Esketamine for Treatment-Resistant Depression: Effectiveness and Value

Afternoon Session – May 23, 2019

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

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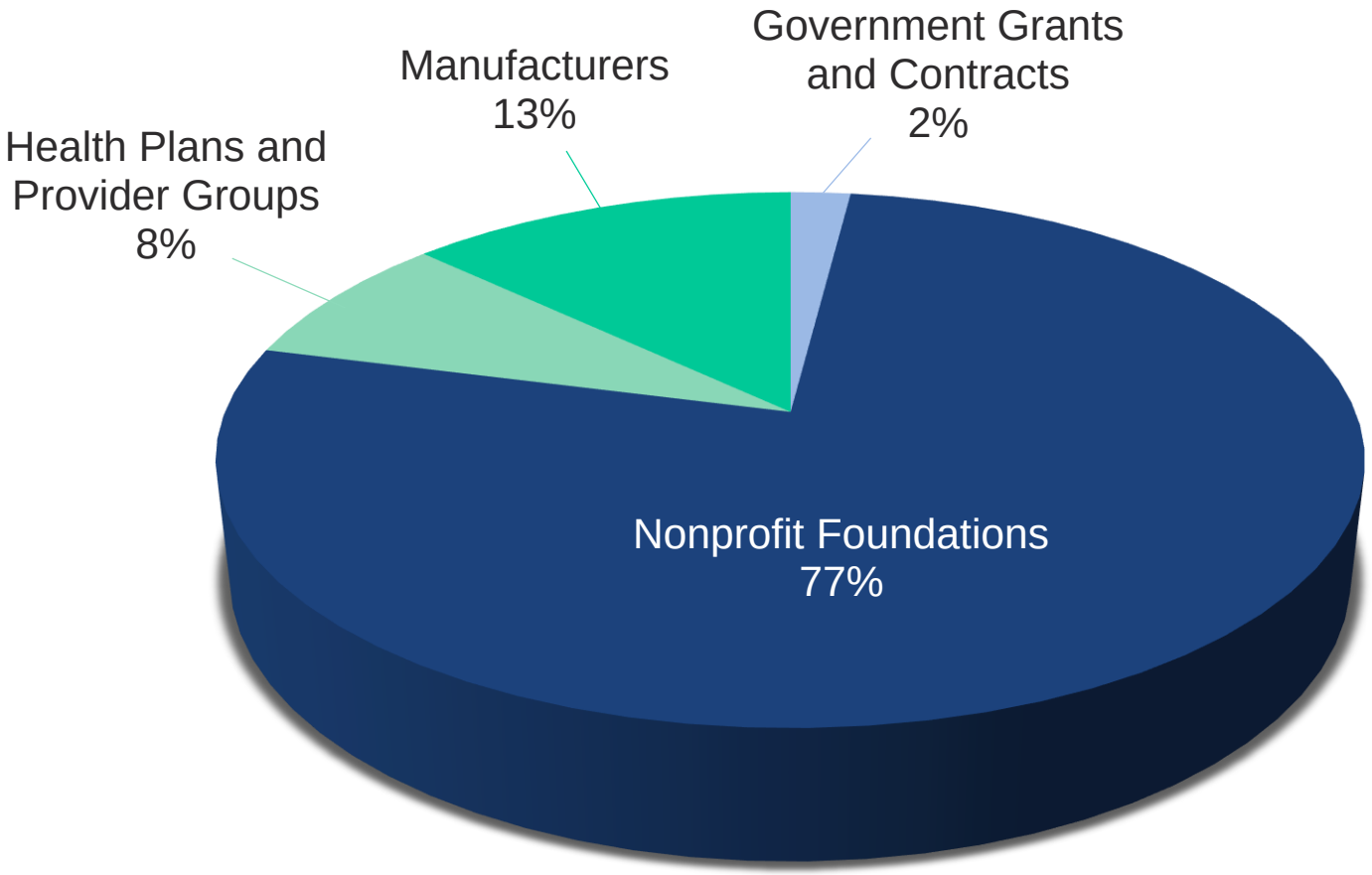
Organizational Overview

- Midwest Comparative Effectiveness Public Advisory Council (CEPAC)

- The Institute for Clinical and Economic Review (ICER)

2019 Funding Sources



ICER Policy Summit and non-report activities

Why are we here today?

- *"While there are numerous medications approved to treat depression in several therapeutic classes – SSRIs, SNRIs and MAO inhibitors—the common experience for people living with TRD is a repetitive cycle of trial and error with multiple combinations of these existing medications."*

  -Mary Giliberti, J.D., Chief Executive Officer, National Alliance on Mental Illness

- *"I used to be suicidal 250-300 days out of the year. Treatment with ketamine lifted me out of this black hole. Now I'm suicidal about once a year."*

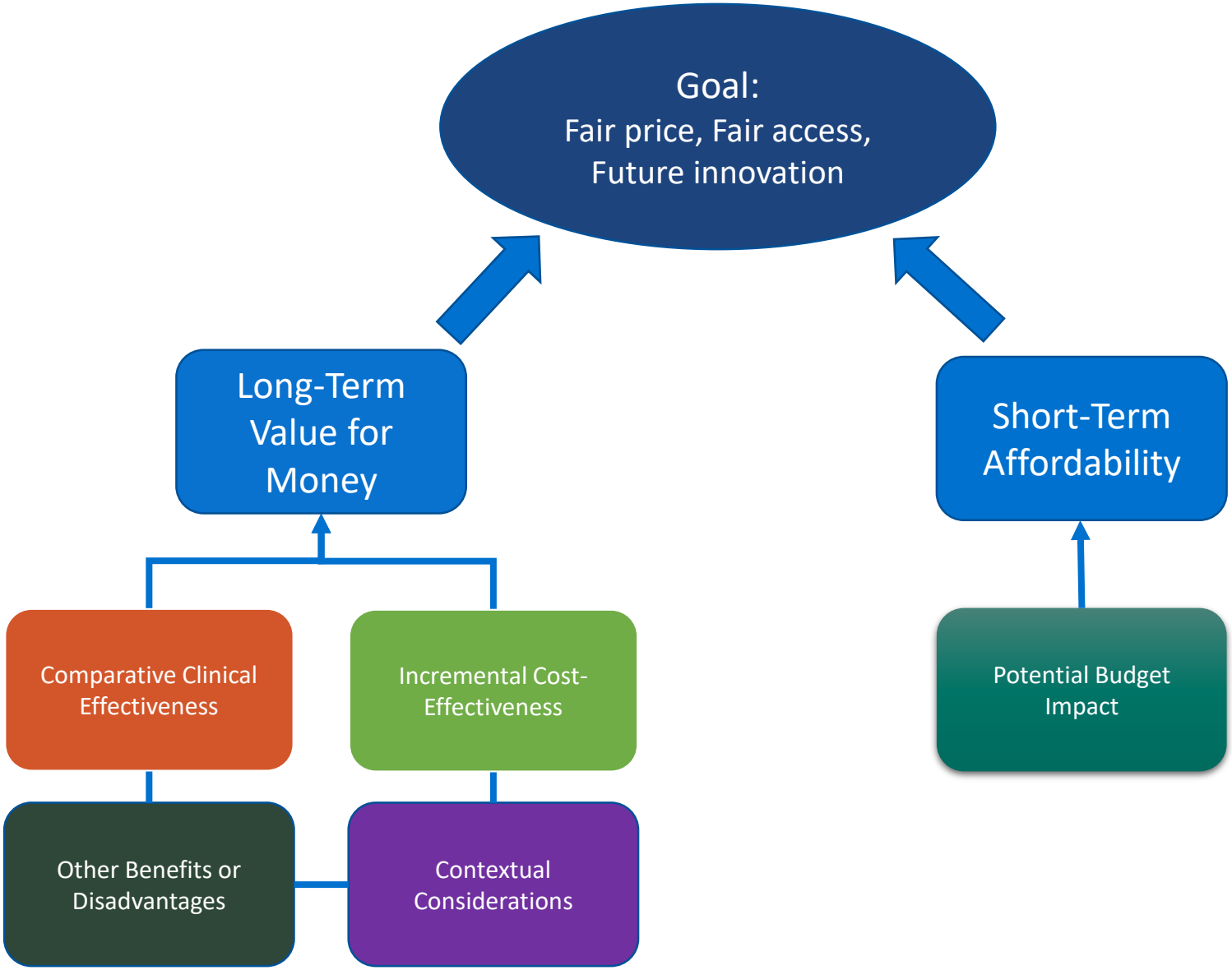
  -Patient with Treatment-Resistant Depression

Why are we here today?

- Increasing health care costs affecting individuals, state and federal budgets
- New mechanisms of action often raise questions about appropriate use, cost
- Patients can have difficulty accessing drugs
  - Step therapy protocols
  - Requirements to switch drugs with new insurance
  - High out-of-pocket costs
- Need for objective evaluation and public discussion of the evidence on effectiveness and value

How was the ICER report developed?

- Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
- Internal ICER staff evidence analysis
- University of Illinois at Chicago cost-effectiveness modeling
- Public comment and revision
- Expert reviewers
  - **Dr. Cristina Cusin**, MD, Massachusetts General Hospital
  - **Dr. William Gilmer**, MD, Northwestern University Feinberg School of Medicine
  - **Phyllis Foxworth**, Depression and Bipolar Support Alliance
- How is the evidence report structured to support CEPAC voting and policy discussion?


Goal:
Fair price, Fair access,
Future innovation
Long-Term Value for Money
Short-Term Affordability
Comparative Clinical Effectiveness
Incremental Cost-Effectiveness
Potential Budget Impact
Other Benefits or Disadvantages
Contextual Considerations

Agenda

Afternoon Session: Esketamine for Treatment-Resistant Depression	
1:00 pm—1:15 pm	Meeting Reconvened Steve Pearson, MD, MSc, President, ICER
1:15 pm—2:15 pm	Presentation of the Evidence • Steven J. Atlas, MD, MPH, Director, Practice Based Research & Quality Improvement, Division of General Internal Medicine, Massachusetts General Hospital • Daniel R. Touchette, PharmD, MA, Professor of Pharmacy; Assistant Director, Center for Pharmacoepidemiology and Pharmacoeconomic Research, University of Illinois at Chicago
2:15 pm – 2:30 pm	Public Comments and Discussion
2:30 pm—3:30 pm	Midwest CEPAC Panel Vote on Clinical Effectiveness and Value
3:30 pm – 3:45 pm	Break
3:45 pm – 4:45 pm	Policy Roundtable Discussion
4:45 pm – 5:00 pm	Reflections from Midwest CEPAC Panel/Adjourn

Clinical and Patient Experts

Cristina Cusin, MD, Assistant Professor in Psychiatry, Massachusetts General Hospital

- *Dr. Cusin served as site PI for an esketamine trial sponsored by Janssen.*

William S. Gilmer, MD, Clinical Professor of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine

- *Dr. Gilmer has received consulting and speaker fee honorarium from Sunovion and Otsuka and owns equity in Organovo, Jounce, and Gilead Sciences.*

Phyllis Foxworth, Vice President of Advocacy, Depression and Bipolar Support Alliance

- *No relevant conflicts of interest to disclose*

Pamela Goloskie, Patient Advocate

- *No relevant conflicts of interest to disclose*

Evidence Review

Steven J. Atlas, MD, MPH

Associate Professor of Medicine

Harvard Medical School

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Key Collaborators

- **Steven J. Atlas, MD, MPH**
  Director, Practice Based Research, MGH
- **Foluso Agboola, MBBS, MPH**
  Director, Evidence Synthesis, ICER
- **Katherine Fazioli**
  Senior Research Assistant, ICER
- **Noemi Fluetsch, MPH**
  Research Assistant, ICER

Disclosures:

We have no conflicts of interest relevant to this report.

Background: Major Depressive Disorder (MDD)

- Symptoms include persistent sadness, hopelessness, loss of interest/appetite, decreased energy, trouble sleeping or concentrating, suicidal thoughts
- Treatment-resistant MDD (TRD) refers to a major depressive episode with an inadequate response to therapy of adequate dosing and duration
- MDD is common, serious, and expensive
  - 16 million (7%) of adults in the United States experience at least one major depressive episode each year
  - ~1/3 of patients with major depressive episode have TRD
  - TRD associated with higher costs of care, decreased work productivity, and accounts for ~$64 billion in total costs

Impact on Patients

- TRD can have a major negative impact on quality of life, ability to work and overall economic well-being
- For many, current medications do not provide long-term relief or have intolerable side effects
- Those with refractory disease may turn to therapies such as electroconvulsive therapy (ECT) or repetitive transcranial magnetic stimulation (rTMS)
  - High relapse rates, time consuming and inconvenient, and especially for ECT, may have cognitive side effects
- As a result, some patients with TRD turn to off-label therapies, such as ketamine

Standard of Care & Management

- Commonly used antidepressant (AD) medications:
  - Selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), and atypical ADs (e.g. bupropion)
- For those not responding or having side effects:
  - Modify AD therapy or augment existing therapies with other medications (e.g. antipsychotics)
  - Depression-focused psychotherapy may be added, but is not considered stand-alone therapy
  - Other strategies such as ECT and rTMS may be tried
- Potential new target for therapy is the N-methyl-D-aspartate (NMDA) receptor
  - Based on ketamine, an anesthetic, improving symptoms

Scope of Review

- To evaluate the clinical effectiveness of esketamine nasal spray plus background AD for TRD
- Comparators:
  - Background AD alone (placebo), ketamine, ECT, rTMS, other ADs, or augmentation with antipsychotics
- Key outcomes & harms

Outcomes	Harms
Symptom improvement	Nausea/vomiting
Clinical response and remission	Dissociation
Relapse	Suicidal ideation
Quality of life	Increased blood pressure

Main Body of Evidence

- Four Phase III multicenter trials of esketamine
  - Three were similarly designed 4-week RCTs
    - TRANSFORM 1 & 2: in patients 18-64 years
    - TRANSFORM 3: in patients aged ≥65 years
  - SUSTAIN 1: withdrawal study to assess relapse prevention
- SUSTAIN 2: open-label, 48-week trial to evaluate long-term safety
- Comparator RCTs that met eligibility criteria
  - Ketamine: One phase II trial
  - rTMS and ECT: 11 sham-controlled trials of rTMS and 1 comparing ECT and rTMS
  - Antipsychotics: 2 trials of olanzapine

Overview of Randomized Trials of Esketamine

Key Trials	Treatment Groups*	N	Age, yrs	Duration of Current Episode, yrs	Failures of ≥ 3 ADs, %	MADRS
TRANSFORM-1	Esketamine 56 mg Esketamine 84 mg Placebo	342	47	3.9	40%	37.5
TRANSFORM-2	Esketamine (flexible) Placebo	223	46	2.2	36%	37.0
TRANSFORM-3	Esketamine (flexible) Placebo	137	70	4.1	39%	35.0
SUSTAIN-1	Esketamine (flexible) Placebo	297	48	NR	NR	38.3

*Patients in all arms also received a newly initiated open-label antidepressant, referred to as background antidepressant.

Key Clinical Outcomes

- **Primary Outcome:**
  - Symptom improvement: change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) at 4 weeks
- **Secondary Outcomes**:
  - Clinical response: ≥50% improvement in MADRS from baseline
  - Clinical remission: MADRS score ≤12
  - Clinical relapse: MADRS score of ≥22 at two consecutive assessments and/or hospitalization for worsening depression, suicide/attempt, or other suggestive event
  - Patient reported outcomes: Patient Health Questionnaire (PHQ-9), Sheehan disability scale (SDS)

Insights from Discussions with Patients

- Patients highlighted the need for new therapies for those not responding to or intolerant of current treatment options
- Emphasized the dramatic impact on all aspects of life: relationships with friends and family, work, disability and economic hardship
- Some have found benefit from off-label use of ketamine and are interested in trying esketamine

Results

Key Finding: Comparability of Trial Evidence

- Key differences in esketamine and comparator trials prevented performing a network meta-analysis
  - Entry criteria: definitions of TRD varied
  - Study population: varying symptom severity and duration
  - Study design: choice of using newly initiated concomitant AD versus continuing a failed AD
  - Outcomes: choice of endpoints and assessment
- Performed meta-analysis of two esketamine trials (TRANSFORM-1 & -2)

Primary Outcome: Change in MADRS at Week 4

Trial	Intervention	Baseline	Δ from Baseline	Esketamine vs. Placebo	
				Mean Difference*	p-value
TRANSFORM-1	Placebo	37.5	-14.8	—	—
	Esketamine 56 mg	37.4	-19.0	-4.1	0.011
	Esketamine 84 mg	37.8	-18.8	-3.2	0.088
TRANSFORM-2	Placebo	37.3	-17.0	—	—
	Esketamine	37.0	-21.4	-4.0	0.020

*LSMD: least square mean difference, estimated using mixed model for repeated measures

- Meta-analysis of TRANSFORM-1 & -2: greater improvement on MADRS score for esketamine compared to placebo (**mean difference -3.8; 95% CI: -6.3, -1.4)**
- TRANSFORM-3: similar improvement was observed, but not statistically significant (mean difference -3.6; 95% CI: -7.2, 0.07)

Clinical Response & Remission at Week 4

Trial	Intervention	N	Response, %	Remission, %
TRANSFORM-1	Placebo	113	37.2	29.2
	Esketamine 56 mg	115	52.2	34.8
	Esketamine 84 mg	114	45.6	33.3
TRANSFORM-2	Placebo	109	47.7	28.4
	Esketamine	114	61.4	46.5

- Results of meta-analysis
  - **Clinical response**: patients on esketamine more likely to achieve clinical response compared to placebo (**relative risk 1.30; 95% CI: 1.08, 1.56)**
  - **Remission**: similar relative risk, but not statistically significant (**relative risk 1.37; 95% CI: 0.99, 1.91)**

Ketamine: Clinical Response & Remission at Week 2

- Phase II, placebo-controlled RCT IV ketamine (Singh 2016)
- Baseline: mean age 44 years, mean MADRS 35, and 15% failed more than 3 ADs in current episode

Trial	Intervention	N	Response, %	Remission, %
Singh 2016	Ketamine	35	51.4	25.7
	Placebo	32	9.4	3.1

- Response and remission rates in the placebo group were much lower compared to the esketamine trials
- Could be due to functional unblinding

Esketamine: Relapse Outcomes

- **SUSTAIN 1:** 705 patients enrolled
  - 176 achieved stable remission
  - 121 achieved stable response
- **Stable remitters (n=176):**
  - Esketamine reduced risk of relapse by 51% (HR 0.49; 95% CI: 0.29, 0.84)
- **Stable responders (n=121):**
  - Esketamine reduced risk of relapse by 70% (HR 0.30; 95% CI: 0.16, 0.55)

Esketamine: Harms

- Patients receiving esketamine had more adverse events, but most were mild to moderate and resolved on dosing day
  - Including nausea, dizziness, dissociation, sedation, and clinically important increases in blood pressure
  - More likely to discontinue treatment over 4-week trial
- No evidence of drug-seeking behavior or misuse/abuse of esketamine in trials, but FDA label includes a boxed warning and requires Risk Evaluation and Mitigation Strategy (REMS)
- In 48-week open label trial, serious adverse events, including suicidal ideation/attempt were reported in ~6% of patients
- During the four phase III esketamine trials, a total of six patients died (only one in controlled phase)
  - 3 deaths were by suicide

Controversies and Uncertainties

- Experts view esketamine as option for chronic, severe MDD failing multiple other therapies
  - Uncertain which patients may derive the most benefit
- Given side effects of esketamine, blinding may have been difficult to maintain and not reported
- Uncertainty about the benefits and risks of long-term use of esketamine for patients with TRD
  - No report of issues related to misuse or abuse but FDA approval requires REMS program to monitor safety

Potential Other Benefits and Contextual Considerations

- Esketamine offers a novel mechanism of action that is similar to ketamine, and may be an option for those not finding relief or tolerating other treatments
- TRD associated with large, unmet burden of illness
  - Unclear who may derive the greatest benefit, such as severity of baseline symptoms, duration of episode or years with MDD, and other psychiatric conditions
- Though patients expressed interest in new therapies, they were cautious about esketamine given the nature of its dosing and administration

Public Comments Received

- Esketamine's manufacturer emphasized results from the Transform-2 trial with flexible dosing as being the most relevant
- ICER performed its meta-analysis using data from Transform-1 & -2
  - Both were Phase III efficacy trials in patients with the same eligibility criteria
  - Used the same dosing options and use of background antidepressants
  - Assessed outcomes at the same time point with identical measures

Summary

- Esketamine Versus Placebo Plus Background AD
  - Improved symptoms and response in adults 18-64 years. Also improved remission and showed similar effects in adults ≥65, but not statistically significant
  - For those responding or in remission, continuing esketamine resulted in decreased rate of relapse
  - Side effects included dissociation and increased BP along with risk of suicidal ideation
  - Limited data on long-term use
- Esketamine Versus Ketamine, TMS, ECT and Augmentation with Olanzapine
  - No head-to-head evidence comparing esketamine with any comparators identified

ICER Evidence Ratings

Esketamine plus Background AD	ICER Evidence Rating
vs. Background AD (Placebo)	Promising but Inconclusive (P/I)
vs. Ketamine, TMS, ECT and Augmentation with Olanzapine	Insufficient (I)

Questions?

Cost-Effectiveness

Daniel R. Touchette, PharmD, MA
University of Illinois at Chicago

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Key Team Members

Nicole Boyer, PhD, University of Chicago

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Varun Kumar, MBBS, MPH, MSc, Institute for Clinical and Economic Review

Disclosures

Financial support provided to the University of Illinois at Chicago from the Institute for Clinical and Economic Review (ICER) and from the University of Chicago to Nicole Boyer.

Brian Talon was employed by the University of Illinois at Chicago through a fellowship sponsored by Takeda Pharmaceuticals in 2016-2018. Robert Schultz is currently employed by the University of Illinois at Chicago through a fellowship sponsored by Takeda Pharmaceuticals.

University of Illinois at Chicago researchers and Nicole Boyer have no additional conflicts to disclose. Conflicts are defined as more than $10,000 in healthcare company stock or more than $5,000 in honoraria or consultancies from health care manufacturers or insurers relevant to this report during the previous year.

Objectives

Primary: To evaluate the lifetime cost-effectiveness of the addition of esketamine nasal spray plus background antidepressant compared to background antidepressant alone for the treatment of treatment- resistant major depressive disorder (TRD).

Secondary: To evaluate the one-year costs of therapy for the addition of esketamine nasal spray compared to intravenous ketamine for the treatment of treatment-resistant major depressive disorder (TRD).

Cost-Effectiveness Analysis Methods in Brief

Base-Case Population

Characteristic	Value
Mean Age in Years	46
Percent Female	67%
Number of Previous Antidepressant Trials, %	
1 or 2	63%
≥ 3	37%
Mean MADRS Score at Baseline	37.4

Intervention and Comparator

Drug	Dose
Esketamine Plus Background Antidepressant	Esketamine: Induction (weeks 1-4): 56 or 84 mg twice weekly Maintenance (weeks 5-8): 56 or 84 mg once weekly Maintenance (after week 8): 56 or 84 mg once weekly to every other week Background Antidepressant: Varies by patient
Background Antidepressant	Varies by patient

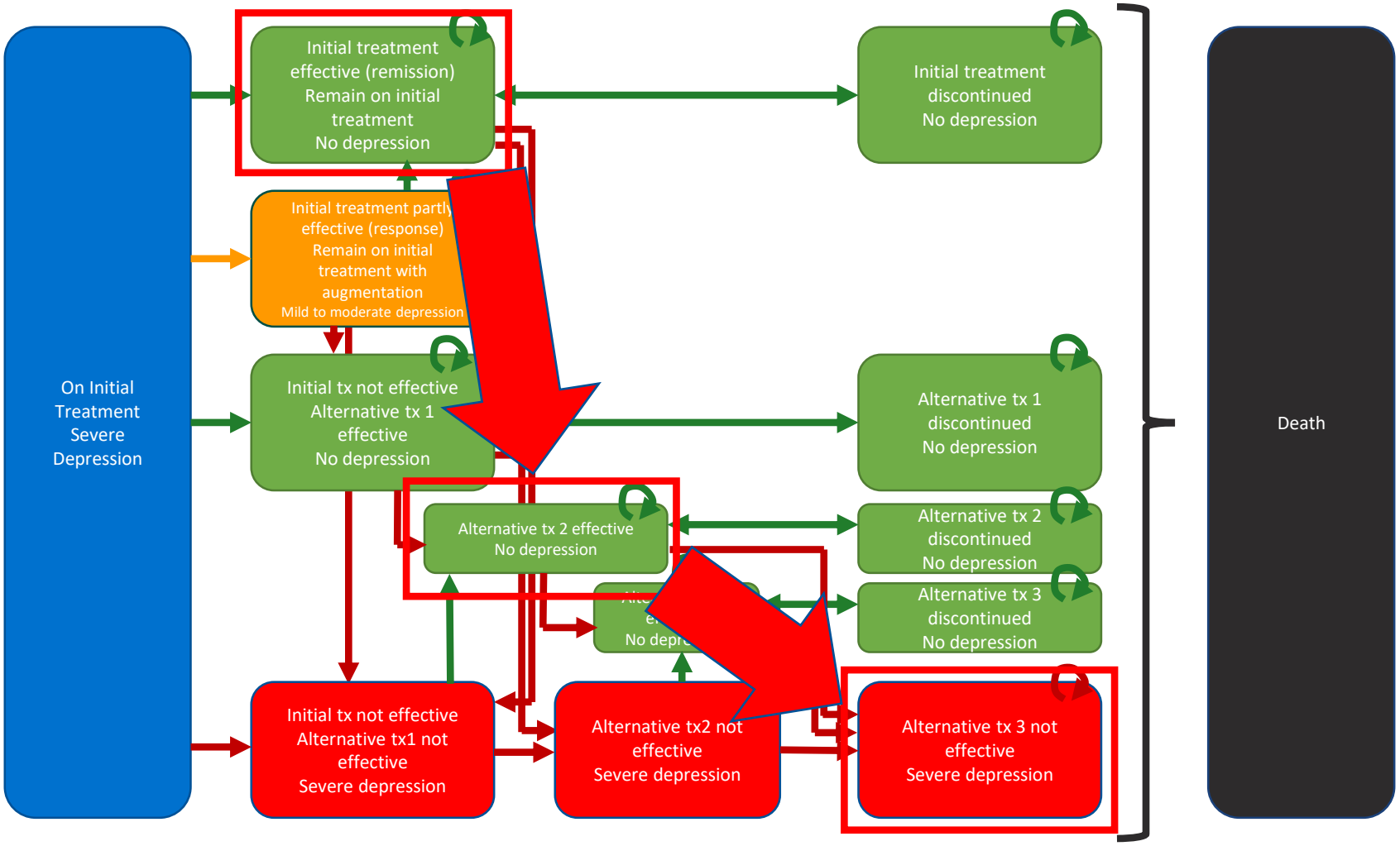
Methods Overview

- **Model:** Semi-Markov with time varying mortality
- **Setting:** United States
- **Perspective:** Health care sector (direct medical care and drug costs)
- **Time Horizon:** Lifetime
- **Discount Rate:** 3% per year (costs and outcomes)
- **Cycle Length:** 3 months
- **Primary Outcome:** Cost per quality-adjusted life year (QALY) gained
- **Other Outcomes:** Cost per life year (LY) gained, cost per depression day avoided

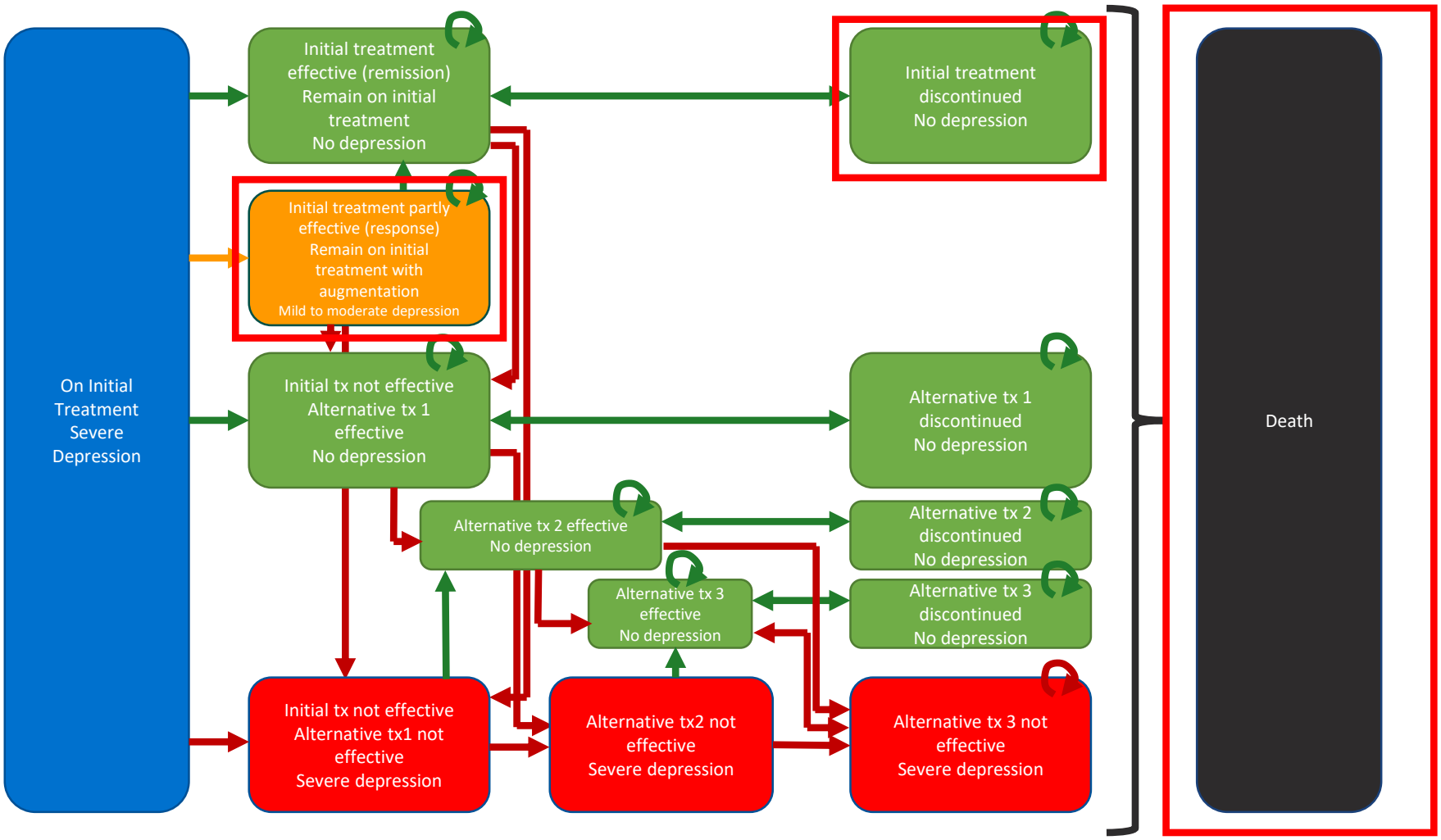
Key Model Inputs

- **Clinical inputs**
  - Esketamine effectiveness determined from clinical and open-label longer-term trials
  - Other model inputs determined from STAR*D trial, a pragmatic study evaluating numerous depression treatments
- **QALY Gains**
  - Utility assigned to model states according to degree of depression experienced
- **Health Sector Costs**
  - Manufacturer-submitted net price
  - Cost of care determined by number of failed prior treatments

Model Structure



Model Structure



Key Assumptions

- Some patients with effective treatment long term had their treatments discontinued
  - Those whose treatments were discontinued for effectiveness and had a relapse restarted their last effective treatment and received benefit from that treatment
- The model only tracked up to three additional alternative therapies; patients with additional failures were pooled in same Markov state
- Patients with effective depression treatment had medical costs equivalent to those with three prior treatment failures (i.e. lowest cost of care from our source publication)
- Treatment did not directly affect mortality (level of depression did affect mortality)

Key Treatment Model Inputs

Probabilities (Per 3-Month Cycle)	Esketamine plus Antidepressant	Antidepressant Alone
Effective Treatment (Tx)	39.5%	28.8%
Partly Effective Tx	19.3%	16.5%
Partly Effective Tx to Effective Tx	19.9%	12.4%
Effective Treatment Loss of Response	13.0%	
Partly Effective Tx Loss of Response	21.0%	47.6%
Effective Initial Treatment to Discontinued with Effect	1.3% per cycle (5% per year)	

Patient Utilities

Parameter	Base-Case Value
No Depression	0.86
Mild-to-Moderate	0.68
Severe	0.50*

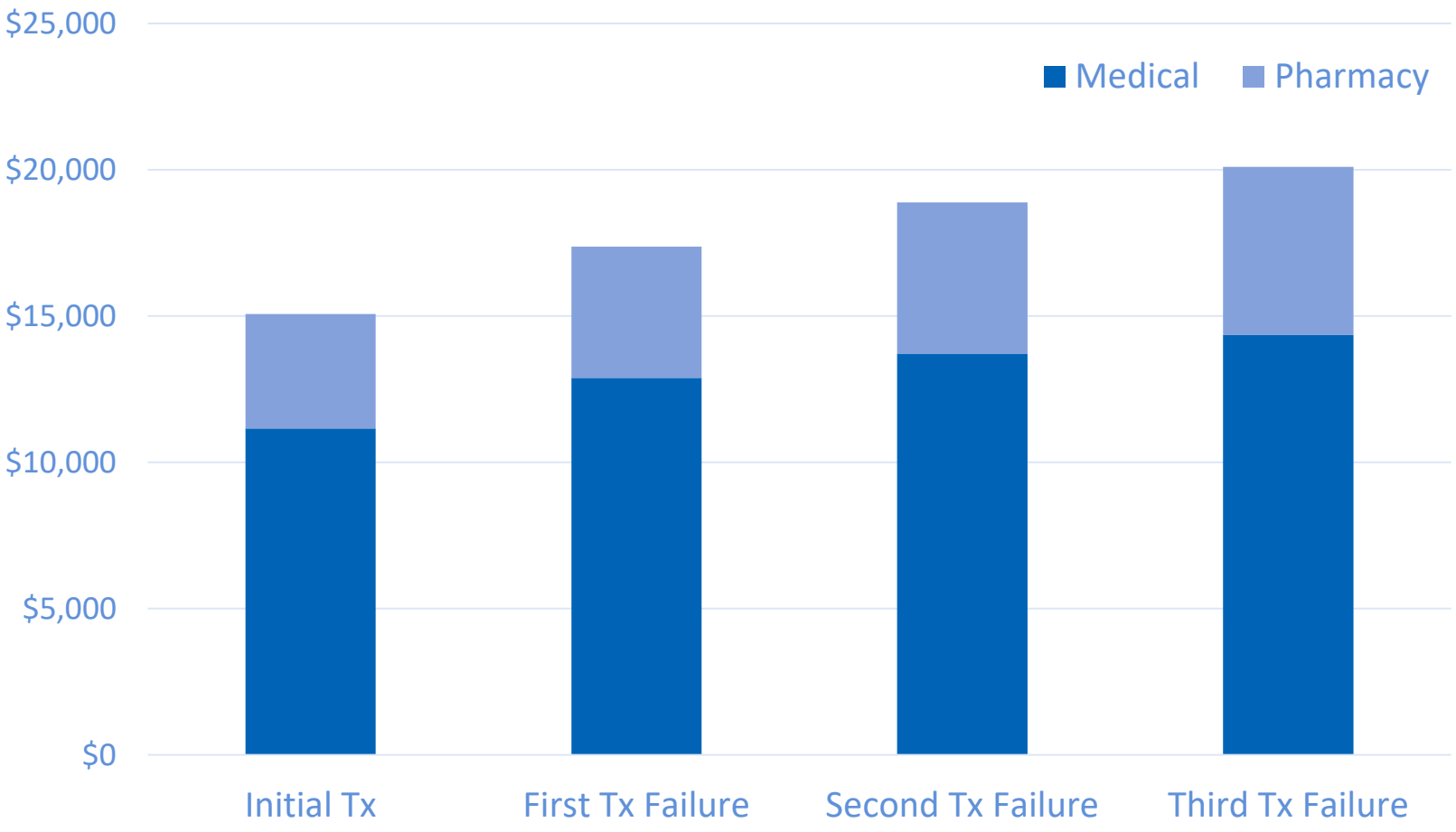
*Very few conditions have utility values approaching 0.5. One review of a broad range of conditions identified “Senility without Psychosis” at a utility of 0.55, “Heart Failure” at 0.64, and “Renal Failure” at 0.65.

Esketamine Pricing and Annual Cost

- A WAC price of $295 per 28 mg device was applied to the utilization doses and proportions of patients receiving each dose

Annual Costs	Base-Case Value
First Year (excluding observation and monitoring)	$28,500
Second Year (excluding observation and monitoring)	$27,000
First Year (including observation and monitoring)	$32,400
Second Year (including observation and monitoring)	$30,800

Direct Medical and Pharmaceutical Costs



Cost-Effectiveness Analysis Results

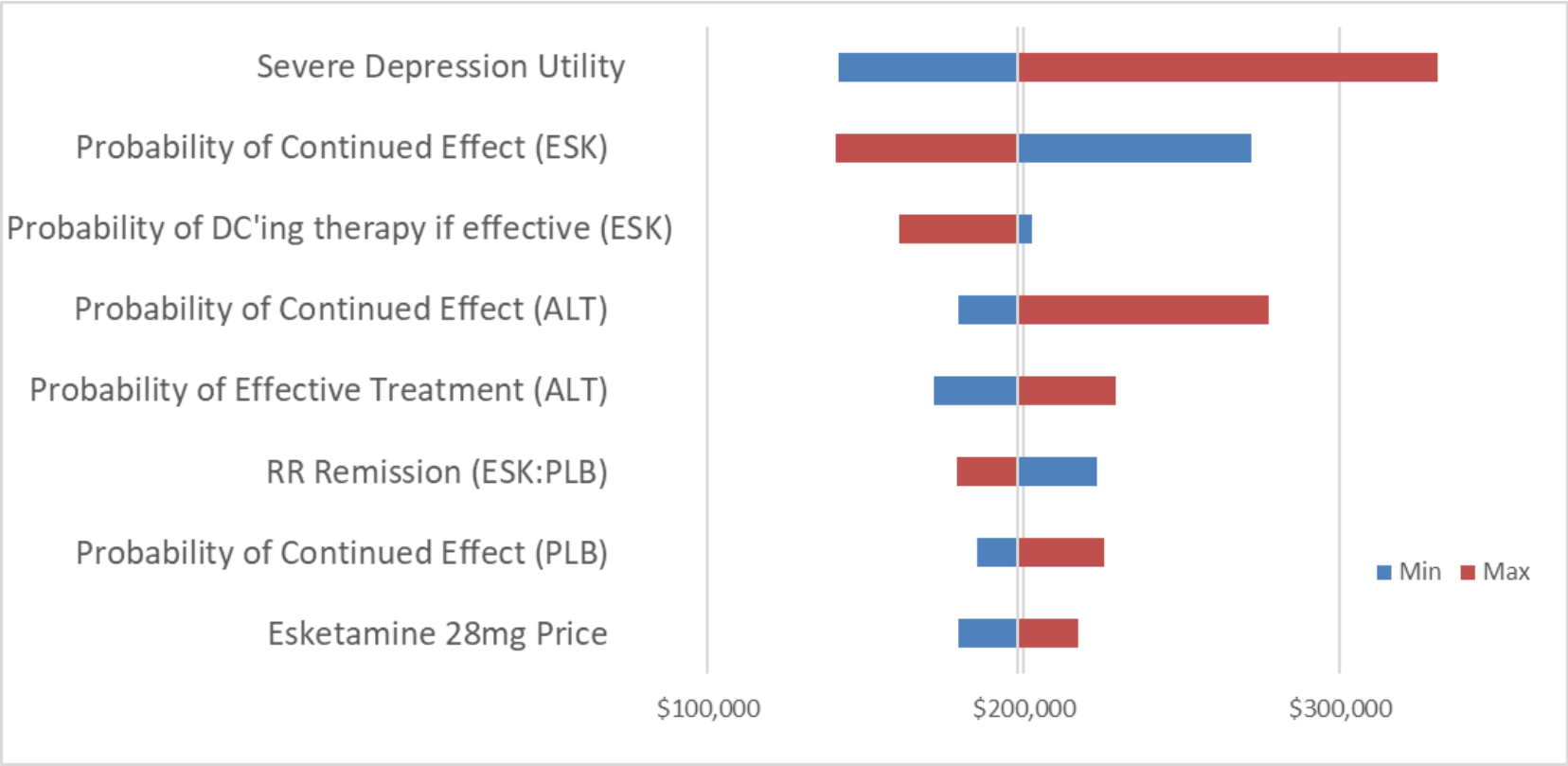
Base-Case Discounted Total Costs of Care and Outcomes

Treatment Pathways	Total Cost	QALYs	LYs	Depression-Free Days
Esketamine plus Background Antidepressant	$448,600	12.66	20.66	373
Background Antidepressant	$410,200	12.47	20.64	123
Difference	$38,400	0.19	0.01	250

Base-Case Incremental Cost-Effectiveness Ratios

Treatment Pathways	Cost Per QALY Gained	Cost Per LY Gained	Cost Per Depression-Free Day
Esketamine plus Background Antidepressant vs. Background Antidepressant	$198,000	$2,592,000	$150

One-Way Sensitivity Analysis (Key Variables)



Probabilistic Sensitivity Analysis

	Cost-Effective at $50,000 Per QALY	Cost-Effective at $100,000 Per QALY	Cost-Effective at $150,000 Per QALY
Esketamine plus Background Antidepressant	0%	1%	15%

Scenario Analysis

- When labor benefits for the proportion of patients who worked were included:
  - $188,000 per QALY gained

Limitations

- Lack of comparative effectiveness data of esketamine to other commonly used TRD treatments
- Number of lifetime treatment failures, severity of depression, and patient course of TRD are likely important factors that are not well-captured in the evidence base
- Caregiver burden, underemployment/ reemployment are important societal costs not captured in evidence base

Public Comments Summary

- Alternative inputs suggested for use in the model
  - TRANSFORM-2 (variable dose study) data alone should be used to inform the treatment effect
  - Discontinuation for long-term effectiveness
  - Mortality risk was underestimated
  - Cost inputs
- Health-related quality of life and utilities do not fully capture patient experience

Cost Analysis Methods in Brief

Drug Regimens

Drug	Dosage	Schedule	Route
Esketamine	56 mg (33% of patients) 84 mg (67% of patients)	Induction (weeks 1-4): Twice weekly Maintenance (weeks 5-8): Once weekly Maintenance (after week 8): Once weekly to every other week	Intranasal, administered in the physician's office
Ketamine	0.5 – 1.0 mg/kg	Twice weekly for two weeks, reduced to every other week or once monthly thereafter	Intravenous, administered in a ketamine clinic

Cost-Analysis Methods Overview

- **Model:** Deterministic model
- **Setting:** United States
- **Perspective:** Health care sector (direct medical care and drug costs)
- **Time Horizon:** Two-years
- **Discount Rate:** None
- **Primary Outcome:** Cost of care

Cost Analysis Methods Overview

- Method of administration compared
  - Esketamine, administered in the physician's office
  - Ketamine, administered in a ketamine clinic
- Costs included
  - Drug acquisition
  - Physician office visit, including administration and observation
- Scenario analysis was conducted from modified societal perspective which includes
  - Employment related costs (i.e. missed days of work)

Cost Analysis Results

	First Year Costs	Annual Costs After First Year	First Year Costs (Including Lost Labor)	Annual Costs After First Year (Including Lost Labor)
Esketamine	$36,500	$30,800	$39,400	$33,300
Ketamine	$3,600	$2,500	$5,300	$3,700

Conclusions

Conclusions

- Long-term cost-effectiveness of esketamine plus antidepressant compare with an antidepressant alone
  - Esketamine provides gains in quality-adjusted survival, primarily in the first five years of treatment
  - Esketamine appears to be priced higher than the modeled benefits support
  - Many patients discontinued treatment with esketamine in longer-term studies; long-term effectiveness of esketamine has not been demonstrated
- Short term costs of esketamine compared with ketamine:
  - There is no evidence directly comparing esketamine to ketamine
  - There is limited evidence for the effectiveness of ketamine for treating patients with TRD
  - Annual costs for ketamine appear to be substantially lower than for esketamine

Questions?

Public Comment and Discussion

Nathaniel Z. Counts, JD
Associate Vice President of Policy
Mental Health America (MHA)

Conflicts of Interest:

- Mental Health America receives more than 25% of its funding from health care companies.

Kevin Einbinder, MA
Vice President of Communications and Programs
Depression and Bipolar Support Alliance (DBSA)

No conflicts of interest to disclose.

Andrew Sperling
Director of Policy Advocacy
National Alliance on Mental Illness (NAMI)

Conflicts of Interest:

- NAMI receives financial assistance from pharmaceutical companies to support specific education programs for people living with mental illness and their families.
- This includes support from Janssen for its "Home Front" program - support groups for military families and "Crisis Intervention Training" for local law enforcement personnel.
- Overall, pharmaceutical company funding constitutes 6.6% of NAMI National's budget.

Voting Questions

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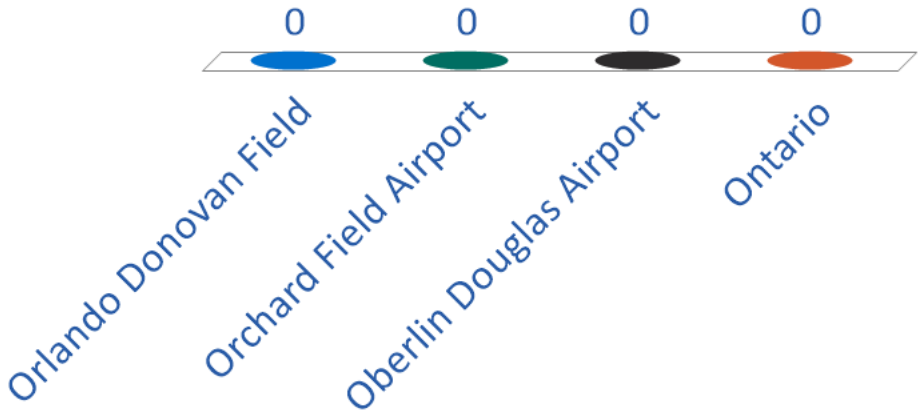
0. What was the original name of Chicago O'Hare airport, which gave it its abbreviation, ORD?

A. Orlando Donovan Airport

B. Orchard Field Airport

C. Oberlin Douglas Airport

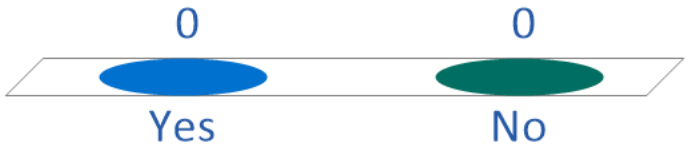
D. Ontario Development Airport



1. Is the evidence adequate to demonstrate that the net health benefit of esketamine plus background antidepressant is superior to that provided by background antidepressant alone?

A. Yes

B. No



2. Is the evidence adequate to distinguish the net health benefit between esketamine plus background antidepressant and ketamine plus background antidepressant?

A. Yes

B. No

(If yes to question 1)

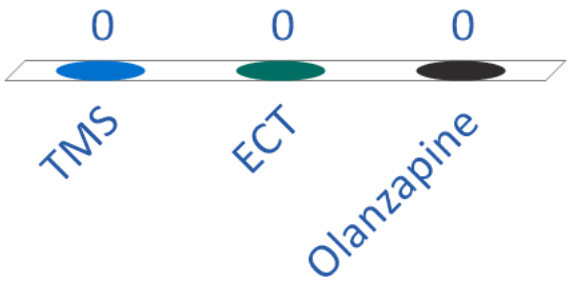
3. Is the evidence adequate to demonstrate that the net health benefit of esketamine plus background antidepressant is superior to that provided by any of the following treatments: TMS, ECT, or olanzapine?

A. Yes
B. No

(If yes to question 3)

4. For which of the following comparator(s) is the evidence adequate to demonstrate a superior net health benefit to that provided by esketamine plus background antidepressant?

A. TMS
B. ECT
C. Olanzapine



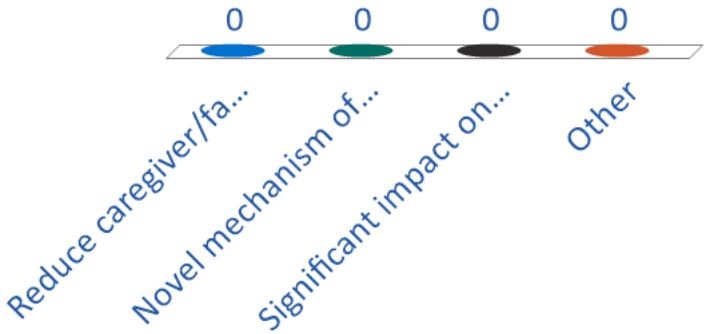
5. Does treating patients with esketamine plus background antidepressant offer one or more of the following potential "other benefits or disadvantages" compared to other approved treatments for TRD?

A. Reduce caregiver/family burden

B. Novel mechanism of action or approach

C. Significant impact on improving return to work/overall productivity

D. Other



6. Are any of the following contextual considerations important in assessing the long-term value for money of esketamine plus background antidepressant?

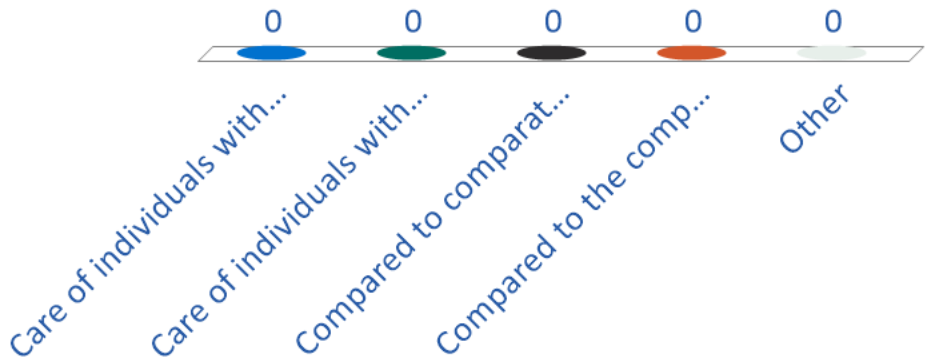
A. Care of individuals with condition of high severity

B. Care of individuals with condition with high lifetime burden of illness

C. Compared to comparator, there is significant uncertainty about long-term risk of serious side effects

D. Compared to the comparator, significant uncertainty about magnitude or durability of the long term benefits of this intervention

E. Other



Break

Meeting will resume at 3:45 pm

Policy Roundtable

Policy Roundtable Participants

Participant	Affiliation	Conflict of Interest
Cristina Cusin, MD	Assistant Professor in Psychiatry, Massachusetts General Hospital	Dr. Cusin served as site PI for an esketamine trial sponsored by Janssen.
Phyllis Foxworth	Vice President of Advocacy, Depression and Bipolar Support Alliance	No conflicts of interest to disclose
Jeremy Fredell, PharmD, BCPS	Director Trend Solutions – Drug Trend & Formulary, Express Scripts	Dr. Fredell is a full-time employee of Express Scripts
Young Fried, PharmD, MSP	Vice President, Pharmacy Plan Services, HealthPartners	Dr. Fried is a full-time employee of HealthPartners.
William S. Gilmer, MD	Clinical Professor of Psychiatry and Behavioral Sciences, Northwestern University Feinberg School of Medicine	Dr. Gilmer has received consulting and speaker fee honorarium from Sunovion and Otsuka; and owns equity in Organovo, Jounce, and Gilead.
Pamela Goloskie	Patient Advocate	No conflicts of interest to disclose

Midwest CEPAC Panel Reflections

Next Steps

- Meeting recording posted to ICER website next week
- Final Report published on or around June 20th
  - Includes description of Midwest CEPAC votes, deliberation, policy roundtable discussion
- Materials available at:

  https://icer-review.org/topic/depression/

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Adjourn