 million** in Canada for 2010

MRSA: Methicillin-resistant *Staphylococcus aureus*

SSSI: Skin and skin structure infections ; cSSSI :Complicated skin and skin structure infections

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Background – cSSSTI Treatment Options

cSSSI Treatment Options

Semi-synthetic penicillins

1st and 2nd generation cephalosporins

Vancomycin

Linezolid

- due to a rise in MRSA-related cSSSI these **treatments often fail**

- **IV only** (thus, outpatient use requires additional at-home services for IV administration)
- **lower drug acquisition cost** than linezolid

- available as **IV and oral formulations** (facilitates transition to the **outpatient setting**)

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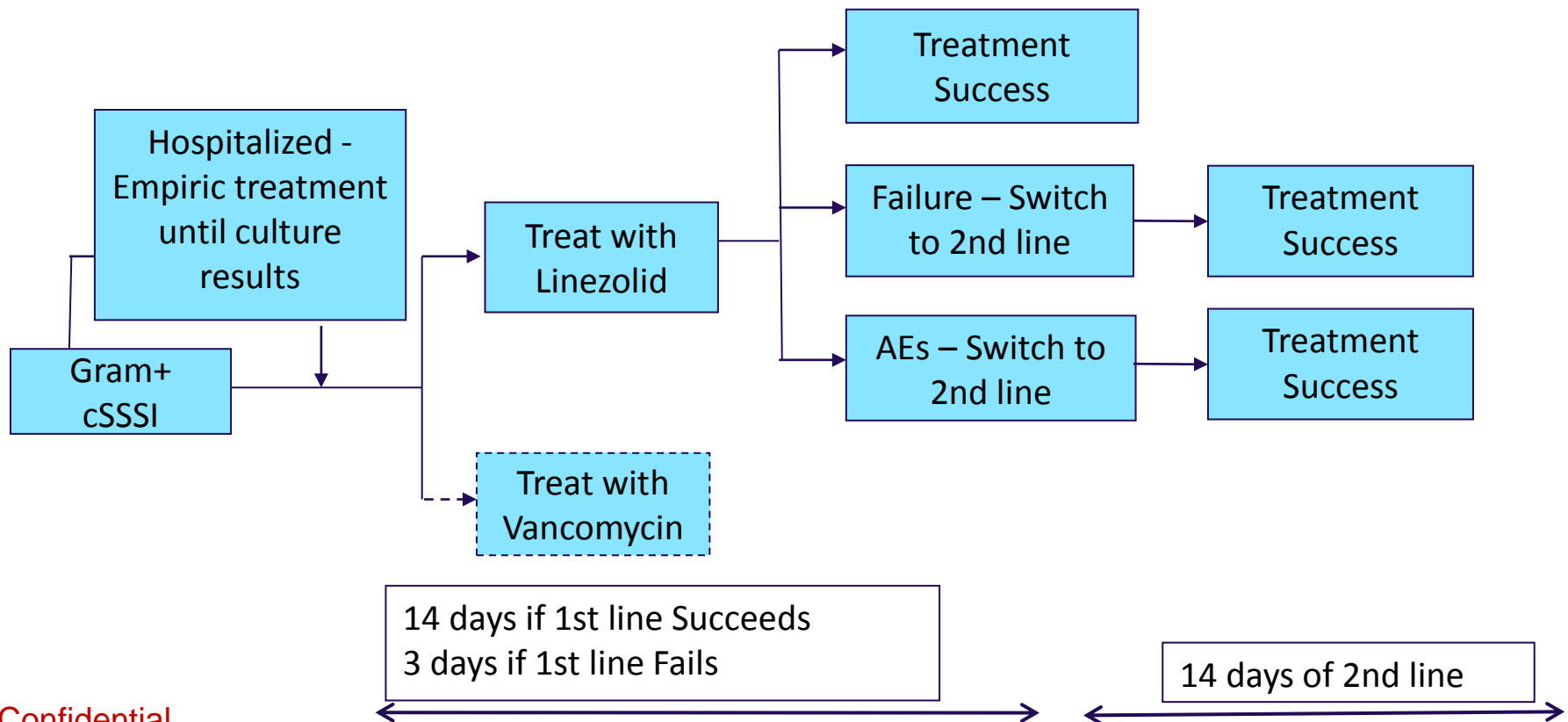
■ Summary and Conclusions

Overview: Linezolid Pharmacoeconomic Model

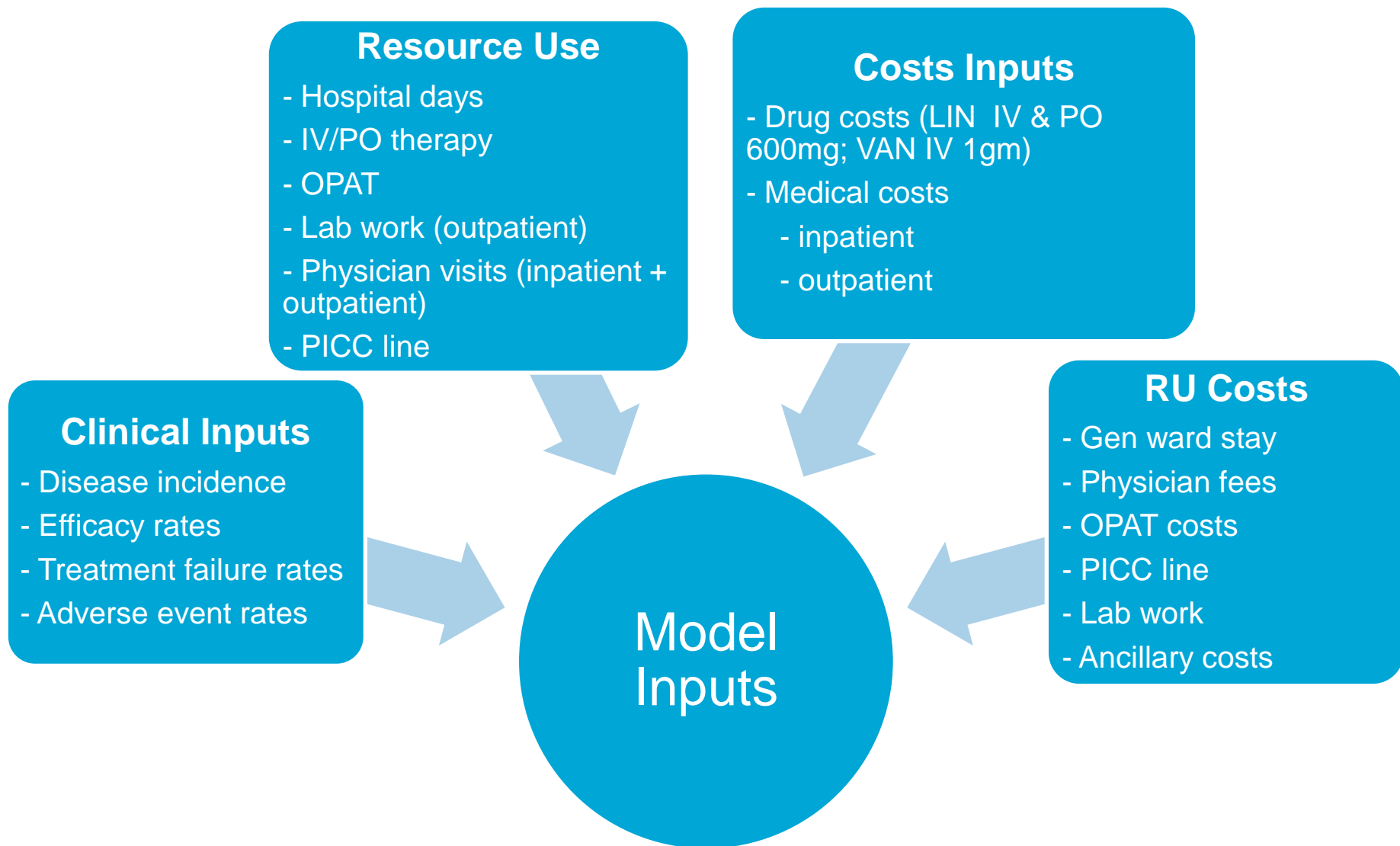
Model Objective	To assess the value of linezolid compared with vancomycin in the treatment of cSSSIs caused by MRSA from a Quebec healthcare system perspective
Model type	Base Case: Cost-minimization analysis
Comparators	Linezolid (IV and oral) vs Vancomycin (IV)
Perspective	Quebec provincial payer perspective: only direct medical costs were included (inpatient and outpatient drug and medical costs)
Costs	Includes inpatient and outpatient costs for both treatments
Time horizon	14 days (in case of only first line treatment) or 17 days (if patient discontinued first line and switched to second line).
Outputs	Incremental cost per patient

Model Structure

- Patients enter the model after a confirmed diagnosis of cSSSI caused by MRSA.
- The model time frame is either 14 days (in case of only first line treatment) or 17 days (if patient discontinued first line and switched to second line)



Model Inputs



Model Assumptions

- Due to limited information in the literature, assumptions made were verified by expert opinion. Key assumptions are summarized below.
 - ◆ Base case scenario for this model was conservative: assumed **equal efficacy and equal length of stay** for both treatments
 - ◆ Patients who experienced treatment failure or adverse events switched from first to **second line after 3 days** of therapy
 - ◆ **Second line treatment** was assumed to be 100% effective
 - ◆ **Resource use** associated with drug failure or adverse events was similar between vancomycin and linezolid.
 - ◆ **Mortality was not included** in the analysis (ref: Bounthavong 2009 and Itani 2010)
 - ◆ **Quebec costs**: hospital related costs for this model were incorporated from a Net Impact Analysis (Pettigrew et al)

Model Results – Base Case¹

Costs per Patient	Linezolid	Vancomycin	Incremental Cost ² per Patient
Total Inpatient Costs	\$2,642	\$2,522	\$120
Inpatient Drug Costs	\$876	\$688	\$188
Drug treatment	\$831	\$510	\$321
Drug administration	\$45	\$178	-\$133
Inpatient Medical Costs	\$1,766	\$1,834	-\$68
Hospital days	\$1,455	\$1,455	\$0
ID specialist	\$130	\$130	\$0
Inpatient Monitoring	\$32	\$100	-\$68
Adverse event costs	\$49	\$49	\$0
Failure costs	\$99	\$99	\$0
Total Outpatient Costs	\$1,622	\$2,631	-\$1,009
Outpatient Drug Costs	\$1,337	\$976	\$361
Drug treatment	\$1,337	\$976	\$361
Drug administration	\$0	\$0	\$0
Outpatient Medical Costs	\$285	\$1,655	-\$1,370
Physician visits	\$39	\$39	\$0
Laboratory work	\$1	\$1	\$0
Home care for IV administration	\$245	\$1,615	-\$1,370
Total Cost of Treatment	\$4,264	\$5,153	-\$889
Total Drug Costs	\$2,214	\$1,664	\$549
Total Medical (Healthcare) Costs	\$2,050	\$3,488	-\$1,438

¹ equal efficacy and length of stay (LOS), outpatient resource use data from literature and expert opinion

² Incremental cost of linezolid vs vancomycin (negative results indicate cost savings with linezolid)

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Summary of Base Case Results

■ Total Treatment costs:

- ◆ potential cost-savings with linezolid of \$889 per patient

■ Inpatient Treatment Costs:

- ◆ potential savings of \$120 per patient with vancomycin
 - Due to higher drug acquisition costs with linezolid

■ Outpatient Treatment costs:

- ◆ potential cost-savings with linezolid of \$1,009 per patient
 - due to lower outpatient treatment costs with linezolid, specifically home-care IV administration

■ Overall:

- ◆ total drugs costs were \$549 higher but treatment costs were over \$1,438 lower with linezolid compared to vancomycin therapy
 - driven by lower outpatient costs for linezolid in the home care setting

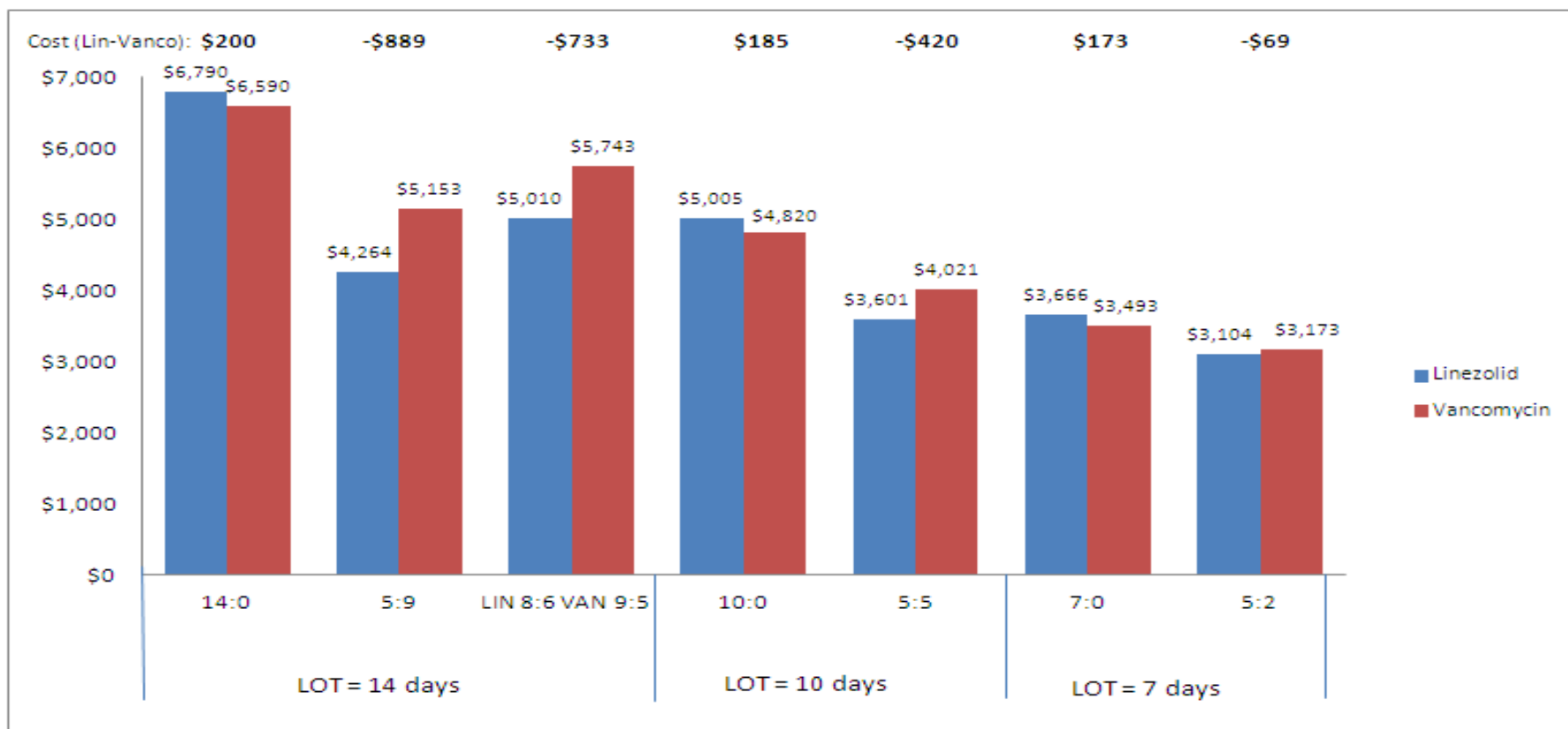
Sensitivity Analyses: Scenario 1 & 2 of 5

Scenarios	Linezolid	Vancomycin	Incremental Cost per Patient
<p><i>Scenario 2: Including 2-day empiric treatment of vancomycin</i></p>			
<p>- Linezolid cost-savings decreased to \$549: Assuming two days of empiric treatment increases inpatient and reduces outpatient stay, which resulted in lower vancomycin costs, and hence, reduced linezolid cost-savings.</p>			
<p><i>Scenario 1: Using Bayesian meta-analysis (Logman 2010⁸) efficacy rates</i></p>			
<p>- linezolid treatment was dominant having lower treatment costs, and higher efficacy rate and QALY (Quality Adjusted Life Years) gained compared to vancomycin treatment</p>			

Scenario 3: Vary treatment duration and inpatient LOS

Vancomycin is cost-saving when inpatient stay is greater, and linezolid is cost-saving when outpatient stay is greater

Treatment cost of linezolid vs. vancomycin under different treatment durations and inpatient LOS

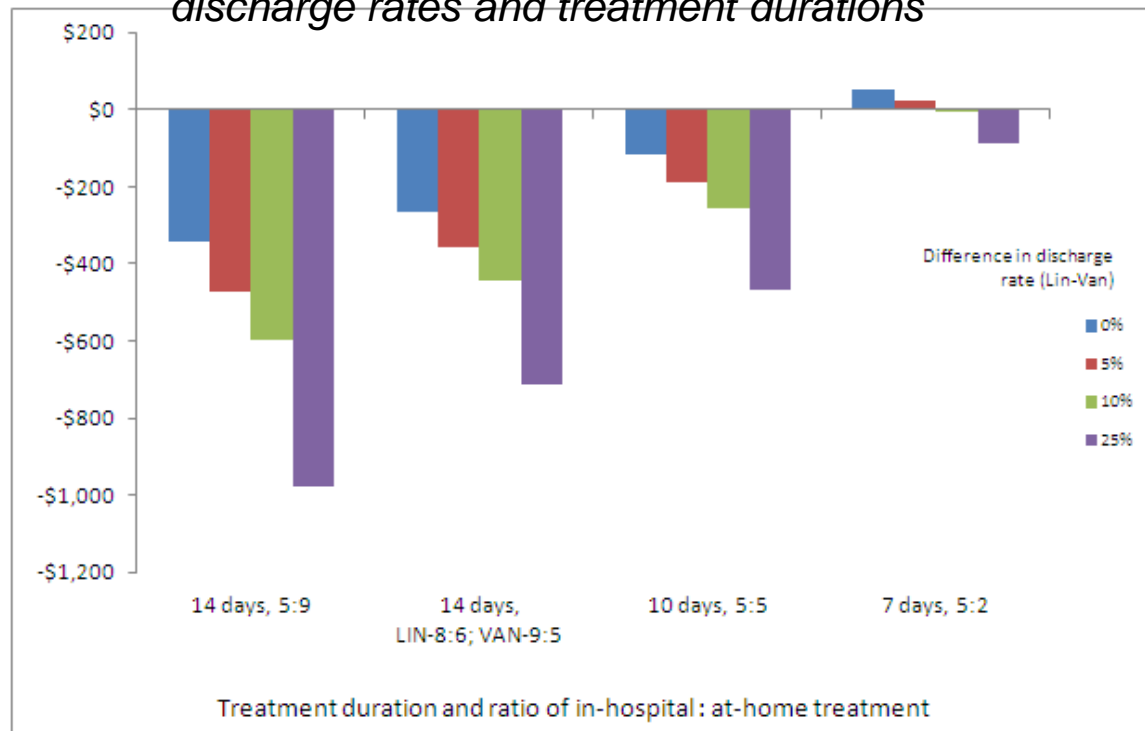


Note: Negative cost differential values indicate per-patient cost-savings for linezolid.

Scenario 4: Testing the different discharge rates

- linezolid shows cost-savings when discharge rate is greater or equal to vancomycin
- shorter treatment durations with lower outpatient stay = lower vancomycin costs.

Difference between linezolid and vancomycin treatment costs per patient under different discharge rates and treatment durations

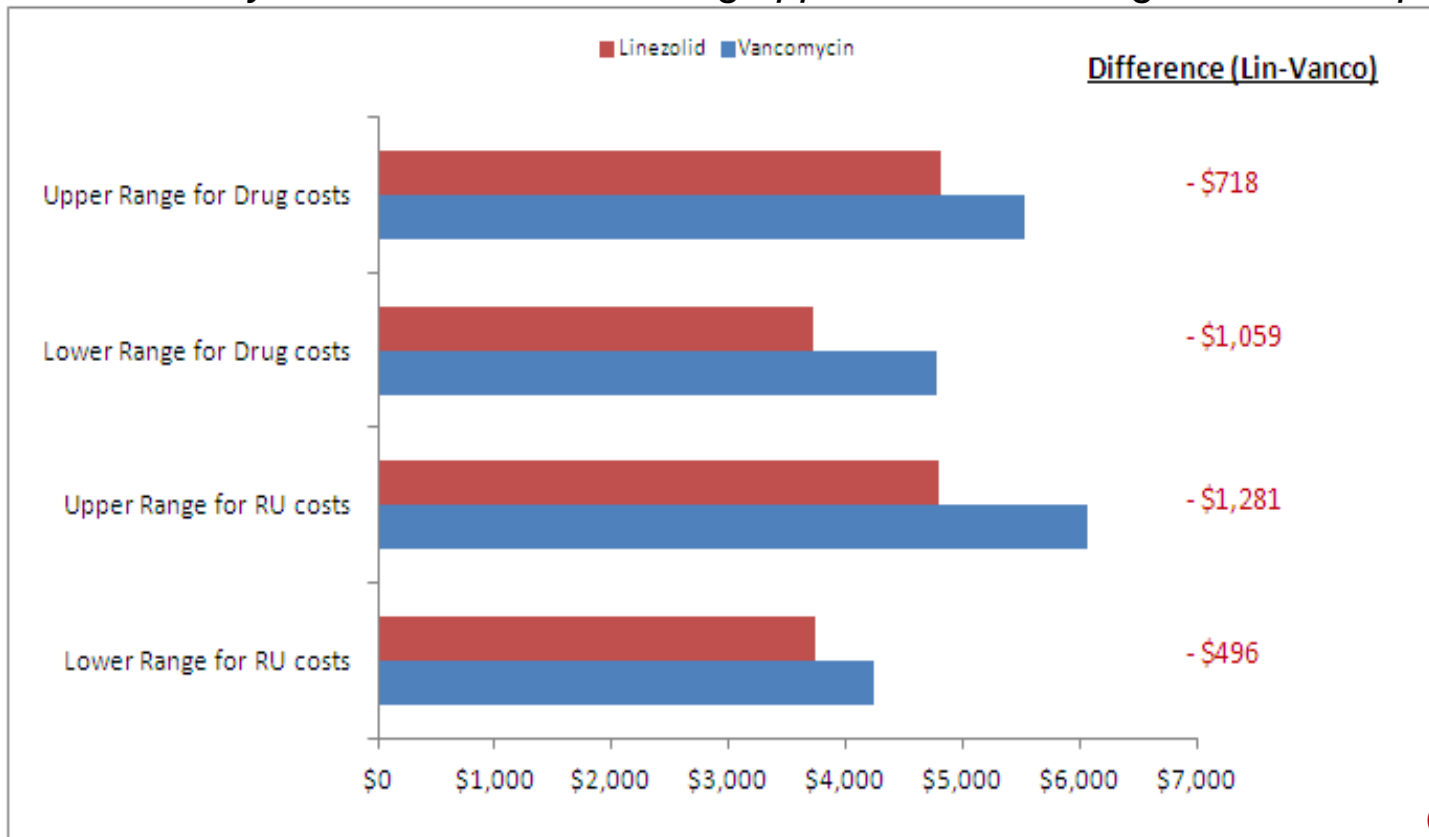


Note: Positive cost differentials indicate per-patient cost savings for Vancomycin; negative cost differentials indicate per-patient cost savings for Linezolid

Scenario 5: Using lower and upper ($\pm 25\%$) ranges for all cost inputs

- Increase of 25% in key resource costs= higher cost-savings with linezolid (\$1,281)
 - Decrease of 25% in key resource costs = less savings with linezolid (\$496)

Linezolid and vancomycin treatment costs using upper and lower ranges for cost inputs



Summary

- economic model provides perspective on the inpatient and outpatient costs associated with cSSSIs
- Equal efficacy and LOS assumption makes the base-case a 'conservative' scenario
- although total **drug acquisition costs** were lower for generic vancomycin, the model suggests **linezolid provides cost-savings in cSSSI** versus vancomycin, primarily in the outpatient setting
 - ◆ linezolid had substantially lower total costs compared to vancomycin.
 - ◆ linezolid offsets its higher drug price by reducing outpatient medical costs, specifically the cost of at-home parenteral administration

Conclusion

- For patients with MRSA cSSSIs, the appropriate ways to decrease hospital LOS and ultimately overall costs would be by **increasing outpatient antibiotics administration**,
 - ◆ i.e. increase the use of oral linezolid and at-home IV vancomycin
 - ◆ However, due to the added costs of outpatient parenteral administration for vancomycin, the use of oral linezolid appears to be economically more efficient

THANK YOU

Limitations

- Due to lack of available evidence, the model is partly based on expert opinion combined with trial-based and peer-reviewed data.
- the assumption that second-line treatment is 100% effective can be considered a simplification,
 - ◆ considered reasonable by clinical experts, as there are no efficacy data for second-line treatments in patients with cSSSI caused by MRSA.
 - ◆ incremental benefit from including a third line treatment was believed to be minimal since >98% patients were included within the first two lines due to the high efficacy rates (~90%).
 - ◆ similar assumptions are used by other published models for cSSSI
- The model does not account for mortality,
 - ◆ evidence suggests that mortality rates are similar between MRSA cSSSI patients treated with linezolid or vancomycin.⁹ Thus, the costs and outcomes due to mortality would be similar for both treatment arms.
- hospital related costs for this model were incorporated from a Net Impact Analysis conducted by Pettigrew et al.,²⁰ which used estimates obtained from a hospital in Quebec. One may dispute the generalizability of these estimates, however, this was the only available source to capture hospital costs specific to Quebec.

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