Vesicular Monoamine Transporter 2 Inhibitors for Tardive Dyskinesia: Effectiveness and Value

Public Meeting – December 5, 2017

ICER
INSTITUTE FOR CLINICAL AND ECONOMIC REVIEW

Wireless Network: Marriott Conference Center Network
PW: ICER2017 (not case sensitive)

Welcome and Introduction

Why are we here today?

- Tardive dyskinesia can profoundly affect patients and families, and new drugs offer the potential for important benefits

Involuntary muscle movements in the mouth and face region, facial grimacing, lip smacking and other symptoms associated with TD carry enormous social stigma. This in turn leads to further social isolation and exacerbation of the negative symptoms associated with psychotic disorders such as schizophrenia. Likewise, in the case of mood disorders such as bipolar disorder the social isolation resulting from TD can further exacerbate symptoms of depression and lack of self-worth.

- ***National Alliance on Mental Illness***

There is no known cure for TD. That is precisely why treatments that improve the quality of life for patients who suffer from this complex disease are significant.

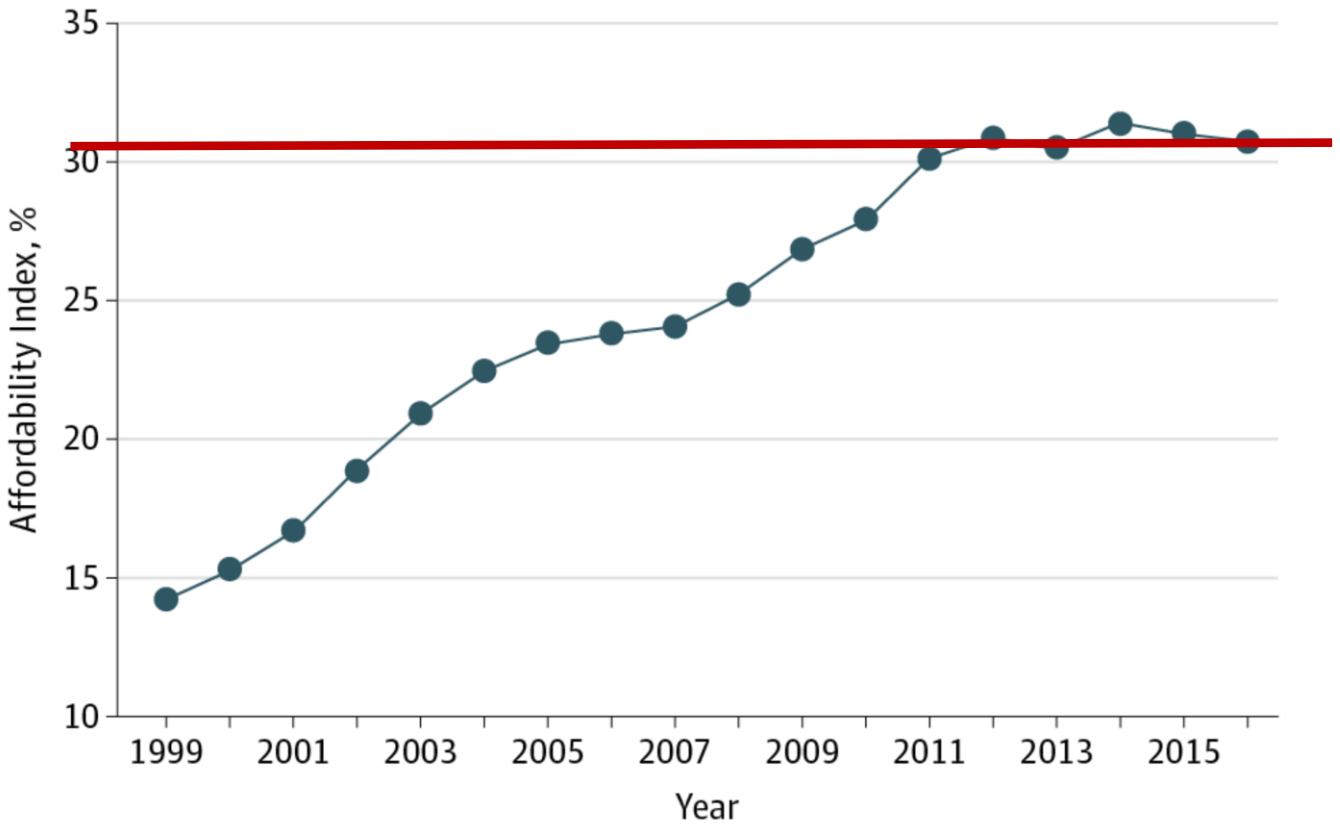
- ***Movement Disorder Policy Coalition***

Welcome and Introduction

Why are we here today?

- New treatment options often raise questions about appropriate use, cost
- Increasing health care costs affecting individuals', state and federal budgets

An Affordability Index



Emanuel EJ, Glickman A, Johnson D. Measuring the Burden of Health Care Costs on US Families: The Affordability Index. JAMA. Published online November 02, 2017. doi:10.1001/jama.2017.15686

Welcome and Introduction

Why are we here today?

- New treatment options often raise questions about appropriate use, cost
- Increasing health care costs affecting individuals', state and federal budgets
- Patients can have difficulty accessing drugs
  - Tight prior authorization criteria
  - Step therapy protocols
  - Requirements to switch drugs with new insurance
  - High out-of-pocket costs
- Potential benefit of objective evaluation and public discussion of the evidence on effectiveness and value of emerging treatment options

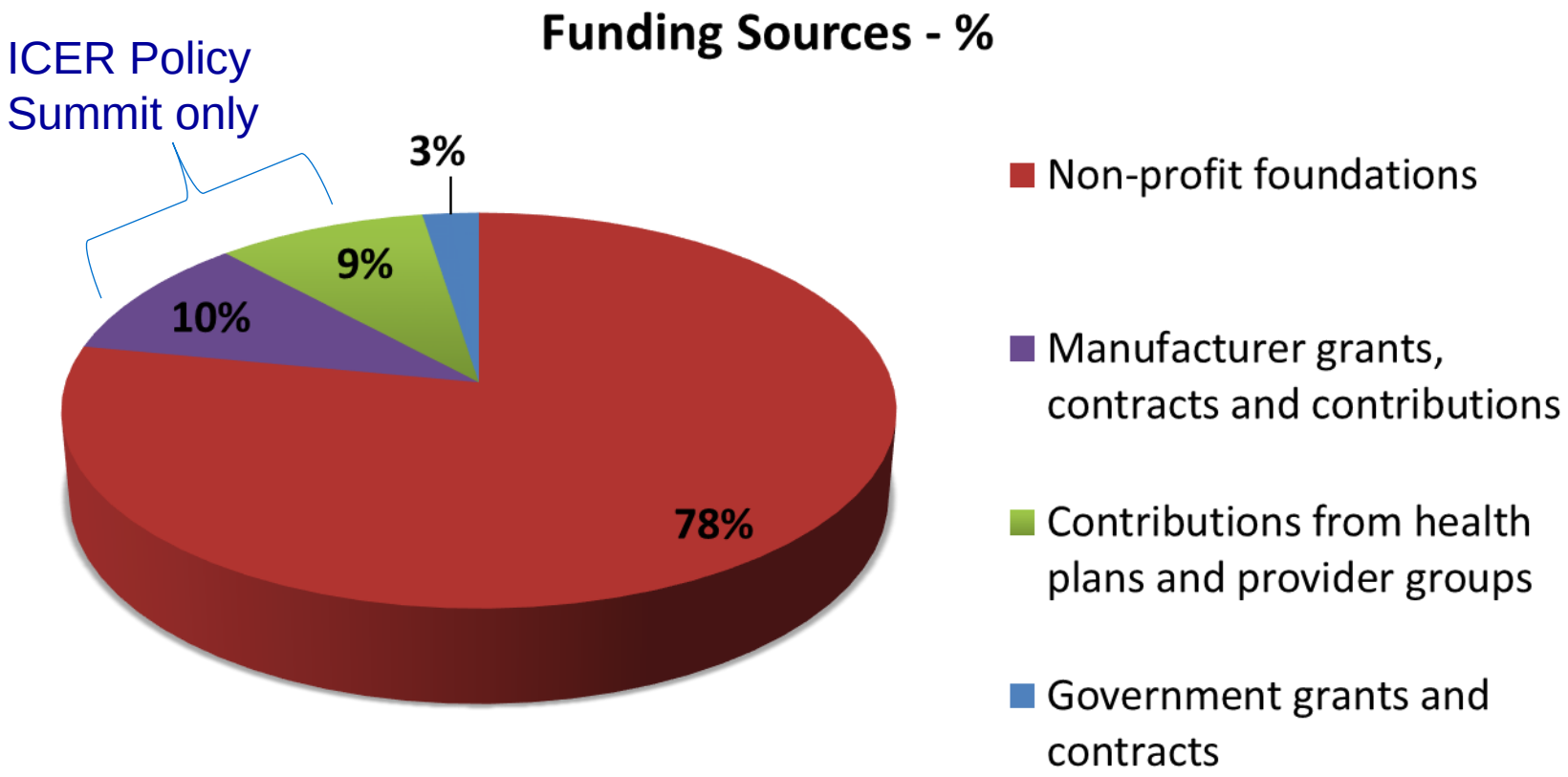
Welcome and Introduction

- New England Comparative Effectiveness Public Advisory Council (CEPAC)

- The Institute for Clinical and Economic Review (ICER)

Sources of Funding, 2017

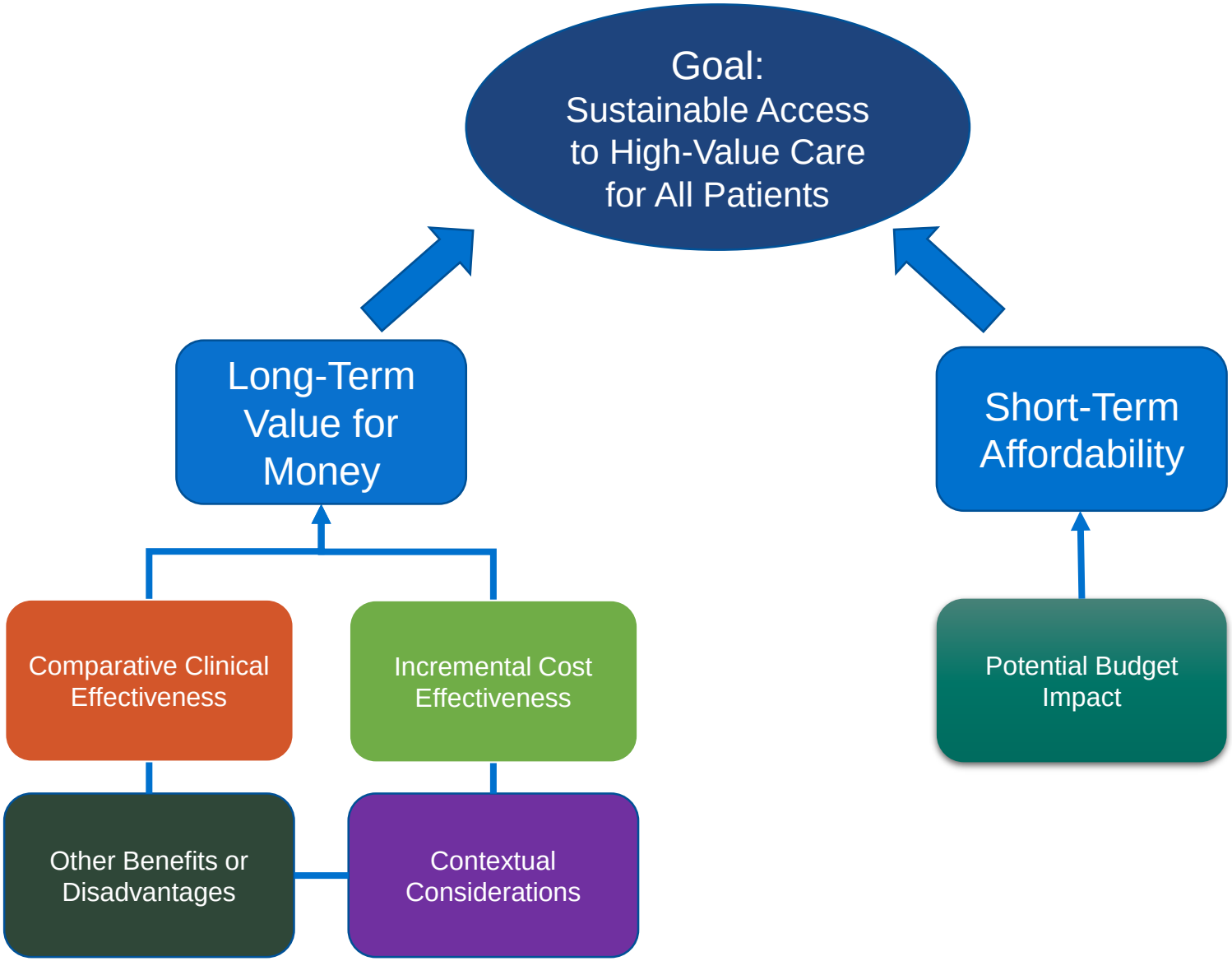
ICER Policy Summit only



Welcome and Introduction

How was the ICER report on treatments for Tardive Dyskinesia developed?

- Scoping with guidance from patients, patient groups, clinical experts, and manufacturers
- ICER evidence analysis and cost-effectiveness modeling
- Survey of patients with TD on the impact on quality of life
- Public comment and revision
- Clinical and patient expert report reviewers
  - **Robert Rosenheck, MD**, Yale Medical School
  - **Daniel Tarsy, MD,** Beth Israel Deaconess Medical Center
  - **Cindy Specht,** Depression and Bipolar Support Alliance (DBSA)
- How is the evidence report structured to support CEPAC voting and policy discussion?


Goal:
Sustainable Access to High-Value Care for All Patients
Long-Term Value for Money
Short-Term Affordability
Comparative Clinical Effectiveness
Incremental Cost Effectiveness
Potential Budget Impact
Other Benefits or Disadvantages
Contextual Considerations

Agenda

10:00am: Welcome and Opening Remarks

10:15 am: Patient Experience Survey

Allen Doederlein, Depression and Bipolar Support Alliance

10:25 am: Presentation of the Evidence

Evidence Review: Steven Atlas, MD ,MPH

Cost Effectiveness: Surrey Walton PhD; Dan Touchette PharmD, MA

11:25 pm: Manufacturer Comments and Discussion

11:45 pm: Public Comments and Discussion

12:15 pm: Lunch

1:00 pm: New England CEPAC Deliberation and Votes

2:00 pm: Policy Roundtable

3:30 pm: Reflections and Wrap Up

4:00 pm: Meeting Adjourned

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Depression and Bipolar Support Alliance

Experiences with Tardive Dyskinesia

Results from DBSA Survey

ALLEN DOEDERLEIN
DEPRESSION AND BIPOLAR SUPPORT ALLIANCE
TUESDAY, DECEMBER 5, 2017

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Disclosures

DBSA receives grants and sponsorships from

ALKERMES
ALLERGAN
JANSSEN PHARMACEUTICALS, INC.,
LUNDBECK
NEUROCRINE
OTSUKA
SUNOVION
TAKEDA
TEVA

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Making Tardive Dyskinesia Real

Today we will cover

- About DBSA
- DBSA Survey Center *Experiences with Tardive Dyskinesia* Survey
- What's it Like? Words from People Who've Experienced Tardive Dyskinesia

DBSA
Depression and Bipolar Support Alliance

About DBSA

The Depression and Bipolar Support Alliance, DBSA, is the leading **peer-directed national** organization focusing on the two most prevalent mental health conditions, **depression and bipolar disorder**.

DBSA envisions wellness for people living with depression and bipolar disorder. Our mission is to provided hope, help, support, and education to improve the lives of people living with mood disorders.

DBSA reaches millions of people each year with

- in-person and online **peer support**
- current, readily understandable **information** about mood disorders
- empowering **tools** focused on an integrated approach to wellness

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Experiences with Tardive Dyskinesia

Background

- DBSA Survey Center on DBSAlliance.org
- Conducted August 14-September 4, 2017
- Prospective participants from
  - DBSA newsletters
  - Individual constituent and local chapter outreach
  - Social media
  - Colleague organizations
- 211 responded

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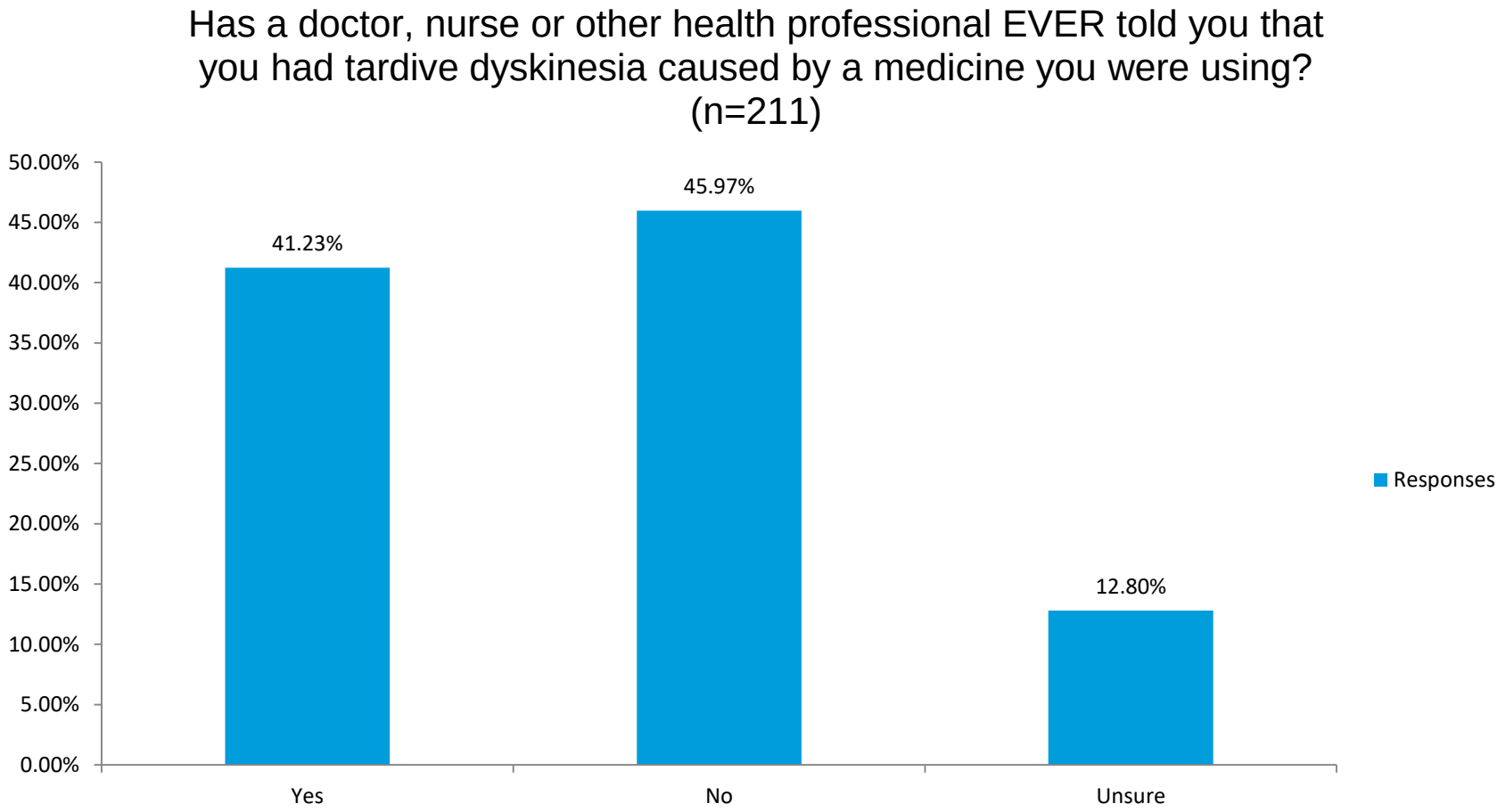
Experiences with Tardive Dyskinesia

Diagnosis



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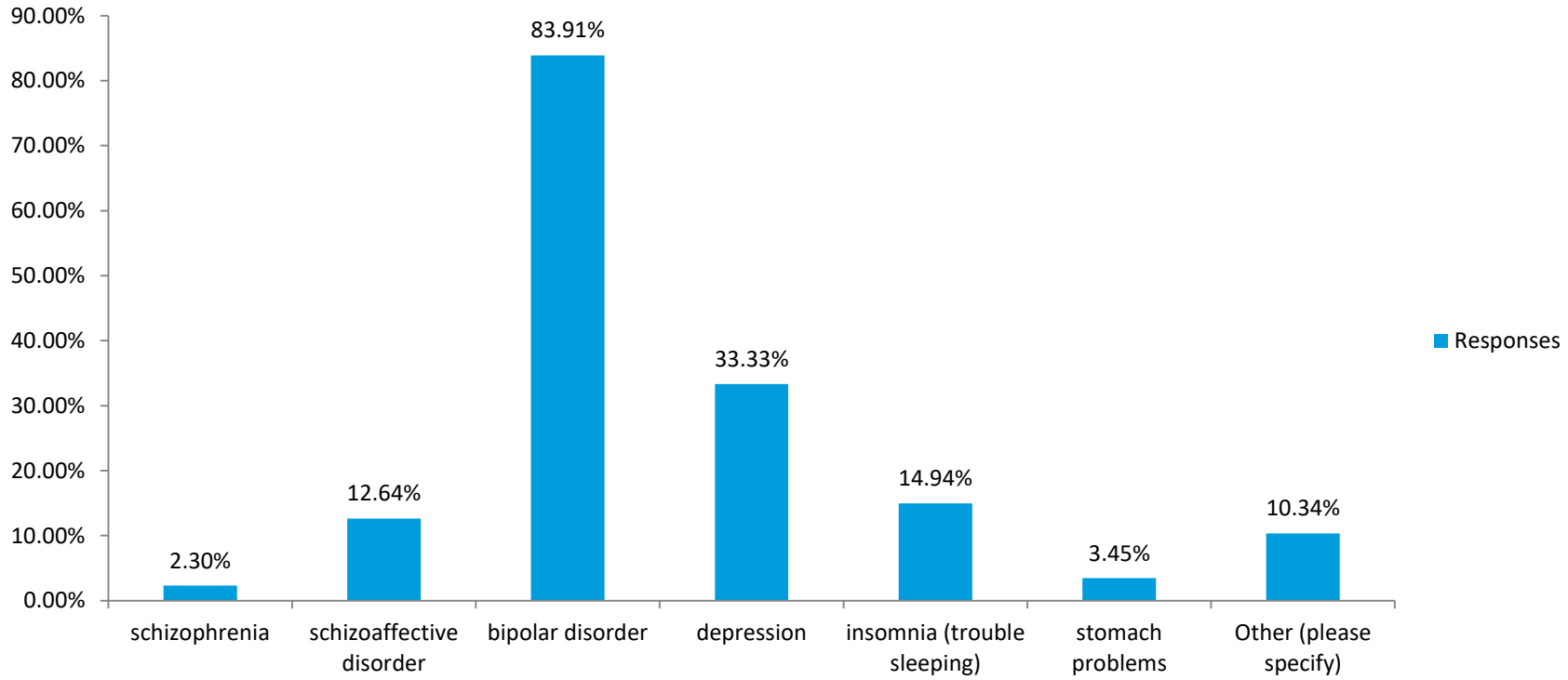
Experiences with Tardive Dyskinesia

Diagnosis

What health conditions do you/did you have that required you to take a medicine that caused tardive dyskinesia? Please check all that apply. (n=87)



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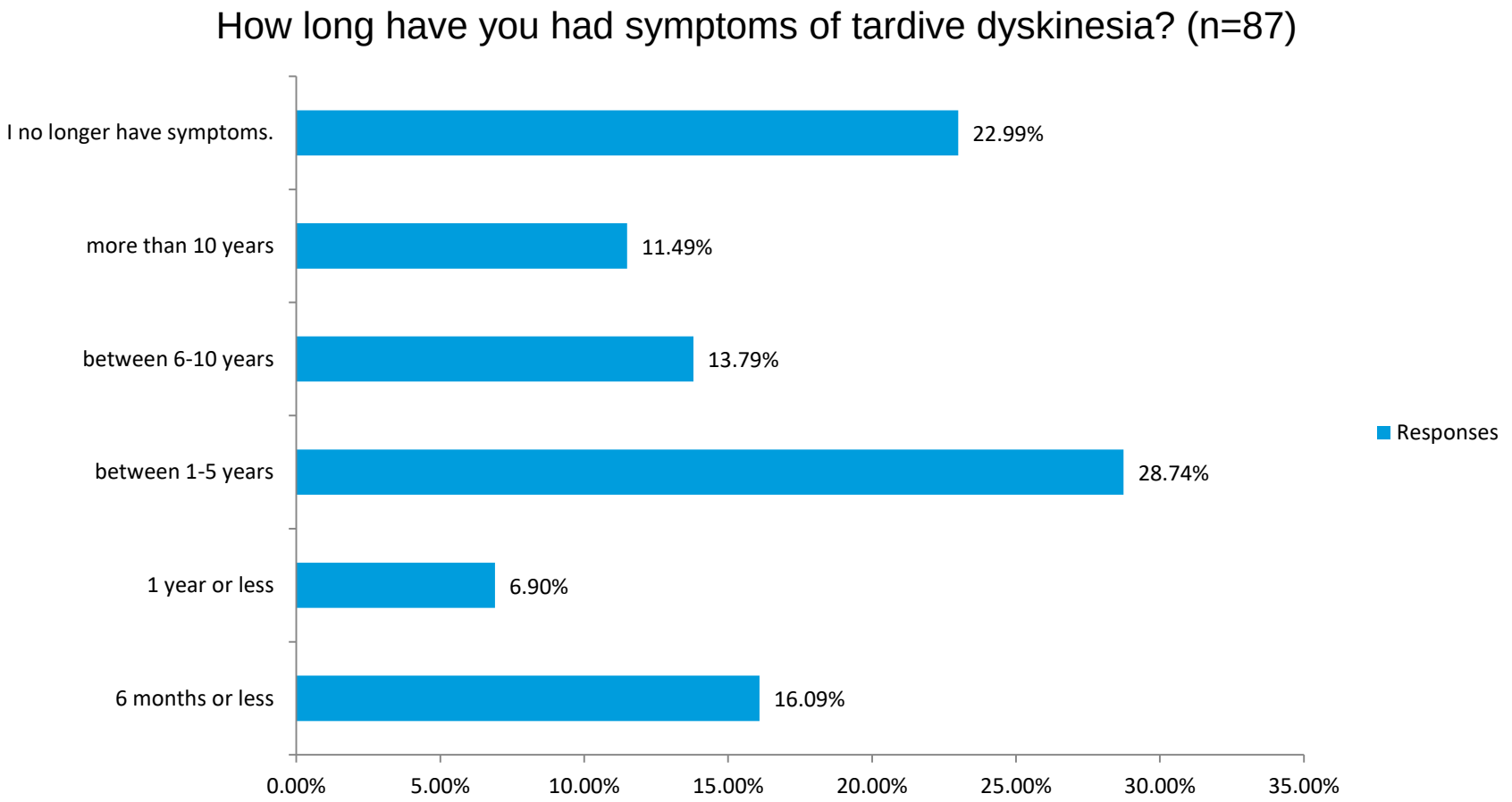
Experiences with Tardive Dyskinesia

Diagnosis



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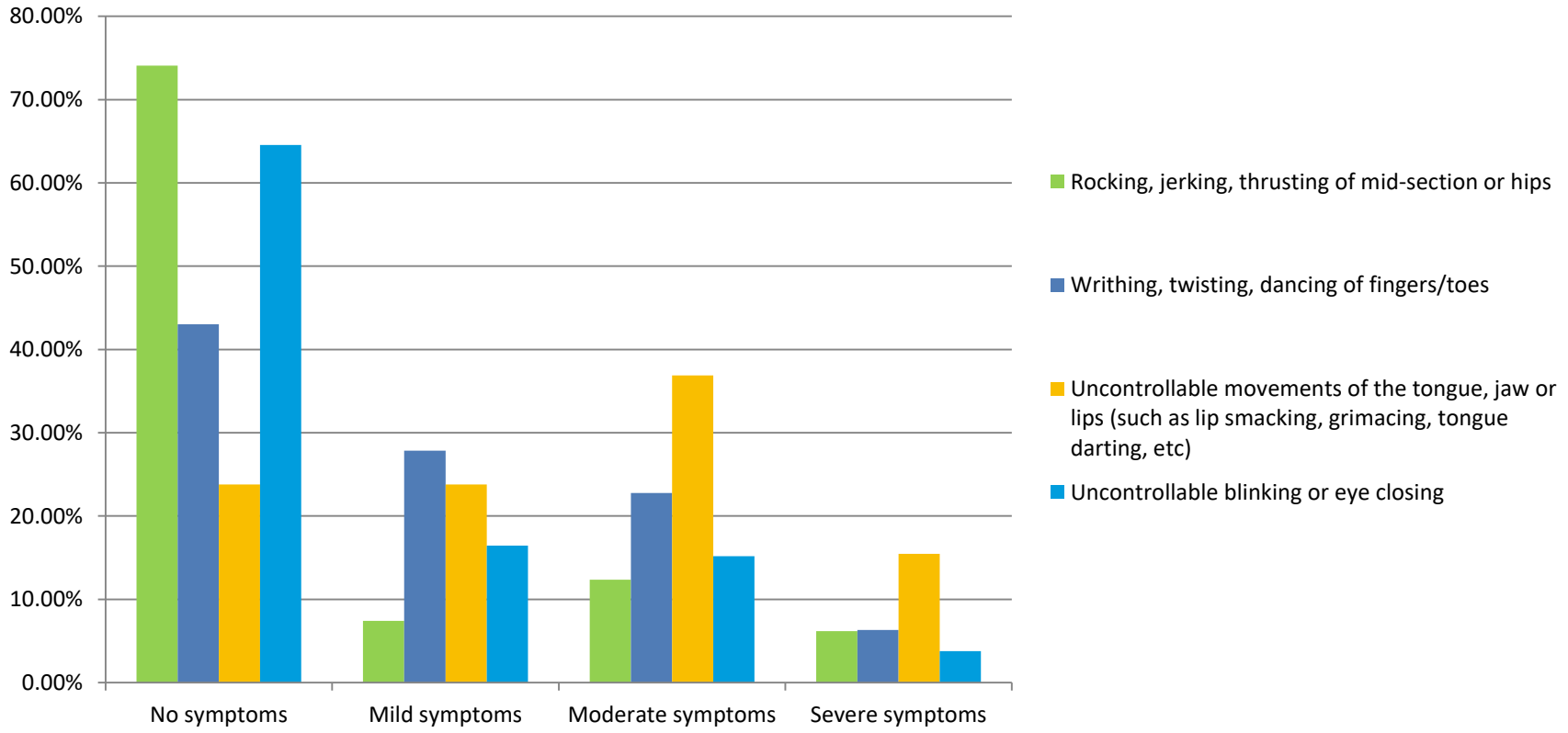
Experiences with Tardive Dyskinesia

Impact

For each of the following tardive dyskinesia symptoms, select the option that best fits your experience (n=86)



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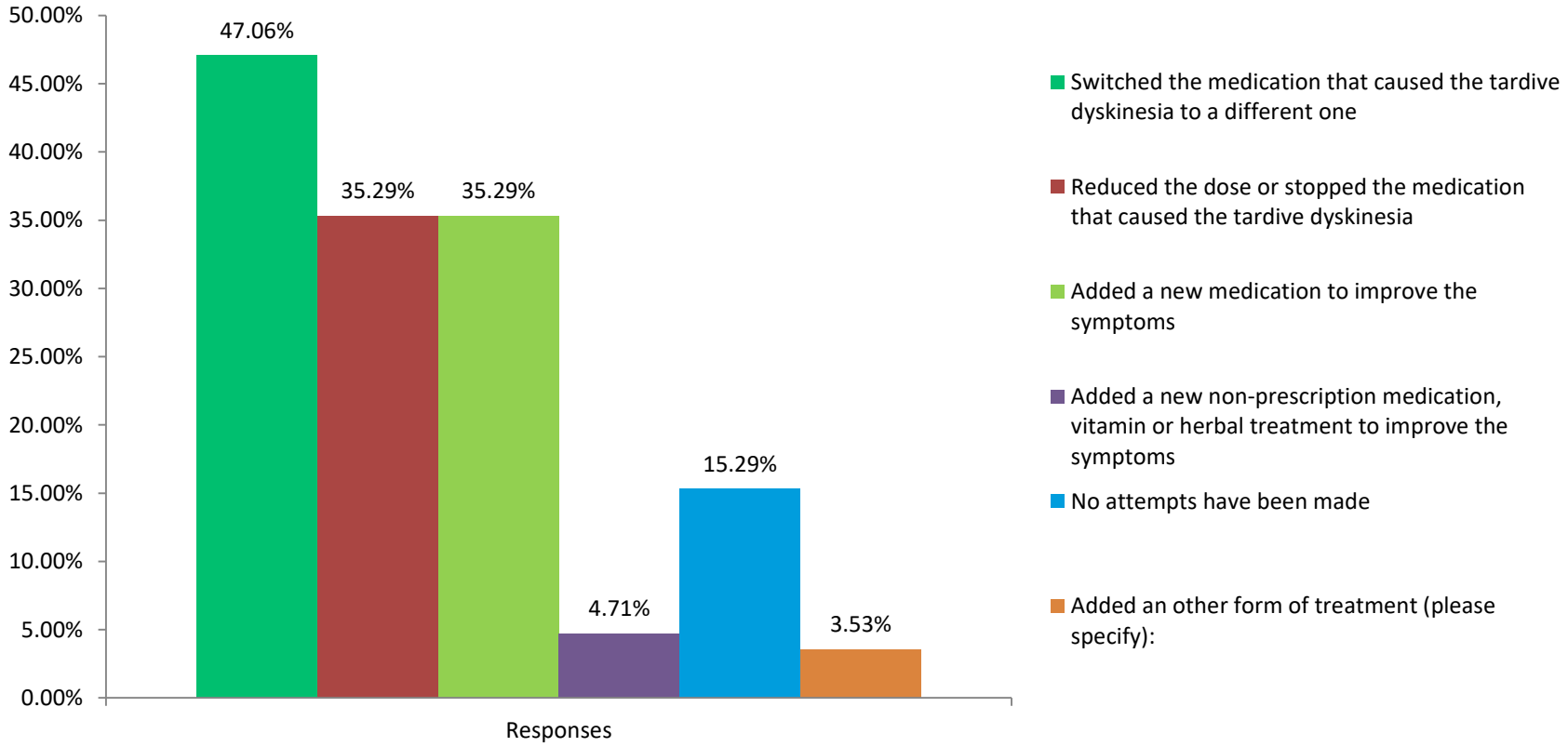
Experiences with Tardive Dyskinesia

Treatment

How has your doctor attempted to address your tardive dyskinesia? Please check all that apply. (n=85)



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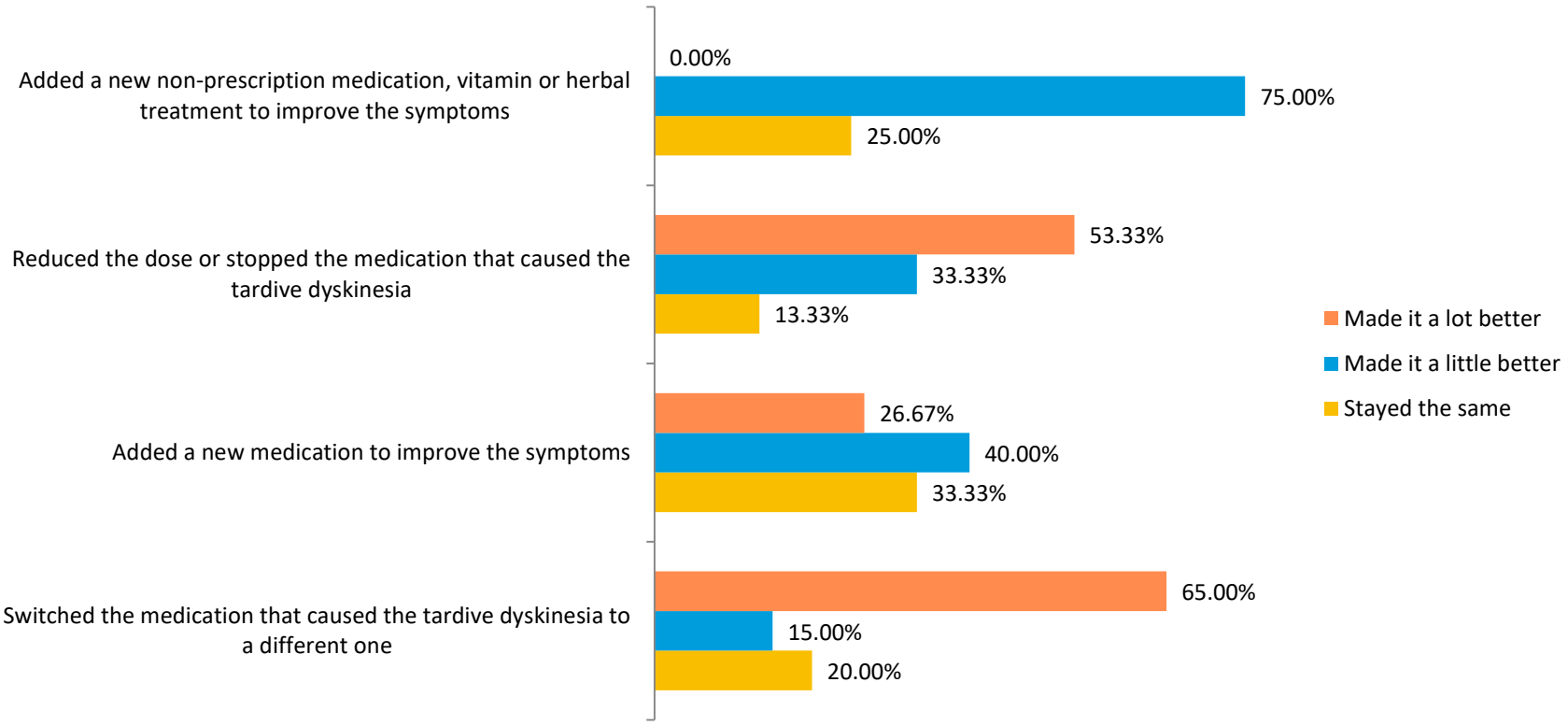
Experiences with Tardive Dyskinesia

Treatment

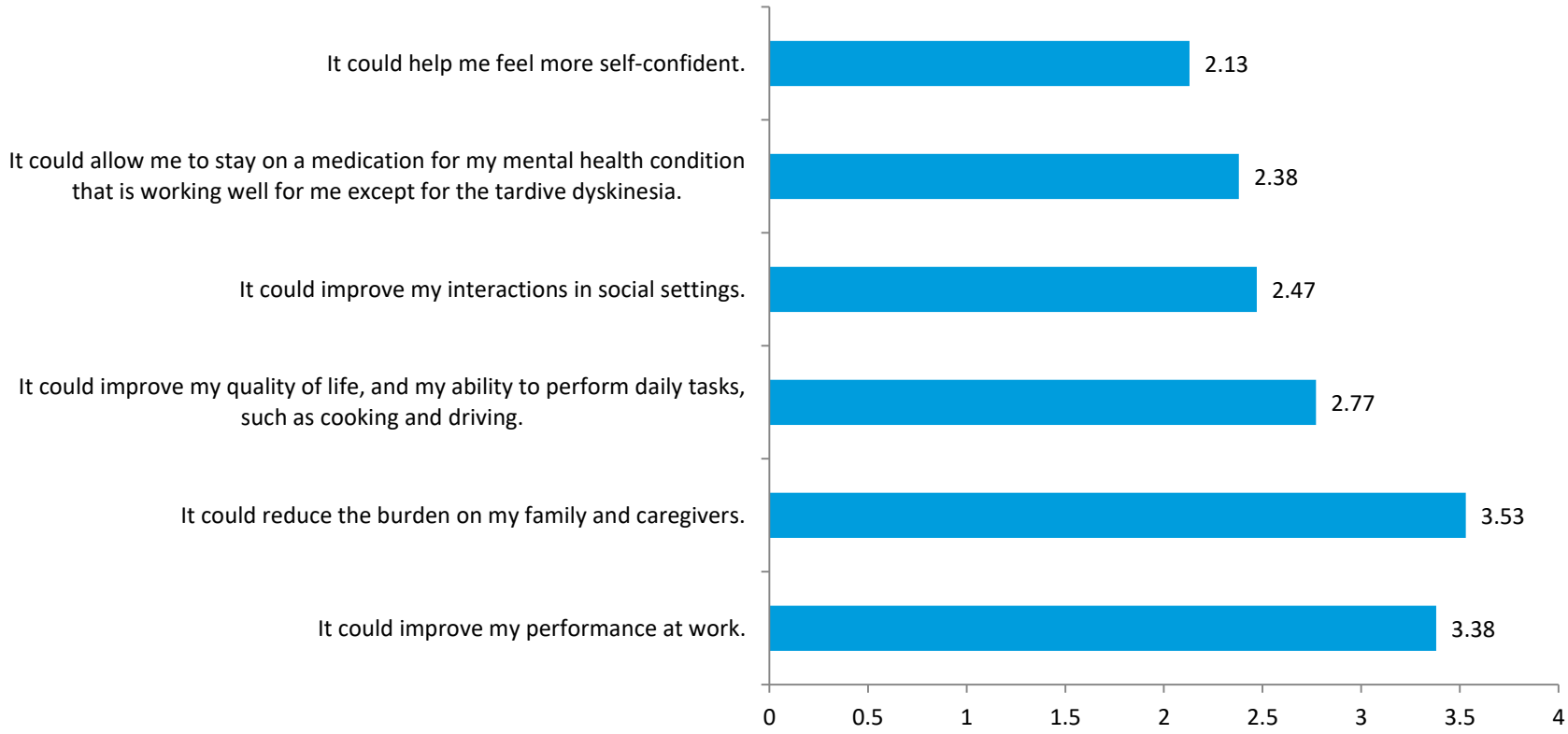
How has your doctor's treatment of your tardive dyskinesia impacted your symptoms? (n=72)



Experiences with Tardive Dyskinesia

Treatment

Please rate from most important (1) to least important (5) the following reasons for treating your tardive dyskinesia? (n=80)



Experiences with Tardive Dyskinesia

Summary and Discussion

- Impact on social and leisure time, family time, and work is significant
- Over 15% of people had not yet tried anything to improve TD symptoms
- For many, treatments that have been tried have been successful in improving the symptoms
- DBSA hopes to utilize survey results to increase awareness of TD and show the negative impact this condition can have

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What's it Like?

Open-ended Survey Responses

- "It has ruined my life due to police ignorance."
- "One of very few medications that helped, but had to stop taking for fear of symptoms becoming permanent."
- "At the time it was completely disabling. Removing the medication that caused it was a must. But now greatly limited by what medications can assist the bipolar. Very frustrating and concerning."
- "I experienced the onset of symptoms in the 1970s…I remember the pharmacists always asking me, 'Are you sure your doc wants you to take these meds at the same time?' By the time I heard about TD, mine was permanent. I am fortunate to have mild symptoms that only affect my self-confidence, outward appearance, my face."

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What's it Like?

Open-ended Survey Responses

- "Very emotionally damaging…It still affects my anxiety when trying to leave the house to this day."
- "I actually stopped eating in front of people because I spit and drooled. It was AWFUL!"
- "My tardive dyskinesia is humiliating, degrading, and I feel like I can't show myself in public because of it. It jeopardizes my mental health treatment, burdens the ones I love the most, and I feel keeps me from finding a romantic partner."

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What's it Like?

Jeff's Story: Living with TD

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What's it Like?

Kim's Story: Living with TD

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Experiences with Tardive Dyskinesia

Thank you

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TUESDAY, DECEMBER 5, 2017

Evidence Review

Steven Atlas, MD, MPH

Director, Primary Care Research and Quality Improvement Network, Massachusetts General Hospital

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Key Review Team Members

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Disclosures:

We have no conflicts of interest relevant to this report.

Topic in Context

- Tardive dyskinesia (TD) is a repetitive, involuntary movement disorder with a delayed onset caused by prolonged use of dopamine receptor blocking agents (DRBAs), most commonly antipsychotic drugs
- 20-50% of individuals taking antipsychotic drugs develop TD, with slightly lower rates for second generation drugs
- Estimated population in the US: 500,000
- No FDA-approved therapies for TD before recent approval of two vesicular monoamine transporter 2 (VMAT2) inhibitors

VMAT2 Inhibitors:

VMAT2 Inhibitors	Brand name	Recommended Dose	FDA Approval
Valbenazine	Ingrezza	80 mg daily dose	April 2017 (TD)
Deutetrabenazine	Austedo	12mg – 48mg/day in two divided dose	April 2017 (HD) August 2017 (TD)
Tetrabenazine*	Xenazine	12.5mg – 100mg/day in two to three divided doses	May 2008 (HD)

*Not approved for TD, but used off label

TD from a Patient Perspective

- Symptoms can vary in terms of severity
- Because it often involves the face, TD can be socially stigmatizing
- Can make it difficult to find and keep a job
- When severe, TD can be disabling and require help from family and other caregivers
- Despite this impact on quality of life, there are no validated patient reported outcome measures

Scope of Review

- To compare clinical effectiveness of VMAT2 inhibitors for treatment of TD due to DRBAs
- Included evidence from all relevant clinical studies, irrespective of use of a comparative study design:
  - Adults 18 or older with symptoms for at least 3 months and history of use of DRBAs
  - Excluded studies that did not meet a minimum sample size of 10 patients
- For safety outcomes included randomized trials of VMAT2 inhibitors for conditions other than TD

Body of Evidence

- 25 TOTAL references on TD in publications and conference abstracts

Valbenazine (3 publications, 5 abstracts)

- 2 RCTs
- 3 open-label extensions (Duration: one 6 weeks & two 48 weeks)

Deutetrabenazine (2 publications, 7 abstracts)

- 2 RCTS
- 1 open-label extension (Duration: 54 weeks)

Tetrabenazine (8 publications)

- 8 nonrandomized studies

Overview of Randomized Trials

	Valbenazine		Deutetrabenazine	
	KINECT 3	KINECT 2	AIM-TD	ARM-TD
Study Type	Phase III RCT	Phase II RCT	Phase III RCT	Phase II/ III RCT
Total # of Patients	234	102	293	117
Mean Age (Years)	56.1	56.2	56.4	54.6
Comorbid Psychiatric Condition (%)				
Schizophrenia/ Schizoaffective	66.1	58	60	68.4
Bipolar Disorder/ Depression	33.9	38	36	48.7
Gastrointestinal Disorder	--	4	--	--

Key clinical outcomes

- **Primary Outcome:**
  - Abnormal Involuntary Movement Scale (AIMS)
    - 7 items measured on a five-point (0-4) scale of severity
    - Total score ranges from 0-28, with higher scores reflecting increased severity
- **Secondary Outcomes**:
  - Clinical Global Impression of Change (CGIC)
  - Patients' Global Impression of Change (PGIC)
  - Single item with score ranging from 1 ("very much improved") to 7 ("very much worse").
  - Reports of "1" or "2" classified as "responders"

Comparability of VMAT2 Trials

- ICER did not attempt to conduct a formal comparison of these VMAT2 inhibitors to each other

	Valbenazine	Deutetrabenazine
Eligibility Criteria	• Moderate - severe TD based on qualitative assessment • Severity based on review of screening videos by multiple external raters	• Moderate - severe TD based on AIMS score ≥6 • Severity criterion required at both screening and baseline assessment • AIMS score assessed by investigator and confirmed by an independent expert via central video rating
Duration of Trials	6 weeks	12 weeks

Results

Valbenazine – Primary AIMS Outcomes

Trials	Baseline AIMS Score (Mean)	AIMS Reduction from Baseline (LS Mean)	≥50% AIMS Improvement (%)
Kinect 3			
Valbenazine 80mg/D	10.4	**-3.2†**	**40.0***
Valbenazine 40mg/D	9.7	**-1.9†**	**23.8***
Placebo	9.9	**-0.1**	**8.7**
Kinect 2			
Valbenazine (Max 75mg/D)	8.0	**-2.6†**	**48.9***
Placebo	7.0	**-0.2**	**18.2**

†statistically significant change; *statistically significant compared to placebo

Valbenazine – Secondary Outcomes

Trials/ Arms	CGIC Responders (%)	PGIC Responders (%)
Kinect 3		
Valbenazine 80mg/D	31.4	**24.3***
Valbenazine 40mg/D	31.7	31.7
Placebo	20.3	42.0
Kinect 2		
Valbenazine (Max 75mg/D)	**66.7***	**57.8***
Placebo	15.9	31.8

* statistically significant compared to placebo

Valbenazine - Harms

- Most common side effects: drowsiness, fatigue, headache, decreased appetite, akathisia, nausea, vomiting, and dry mouth
- No evidence of increased rates of depression and suicidal ideation compared to placebo at six weeks

Deutetrabenazine – Primary AIMS Outcomes

Trials	Baseline AIMS Score (Mean)	AIMS Reduction from Baseline (LS Mean)	≥50% AIMS Improvement (%)
AIM-TD			
DTBZ 36mg/D	10.1	**-3.3†**	**33***
DTBZ 24mg/D	9.4	**-3.2†**	**35***
Placebo	9.5	-1.4	12
ARM-TD			
DTBZ	9.6	**-3.0†**	--
Placebo	9.6	-1.6	--

†statistically significant change; *statistically significant compared to placebo

Deutetrabenazine: Secondary Outcomes

Trials	CGIC Responders (%)	PGIC Responders (%)
AIM-TD		
DTBZ 36mg/Day	44	40
DTBZ 24mg/Day	**49***	45
Placebo	26	31
ARM-TD		
DTBZ	48.2	42.9
Placebo	40.4	29.8

*statistically significant compared to placebo

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Deutetrabenazine - Harms

- Similar side effects to valbenazine: drowsiness, headache, and fatigue
- Other common side effects: diarrhea, insomnia, anxiety, and nasopharyngitis
- No evidence of increased rates of depression and suicidal ideation compared to placebo at 12 weeks (despite boxed warning from earlier indication)

Tetrabenazine

- May reduce symptoms of TD
- Lack of randomized controlled trials
- Variety of non-standardized outcome measures
- Difficult to make qualitative or quantitative comparisons to other VMAT2 inhibitors
- Harms: drowsiness, fatigue, insomnia, fall, agitation, parkinsonism, akathisia, and anxiety
- Boxed warning for HD: increased depression and suicidality

Controversies and Uncertainties

- Trials of valbenazine and deutetrabenazine only compared to placebo
  - No direct comparisons to each other or non-FDA approved TD treatments
- No randomized controlled trials of tetrabenazine in TD patients
- Variation in patient- and clinician-reported outcomes of VMAT2 inhibitors in TD patients
- Lack of comparative efficacy and safety data to support long-term use of VMAT2 inhibitors

Summary

	AIMS	CGIC	PGIC
Valbenazine	Greater reduction in AIMS scores and more patients with ≥50% AIMS improvement compared to placebo	Conflicting study findings with no consistent benefit over placebo on the CGIC scale	Conflicting study findings with no consistent benefit over placebo on the PGIC scale
	AIMS	**CGIC**	**PGIC**
Deutetrabenazine	Greater reduction in AIMS scores and more patients with ≥50% AIMS improvement compared to placebo	Did not demonstrate a statistically significant benefit over placebo on the CGIC scale	Did not demonstrate a statistically significant benefit over placebo on the PGIC scale

Ratings

VMAT2 Inhibitors	ICER Evidence Rating
Valbenazine	Promising but Inconclusive (P/I)
Deutetrabenazine	Promising but Inconclusive (P/I)
Tetrabenazine	Insufficient (I)

Other Benefits/Considerations

- VMAT2 inhibitors are the first FDA-approved therapies for TD
  - Patients and clinicians optimistically view VMAT2 inhibitors as important advancement in a frequently irreversible condition
- VMAT2 inhibitors could potentially improve control of underlying psychiatric condition with better adherence to antipsychotics
- VMAT2 inhibitors could facilitate TD patients' ability to find a job and/or maintenance of job
- Their use may decrease caregiver or family burden

Comments Received

- Tetrabenazine should not be included in this review because it is not FDA approved for TD
- ICER should withhold judgment on these therapies until more data is available
- By effectively treating TD, VMAT2 inhibitors may help patients and their caregivers return to work and not need government health insurance
- TD can worsen social isolation and exacerbate the negative symptoms associated with schizophrenia and serious mood disorders

Cost Effectiveness

Surrey Walton, PhD,

University of Illinois at Chicago College of Pharmacy

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Key Review Team Members

Want to acknowledge important input and assistance from Varun Kumar and Rick Chapman from ICER and Kate Harrigan from UIC

Disclosures:

We have no conflicts of interest to disclose.

Objective

To model the health system costs and patient outcomes associated with treating symptoms of tardive dyskinesia (TD) using valbenazine and deutetrabenazine compared with placebo in a representative population of U.S. adults aged 18 and older with the underlying conditions of schizophrenia, schizoaffective disorders, and affective disorders.

Methods in Brief

Methods Overview

- Model: Semi-Markov model with time-dependent mortality rates
- Setting: United States
- Perspective: Payer (direct medical care and drug costs)
- Time Horizon: Lifetime
- Discount Rate: 3% per year (costs and outcomes)
- Cycle Length: 1 year
- Outcomes by Intervention: Costs, Quality-Adjusted Life Year (QALY)
- Primary Outcome: Cost per QALY Gained

Details on the Patient Population

- Adult U.S. population
- Age: 18-64
- Underlying conditions:
  - Schizophrenia or schizoaffective disorder
  - Affective disorder
- Patients with schizophrenia/schizoaffective disorder
  - Mean age of 38 years
  - 52.5% female
  - Represents 70.2% of modeled population
- Patients with affective disorder
  - Mean age of 40 years
  - 64.8% female
  - Represents 29.8% of modeled population

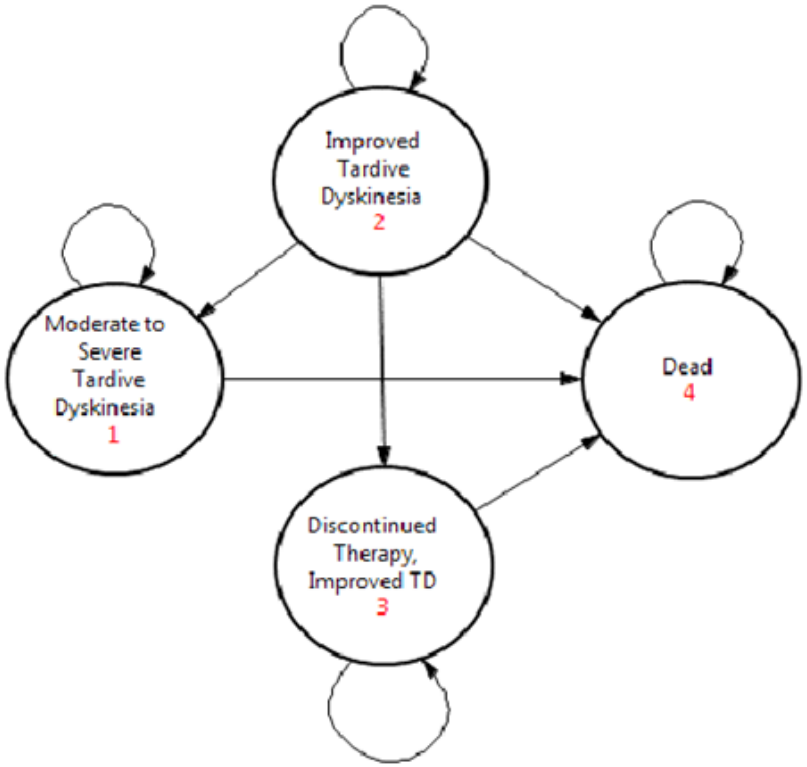
Parameters: Drug Regimens

	Dosage	Schedule	Route	Duration
Valbenazine	80 mg	1x80 mg capsule daily	Oral	Until Discontinuation or Death
Deutetrabenazine	36 mg*	2x9 mg tablets twice daily	Oral	Until Discontinuation or Death

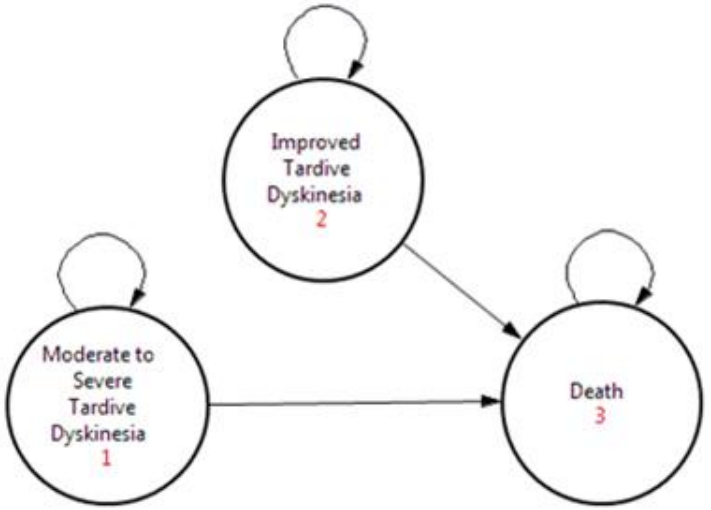
The rationale for using the maximal dose is that in clinical practice patients will be titrated to maximum medication effectiveness without intolerable side effects.
*Data on the efficacy of 48 mg deutetrabenazine on 50% reduction in AIMS score was not available from clinical trials. Therefore the 36 mg dose and cost were used to estimate cost-effectiveness.

Model Overview

Treatment Model



Placebo Model



Key Assumptions

- Patient response to treatment is reflected in their *initial* health states and all treated patients incurred one month of treatment costs.
- Patients not responding to treatment with valbenazine or deutetrabenazine discontinue their treatment in that first month and enter the model with moderate to severe TD.
- Response to treatment remains constant for all responders thereafter unless they subsequently discontinue treatment.
- Patients not responding to treatment were assumed to have two additional primary care and two additional neurologist visits per year.

Key Assumptions

- Long-term discontinuation rates were modeled from open-labeled studies with less than one year of observation. Following the first cycle, discontinuation rates were modeled as being 50% of that observed in the first cycle.
- Following discontinuation a percentage of patients, based on the placebo results, remain in the Improved TD state.
- All patients who discontinue treatment stop incurring costs associated with the treatment.
- TD treatments do not have a direct effect on mortality.
- For the base-case, treatment of TD has no effect on the outcomes or costs of treating the underlying conditions.
    - A scenario analysis was developed incorporating an effect of treatment on improving treatment of underlying conditions

Key Model Inputs: Treatment Response and Long Term Discontinuation

Model Inputs	Valbenazine		Deutetrabenazine	
	Value	Reference	Value	Reference
Proportion of PLACEBO Responders with ≥50% Reduction in AIMS	8.7%	Hauser 2017	12.0%	Anderson 2017
Proportion of TREATMENT Responders with ≥50% Reduction in AIMS	40.0%	Hauser 2017	33.1%	Anderson 2017
Annual Discontinuation Rate (First Year)*	17.6%	Remington 2016 Hauser 2017	13.0%	Anderson [2] 2017

*Assumed 50% decrease after 1st year

Key Model Inputs: Drug Costs

Drug and Daily Dose	Annual WAC	Annual Net Price (at 27% discount)	Source
Valbenazine 80 mg	$75,789	$55,326	Redbook 2017 Aitkin et al. 2016
Deutetrabenazine 36 mg	$90,071	$65,751	Redbook 2017 Aitkin et al. 2016

Key Model Inputs: Utilities

Model Inputs	Base Case Value	Reference	Notes
Baseline Utility for Modeled Population	0.82	Wang 2004 Calvert 2006	Weighted average of patients with schizophrenia disorders (0.83) and bipolar disorders (0.80).
Utility Decrement from Moderate to Severe TD	0.095	Lenert 2004	Assumed constant across age and underlying condition.

Results

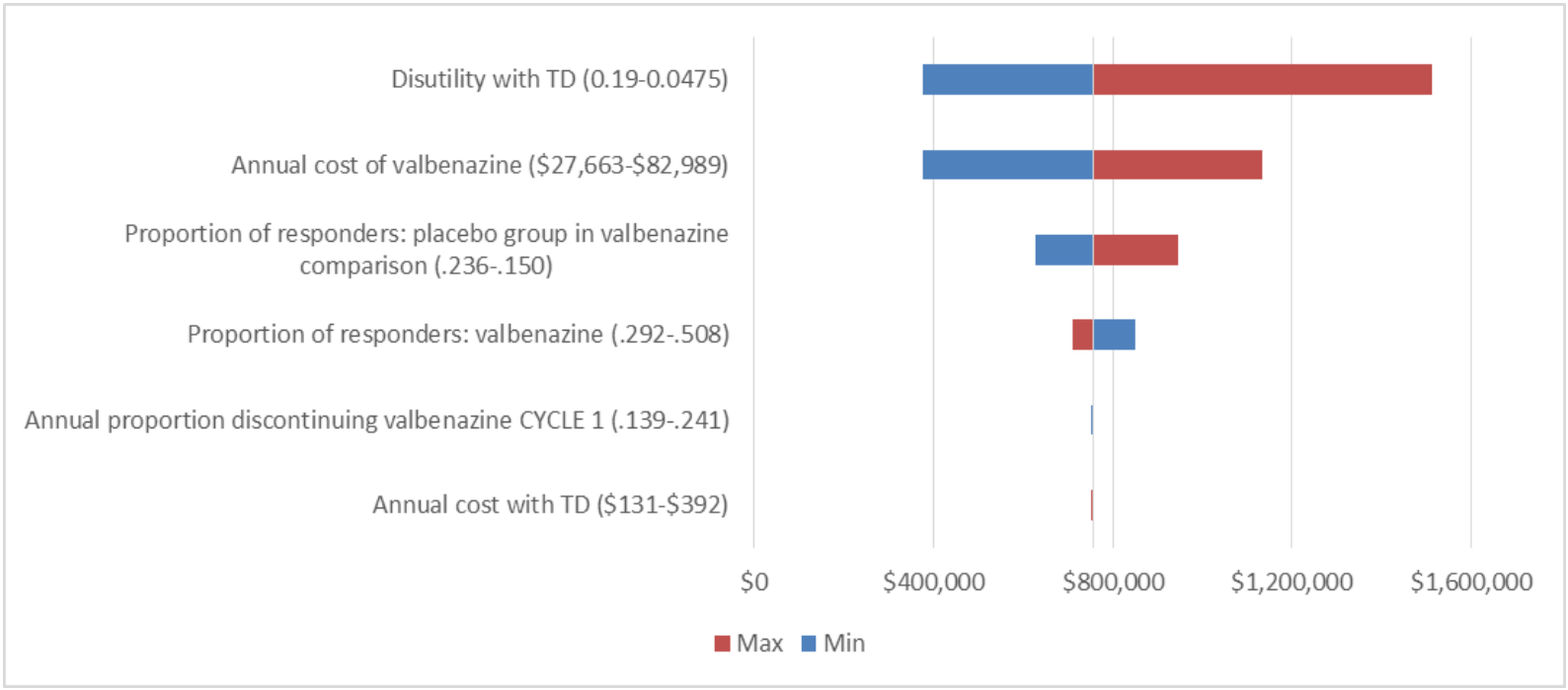
Model Results: Base Case

Model Inputs	Valbenazine		Deutetrabenazine	
	Valbenazine	Placebo	Deutetrabenazine	Placebo
Total Costs	$185,167	$6,876	$220,423	$6,627
Total QALYs	15.35	15.12	15.37	15.18

Model Results: Base Case Cost per QALY

Regimen	Incremental Costs	Incremental QALYs	Incremental Cost-Effectiveness Ratios versus Placebo
Valbenazine	$178,291	0.24	**$752,080**
Deutetrabenazine	$213,795	0.19	**$1,100,773**

One Way Sensitivity Analysis: Tornado Diagram for Valbenazine



Note for comparison 0.159 disutility associated with new-onset depression.[Roberts, 2014]

Model Results: Scenario Analyses for Improvement in Underlying Conditions

Base Case Vs. Placebo	Underlying Condition	Incremental Cost Per QALY
Valbenazine	Schizophrenia/ Schizoaffective Disorders	$552,589
Deutetrabenazine	Schizophrenia/ Schizoaffective Disorders	$779,342
Valbenazine	Bipolar Disorder	$604,568
Deutetrabenazine	Bipolar Disorder	$874,934

Sensitivity and Scenario Analyses

- Including potential productivity gains based on available literature related to employment levels for patients with and without TD and median US salaries resulted in small improvements in the incremental ratios
  - Valbenazine: $728,000 per QALY gained
  - Deutetrabenazine: $1,077,000 per QALY gained

- None of the sensitivity or scenario analyses resulted in incremental cost-effectiveness ratios of below $150,000 per QALY gained.

Model Results: Threshold Analysis

Drug	Annual WAC	Annual Net Price (at 27% discount)	Annual Price to Achieve $50,000 per QALY	Annual Price to Achieve $100,000 per QALY	Annual Price to Achieve $150,000 per QALY
Valbenazine 80 mg per day	$75,789	$55,326	$3,941	$7,600	$11,260
Deutetrabenazine 36 mg per day	$90,071	$65,751	$3,205	$6,181	$9,158

Limitations

- The effectiveness of the treatment is based on limited intermediate measures from the clinical trials.
- We used a utility value for complete removal of moderate to severe TD for a 50% improvement in the AIMS score.
- In general, there are relatively few and relatively limited studies available from which to build models for TD patients particularly in terms of the scenario analyses mentioned here.
- As with all models the results reflect averages for the patient population as described above.

Summary

- Valbenazine and Deutetrabenazine are projected to improve patient health.
- At the current prices the projected base case incremental cost effectiveness ratios for both drugs are well above usual thresholds.
- While the model results did vary across the rate of symptom relief with no treatment, the disutility of TD, and the price of the drugs, all of the sensitivity analyses and scenario analyses resulted in incremental cost effectiveness ratios above usual thresholds.

Public Comments

- The impact of TD is not adequately measured by QALYs and/or the utility decrement from moderate to severe TD is too small.
- Reduction of TD symptoms will result in better adherence to medications for underlying conditions and therefore better outcomes in those underlying conditions along with lower costs.
- Reduction of TD symptoms will have a substantial impact on productivity.
- Reduction of TD symptoms will have positive spillover effects on family and caregivers.

Manufacturer Public Comments and Discussion

Manufacturer Public Comments and Discussion

Name	Title	Company
Chuck Yonan, PharmD	Senior Director of Health Economics Outcomes Research, Medical Affairs	Neurocrine Biosciences
Victor Abler, DO	Senior Global Medical Director, Neurodegenerative Disorders	Teva Pharmaceuticals

Public Comment and Discussion

Nathaniel Counts, JD; Senior Director of Policy, Mental Health America

Conflicts of interest:

- Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies
- Any other relationship that could reasonably be considered a financial conflict of interest, please note below

If yes, please describe the relationship(s) below.

I am a non-officer employee of an organization which receives more than 25% of its funding from health care companies, including multiple life sciences manufacturers, health plans or managed care organizations, life sciences manufacturer associations, and hospital systems. A public list of funds received by funder by program is available on our website.

I am on the Board of Directors of an organization that receives more than 25% of its funding from health care companies, including life sciences manufacturers.

Allen Doederlein, President, Depression and Bipolar Support Alliance

Conflicts of interest:

Status or position as an officer, board member, trustee, owner or employee of a health care company, or an organization which receives more than 25% of its funding from health care companies.

If yes, please describe the relationship(s) below.

DBSA's mean level of support from healthcare companies across 2014-2016 was 42%, which is roughly on par with DBSA's funding since c. 2005. Healthcare company contributions are accepted only for DBSA-initiated programming for which DBSA has sole creative, approval, and dissemination authority

Dr. Daniel Tarsy, MD, Professor of Neurology, Harvard Medical School Parkinson's Disease and Movement Control Disorder Center

Conflicts of interest:

I have no conflicts of interest.

If yes, please describe the relationship(s) below.

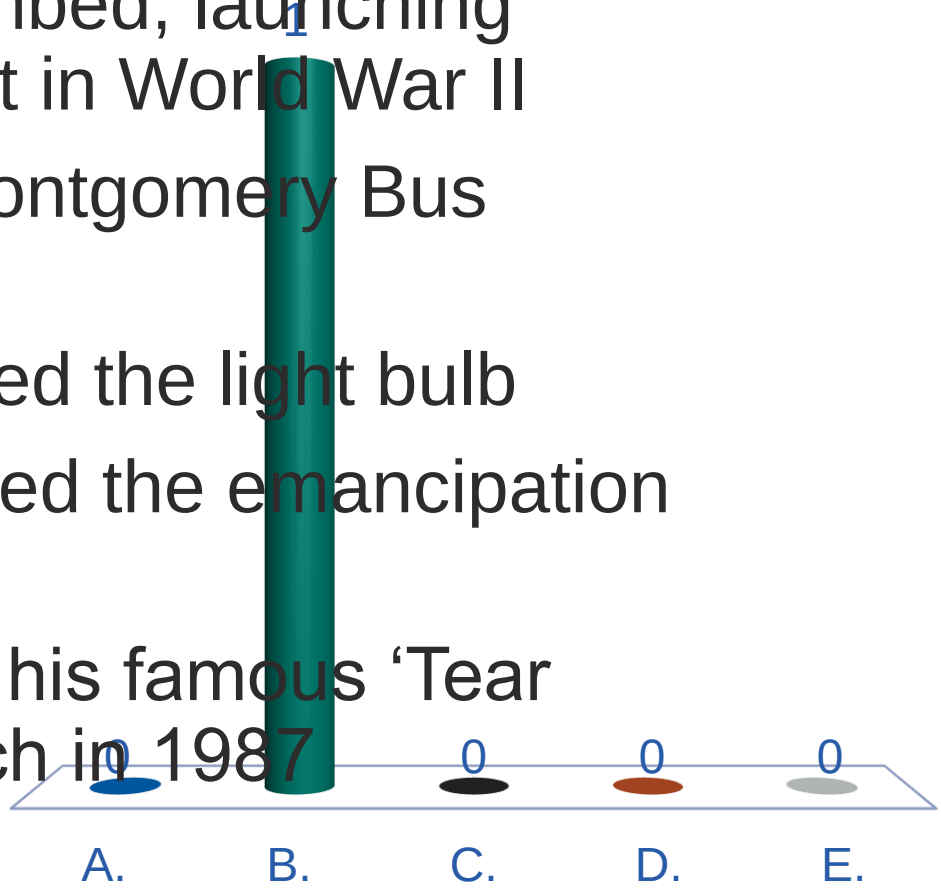
Lunch

Meeting will resume at 1:00 pm

Voting Questions

What famous historic event in American History occurred on December 5?

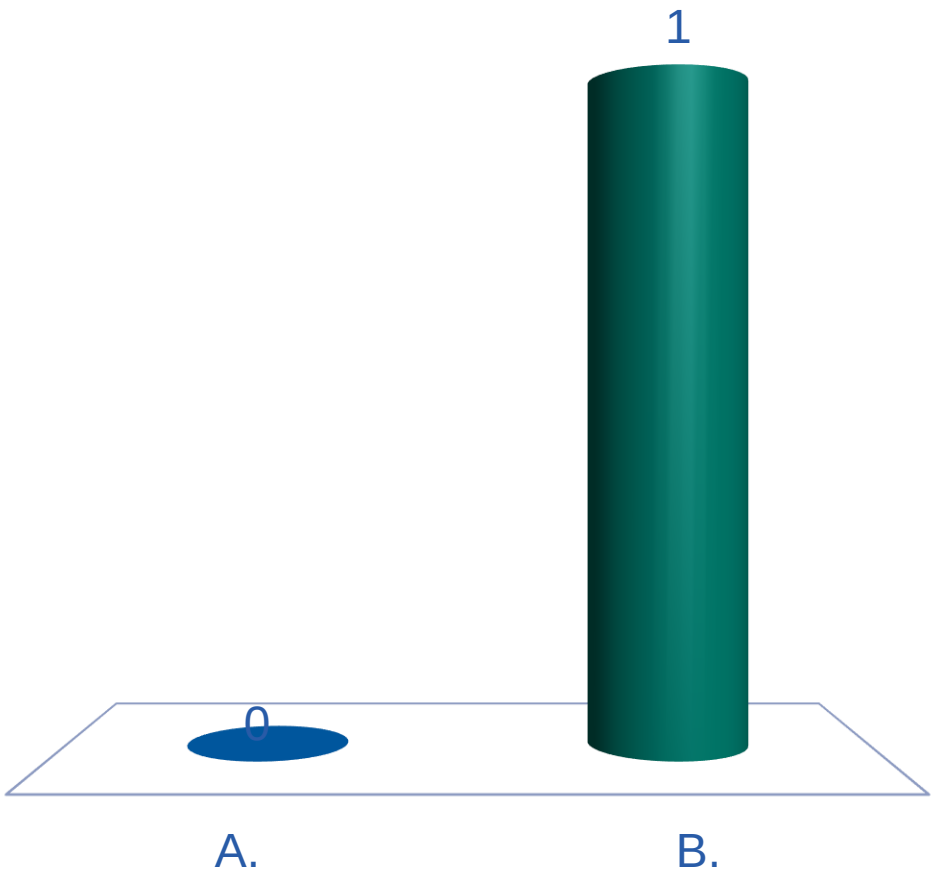
A. Pearl Harbor was bombed, launching American involvement in World War II
B. The first day of the Montgomery Bus Boycott
C. Thomas Edison created the light bulb
D. Abraham Lincoln issued the emancipation proclamation
E. Ronald Reagan gave his famous ‘Tear Down this Wall’ speech in 1987



1. Is the evidence adequate to demonstrate a positive net health benefit from treating patients with TD with valbenazine?

A. Yes

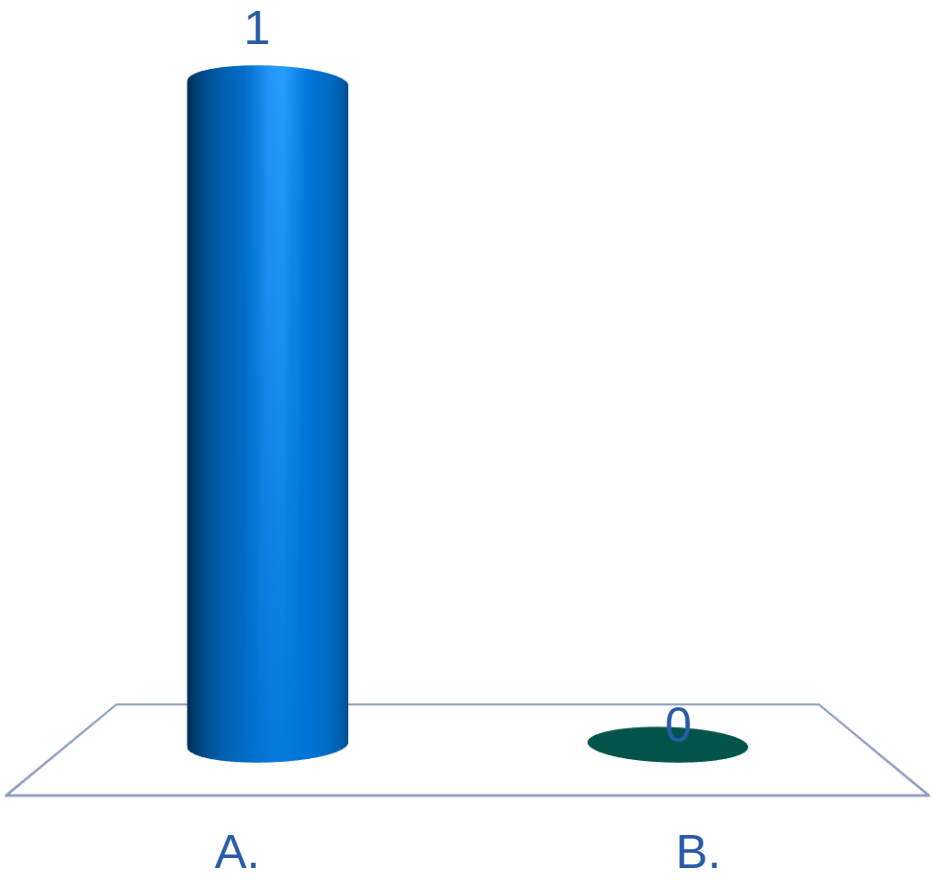
B. No



2. Is the evidence adequate to demonstrate a positive net health benefit from treating patients with TD with deutetrabenazine?

A. Yes

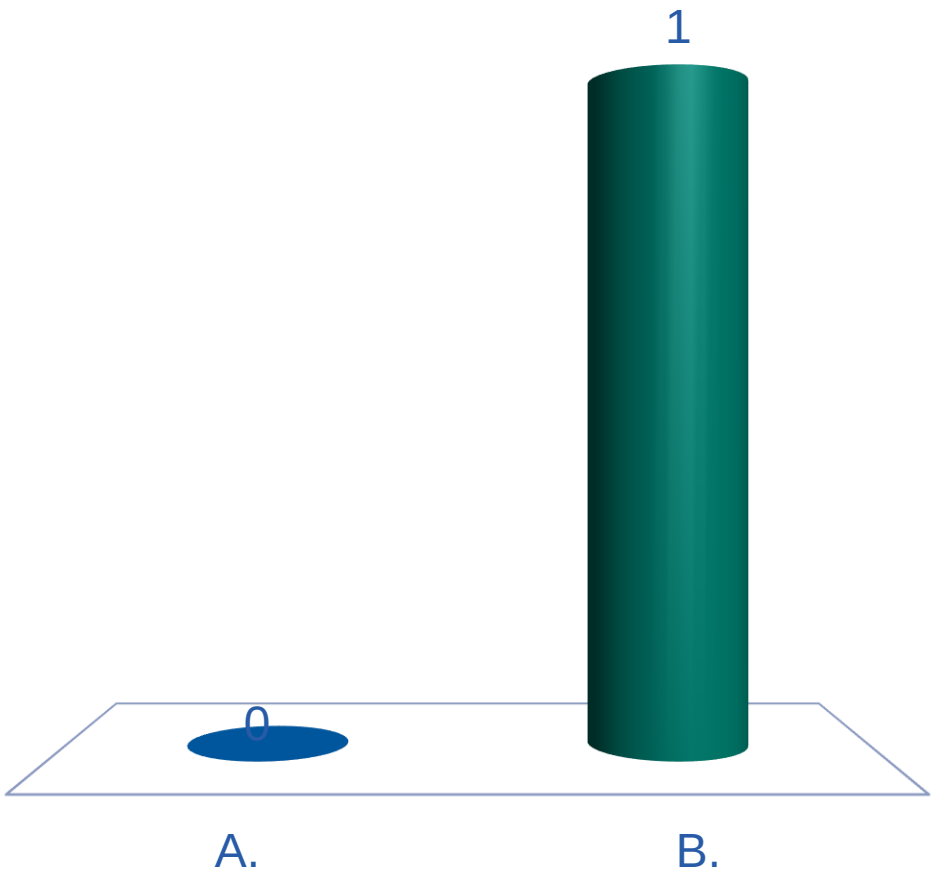
B. No



3. Is the evidence adequate to demonstrate a positive net health benefit from treating patients with TD with tetrabenazine?

A. Yes

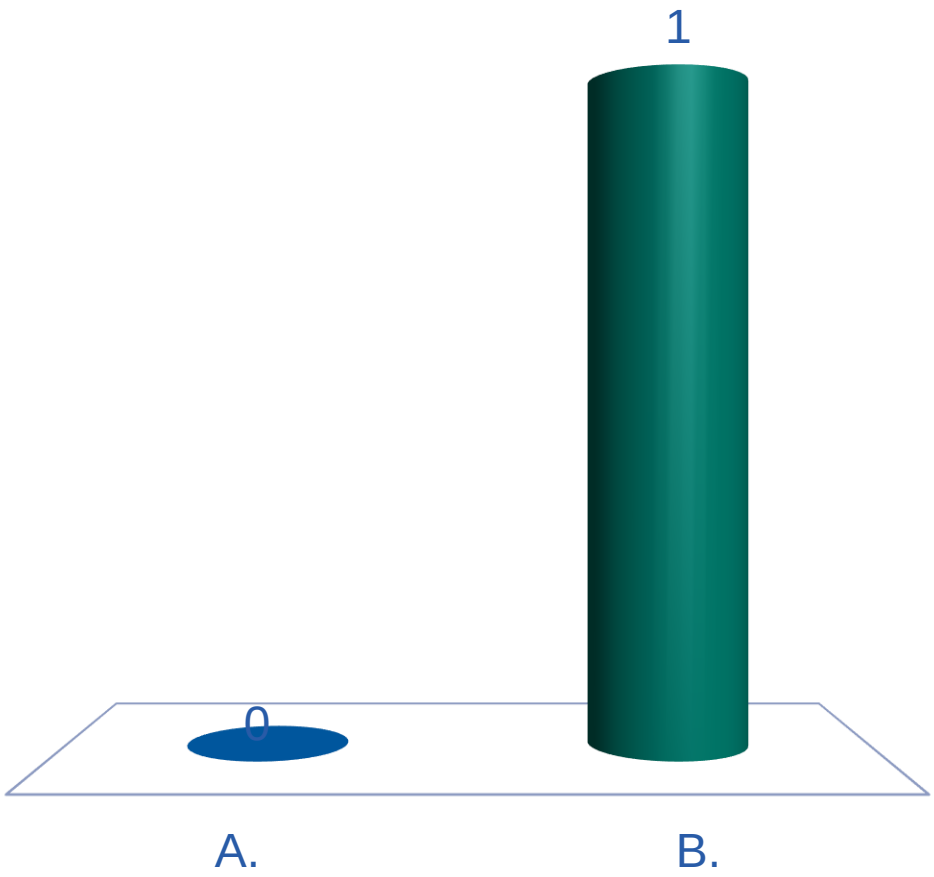
B. No



4. Is the evidence adequate to distinguish between the net health benefit of valbenazine and deutetrabenazine in the treatment of TD?

A. Yes

B. No



Does treating patients with one of the new FDA approved drugs offer one or more of the following "other benefits"? (select all that apply)

A. This intervention provides significant direct patient health benefits that are not adequately captured by the QALY.

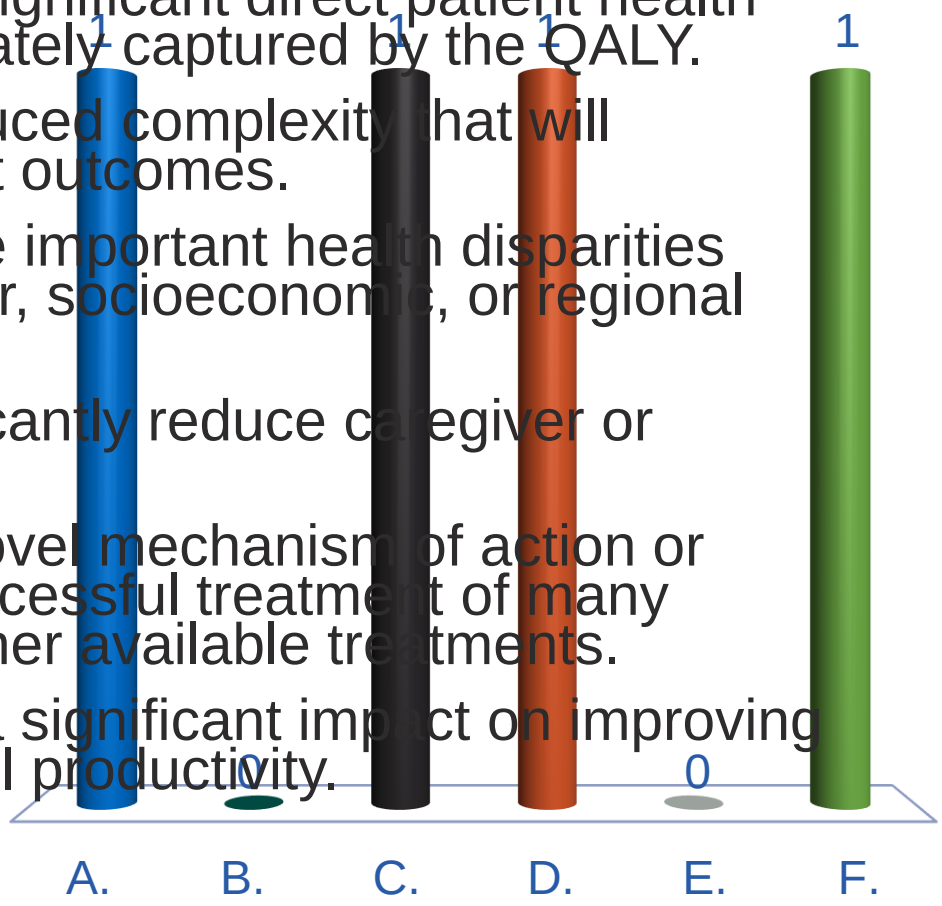
B. This intervention offers reduced complexity that will significantly improve patient outcomes.

C. This intervention will reduce important health disparities across racial, ethnic, gender, socioeconomic, or regional categories.

D. This intervention will significantly reduce caregiver or broader family burden.

E. This intervention offers a novel mechanism of action or approach that will allow successful treatment of many patients who have failed other available treatments.

F. This intervention will have a significant impact on improving return to work and/or overall productivity.



Are any of the following contextual considerations important in assessing the new FDA approved drugs' long-term value for money in patients with tardive dyskinesia? (select all that apply)

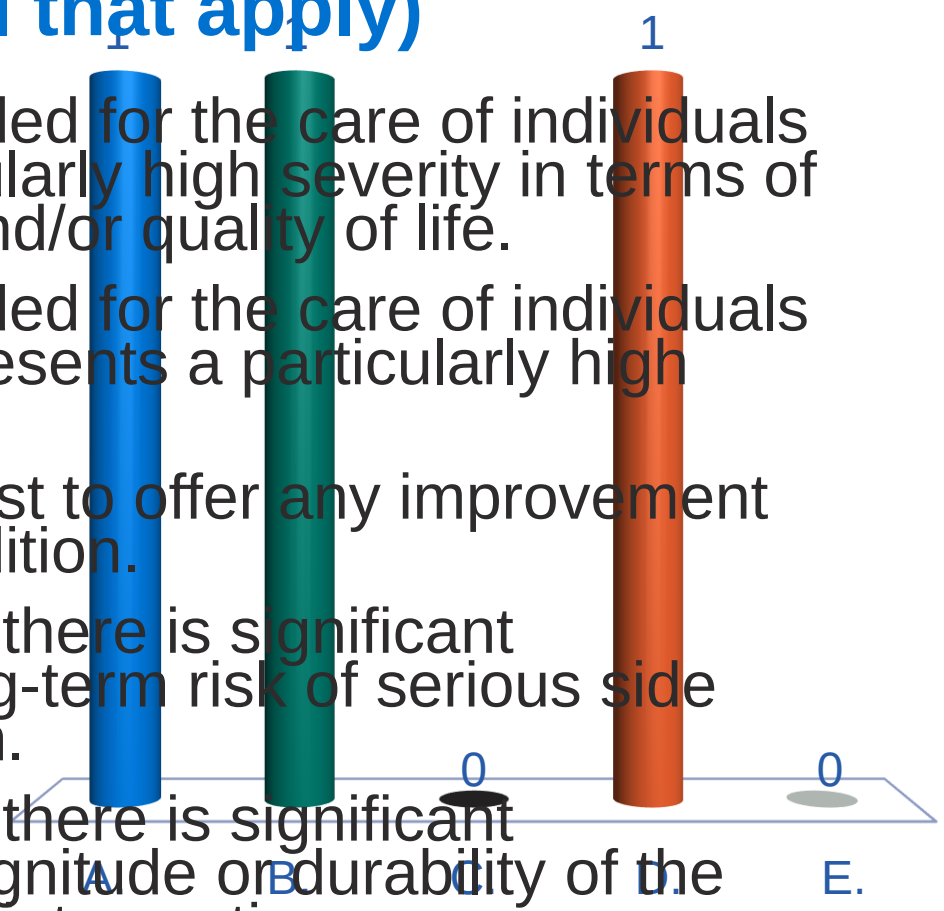
A. This intervention is intended for the care of individuals with a condition of particularly high severity in terms of impact on length of life and/or quality of life.

B. This intervention is intended for the care of individuals with a condition that represents a particularly high lifetime burden of illness.

C. This intervention is the first to offer any improvement for patients with this condition.

D. Compared to usual care, there is significant uncertainty about the long-term risk of serious side effects of this intervention.

E. Compared to usual care, there is significant uncertainty about the magnitude or durability of the long-term benefits of this intervention.



Policy Roundtable

Policy Roundtable

Victor Abler, DO. Senior Global Medical Director for Neurodegenerative Diseases Teva Pharmaceuticals	**Barbara Henry, RPh.** Lead Clinical Pharmacy Specialist Harvard Pilgrim
Teri Brister, PhD. Director Knowledge Integration Information National Alliance on Mental Illness	**Paul Jeffrey, PharmD.** Director of Pharmacy MassHealth
Oliver Freudenreich, MD. Co-Director, Schizophrenia Clinical Research Program Mass General Hospital	**Daniel Tarsy, MD.** Professor of Neurology; Parkinson's Disease and Movement Disorders Center Beth Israel Hospital; Harvard Medical School
Patrick Hendry Vice President of Peer Advocacy Support and Services Mental Health America	**Chuck Yonan, PharmD.** Senior Director HEOR, Medical Affairs Neurocrine Bioscience

New England CEPAC Panel Reflections and Closing Remarks

Adjourn