

LONG-TERM COST-EFFECTIVENESS OF ESKETAMINE FOR THE TREATMENT OF TREATMENT-RESISTANT DEPRESSION

Touchette DR,¹ Boyer N,² Atlas SJ,³ Agboola F,⁴ Talon B,¹ Schultz BG,¹ Kumar VM,⁴ Fazioli K,⁴ Fluetsch N,⁴ Rind DM.⁴

¹University of Illinois at Chicago College of Pharmacy, Chicago, IL

²University of Chicago Hospital Medicine, Chicago, IL

³Division of General Internal Medicine, Massachusetts General Hospital, Boston, MA

⁴Institute for Clinical and Economic Review, Boston, MA

OBJECTIVE

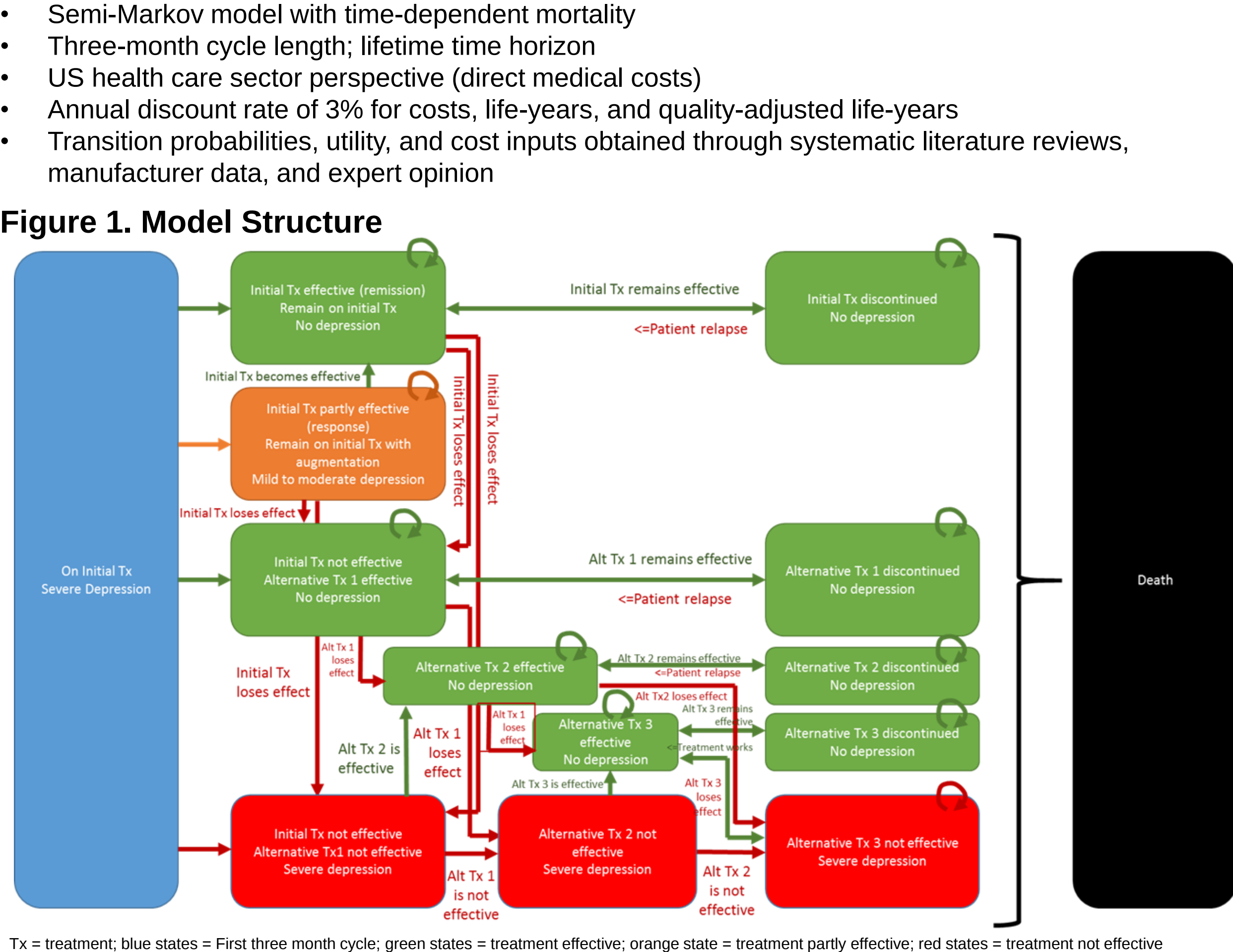
Treatment-resistant major depressive disorder commonly refers to major depressive disorder for which there is an inadequate response to two or more anti-depressant (AD) treatments of adequate dosing and duration. The objective of this analysis was to evaluate the lifetime cost-effectiveness of adding esketamine nasal spray, a new treatment for treatment-resistant depression, to a regimen of background AD treatment compared with AD alone in patients with treatment-resistant depression.

METHODS

Table 1. Base Case Key Model Inputs

Parameters	Esketamine	No Additional Treatment
Probability, Effective Initial Treatment	39.5% ^{1,2}	28.8% ^{1,2}
Probability, Partly Effective Initial Treatment	19.3% ^{1,2}	6.5% ^{1,2}
Probability, Effective Treatment in Subsequent Cycles After Partly Effective Treatment	19.9% ³	12.4% ³
Probability, Loss of Initial Treatment Effect in Subsequent Cycles After Effective Treatment	13.0% ³	13.0% ³
Probability, Loss of Effect in Subsequent Cycles After Partly Effective Treatment	21.0% ³	47.6% ³
Probability, Alternative Treatment Being Effective	13.0% ⁴	13.0% ⁴
Probability, Patients Discontinuing Therapy After Long-Term Effectiveness	1.3% ⁵	1.3% ⁵
Utility, No Depression	0.86 ⁶	0.86 ⁶
Utility, Mild to Moderate Depression	0.68 ⁷	0.68 ⁷
Utility, Severe Depression	0.50 ⁷	0.50 ⁷
Cost, Esketamine*		
First cycle (includes titration)	\$9322 ^{2,8-10}	n/a
All other cycles (stable dose)	\$7704 ^{2,8-10}	n/a

*Based on WAC of \$295 per 28 mg device



Tx = treatment; blue states = First three month cycle; green states = treatment effective; orange state = treatment partly effective; red states = treatment not effective

RESULTS

Table 2. Base-Case Discounted Costs and Outcomes

Treatment Arm	Total Drug Costs	Total Tx Strategy Costs	Total QALYs	Total LYs	Total Depression-Free Days
Esketamine	\$42,600	\$448,600	12.66	20.66	373
No Additional Treatment	\$0	\$410,200	12.47	20.64	123
Difference	\$42,000	\$38,400	0.19	0.01	250

Tx: treatment; QALY: quality-adjusted life year, LY: life year

Table 3. Incremental Cost-Effectiveness Ratios for Base-Case Analysis

Treatment	Cost per QALY Gained	Cost per LY Gained	Cost per Depression-Free Day
Esketamine vs. No Additional Treatment	\$198,000	\$2,592,000	\$150

QALY: quality-adjusted life year, LY: life year

Figure 3. Acceptability Curve for Esketamine Compared With No Additional Treatment at Varying Willingness-to-Pay Thresholds

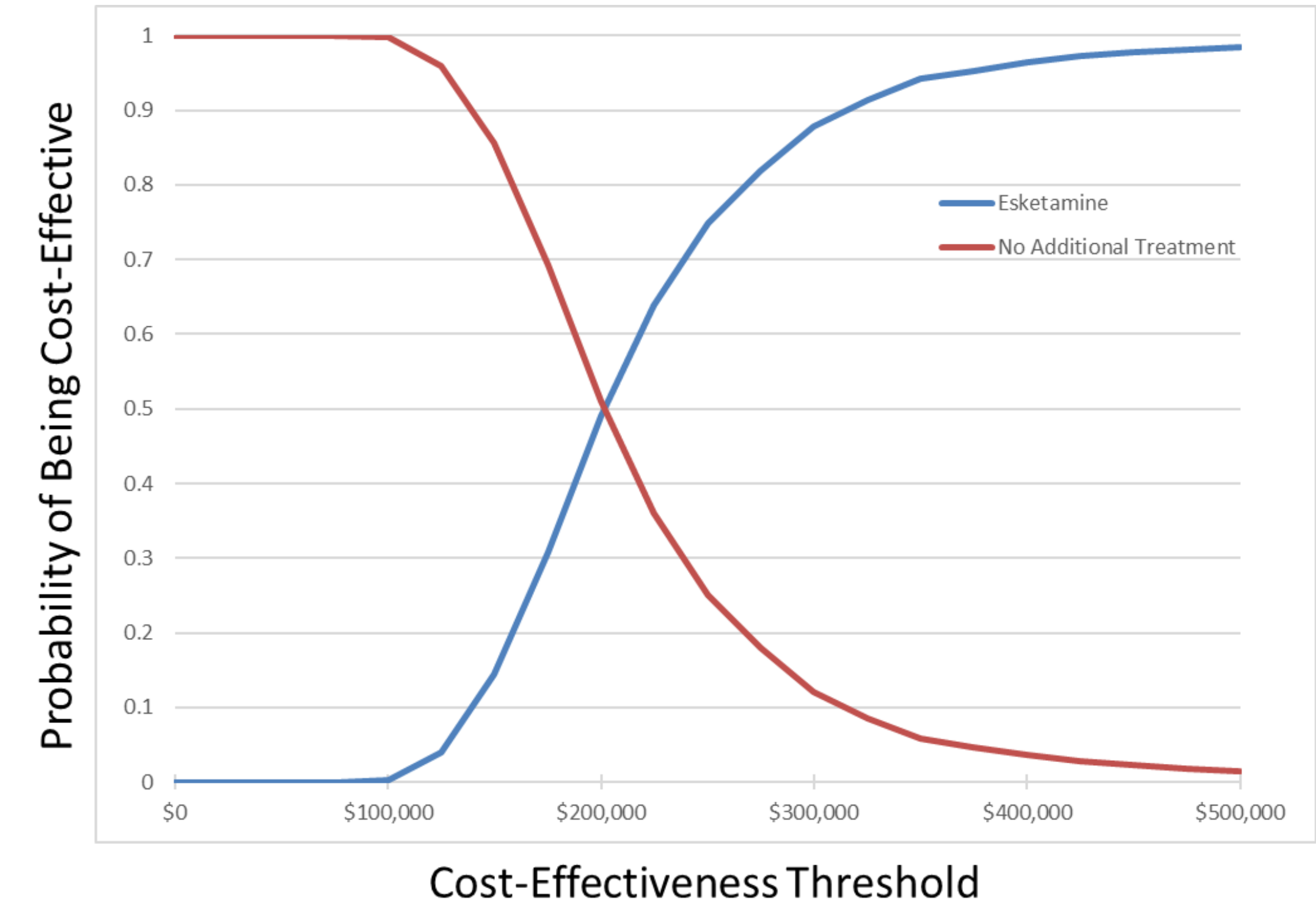
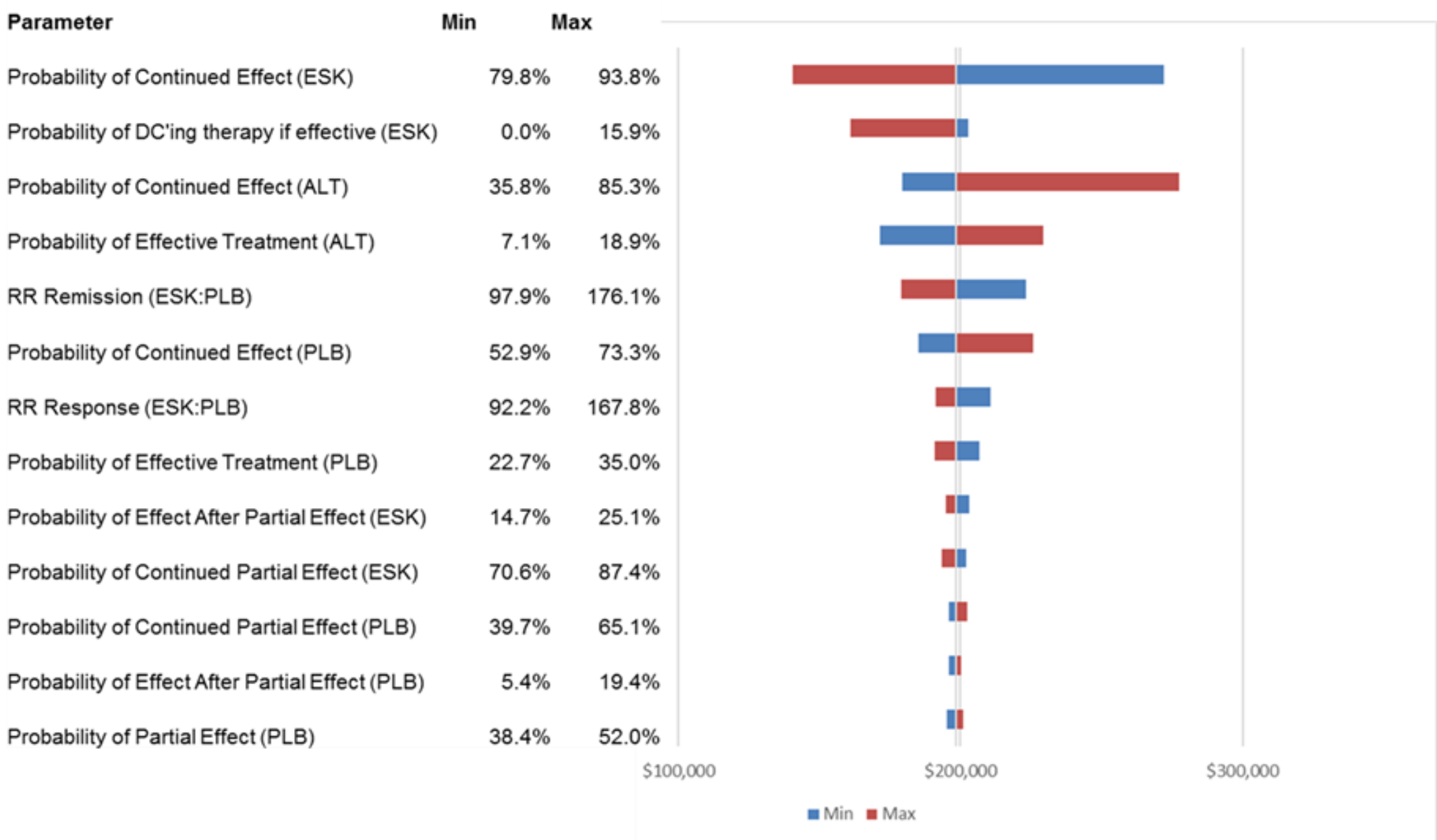
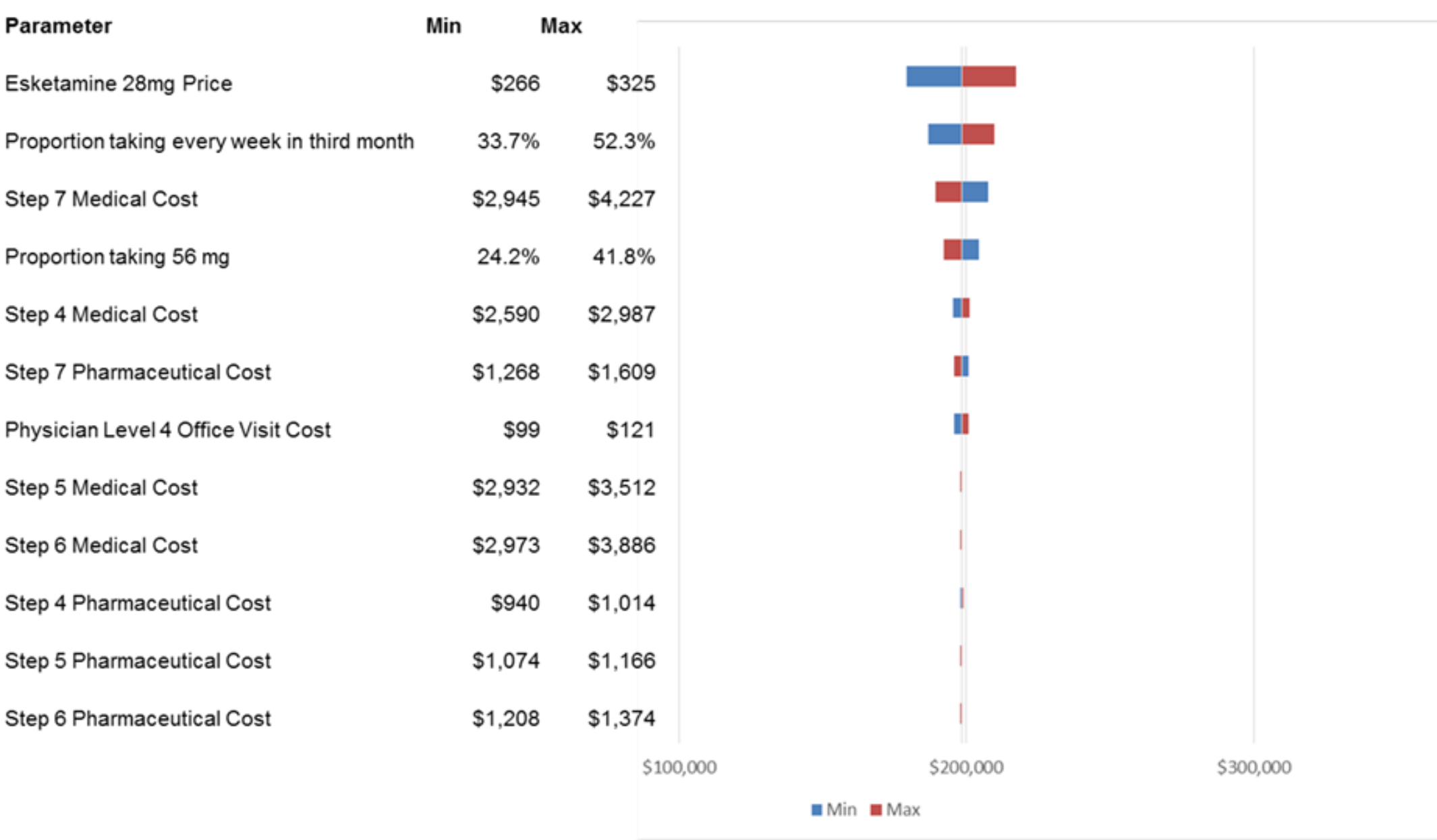


Figure 2. One-Way Sensitivity Analyses Tornado Diagrams of Esketamine Versus No Additional Treatment

Probabilities



Costs



CONCLUSION

- Although esketamine appears to provide important relief depressive symptoms for some patients deriving suboptimal benefit from other treatments, the estimated lifetime cost-effectiveness of esketamine far exceeds commonly cited cost-effectiveness thresholds.
- Due to a high discontinuation rate observed in open-label studies, the majority of esketamine's cost and benefits occurred in the first five years of therapy.
- The complex Risk Evaluation and Mitigation Strategies (REMS), designed to mitigate serious adverse outcomes resulting from sedation and dissociation, as well as reduce abuse and/or misuse, further complicate therapy with esketamine.
- Treatment-resistant depression is a debilitating disease with few treatment options. There is a need for effective and affordable treatments.
- Limitations:**
 - No or low-quality studies evaluating potential comparators, such as ketamine.
 - Limited information on important modifiers of treatment effect, such as:
 - Number of failed treatments during a person's lifetime
 - Pattern and frequency of depression episodes
 - Episode severity

REFERENCES

- Fedgchin M, Trivedi M, Daly E, et al. Randomized, Double-Blind Study of Fixed-Dosed Intranasal Esketamine Plus Oral Antidepressant vs. Active Control in Treatment-Resistant Depression. 9th Biennial Conference of the International Society for Affective Disorders and the Houston Mood Disorders Conference. 2018.
- Popova V, Daly E, Trivedi M, et al. Randomized, Double-Blind study of Flexibly-dosed Intranasal Esketamine Plus Oral Antidepressant vs. Active Control in Treatment-Resistant Depression. Annual Meeting of the American Society of Clinical Psychopharmacology. 2018.
- Daly E, Trivedi M, Janik A, et al. A Randomized Withdrawal, Double-blind, Multicenter Study of Esketamine Nasal Spray Plus an Oral Antidepressant for Relapse Prevention in Treatment-resistant Depression. Annual Meeting of the American Society of Clinical Psychopharmacology (ASCP). 2018.
- Rush AJ, Trivedi MH, Wisniewski SR, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR*D report. The American journal of psychiatry. 2006;163(11):1905-1917.
- Expert Opinion.
- Sullivan PW, Ghushchyan V. Preference-Based EQ-5D index scores for chronic conditions in the United States. Medical decision making : an international journal of the Society for Medical Decision Making. 2006;26(4):410-420.
- Janicak PG, Dunner DL, Aaronson ST, et al. Transcranial magnetic stimulation (TMS) for major depression: a multisite, naturalistic, observational study of quality of life outcome measures in clinical practice. CNS spectrums. 2013;18(6):322-332.
- Wajs E, Aluisio L, Morrison R, et al. Long-Term Safety of Esketamine Nasal Spray Plus Oral Antidepressant in Patients with Treatment-Resistant Depression: Phase 3, Open-Label, Safety and Efficacy Study (SUSTAIN-2). Annual Meeting of the American Society of Clinical Psychopharmacology. 2018.
- Food and Drug Administration (FDA). Spravato (Esketamine) Label. 2019; <http://www.janssenlabels.com/package-insert/product-monograph/prescribing-information/SPRAVATO-pi.pdf>.
- Redbook. 2019. Micromedex Online. Accessed March 12, 2019.

DISCLOSURE

DRT, NB, BT, and BGS were supported by a grant from the Institute for Clinical and Economic Review (ICER) to the UIC College of Pharmacy. SJA was supported by a grant from ICER to Massachusetts General Hospital. FA, VMK, KF, NF, and DMR are employees of ICER.