Daily intravenous ketamine for treatment-resistant depression: a cost-effectiveness analysis alongside the clinical trial

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OBJECTIVES

We conducted a cost-effectiveness analysis alongside a randomized controlled trial (RCT) evaluating the use of daily intravenous ketamine over three days for treatment-resistant depression (TDR) compared to an active placebo.

METHODS

We utilized person-level data from the RCT conducted at Siriraj Hospital, Mahidol University, Thailand, to assess the cost-effectiveness of ketamine compared to midazolam, the active placebo. Both treatments were administered intravenously over three consecutive days during a four-day hospitalization, with a follow-up period of one month. The effectiveness of each treatment for TDR was measured in quality-adjusted life-years (QALYs) using the EuroQol 5-Dimension 5-Level questionnaire, the Montgomery–Åsberg Depression Rating Scale (MADRS), and the Clinical Global Impression–Severity (CGI-S). Costs associated with outpatient and inpatient visits were calculated from a societal perspective, encompassing both direct medical costs (treatment for TDR and any adverse events) and direct non-medical costs. A probabilistic sensitivity analysis was performed.

RESULTS

(1 USD = 34.64 THB)

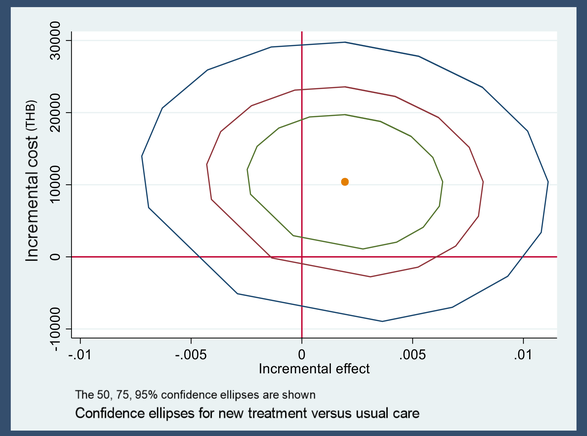
Among the 20 participants included in the RCT, 18 provided complete data for the analysis. The number of participants in the ketamine and midazolam groups was equal. Median costs of the ketamine and the midazolam groups were 374 USD (interquartile range [IQR] 281–577) and 291 USD (IQR 244–525), respectively. Average QALYs were 0.063±0.006 for ketamine and 0.061±0.009 for midazolam. The incremental cost-effectiveness ratios (ICERs) for ketamine compared to midazolam were 154,470 USD per QALY gained, 39 USD per 1 point decrease in MADRS, and 225 USD per 1 point decrease in CGI-S. The ICER per one remission achieved was 1,352 USD. Sensitivity analysis indicated an 8.2% probability of ketamine being cost-effective at Thailand's willingness-to-pay threshold of 4,619 USD per QALY gained

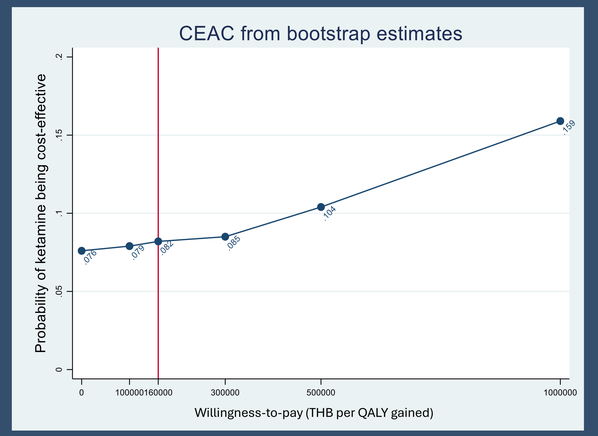
CONCLUSIONS

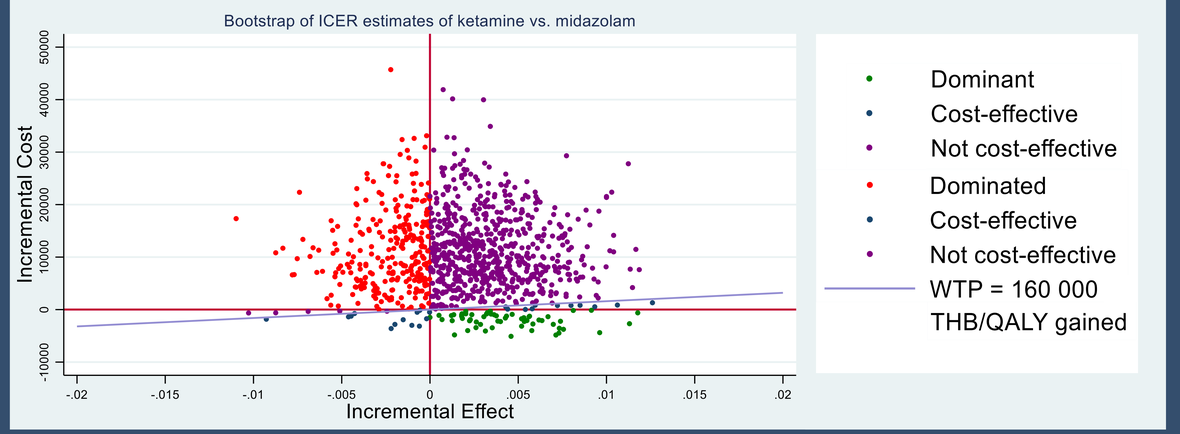
This study highlights the incremental effectiveness of ketamine at its higher cost, compared to midazolam. Variability in the cost-effectiveness of ketamine for TDR across different outcome measures was observed, underscoring the need for further research to elucidate its optimal regimen and economic implications.

Variables	Midazolam (n=9)	Ketamine (n=9)	*p*-value
Total cost (USD) mean ± SD median (IQR)	 368 ± 142 291 (244, 525)	 669 ± 673 374 (281, 577)	0.508
Total QALY (mean ± SD)	0.061 ± 0.009	0.063 ± 0.006	0.612
MADRS at 1 month (mean ± SD)	22.89 ± 8.54	15.11 ± 9.60	0.088
MADRS response, n (%)	2 (22.2%)	4 (44.4%)	0.620
MADRS remission, n (%)	1 (11.1%)	3 (33.3%)	0.576
CGI-S at 1 month (mean ± SD)	3.44 ± 1.13	2.11 ± 1.05	0.020

CGI-S, Clinical Global Impression–Severity; IQR, interquartile range; MADRS, Montgomery–Åsberg Depression Rating Scale; n, number; QALY, quality –adjusted life-year; SD, standard deviation; USD, United State dollar







Ethics approval and consent to participate

All the study protocols and materials have been reviewed and approved by the Institutional Review Board of Faculty of Medicine Siriraj Hospital, Mahidol University (Protocol No. 109/2564; Certificate of Approval No. Si 553/2021).
All participants received all essential information regarding the study protocols before contributing informed consent. This research confirm that all methods were carried out in accordance with the Declaration of Helsinki.
The trial is registered on ClinicalTrials.gov (NCT05026203).

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