HPR160

Relationships Between ICER Clinical Evidence Ratings and FDA Approval Decisions

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Objective

This analysis aimed to determine whether relationships exist between Institute for Clinical and Economic Review (ICER) comparative clinical effectiveness ratings and FDA approval decisions.

Background

- ICER conducts assessments of interventions by systematically evaluating their comparative clinical effectiveness. ICER thoroughly reviews available evidence to determine the net health benefits of an intervention compared to alternatives.[1]
- ICER assigns overall comparative clinical effectiveness evidence ratings to each of the interventions evaluated in an appraisal using the ICER clinical effectiveness rating matrix (**Figure 1**).[2]
- ICER convenes three independent appraisal committees — The California Technology Assessment Forum (CTAF), The Midwest Comparative Effectiveness Public Advisory Council (Midwest CEPAC), and The New England (NE) CEPAC. These committees deliberate and vote on whether the evidence in an assessment demonstrates a net health benefit for the intervention.[3]
- The objective of this analysis was motivated by a recent ICER assessment of MDMA-assisted psychotherapy for post-traumatic stress disorder which concluded with an "Insufficient" evidence rating.[4] Thereafter, the FDA issued a complete response letter requesting an additional Phase 3 trial, highlighting insufficient data for approval.[5]

Methods

- Completed ICER assessments published from the beginning of 2018 to the end of 2024 were reviewed. Key information was extracted from the ICER assessments, including, the intervention of interest, comparators, clinical evidence rating, and appraisal committee voting results.
  - For interventions with multiple comparators, the evidence rating compared to "usual care" was prioritized.
- Interventions with more ICER advisory board votes for a net health benefit than against were deemed to have a positive voting result, those with more votes against, a negative result.
- FDA approval decisions were reviewed for all interventions assessed within the included ICER reports and were categorized as approved (including full and conditional approvals) or not approved (including withdrawn and not approved decisions).
- Clinical evidence ratings and net health benefit voting results were compared with FDA decision status and descriptive statistics were calculated.

Results

- A total of 63 ICER assessments were reviewed. Fifty-four were included for analysis encompassing 98 interventions.
  - Nine were excluded with reasons for exclusion including outdated FDA decisions, incompleteness, or repetition.
- As assessed by ICER, of the 98 interventions, 18 received a high certainty rating with 15.8% (16/98) assessed to have "Superior", 1% (1/98) "Incremental" and 1% (1/98) "Comparable" net health benefits, respectively.
- Sixty-four interventions had moderate certainty ratings with 28.6% (28/98) assessed to have "Incremental or Better", 10.2% (10/98) "Comparable or Better", 8.2% (8/98) "Comparable or Incremental", and 18.3% (18/98) "Promising but Inconclusive" benefit respectively.
- Sixteen interventions, 15.8% (16/98), were assessed to have low certainty and "Insufficient" evidence.
- Excluding pending FDA decisions, 100% (16/16) of interventions with high certainty evidence, 89.1% (57/64) with moderate certainty, and 81.3% (13/16) with low certainty were approved, respectively (**Figure 2**).
- Interventions with a positive ICER advisory board voting result (59/98) had a higher FDA approval rate (94.7%) than those with a negative result (29/98; 86.2% approval rate; **Figure 3**).
  - Ten interventions were not voted on by an ICER advisory board (10/98; 70% approval rate).
- Interventions voted on by the CTAF had the highest approval rate at 95.5% (21/22), compared to 89.7% (26/29) for the NE CEPAC and 89.2% (33/37) for the Midwest CEPAC. There were variations in the proportion of interventions with low, moderate, and high certainty evidence across each advisory board (**Figure 4**).

Conclusion

Interventions assessed by ICER were approved by the FDA 89.5% of the time (86/96), with a strong alignment between high-and moderate-certainty ICER clinical evidence ratings and FDA approval. All 10 interventions not approved by the FDA received one of the three lowest-certainty ICER evidence ratings (C++, P/I, or I), while all five higher-certainty ratings received 100% approval. This trend highlights a potential alignment in ICER's and the FDA's clinical evidence evaluation methods.

FIGURE 1

ICER comparative clinical effectiveness rating matrix

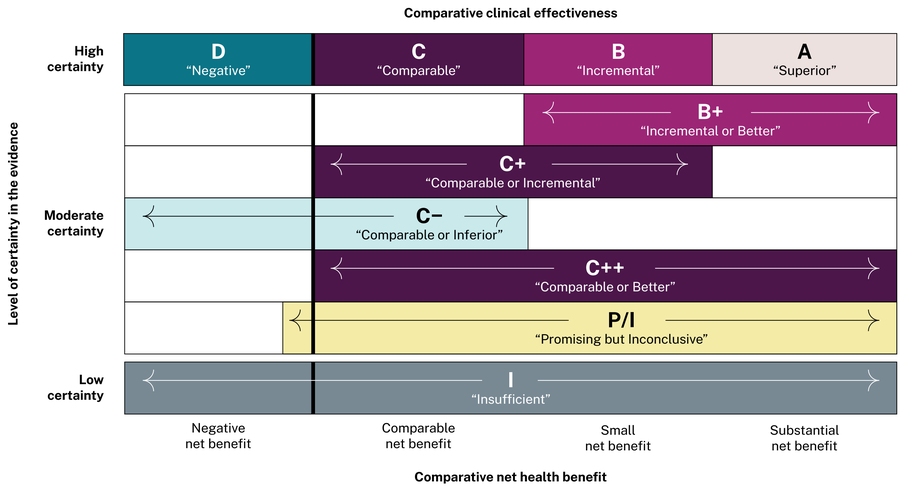


FIGURE 2

FDA approval decisions by ICER evidence rating

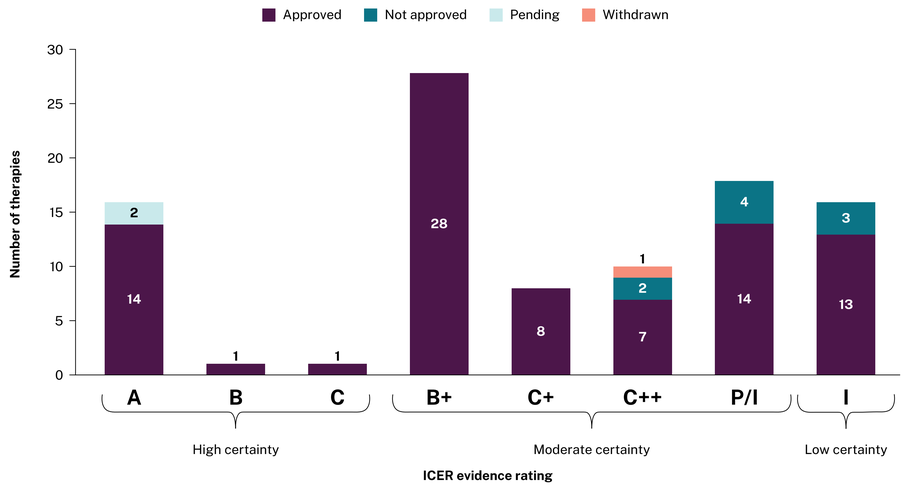
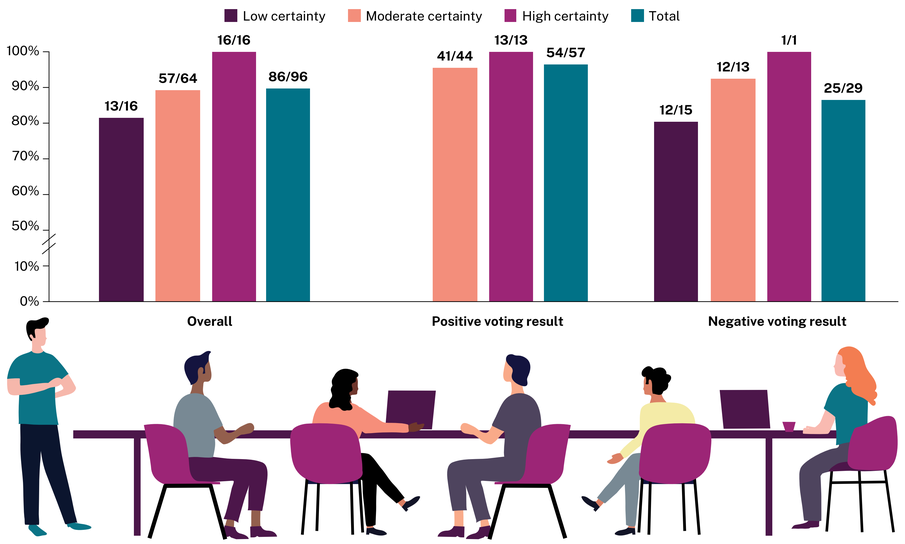


FIGURE 3

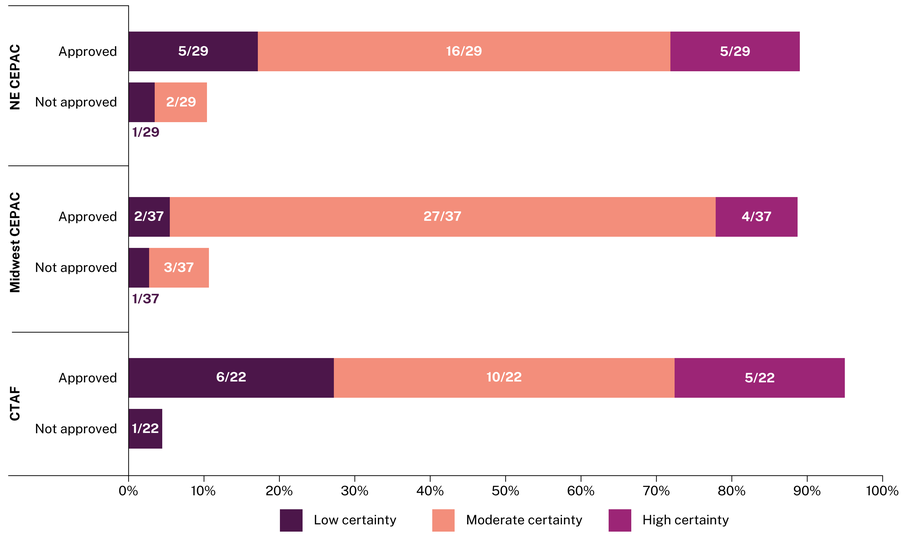
FDA approval rates of assessed interventions by ICER evidence rating and advisory board voting results



Interventions with pending FDA decisions (n=2) and interventions with no advisory board voting (n=10) are not presented.

FIGURE 4

FDA approval rates of assessed interventions by each ICER advisory board and evidence certainty



Interventions with pending FDA decisions (n=2) and interventions with no advisory board voting (n=10) are not presented.

Abbreviations: CEPAC: Comparative Effectiveness Public Advisory Council; **CTAF:** The California Technology Assessment Forum; **FDA:** US Food and Drug Administration; **ICER:** Institute for Clinical and Economic Review; **MDMA:** 3,4-methylenedioxymethamphetamine; **NDA:** New drug application; **NE:** New England.

References: [1]ICER (2025) Considering Clinical, Real-World, and Unpublished Evidence. Available at: https://icer.org/our-approach/methods-process/considering-clinical-real-world-and-unpublished-evidence/ [Last accessed 10 April 2025]; [2]ICER (2025) Evidence Rating Matrix. Available at: https://icer.org/evidence-rating-matrix/ [Last accessed 10 April 2025]; [3]ICER (2025) Independent Appraisal Committees. Available at: https://icer.org/who-we-are/people/independent-appraisal-committees/ [Last accessed 10 April 2025]; [4]ICER (2024) Midomafetamine-Assisted Psychotherapy for Post-Traumatic Stress Disorder, Final Evidence Report. Available at: https://icer.org/wp-content/uploads/2024/06/PTSD_Final-Report_For-Publication_06272024.pdf; [5]Lykos Therapeutics (2024) Lykos Therapeutics Announces Complete Response Letter for Midomafetamine Capsules for PTSD. Available at: https://news.lykospbc.com/2024-08-09-Lykos-Therapeutics-Announces-Complete-Response-Letter-for-Midomafetamine-Capsules-for-PTSD/ [Last accessed 10 April 2025]. **Acknowledgements:** The authors thank Jessica Brown, Costello Medical, for graphic design assistance. **Disclosures:** PM and CD report employment with Costello Medical, Boston, MA.

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