Cost-effectiveness of Sulbactam-durlobactam Versus Colistin in Treating Carbapenem-resistant *Acinetobacter baumannii* Infections in Critical Care Settings in the United States: A Decision Analysis

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Background

- Carbapenem-resistant *Acinetobacter baumannii* (CRAB) infections present a critical public health challenge in the United States, demanding effective treatment strategies due to limited options and significant healthcare burdens.[1]
- The attributable healthcare costs of CRAB infection in the United States were estimated at $281 million in 2017 with 90-day mortality rates of 30.3% in 2018.[2,3]
- Patients in critical care settings are at high risk of being colonized with CRAB (Odds ratio: 5.48 [95% confidence interval (CI),3.38-8.91]) compared with patients treated in acute care settings.[3] Incident cases of acute kidney injury (AKI) have been reported in a substantial subset of patients treated with colistin.[4]

Objectives

- This study aimed to assess the cost difference and cost-effectiveness of sulbactam-durlobactam compared to colistin in managing patients in critical care with CRAB infections from the perspective of a hospital critical care setting in the United States.
- In addition, deterministic sensitivity and scenario analyses were performed to assess the cost-effectiveness of sulbactam-durlobactam compared to colistin in different clinical scenarios.

Methods

- **Data source:** The decision-analytic model was developed to evaluate treatments (sulbactam-durlobactam versus colistin) used in the Acinetobacter Treatment Trial Against Colistin (ATTACK) trial in treating CRAB infections in critical care settings in the United States.[5]
- **Design:** The model incorporated survival, CRAB outcome (complete or incomplete clinical cure), and the incidence of and inpatient costs associated with acute kidney injury (AKI). Mean treatment duration was 10 days (7-14 days). Patients with incomplete clinical cure were assumed to have switched to cefiderocol, with a follow-up of 14±2 days to assess outcomes.
- **Outcomes:** Measured outcomes included the expected cost for each treatment, per-patient cost per additional life saved, QALYs gained, and incremental cost-effectiveness ratio (ICER). The model represented a 32-day time horizon.
- **Utility:** Health utilities scores were obtained from Nisula et al 2013 study, and estimated for patients in the intensive care unit, with or without AKI risk, injury, and failure. Utility scores ranged from 0.63 to 0.69.[6]
- **Costs:** The model incorporated direct medical costs (RED Book Online) comprising wholesale acquisition costs for the antibiotics, the cost of managing recurrent infections, and the cost of managing AKI. Costs were adjusted to 2023 US dollars.
- **Sensitivity Analysis:** One-way deterministic sensitivity analysis (DSA) of input parameters was performed and varied between ±50% as used in previous studies.
- **Scenario Analyses:** The first scenario modeled alternative optimal treatment as the preferred treatment for patients with treatment failure in both treatment arms relative to switching to cefiderocol as assessed in the base case.[7] The second scenario modified the base model by modeling the risk of developing AKI prior to death, and treatment outcomes were set to equal for both therapies in the third analysis.
- Data analysis was performed with TreeAge software (Williamstown, MA).

Results

Table 1: Model Input Ranges and Sources

Parameter	Input	Range	Sources
Path Probabilities			
Survival with complete cure			
Sulbactam-durlobactam	0.50	0.250-0.750	ATTACK
Colistin	0.27	0.135-0.405	ATTACK
Survival with incomplete cure			
Sulbactam-durlobactam	0.31	0.155-0.465	ATTACK
Colistin	0.41	0.205-0.615	ATTACK
Sulbactam-durlobactam			
AKI-Risk	0.07	0.035-0.105	ATTACK
AKI-Injury	0.02	0.010-0.030	ATTACK
AKI-Failure	0.04	0.020-0.060	ATTACK
Colistin			
AKI-Risk	0.15	0.075-0.225	ATTACK
AKI-Injury	0.17	0.085-0.255	ATTACK
AKI-Failure	0.06	0.030-0.090	ATTACK
28-day all-cause mortality			
Sulbactam-durlobactam	0.19	0.095-0.285	ATTACK
Colistin	0.32	0.160-0.480	ATTACK
Health utilities			
Survival without AKI	0.69	0.345-1.000	Nisula et al 2013[6]
Survival with AKI-Risk	0.69	0.345-1.000	Nisula et al 2013
Survival with AKI-Failure	0.68	0.340-1.000	Nisula et al 2013
Survival with AKI-Injury	0.63	0.315-0.945	Nisula et al 2013
Costs (in 2023 US dollars)			
Sulbactam-Durlobactam*	$19,000	$13,300-$26,600	RED BOOK Online
Colistin*	$840	$588-$1,176	RED BOOK Online
Cefiderocol*	$119,543	$83,680-$167,360	RED BOOK Online
AKI-Risk**	$14,226	$7,113 - $21,339	Hobson et al. 2015
AKI-Injury**	$28,453	$14,227 - $42,680	Hobson et al. 2015
AKI-Failure**	$50,790	$25,395 - $76,185	Hobson et al. 2015

* Drug costs are wholesale acquisition costs and represent the 10-day treatment duration costs;
** Acute medical costs of inpatient management only; AKI- Acute Kidney Injury;

Table 2: Base case for sulbactam-durlobactam compared to colistin

Strategy	Colistin	Sulbactam-durlobactam	Incremental
10-day drug cost	$840	$19,000	$18160
Total costs	$56,665	$58,971	$2306
QALYs	0.46	0.56	0.10
28-day survival	0.46	0.66	0.20
cost per QALY			$23,060
cost per additional life saved			$11,530
	AKI-Risk	AKI-Injury	AKI-Failure
Cost of AKI	$14,226	$28,453	$50,790

Table 3: Scenario analyses

Scenario	Cost	QALY	28-day survival	ICER (US$ per additional life saved)	ICER (US$ per QALY)
Scenario 1: Patients in both treatment arms from base case switched to optimal alternative therapy following incomplete response to initial treatment					
Colistin	$15,443	0.46	0.46		
Sulbactam-durlobactam	$22,174	0.56	0.66	**33,655**	**67,310**
Scenario 2: Modeled the risk of developing AKI among patients who died and in patients who survived with or without incomplete treatment.					
Sulbactam-durlobactam	$59,513	0.56	0.66		
Colistin	$59,871	0.46	0.46	**dominated**	**dominated**
Scenario 3: Modeled equal treatment outcomes for both treatments based on the proportions of patients surviving with or without a complete cure in the colistin group.					
Colistin	$56,665	0.46	0.46		
Sulbactam-durlobactam	$70,458	0.47	0.55	**153,256**	**1,379,300**

Figure 1: Decision tree for the base case analysis

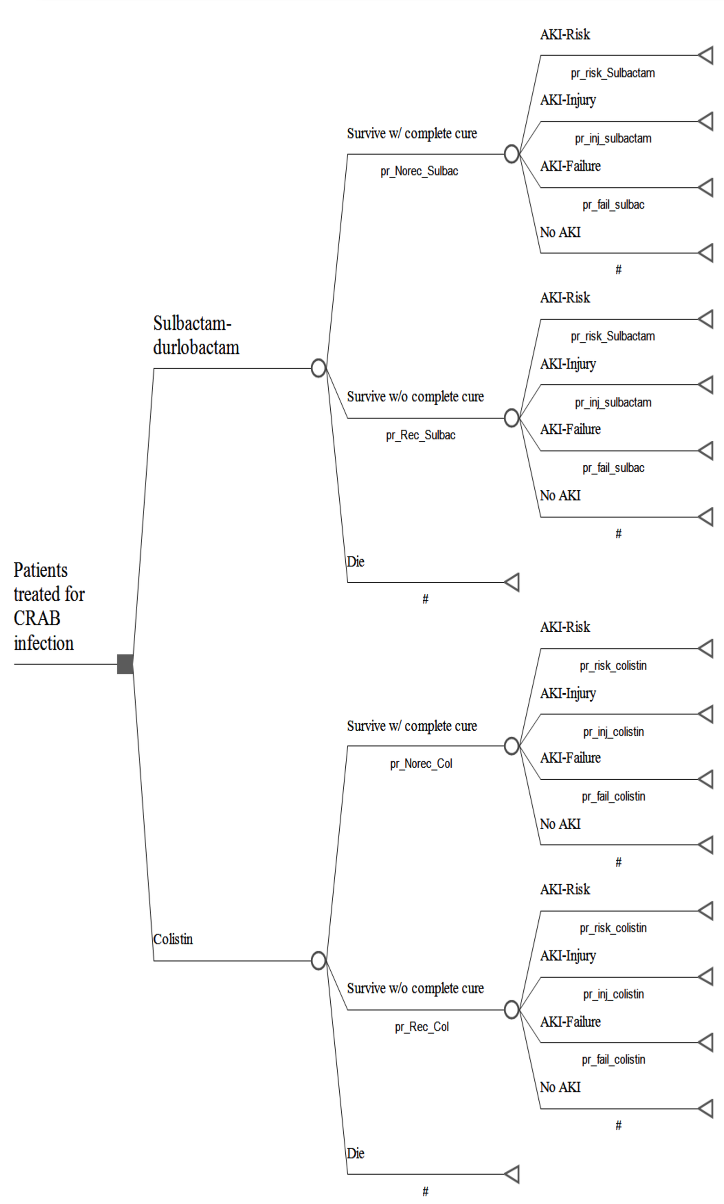


Figure 2: Decision tree for second scenario analysis

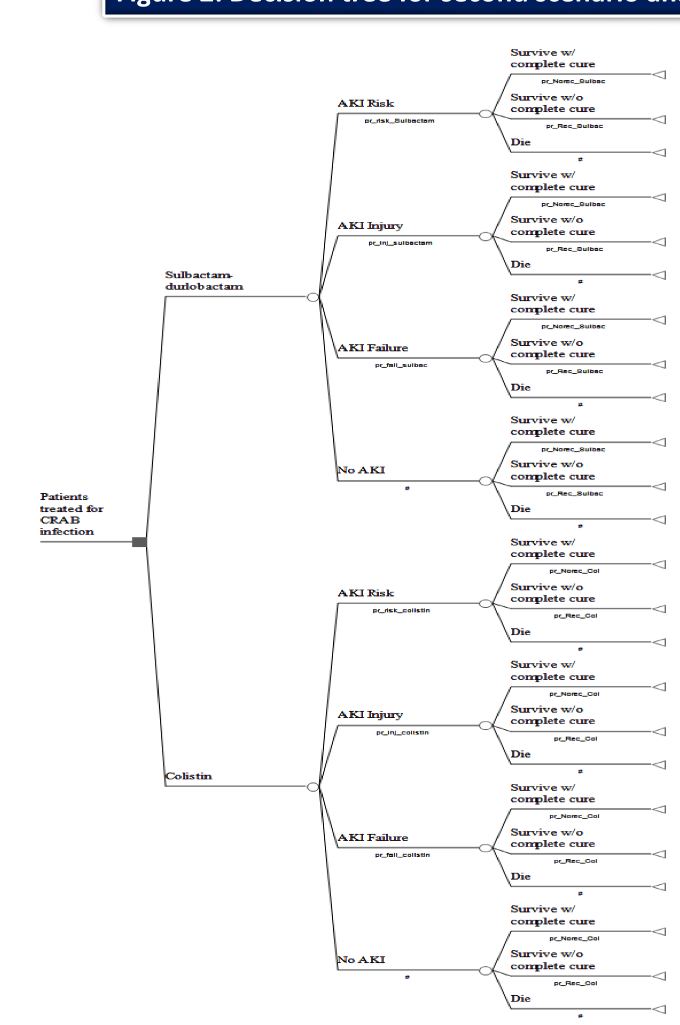
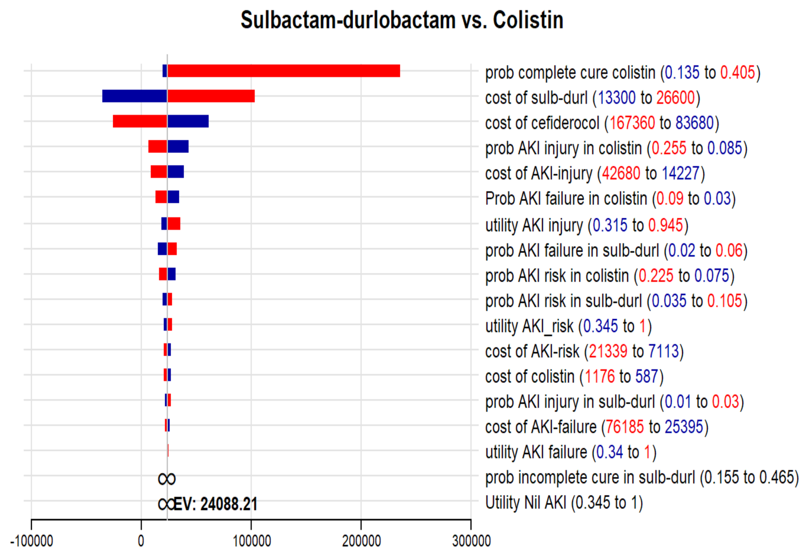


Figure 3: Tornado Diagram ICER (QALY)



The following variables had less than a 5% change in the ICER and are not shown in the diagram. (prob of complete cure sulbactam-durlobactam, prob incomplete cure col, survival col, survival sulbactam-durlobactam.)

Results/Discussion

- The estimated per-patient cost, including expenses for medication and managing AKI, was $58,971 for sulbactam-durlobactam compared to $56,665 for colistin with a cost difference of $2,306.
- Sulbactam-durlobactam demonstrated an ICER of $11,530 per additional life saved and $23,060 per QALY compared to colistin as shown in Table 2. This ICER falls significantly below the WTP threshold of $100,000 per QALY gained, a commonly used threshold in the United States.[8]
- The results of the deterministic sensitivity analysis are presented in the Tornado diagram (Figure 3). In terms of cost per QALY, variation in the proportion surviving with complete clinical cure among colistin-treated patients significantly influenced the ICER ($19,520 to $235,189 per QALY).
- Other sensitive parameters include variation in treatment cost associated with sulbactam-durlobactam (-$35,443 to $103,463 per QALY) and cefiderocol (-$25,852 to $61,544 per QALY).
- In the first scenario analysis, patients treated with sulbactam-durlobactam compared to colistin had an ICER of $33,655 per additional life saved and $67,310 per QALY, while colistin was dominated in the second scenario analysis which modeled the risk of AKI before death (Table 3).
- The third scenario which modeled equal treatment outcomes based on the proportions of patients surviving with or without a complete cure in the colistin group demonstrated sulbactam-durlobactam to be cost-effective at $1,379,300 per QALY gained.
- The generalizability of the results from our study is limited to patients with CRAB infections in critical care settings in the United States.
- Our study modeled a 32-day time horizon based on the ATTACK clinical trial, however, patients in inpatient settings have varying lengths of stay.

Conclusions

- Although medication costs were higher for sulbactam-durlobactam compared with colistin, the cost difference lessened when including the costs of managing acute kidney injury and its associated disutility.
- Incorporating the efficacy difference observed in the ATTACK trial yielded a cost-effectiveness ratio of $23,060 per QALY gained and hence could be considered cost-effective for the treatment of CRAB infections among patients in critical care in the United States.

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