



AIMS Is Nothing but a Number: Focusing on *Function and Family in Tardive Dyskinesia*

MasterClass



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Ashley Walters: Has no relationships to report

Elizabeth Walters: Has no relationships to report

Disclosures

- The faculty have been informed of their responsibility to disclose to the audience if they will be discussing off-label or investigational use(s) of drugs, products, and/or devices (any use not approved by the US Food and Drug Administration).
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Learning Objectives

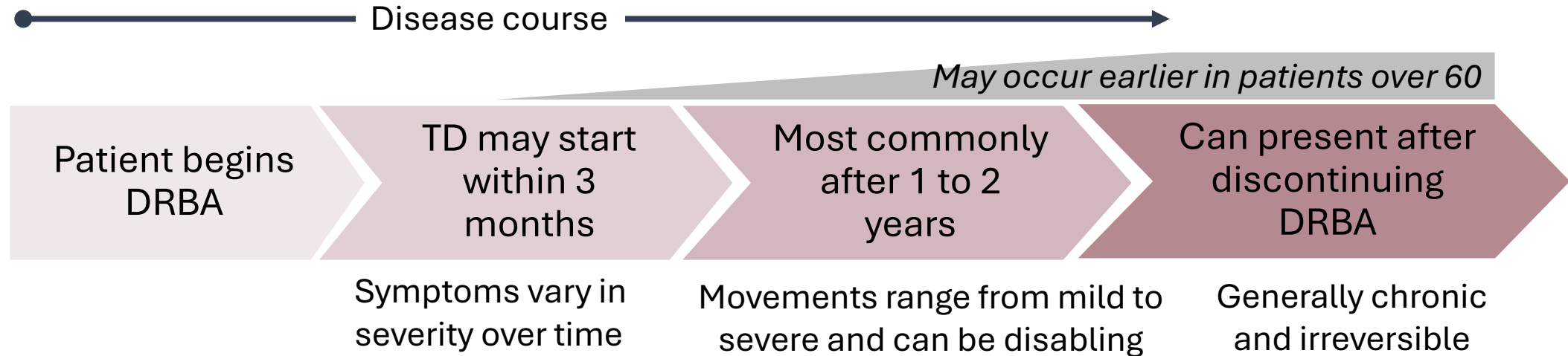
- Define and describe the importance of functional and QoL restoration as long-term treatment goals for patients with TD as well as their caregivers
- Identify subtle manifestations of TD, differentiate it from other movement disorders, and utilize validated tools to assess its functional and QoL impacts on patients and caregivers
- Evaluate clinical and real-world evidence associated with VMAT-2 inhibitors and strategies to optimize their efficacy and safety in the treatment of TD

Overview of TD

Basics of Tardive Dyskinesia

Tardive = tending to or characterized by lateness especially in development

Dyskinesia = distortion or impairment of voluntary movement

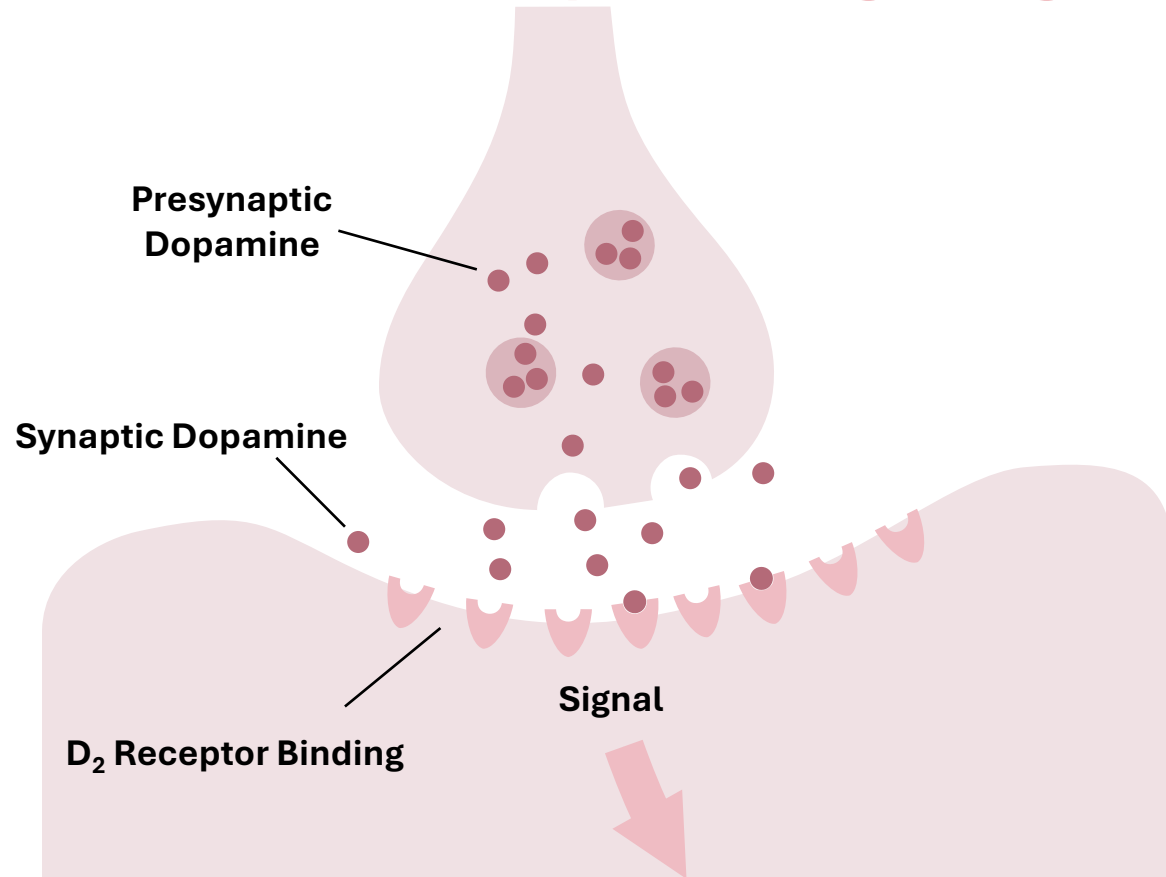


DRBA = Dopamine receptor blocking agent.

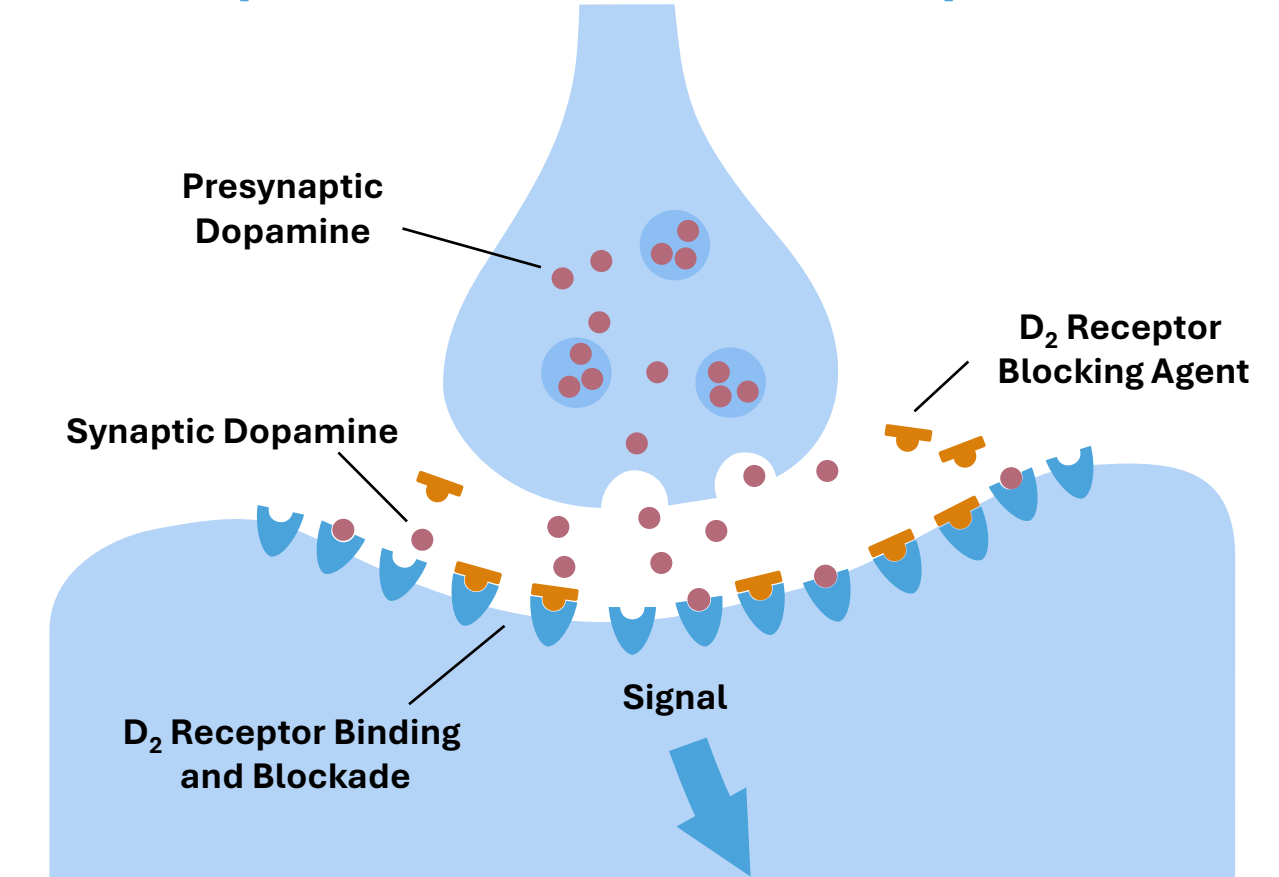
Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-78. Lerner PP, et al. *Psychiatry Clin Neurosci*. 2015;69(6):321-34. Merriam-Webster Medical Dictionary. Accessed May 12, 2025. <https://www.merriam-webster.com/medical/tardive>. O'Brian A. *Int J Geriatr Psychiatry*. 2016;31(7):683-93.

Chronic D₂ Blockade Triggers Compensatory Receptor Adaptations

Homeostatic Dopamine Signaling



Impact of Chronic DRBA Exposure



DRBA=Dopamine Receptor Blocking Agent
Stahl SM. *CNS Spectr.* 2018;23(4):239-247.

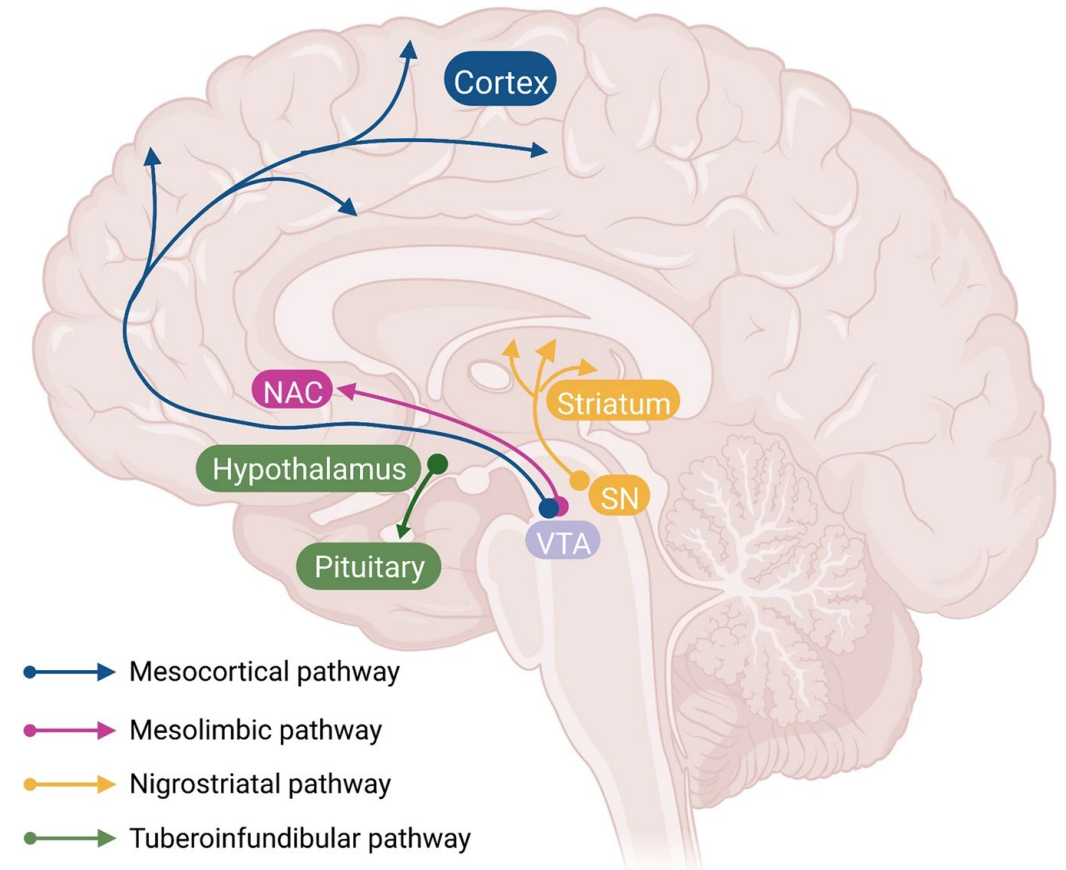
↑ in D₂ Receptor
Number and Density

↑ in Receptor
Sensitivity

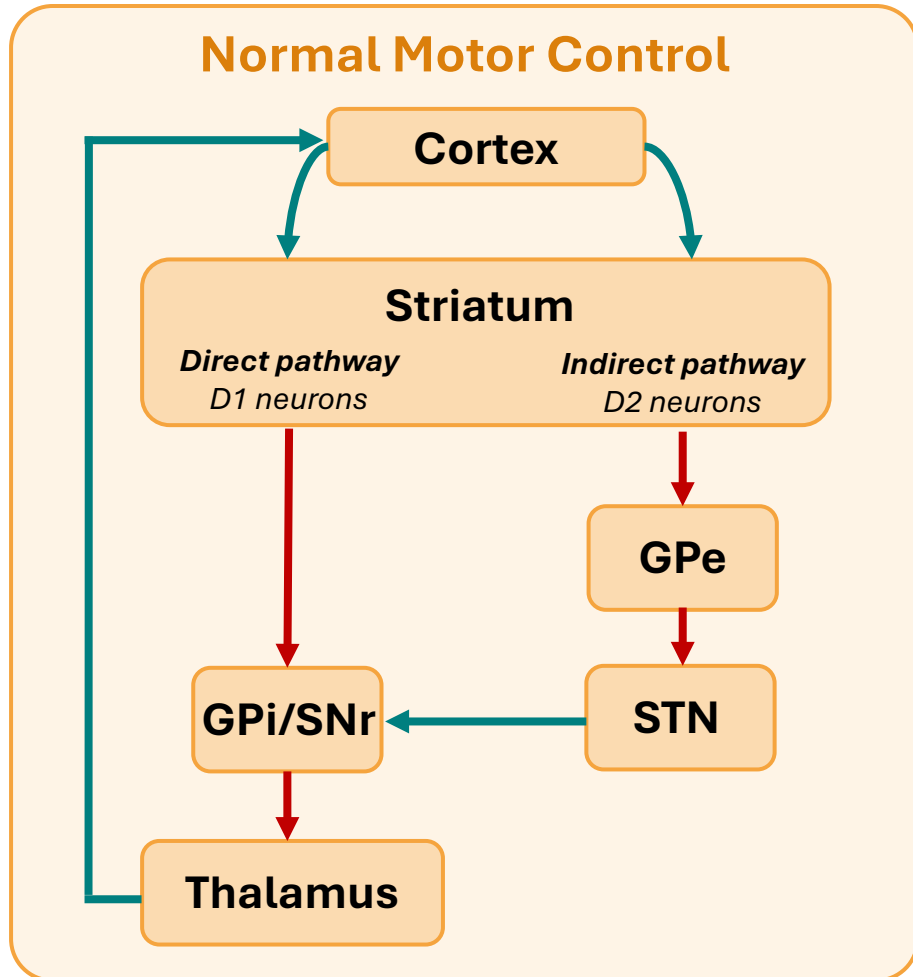
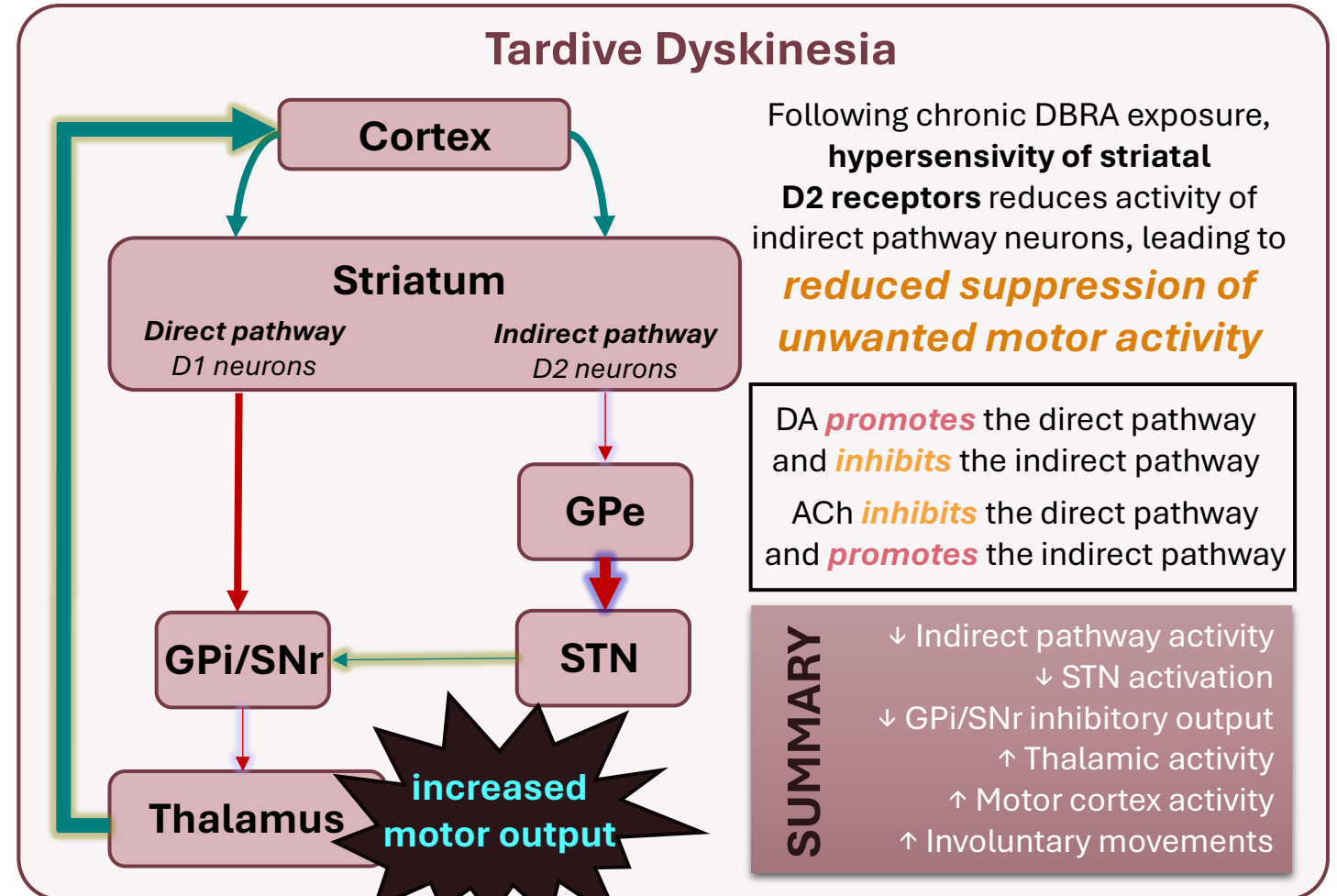
Maladaptive signaling resulting
in abnormal movements

TD Emerges Within the Nigrostriatal Motor Pathway

- **Substantia Nigra → Dorsal Striatum**
 - Dopaminergic projections
 - Critical for movement initiation, modulation, and ***suppression of unwanted motor activity***
 - High density of D2 receptors in striatum



Indirect Pathway Dysfunction Promotes Involuntary Movements



Red = inhibitory projections; **teal** = excitatory projections; DA = dopamine; ACh = acetylcholine; DBRA = dopamine receptor blocking agent, D1 = dopamine D1 receptor, D2 = dopamine D2 receptor, GPe = globus pallidus externa, STN = subthalamic nucleus, GPi = globus pallidus interna, SNr = substantia nigra pars reticulata.

Takeuchi H, Mori Y, Tsutsumi Y. 2022;12:20451253221117313. Published 2022 Oct 21.

TD Is More Than a Movement Disorder



Physical

- Difficulty using utensils, writing, typing, dressing
- Difficulty speaking, chewing, or swallowing
- Difficulty walking or maintaining balance
- Problems breathing
- Pain due to TD
- Difficulty sitting still/falling asleep



Social interactions

- Difficulty participating in social events
- Self-consciousness / embarrassment
- Avoidance of interaction with others
- Reduced quality of interpersonal communication



Vocational/ Educational/ Recreational

- Problems gaining or maintaining employment
- Problems with recreational/vocational/educational performance
- Challenges getting to work/school or to other activities
- Difficulty sitting still/falling asleep
- Difficulty performing tasks independently



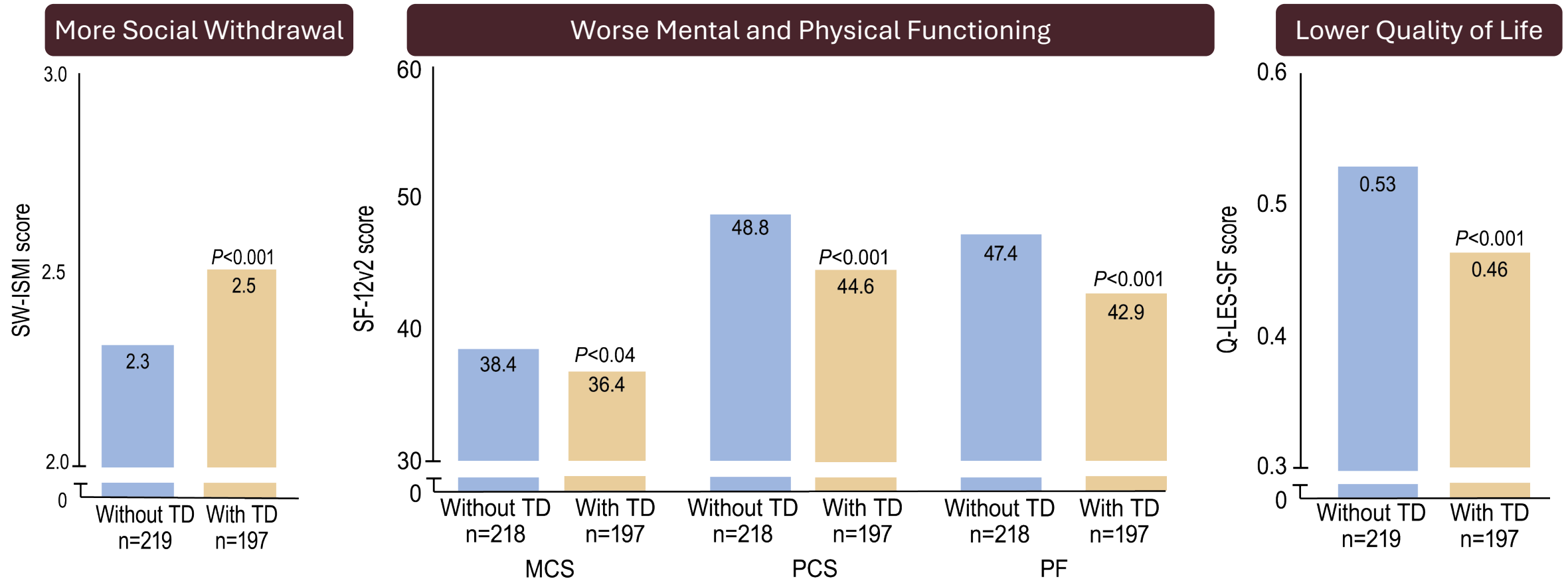
Psychological/ Psychiatric

- Sadness, depression
- Anxiety, worry, concern
- Low self-esteem
- Hopelessness, loss of sense of purpose
- Poor concentration, attention, memory
- Worsening or recurrence of previous symptoms/disorder
- Difficulty with appropriate treatment of mental disorder
- Unhealthy coping strategies

TD Negatively Impacts Life No Matter the Underlying Diagnosis



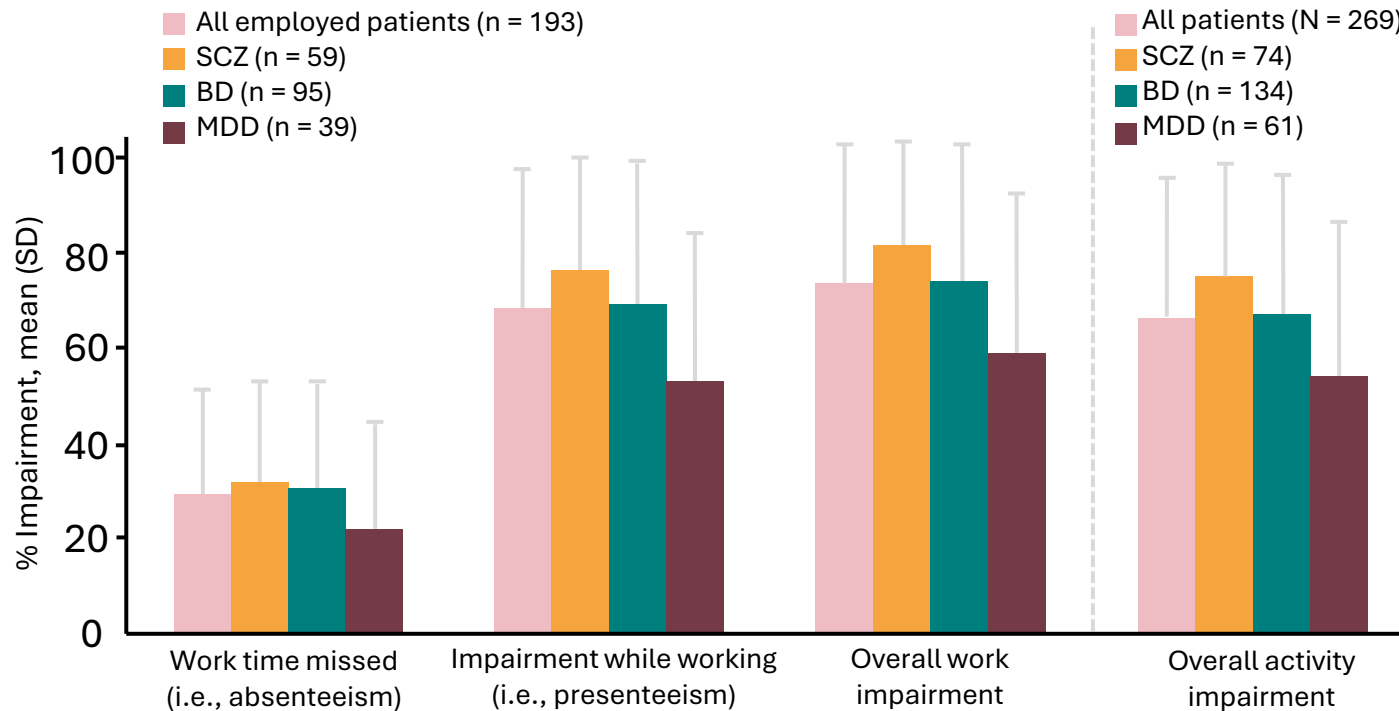
Survey of patients with clinician-confirmed diagnosis of BD, MDD, or SCZ shows those with TD have significantly:



BD = bipolar disorder; MDD = major depressive disorder; SCZ = schizophrenia; SW-ISMI = Social Withdrawal Subscale of the Internalized Stigma of Mental Illness Scale; MCS = Mental Component Summary of the SF-12; PCS = Physical Component Summary of the SF-12; PF = Physical Functioning of the SF-36v2; Q-LES-Q SF = Quality of Life Enjoyment and Satisfaction Questionnaire Short Form.

McEvoy J, et al. *Qual Life Res.* 2019;28(12):3303-3312.

Individuals with TD Report Substantial Impacts on Work and Professional Activities

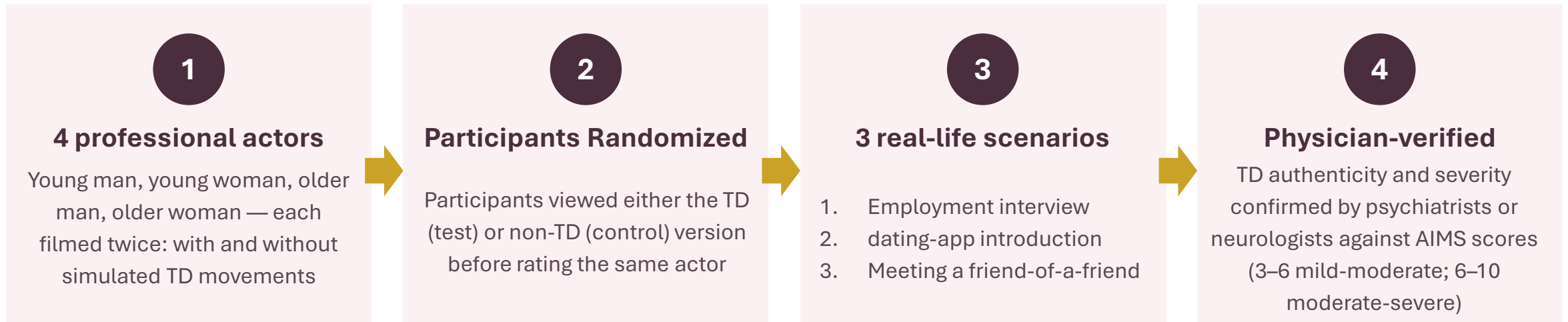
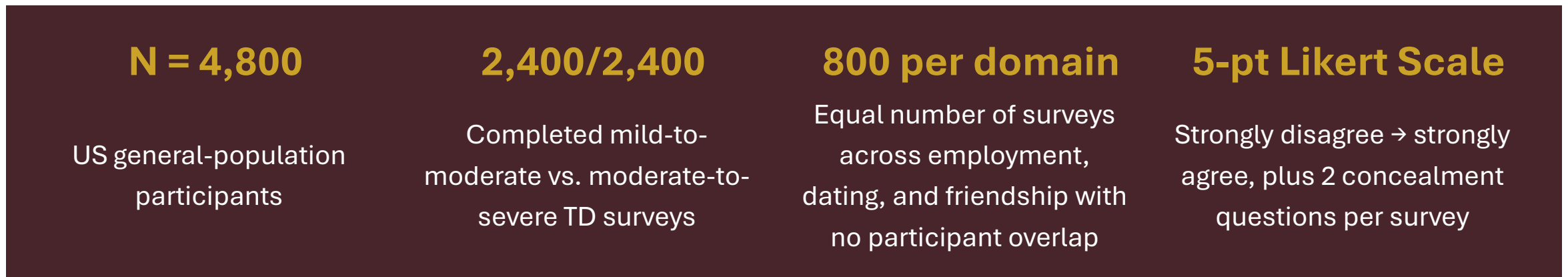


At least **25%**
of individuals with
schizophrenia, BD, or MDD
reported **a substantial impact
of TD** when applying for jobs,
attaining a job, and seeking a
promotion or new
responsibilities at work

SCZ=Schizophrenia; BD=Bipolar Disorder; MDD=Major Depressive Disorder.

Jain R, et al. *J Clin Psychiatry*. 2023;84(3):22m14694.7

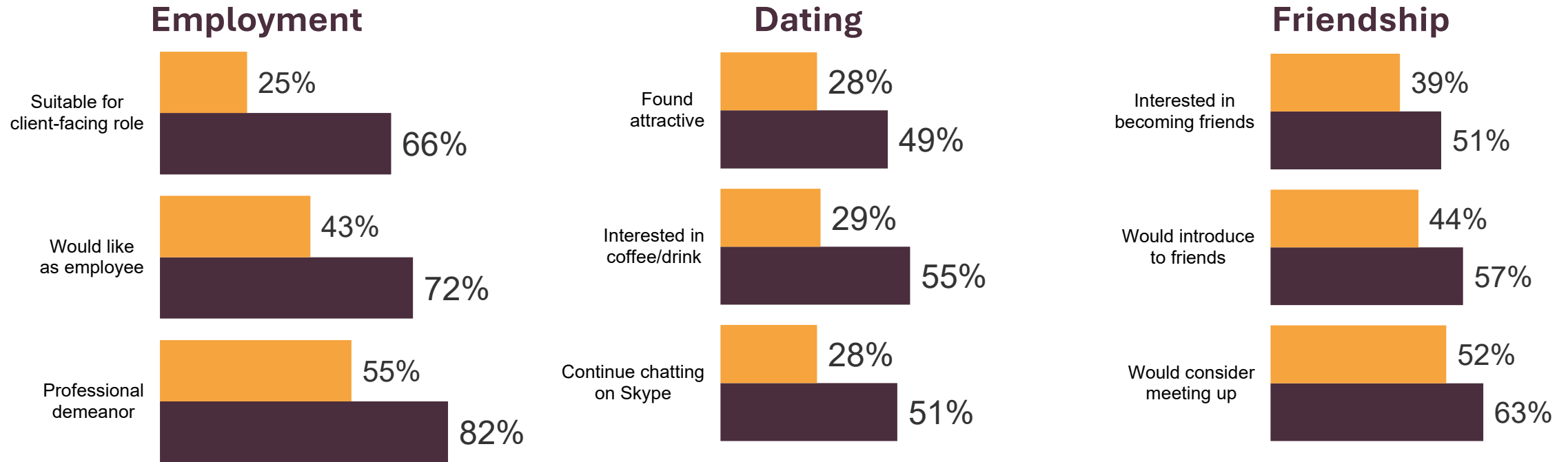
Putting TD Stigma to the Test



Across Employment, Dating, and Friendship, TD Movements Reduced Favorable Perceptions

% of participants who agreed / strongly agreed after viewing an actor with vs. without mild-to-moderate TD movements

■ Actor without TD (control) ■ Actor with TD (test)



The actors demonstrating TD movements were less likely to be considered favorably in professional, romantic, and social capacities.





Key Learning Points

- Tardive dyskinesia is a persistent movement disorder resulting from exposure to dopamine receptor blocking medication that may endure despite medication adjustment or discontinuation
- Observable movements represent only part of the disease burden. TD also contributes to **worse mental and physical functioning, more social withdrawal, and lower quality of life**
- Routine screening, early recognition, and timely intervention are essential components of comprehensive care that can preserve psychiatric stability, dignity, and quality of life

Detection and Assessment of TD in Psychiatric Practice

How Common is TD?

~1 in 4

people treated with
an antipsychotic
experience TD*

Overall prevalence: 25.3%

FGAs: 30%

SGAs: 20.7%

SGAs without prior
FGA treatment: 7.2%

~5%

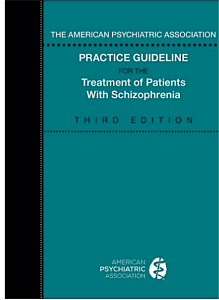
of diagnosed
patients receive
available treatment

~15%

of patients with TD
are diagnosed

*Based on a meta-analysis of 41 studies (N=11,493; mean age=42.8 years, 66.4% male, 77.1% schizophrenia spectrum).
Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-e278.

Structured Screening Is Standard of Care: APA Guideline Recommendations



11%

**of patients on
antipsychotics receive
regular TD screenings,
according to one study**

Risk Factors

3–5× risk if > 50 years old

History of akathisia, dystonia, or Parkinsonism (“EPS”)

Dosage, duration, and potency of DRBA

Substance use disorder

Mood disorder > Psychotic disorder diagnosis

AP = antipsychotic.

Keller WR, et al. *J Nerv Ment Dis*. 2014;202(1):6-12. Caroff SN, et al. *J Clin Psychiatry*. 2020;81(2):19cs12983. American Psychiatric Association. *Practice Guideline for the Treatment of Patients with Schizophrenia*. 3rd ed. APA Publishing; 2021. Aquino CC, Lang AE. *Parkinsonism Relat Disord*. 2014;20 Suppl 1:S113-117. Jankelowitz SK. *Neuropsychiatr Dis Treat*. 2013;9:1371-1380. D’Abreu A, et al. *J Neurol Sci*. 2018;389:17-20.

Is It Tardive Dyskinesia (TD) or Drug-Induced Parkinsonism (DIP)?

Characteristic	Tardive Dyskinesia	Drug-Induced Parkinsonism
Onset	Delayed (months-years) after initiation of an antipsychotic	Immediate (hours-days-weeks) after initiation of an antipsychotic or after dose is increased
Motor symptoms observed	Arrhythmic movements (generally choreo-athetoid) of the face, trunk and extremities	Rhythmic tremor (3-6 Hz), rigidity, shuffling gait; akathisia may be present
Immediate (hours-days-weeks) effects of increasing antipsychotic dose	Improves	Worsens
Immediate (hours-days-weeks) effects of decreasing antipsychotic dose	Worsens	Improves
Effects of anticholinergic medications (eg, benztropine)	Can worsen	Improves
Pharmacotherapeutic treatment options	<u>FDA Approved</u> : VMAT2 inhibitors (deutetrabenazine and valbenazine) <u>Off-Label</u> : amantadine, clonazepam, ginkgo biloba, tetrabenazine	Anticholinergics (for example, benztropine), amantadine

DIP = drug-induced parkinsonism; VMAT2 = vesicular monoamine transporter 2.

Ward KM, Citrome L. *Neurol Ther*. 2018;7(2):233-248.

AIMS Rating Scale Is Used to Assess the Severity of TD Symptoms

Movement Ratings		Score				
Facial & Oral Movements	1. Muscles of facial expression	0	1	2	3	4
	2. Lips and perioral area	0	1	2	3	4
	3. Jaw	0	1	2	3	4
	4. Tongue	0	1	2	3	4
Extremity Movements	5. Upper (arms, wrists, hands, fingers)	0	1	2	3	4
	6. Lower (legs, knees, ankles, toes)	0	1	2	3	4
Trunk Movements	7. Neck, shoulders, hips	0	1	2	3	4
Global Judgments	8. Severity of abnormal movements overall	0	1	2	3	4
	9. Incapacitation due to abnormal movements	0	1	2	3	4
	10. Patient awareness of abnormal movements	0	1	2	3	4
Dental Status	11. Current problems with teeth/dentures?	No	Yes			
	12. Are dentures usually worn?	No	Yes			

- AIMS is a clinician-rated scale
 - Items 1–4 assess orofacial movements
 - Items 5–7 assess extremity and truncal movements
 - Item 8 assesses the overall severity of movements
- Scoring
 - Total score is calculated using items 1–7 for a total (max) score of 28
 - Item 8 score is based on the highest single score in any of the items 1–7

0=None 1=Minimal 2=Mild
3=Moderate 4=Severe

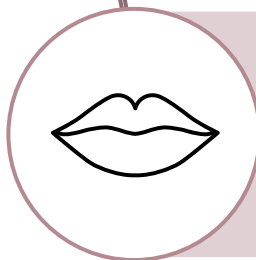
Gharabawi GM, et al. *Schizophr Res.* 2005;77(2-3):119-128. Guy W. *ECDEU Assessment Manual for Psychopharmacology, Revised 1976*. U.S. Dept. of Health, Education, and Welfare; Public Health Service; Alcohol, Drug Abuse, and Mental Health Administration; National Institute of Mental Health; 1976:534-537. STABLE National Coordinating Council Resource Toolkit Workgroup. STABLE Resource Toolkit. BCBST. Accessed February 2025. <https://www.bcbst.com/docs/providers/Behavioral-health-toolkit/stable-resource-toolkit.pdf>. OHSU. Abnormal Involuntary Movement Scale (AIMS). Accessed February 12, 2021. <https://www.ohsu.edu/sites/default/files/2019-10/%28AIMS%29%20Abnormal%20Involuntary%20Movement%20Scale.pdf>.

Looking for Involuntary Movements Beyond the Formal AIMS



Observe Throughout the Visit

i.e., waiting room, walking to exam room, during conversation



Use a Quick Semi-Structured Screen

- Ask patient/caregiver about abnormal movements
- Visually assess face & tongue: at rest, with speech, and with activation



**If Abnormal Movements Are Observed,
Perform Full AIMS**

Telepsychiatry and TD: Challenging, Yet Better Than Nothing

Why It's Challenging

- A full AIMS is more challenging via video, but not impossible
- Limited ability to assess full-body movements
- No formal TD telehealth guidelines

What You Can Do Now

- A suboptimal AIMS is better than no AIMS. Most (though not all) exam components can be conducted via telepsychiatry
- Involve family/support for movement observation
- Consider asynchronous video capture

Scan here to see a
telehealth
AIMS demo!



Key Learning Points

- Tardive dyskinesia remains prevalent among patients receiving DRBAs for psychiatric disorders, reinforcing the necessity of routine systematic screening throughout treatment
- Accurate detection requires vigilance, as TD may be subtle, underrecognized, and must be differentiated from other drug-induced or primary movement disorders.
- The Abnormal Involuntary Movement Scale (AIMS) is the standard clinical tool for assessment, but its optimal use, including via telehealth, requires structured administration and recognition of its limitations in capturing overall disease burden

Treatment of TD with VMAT-2 Inhibitors

The Anticholinergic Controversy

Used **extensively**, and often **prophylactically**, upon the initiation of antipsychotic medication to manage DIP

However, anticholinergics can **increase the risk of developing TD**, can **worsen comorbid TD**, and **negatively impact cognition**

Avoid in the elderly due to an increased risk of delirium

Peripheral side effects such as blurred vision, dry mouth, constipation, and urinary retention can also be encountered

If prescribed, a typical duration of anticholinergic use is 3 months, and they should be **periodically stopped to assess the need for continued use**

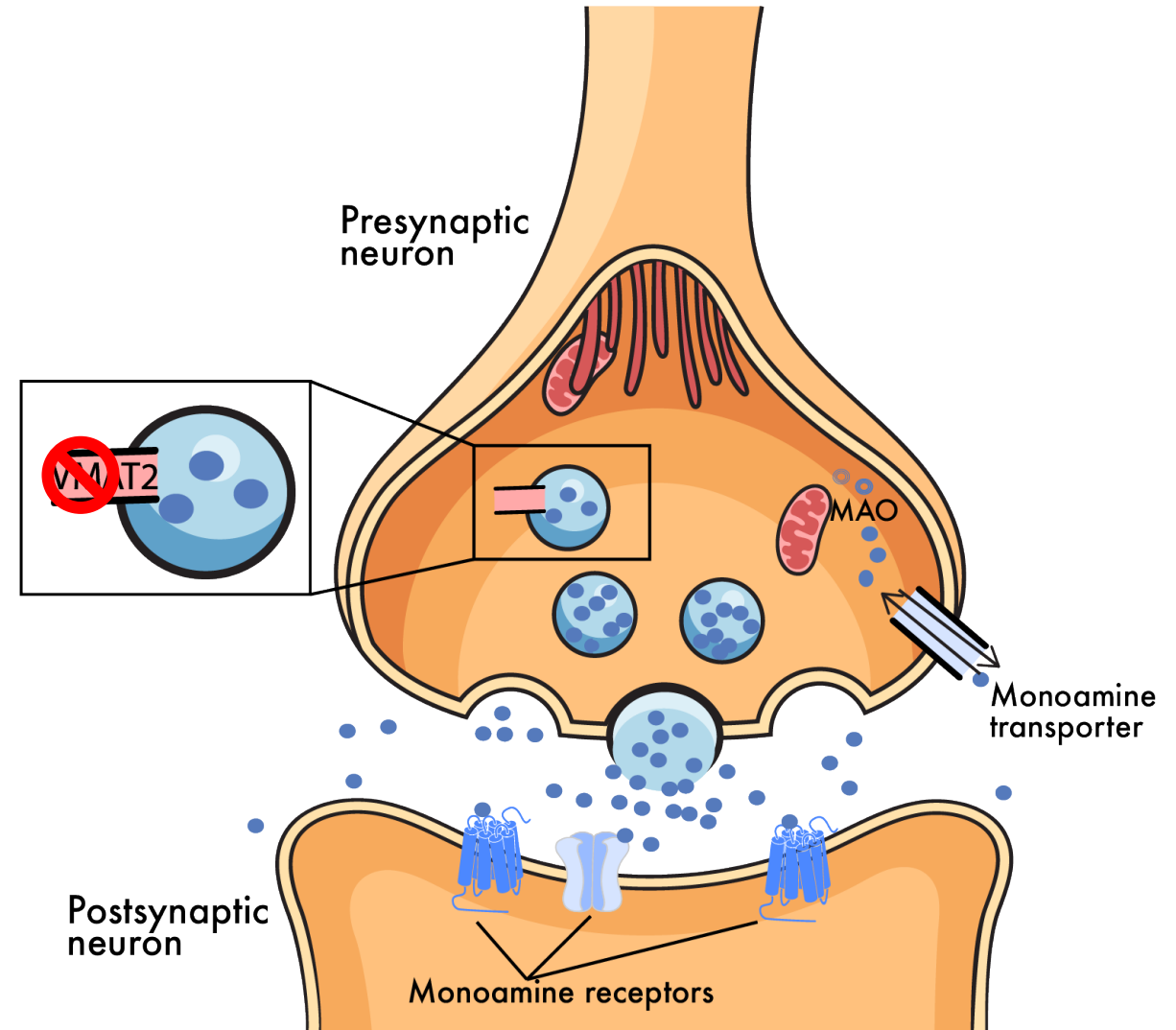
Consider **amantadine as an alternative to anticholinergic medication** to manage DIP

DIP = drug-induced Parkinsonism.

Ward KM, Citrome L. *Neurol Ther.* 2018;7(2):233-248. Vanegas-Arroyave N, et al. *CNS Drugs.* 2024;38(4):239-254.

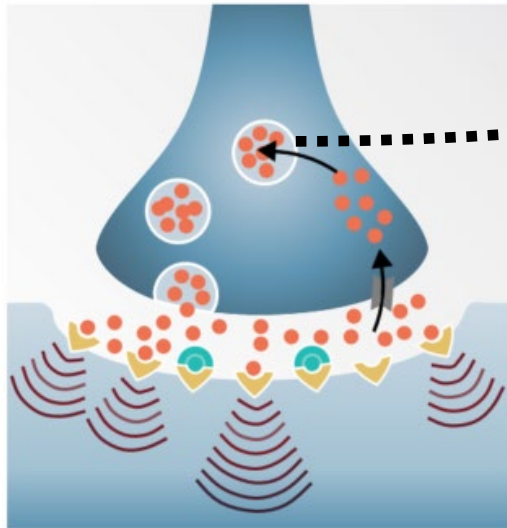
What Are VMAT-2 Inhibitors?

- VMAT-2 packages and transports monoamine neurotransmitters into synaptic vesicles
 - Serotonin
 - Dopamine
 - Histamine
 - Norepinephrine
- Inhibiting VMAT-2 decreases the amount of neurotransmitter released when a neuron fires
- VMAT-2 inhibitors
 - Reduce dopamine release in the dorsal striatum
 - Reduce dyskinetic movements resulting from the **hyperdopaminergic** state of TD

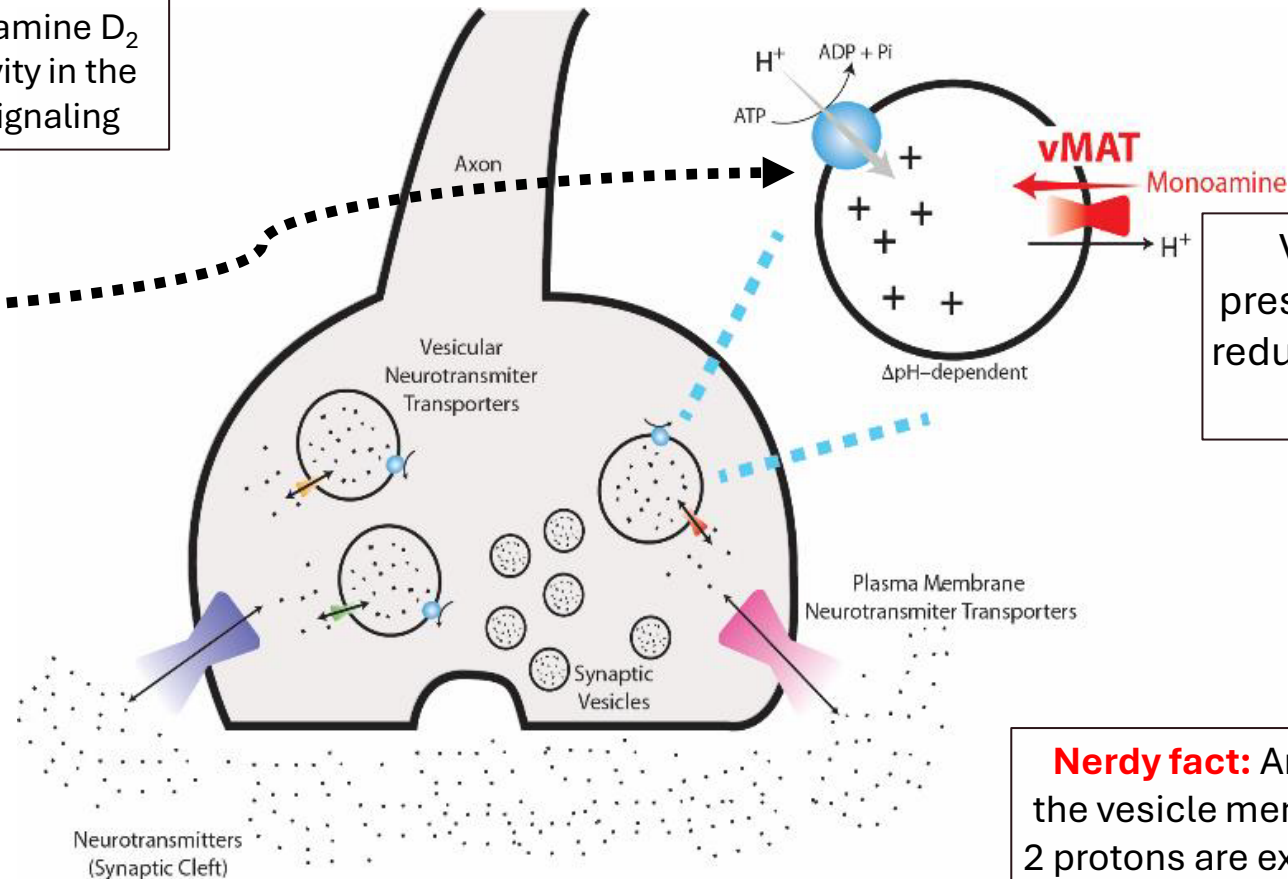


Reversible VMAT-2 Inhibitor: Mechanism of Action

TD Pathophysiology: Postsynaptic dopamine D₂ receptor upregulation and supersensitivity in the indirect pathway – not enough “stop” signaling



 D₂ receptor  Antipsychotic
 Dopamine transporter  Dopamine



VMAT2 inhibitors decrease presynaptic dopamine release by reducing the amount of dopamine packaged into vesicles.

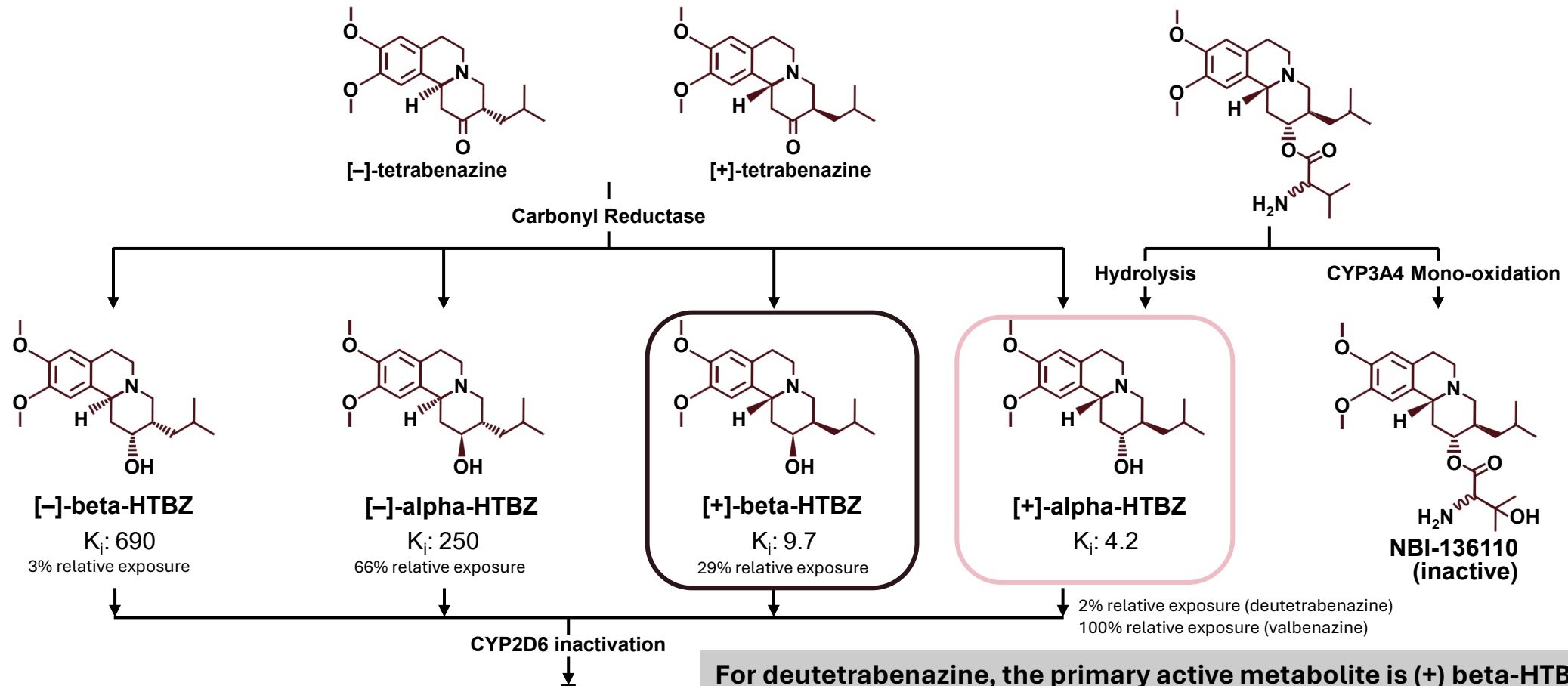
Nerdy fact: An ATP-driven proton pump on the vesicle membrane creates a pH gradient. 2 protons are exchanged for each monoamine molecule transported by VMAT2.

Stahl SM. *CNS Spectr.* 2017;22(6):427-434. Meyer JM. *CNS Spectr.* 2016;21(S1):13-24. Yaffe D, et al. *Proc Natl Acad Sci U S A.* 2016;113(47):E7390-E7398.

Differences in Metabolism of Valbenazine and Tetrabenazine/Deutetabenazine

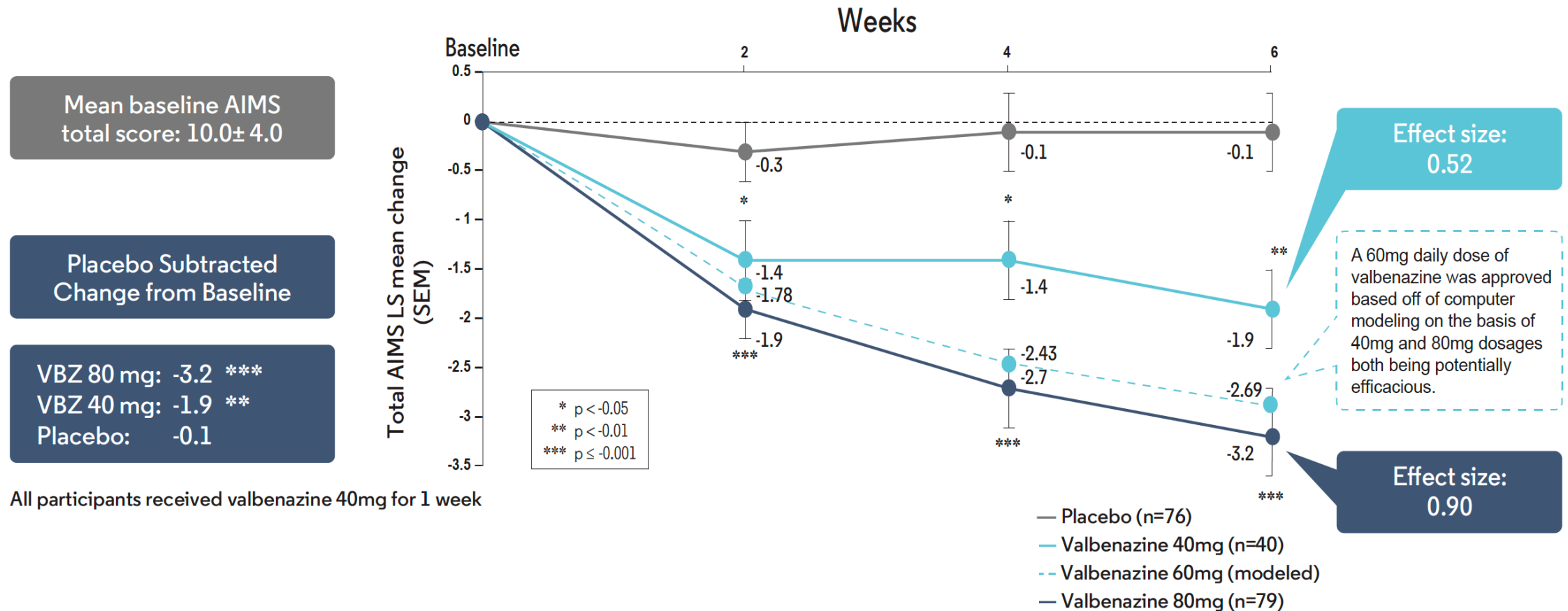
Tetrabenazine or Deutetabenazine

Valbenazine



Valbenazine: Clinical and Real-World Evidence in TD

6-Week Placebo-Controlled Fixed-Dose Study of Valbenazine (KINECT-3)



VBZ = valbenazine.

Hauser RA, et al. *Am J Psychiatry*. 2017;174(5):476-484.

Valbenazine Safety and Tolerability in Short-Term Studies

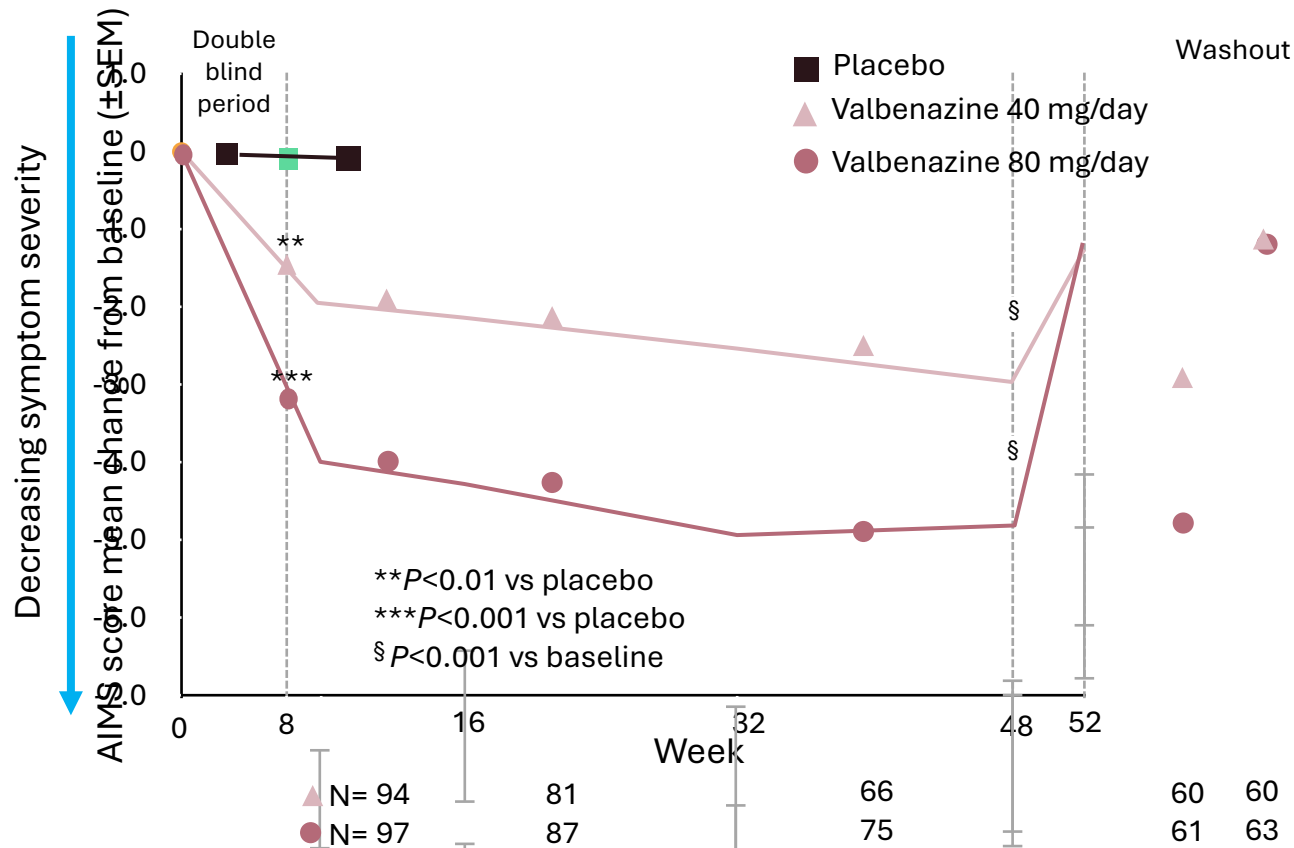
**Adverse Events in 6-Week Valbenazine DBPC Studies in North America
Reported at ≥ 2% and Greater Than Placebo**

Adverse Event	Valbenazine (n=262) (%)	Placebo (n=183) (%)
Somnolence	10.9%	4.2%
Anticholinergic effects	5.4%	4.9%
Balance disorders/fall	4.1%	2.2%
Headache	3.4%	2.7%
Akathisia (akathisia, restlessness)	2.7%	0.5%
Vomiting	2.6%	0.6%
Nausea	2.3%	2.1%
Arthralgia	2.3%	0.5%

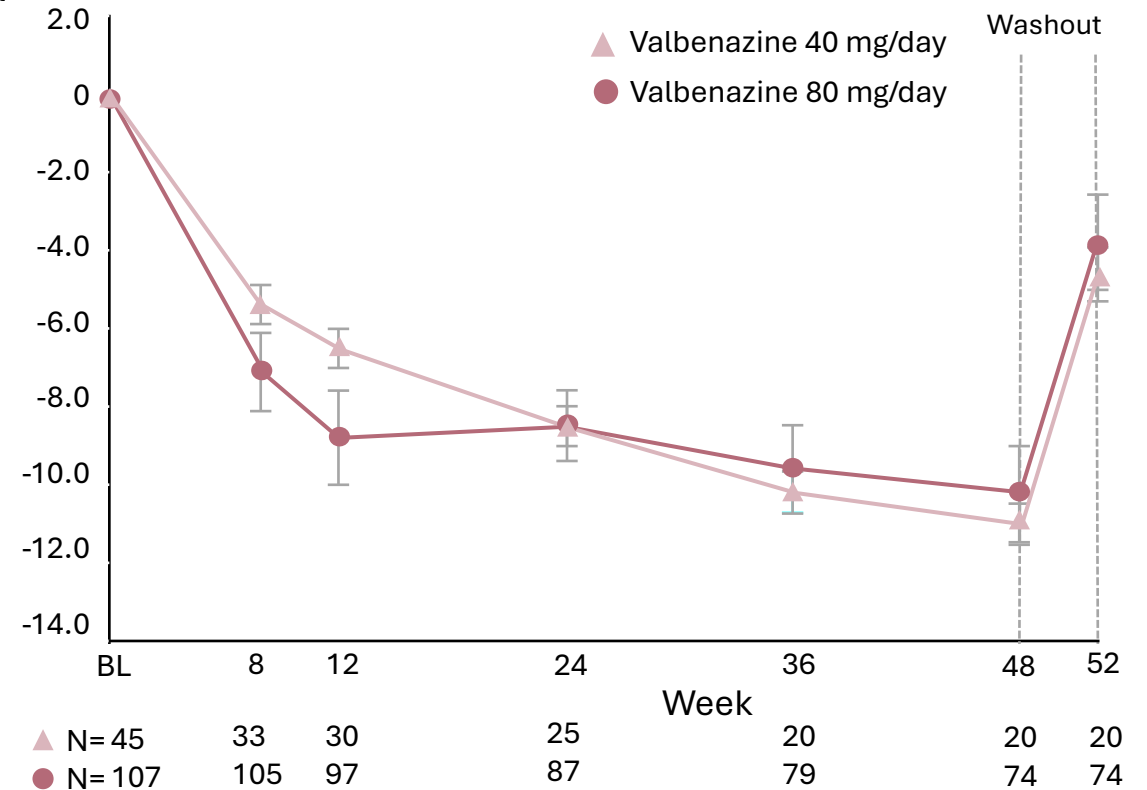
Discontinuation due to AEs occurred in 3% of patients taking valbenazine vs 2% of patients taking placebo

Long-Term Studies of Valbenazine

KINECT-3 Open Label Extension Study



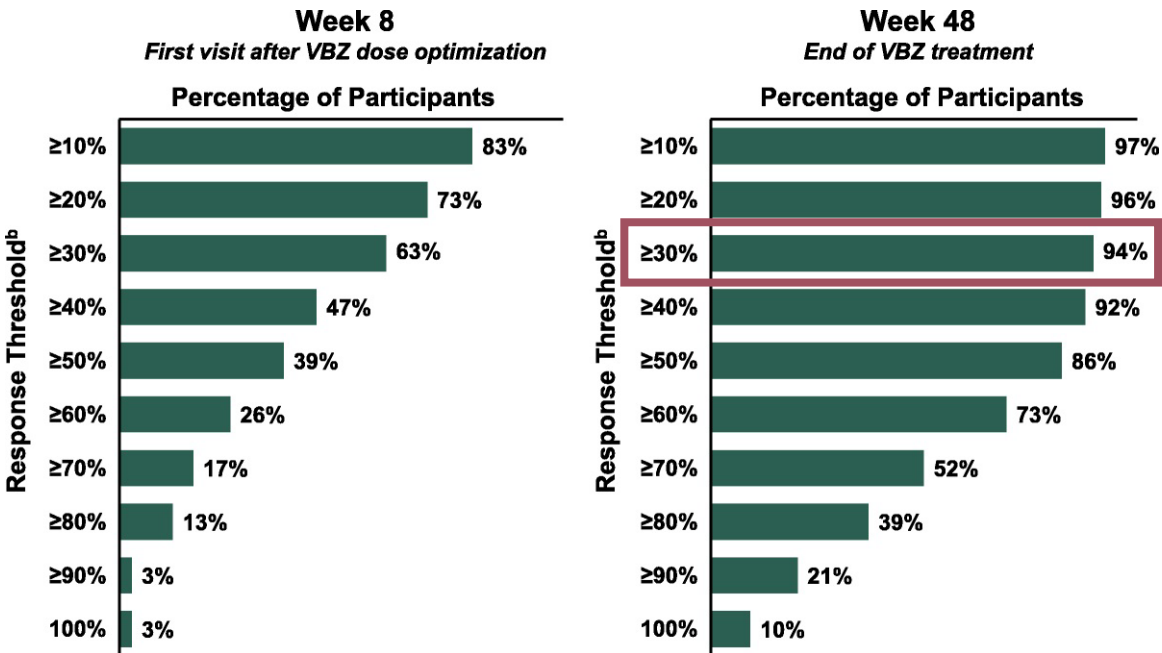
KINECT-4 Study



No new safety signals or concerns emerged in either study

Range of Total AIMS Score Response Thresholds at Week 8 and Week 48 with Valbenazine: KINECT 4 Study

94% treatment completers met the response threshold of $\geq 30\%$ AIMS improvement at week 48



Sustained Response with Valbenazine Treatment

$\geq 50\%$ AIMS improvement at Week 8 and at Week 48 (sustained response)	<div><div>95%</div><div>n/N = 38/40</div></div>
<50% AIMS improvement at Week 8 but $\geq 50\%$ AIMS improvement at Week 48	<div><div>81%</div><div>n/N = 51/63</div></div>
$\geq 50\%$ AIMS improvement at Week 48	<div><div>86%</div><div>n/N = 89/103</div></div>

Formulations and Administration of Valbenazine

Valbenazine	
Dosage forms	<ul style="list-style-type: none">• 40, 60, 80 mg capsules• 40, 60, 80 mg sprinkle capsules
Dosing	<ul style="list-style-type: none">• Start 40 mg once daily with or without food• Increase to 60 or 80 mg/day after 1 week• Sprinkle capsules are broken open and sprinkled on soft food
Drug-drug interactions	<ul style="list-style-type: none">• MAOIs• Strong CYP3A4 inducers• Maximum dose 40 mg with strong CYP2D6 or strong CYP3A4
Contraindications	<ul style="list-style-type: none">• Known hypersensitivity to valbenazine or any components of capsule

The valbenazine sprinkle capsule is bioequivalent to the original formulation and may be sprinkled onto soft foods such as:



apple sauce



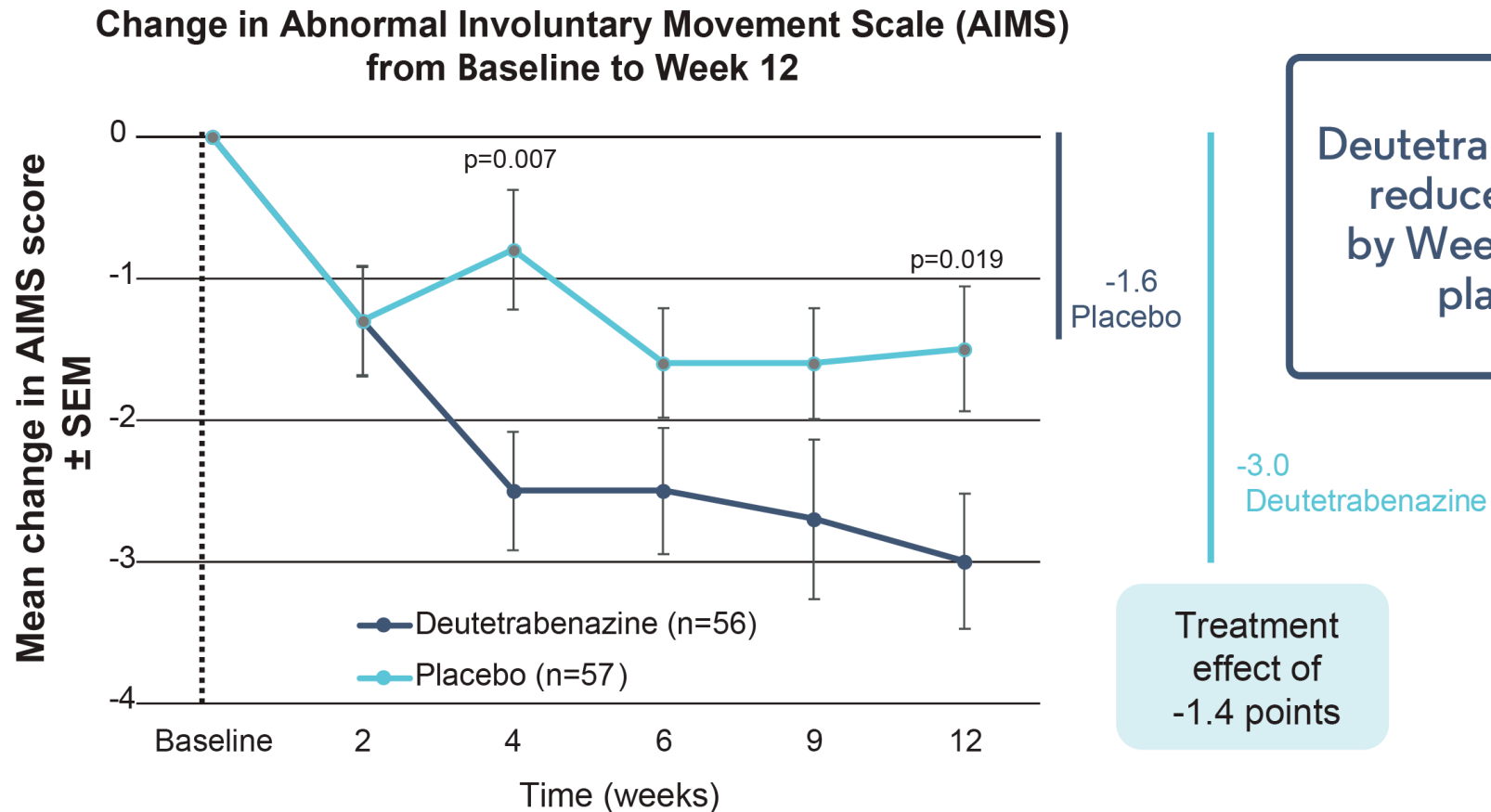
yogurt



pudding

Deutetrabenazine: Clinical and Real-World Evidence in TD

Flexible-Dose Study of Deutetrabenazine (ARM-TD)



Deutetrabenazine significantly reduced AIMS total score by Week 12 compared with placebo (p=0.019)

Mean dose at the end of titration was 38.8 mg/day

Deutetrabenazine Safety and Tolerability in Short-Term Studies

Adverse Reaction	Deutetrabenazine (n=279)	Placebo (n=131)
Headache	5%	8%
Somnolence	4%	7%
Diarrhea	4%	4%
Nasopharyngitis*	4%	2%
Fatigue	4%	5%
Insomnia*	4%	1%
Anxiety	4%	5%
Upper respiratory tract infection	3%	4%
Dry mouth	3%	5%
Nausea	2%	7%
Weight increased	2%	3%
Urinary tract infection	2%	2%
Depression/Dysthymic Disorder	2%	1%
Akathisia/Agitation/Restlessness*	2%	1%
Arthralgia	2%	1%

* AEs occurring at a greater rate in patients taking deutetrabenazine than in patients taking placebo

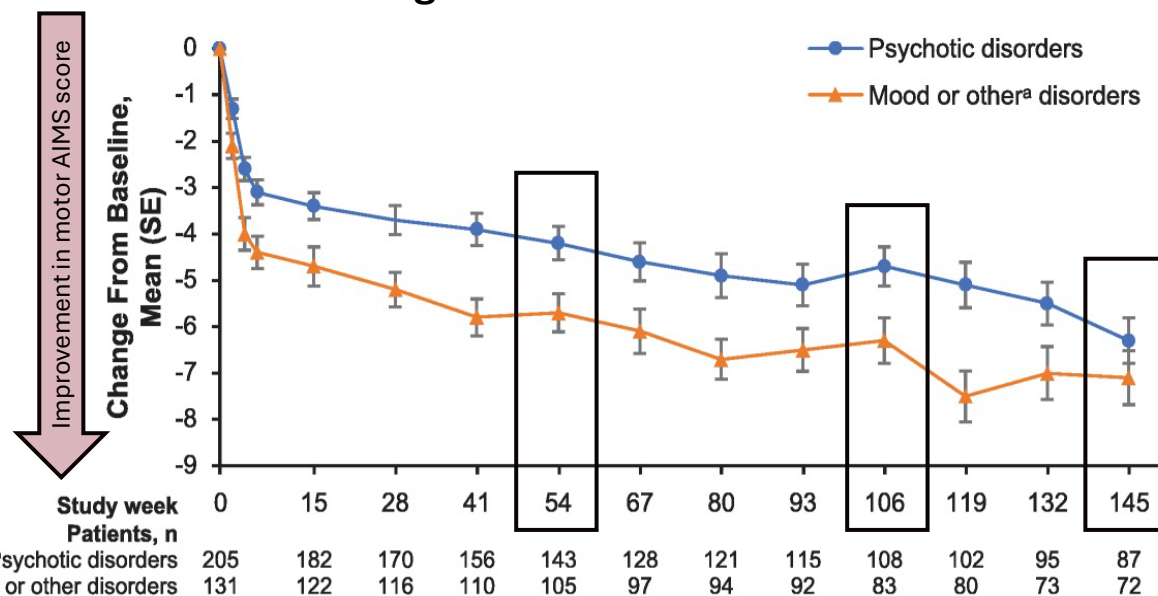
Discontinuation due to AEs occurred in 4% of patients taking deutetrabenazine vs 3% of patients taking placebo

AE = adverse effect.

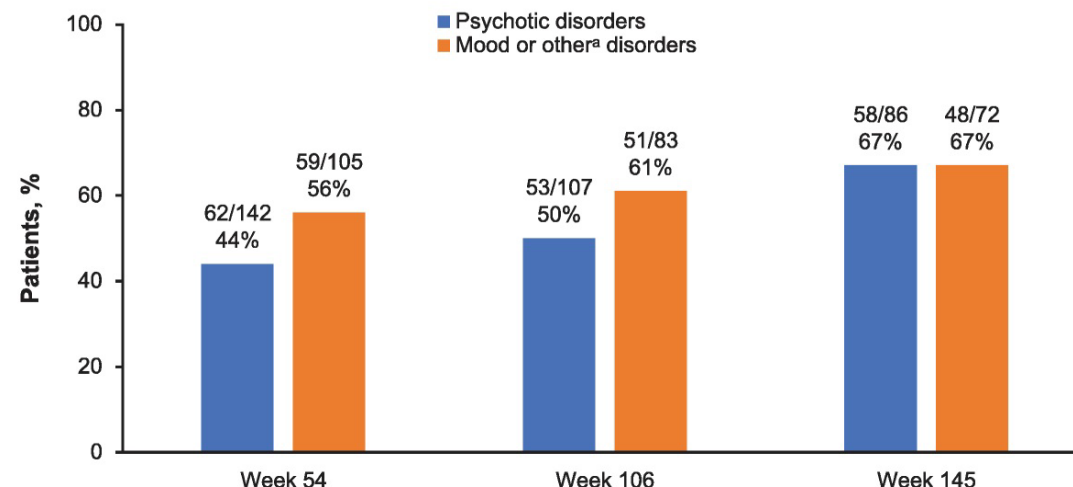
Anderson KE, et al. *Lancet Psychiatry*. 2017;4(8):595-604. Fernandez HH, et al. *J Neurol Neurosurg Psychiatry*. 2019;90(12):1317-1323.

Deutetrabenazine Improves TD Over 3 Years Independent of Diagnosis...

Change in Total Motor AIMS Score



Proportion of Patients Achieving $\geq 50\%$ Improvement in Total Motor AIMS Score

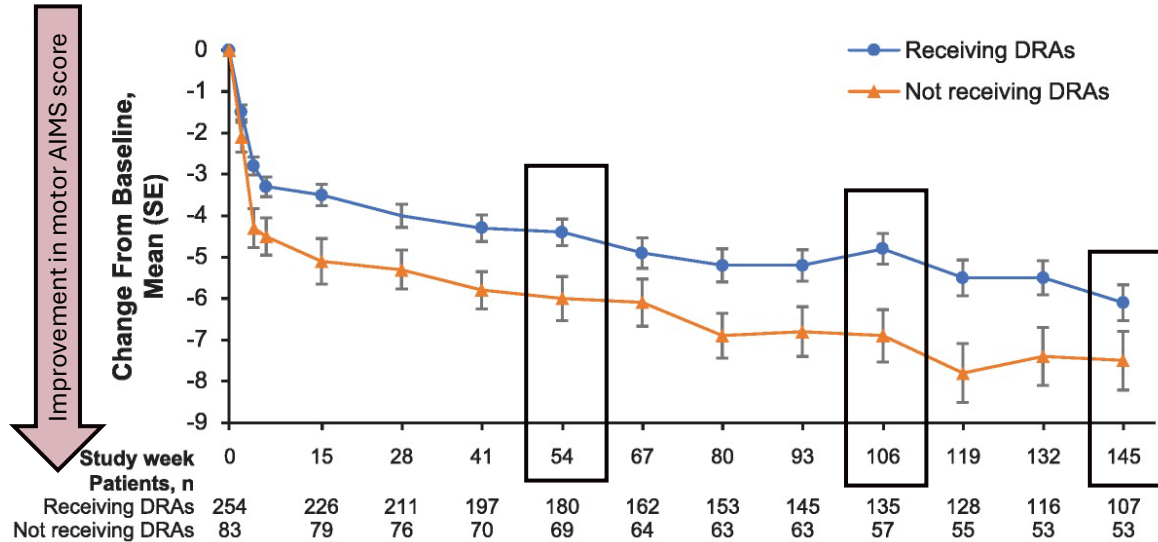


Deutetrabenazine produced **sustained, clinically meaningful reductions in AIMS scores over 3 years**, with similar long-term benefits across both psychotic and mood/other disorder populations.

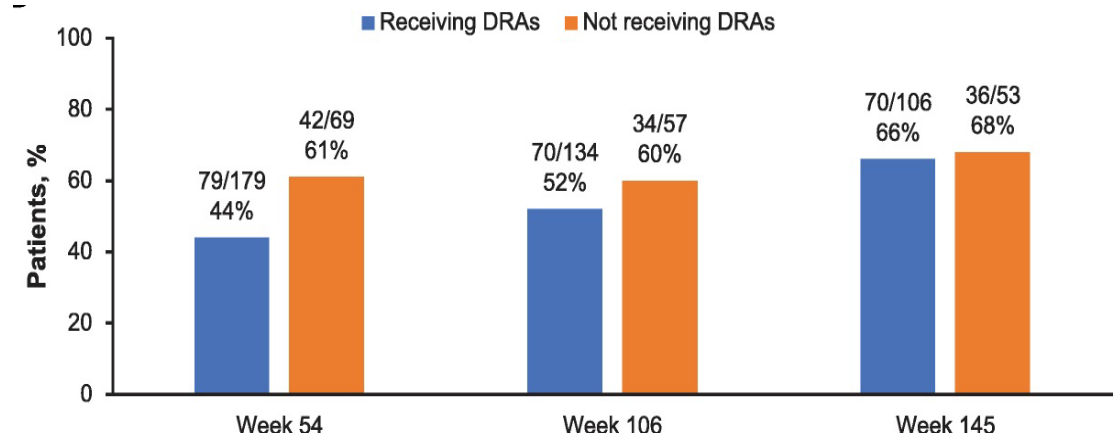
^aExamples of other disorders include abdominal discomfort, alcohol withdrawal syndrome, gastroesophageal reflux disease, insomnia, neurosis, and tic.
Hauser RA, et al. *J Clin Psychopharmacol*. 2024;44(4):386-396.

...And Independent of DBRA Use

Change in Total Motor AIMS Score



Proportion of Patients Achieving $\geq 50\%$ Improvement in Total Motor AIMS Score



Nominal P values for the comparison of the DRA subgroups were 0.018, 0.348, and 0.813 at weeks 54, 106, and 145, respectively, and were not controlled for multiplicity.

Deutetrabenazine is associated with **durable improvement in AIMS scores over 3 years**, with similar efficacy observed irrespective of ongoing dopamine receptor antagonist use.

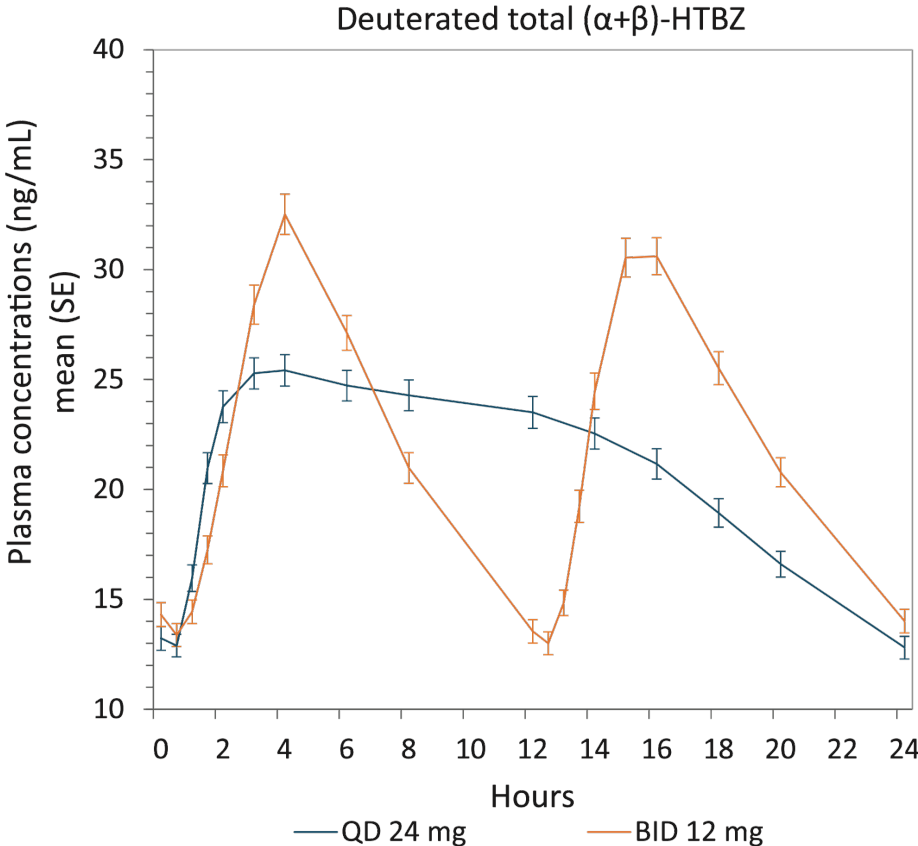
DRA=Dopamine Receptor Antagonist.

Hauser RA, et al. *J Clin Psychopharmacol.* 2024;44(4):386-396.

Pharmacology and Formulations of Deutetrabenazine

	Deutetrabenazine XR
Dosage forms	Tablets: 6 mg, 12 mg, 18 mg, 24 mg, 30 mg, 36 mg, 42 mg, and 48 mg
Dosing	Start 12 mg qD once daily with or wi/o food, increase by 6 mg weekly to a at least 24 mg qD
Active metabolites	(+)deuterated β -HTBZ (primary), (+)deuterated α -HTBZ
CYP Interactions	Max dose 36 mg with strong 2D6 inhibitors. Not studied in 2D6 PM, but expected to be comparable to strong 2D6 inhibition
Contraindications	Use with MAOIs or other VMAT inhibitors, Suicidal, or inadequately treated depression in Huntington's, Hepatic impairment

Deutetrabenazine XR Once Daily is Bioequivalent to Deutetrabenazine BID



XR = extended release; BID = twice daily; QD = once daily; PM = poor metabolizer; MAOI = monoamine oxidase inhibitor.
Deutetrabenazine PI. Drugs@FDA: FDA-Approved Drugs. Accessed February 2025.
https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208082s016s017lbl.pdf. Sunzel EM, et al. *Clin Pharmacol Drug Dev.* 2024;13(3):224-232.

Overview of VMAT-2 Inhibitors Approved for TD

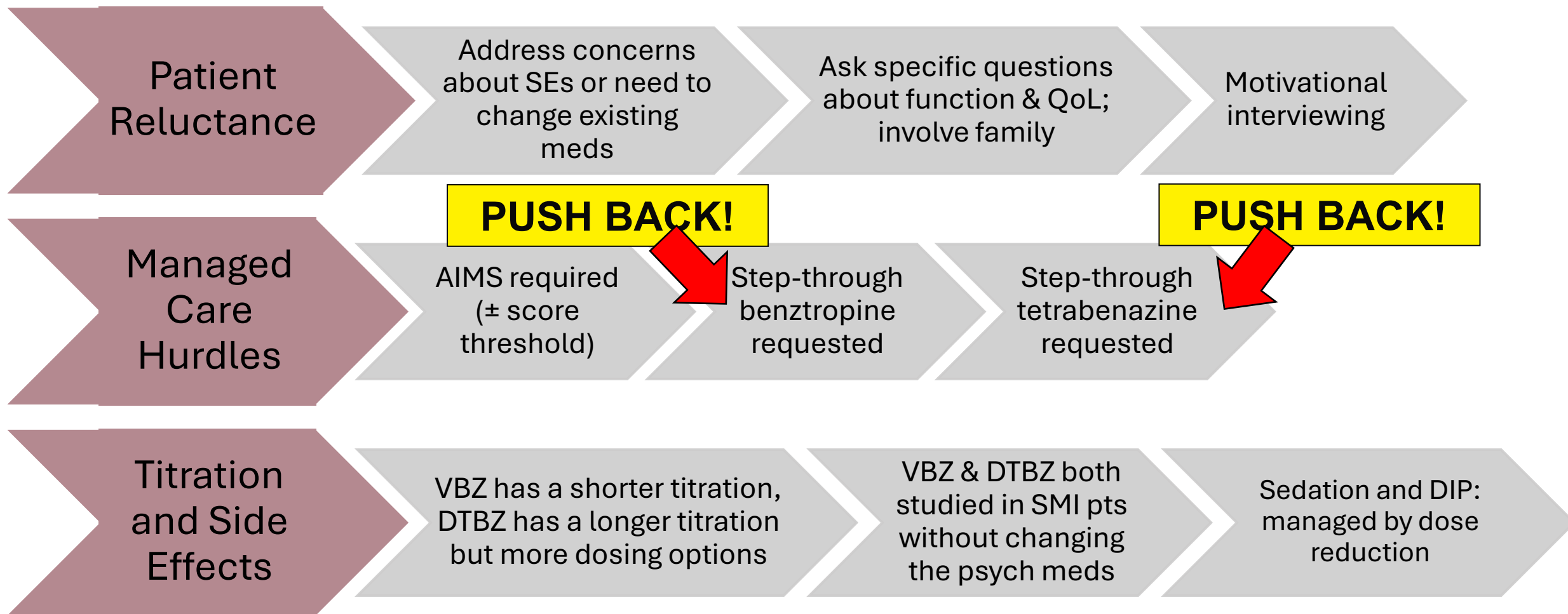
	Valbenazine	Deutetrabenazine Extended-Release
Dosage forms	Capsules and Sprinkle Capsules: 40 mg, 60 mg, and 80 mg	Tablets: 6 mg, 12 mg, 18 mg, 24 mg, 30 mg, 36 mg, 42 mg, and 48 mg; once daily with or without food
Metabolism/ CYP Interactions	Hepatic – Max dose 40 mg with strong CYP 2D6 or 3A4 inhibitors or in 2D6 poor metabolizers (PM); do not give with CYP 3A4 inducers	Hepatic – Max dose 36 mg with strong CYP 2D6 inhibitors. Not studied in 2D6 PM but effects expected to be comparable to strong 2D6 inhibition
Active metabolites	(+)α-HTBZ	(+)deuterated β-HTBZ (primary), (+)deuterated α-HTBZ
Titration	40 mg qD x 1 week, increasing to 80 mg qD	12 mg qD, increasing weekly by 6 mg based on efficacy and tolerability

Both deutetrabenazine and valbenazine are efficacious and well-tolerated in treating TD regardless of psychiatric diagnosis

Neither requires discontinuation or change in antipsychotic or psychotropics

Neither was shown to worsen psychiatric illness or increase suicidality in TD trials; both have warnings about DIP

Using Novel VMAT-2 Inhibitors: Practical Concerns



Comment: NEVER abruptly discontinue anticholinergic medication

SE = side effect; QoL = quality of life; VBZ = valbenazine; DTBZ = deutetrabenazine; SMI = serious mental illness; pts = patients.

Key Learning Points

- VMAT-2 inhibitors reduce the packaging of monoamine neurotransmitters into synaptic vesicles
- There are two VMAT-2 inhibitors approved in the US for the treatment of adults with TD: **valbenazine** and **deutetrabenazine**
 - Both are efficacious and well-tolerated in short- and long-term studies
- Initiation of VMAT-2 inhibitor **does not require discontinuation or change of antipsychotic therapy**

Newer Tools Focused on Patient-Reported Functional and QoL Impacts

Beyond the AIMS: Tardive Dyskinesia Impact Scale (TDIS)



TDIS is a validated 11-item patient-reported questionnaire that assesses how TD affects daily function over the previous 7 days.

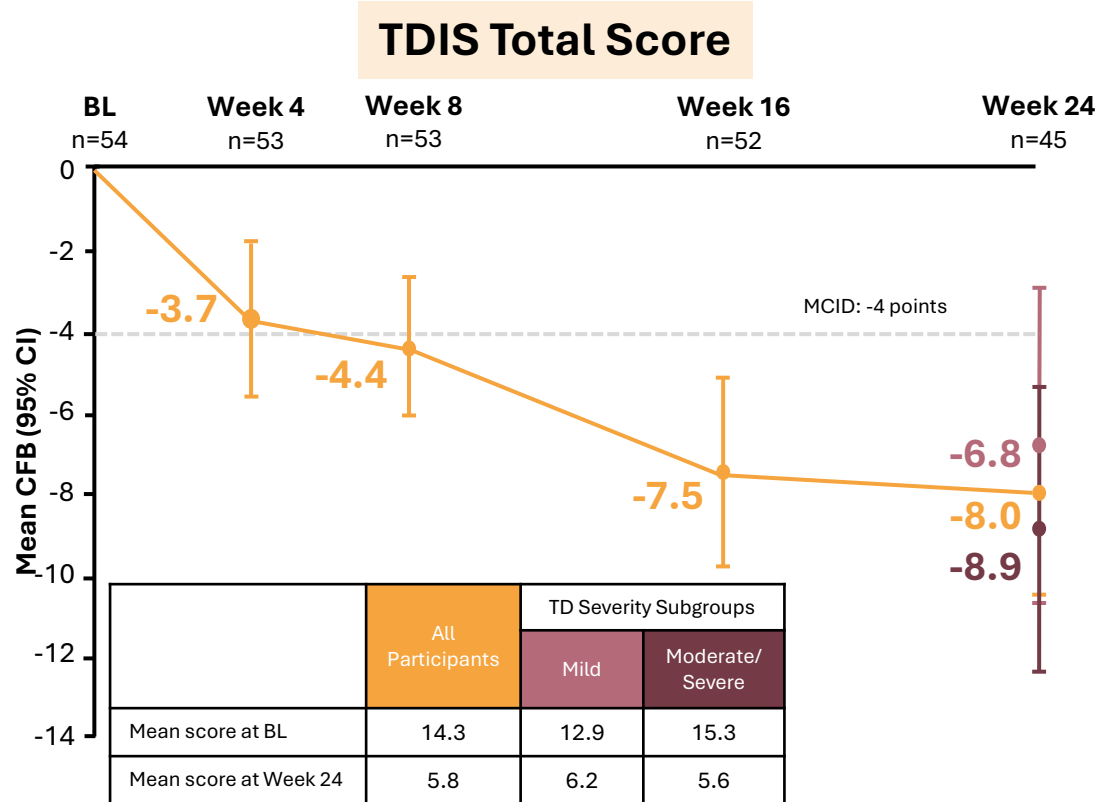
- Designed to fill a gap, as there is no validated patient-reported outcome measure specific to TD
- 11-item questionnaire captures physical and socio-emotional effects of TD
- TDIS has been shown to be responsive to changes in treatment (e.g., decrease in TD movements, decrease in AIMS score)

Domain	TDIS item	Corresponding TDRS item
Mouth/throat function	1. Speech	Item 2. Speech
	2. Mouth noises	Not applicable
	3. Swallowing	Item 3. Chewing and swallowing
Dexterity	4. Gripping	Item 4. Eating tasks Item 5. Dressing Item 6. Hygiene Item 8. Hobbies
	5. Writing	Item 7. Handwriting
Mobility	6. Walking	Item 9. Walking and balance
	7. Balance	
Pain	8. Leg pain	Item 12. Dyskinesia pain
Social	9. Unwanted attention	Item 10. Public and social settings
Emotional	10. Embarrassed	Not applicable
	11. Self-conscious	

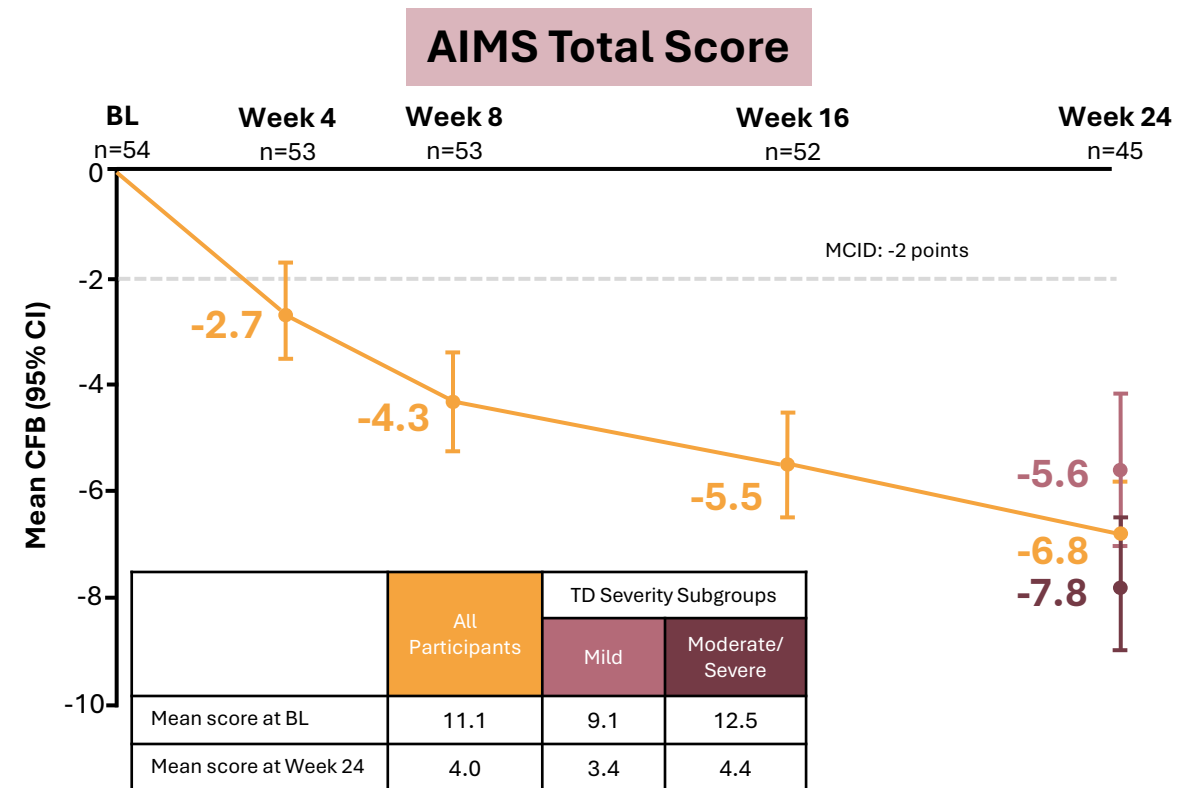
TDIS = Tardive Dyskinesia Impact Scale.

Farber RH, et al. *J Patient Rep Outcomes*. 2024;8(1):2.

Valbenazine Improves the Impacts and Symptoms of TD: Results From the Phase 4 KINECT-PRO™ Study



TDIS total score ranges from 0 to 44, with higher scores indicating worse impact. The total score is summed from the 11-item scores, each of which range from 0 (no impact) to 4 (extreme impact).



AIMS total score ranges from 0 to 28, with higher scores indicating greater symptom severity. AIMS total score is comprised of the summed scores of AIMS items 1-7, each of which rate dyskinesia severity from 0 (no dyskinesia) to 4 (severe dyskinesia).

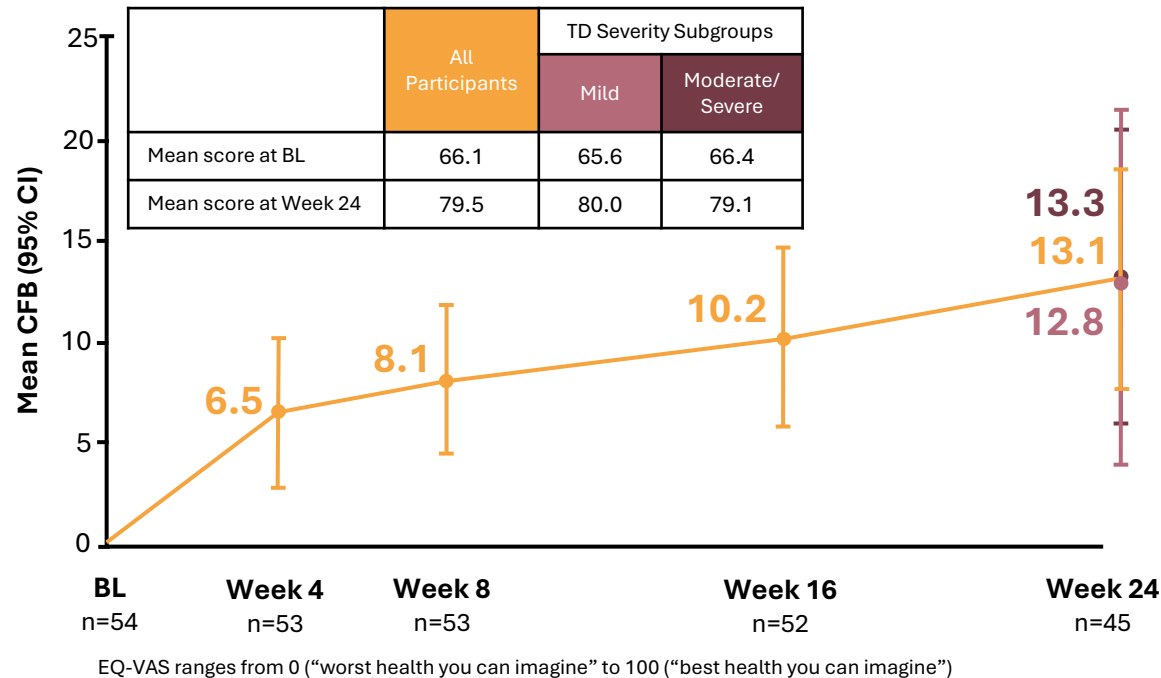
Valbenazine significantly reduced TDIS and AIMS Total Scores from baseline (MCID=-4 and -2, respectively)

BL = baseline, CI = confidence interval; CFB = change from baseline; MCID = minimal clinically important difference

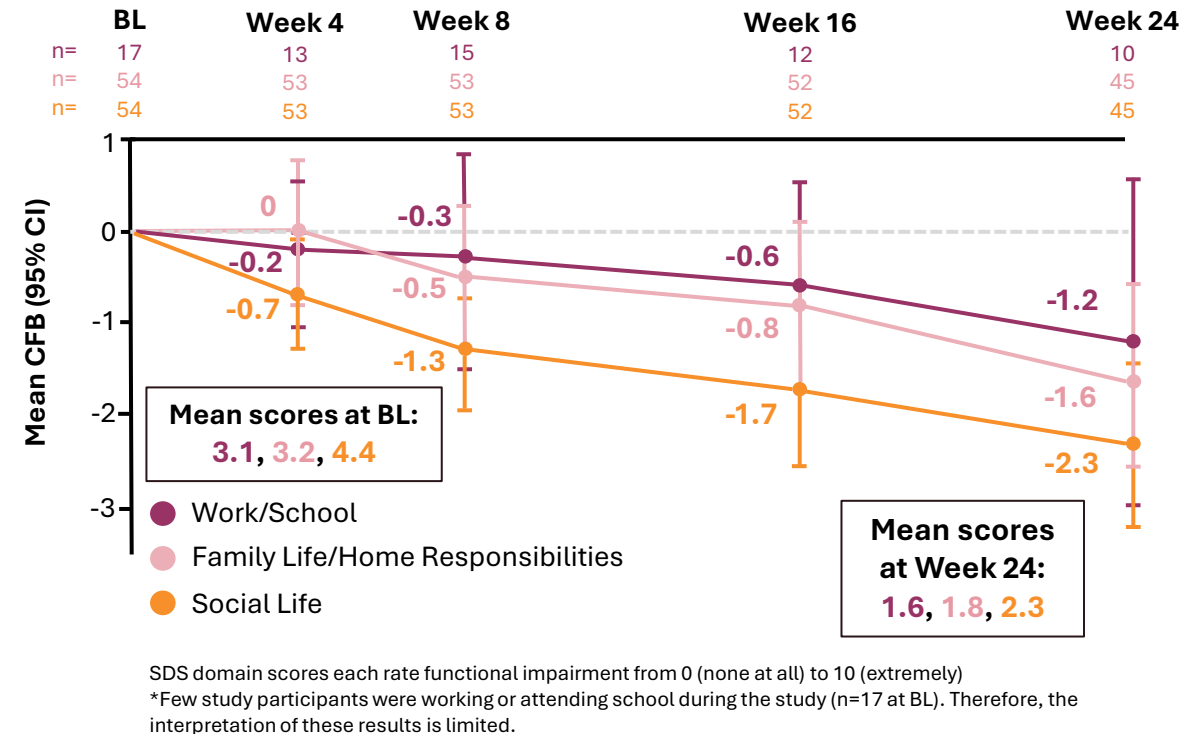
Correll CU, et al. *CNS Spectrums*. Published online 11 August 2026.

Valbenazine Improves the Impacts and Symptoms of TD: Results From the Phase 4 KINECT-PRO™ Study

EQ-VAS Score

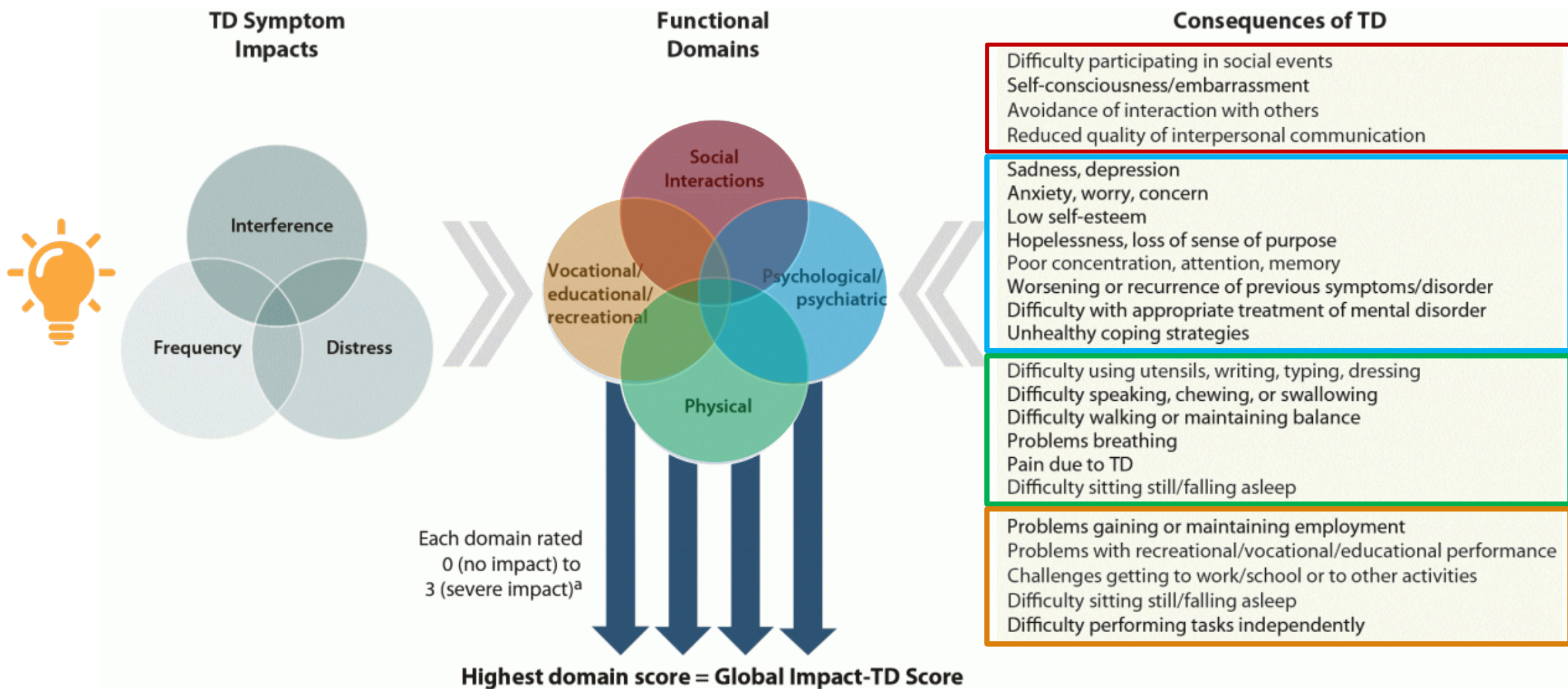


SDS Domain Score



Valbenazine significantly improved self-reported health-related QoL and reduced disability impairments

IMPACT-TD Scale: Design and Real-World Validation



Numerical ratings were done in the trial but are not required for use in clinical practice!

Interim Analysis of Real-World IMPACT-TD Registry Indicates that Mild Movements Can Have Major Impact

Percentage of Patients With Moderate/Severe Impact per Baseline Body Region AIMS (Score of 1 or 2)

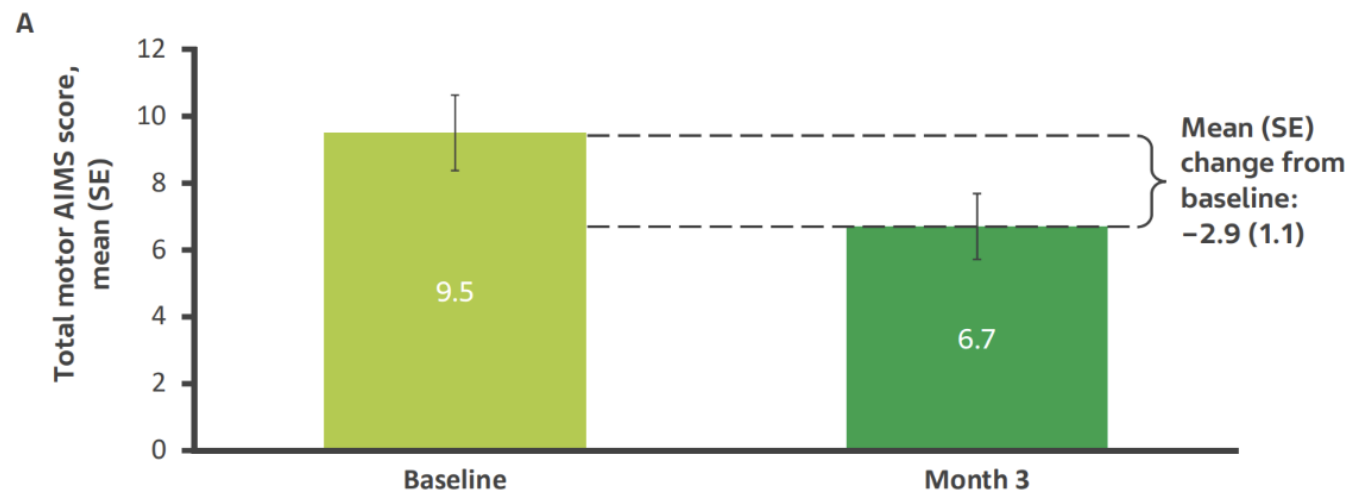
Body region AIMS score, 1 or 2	IMPACT-TD ClinRO domains				
	Social	Psychological	Physical	Vocational	Global
Muscles of facial expression (n=260)	49	58	45	47	71
Lips and perioral region (n=225)	52	59	48	49	72
Jaw (n=201)	53	57	51	50	74
Tongue (n=238)	52	67	52	58	81
Upper extremities (n=236)	50	62	45	53	77
Lower extremities (n=174)	49	55	52	46	74
Trunk (n=108)	58	61	56	47	75

The percentages of patients shown in the table cells are coded from green (0%) to red (100%)

Among participants with an **individual** AIMS item score of **1 or 2** in any body region, **71% to 81%** experienced **moderate/severe global TD impact**.

Analyses from the IMPACT-TD Registry Indicate that Treating TD with a VMAT2 Inhibitor Can Improve QoL

Interim results among individuals newly initiating deutetrabenazine (N=26) indicate **improvement in abnormal movement severity (AIMS)** and **patient-reported QoL**



^aAIMS data presented for n=26; one participant excluded due to missing baseline data.

Up to **77% of participants** experienced meaningful improvements in specific life areas impacted by TD

QoL = quality of life

Finkbeiner S, et al. *Real-world use of deutetrabenazine reduces tardive dyskinesia severity and improves quality of life: patient-reported outcomes in the IMPACT-TD study*. Poster presented at: Neuroscience Education Institute Congress; November 6–9, 2025; Colorado Springs, CO.

Key Learning Points



- TD has impacts across physical, psychological, social, and vocational/educational/recreational domains
- Tardive Dyskinesia Impact Scale (TDIS) is a patient-reported 11-item questionnaire designed to assess **how TD affects daily function over the previous 7 days**
- The IMPACT-TD scale assesses these functional domains based on **interference, distress, and/or frequency**

Faculty and Patient/Caregiver Panel Discussion

Selecting, Adjusting, and Switching Between VMAT-2 Inhibitors

Drug-Drug Interactions and Contraindications (e.g., Hepatic Impairment)

Managing Adverse Events

VMAT2 Inhibitors for Tardive Dyskinesia

Choosing Between Valbenazine and Deutetrabenazine
Great News: Both Work!

2

FDA-approved
VMAT2 inhibitors

A

Level of evidence
for TD treatment

0

Head-to-head
trials exist

Selecting Between Agents

Feature	Valbenazine	Deutetrabenazine
Dosing frequency	Once daily	Twice daily (or once daily XR)
Titration	40 mg → 80 mg after 1 week	6 mg BID, +6 mg/day weekly (max 48 mg)
Food requirement	With or without food	Deutetrabenazine: with food; XR: either
Hepatic impairment	Reduce to 40 mg (moderate/severe)	Contraindicated
CYP2D6 poor metabolizers	Max 40 mg/day	Max 36 mg/day
Key CYP interactions	CYP2D6 and CYP3A4	Primarily CYP2D6

 ***Hepatic impairment is a critical differentiator***

Drug Interactions, Contraindications & Switching

Contraindications and Other Important Restrictions

- MAOIs:
 - Valbenazine: avoid concomitant use and use within 14 days after discontinuing an MAOI.
Deutetrabenazine: concomitant MAOI use is contraindicated; the therapies should be separated by 14 days.
- Reserpine: deutetrabenazine contraindicated; wait ≥ 20 days after stopping
- Concomitant VMAT2 inhibitors: deutetrabenazine contraindicated with tetrabenazine or valbenazine
- Deutetrabenazine specific contraindications: hepatic impairment, Huntington's patients who are suicidal or inadequately treated depression. Valbenazine: hypersensitivity

Switching Between Agents

No clinical trial-validated conversion or label-specified washout protocol exists for switching between valbenazine and deutetrabenazine. Avoid concurrent administration and initiate the new agent using its labeled starting dose; individualize the timing of the switch.

Managing Adverse Effects



Parkinsonism

Reduce dose or discontinue; distinguish from antipsychotic-induced parkinsonism.



Somnolence/ Sedation

Review sedating medications; reduce dose if clinically significant.



Akathisia

Consider dose reduction; distinguish from antipsychotic-related akathisia.



QTc Prolongation

Avoid in congenital long-QT syndrome; assess QTc in patients with additional risk factors.



Depression/Suicidality

Both carry boxed warnings for patients with Huntington disease; deutetrabenazine is contraindicated with suicidality or inadequately treated depression. No increased risk was identified in short-term TD trials, although data remain limited.

Patient & Caregiver Advocate:

Living with TD and Navigating Effective Treatment

Shared-Decision-Making with Patients and Caregivers

Patient and Caregiver Resources

Caregiver Action Network (CAN)

is the nation's leading family caregiver organization. It works to improve the quality of life for family caregivers who care for loved ones with chronic conditions, disabilities, or diseases, including **TARDIVE DYSKINESIA**.



WHAT IS TD?

A movement condition from long-term psychiatric medications causing involuntary, repetitive movements in the face, mouth, or body.

EARLY SIGNS TO WATCH	WHAT INCREASES RISK	WHAT YOU CAN DO
<i>Small, repeated movements, including:</i> <ul style="list-style-type: none">Lip smackingGrimacingFinger tappingTongue movingRapid blinkingBody rocking <i>May come and go; worsen with stress or fatigue</i>	Long-term antipsychotic use Most common trigger Older (1st-gen) medications Higher-risk profile Higher doses + longer treatment Risk grows over time <i>TD can appear months or years after starting or stopping medication.</i>	TRACK Document movements, medication changes, side effects SPEAK UP Tell the doctor what you see. Ask: Could this be TD? ASK ABOUT OPTIONS Safer meds? Adjust treatment? Treatments for TD?

KEY RESOURCES

Caregiver Action Network caregiveraction.org/understanding-tardive-dyskinesia

Patient Advocate Foundation patientadvocate.org

Movement Disorder Policy Coalition movementdisorderspolicy.org

Treatment Advocacy Center treatmentadvocacycenter.org

National Alliance on Mental Illness (NAMI) nami.org

Depression and Bipolar Support Alliance dbsalliance.org

Dystonia Medical Research Foundation dystonia-foundation.org



Visit the Resource Center



- Patient videos
 - Expert insights
 - Latest news
 - Complimentary CME
- ...and more!

<https://www.TD-360.com>

or scan this
QR code



Practical Take-Aways



Incorporate regular TD screening (e.g., AIMS at baseline and periodically) for all patients receiving dopamine receptor–blocking agents because early detection improves long-term neurologic and treatment outcomes



Even mild TD can significantly impair function, social interaction, and quality of life, so clinicians should ask targeted questions about daily activities and psychosocial effects



Consider VMAT-2 inhibitors (e.g., valbenazine or deutetrabenazine) to reduce dyskinetic movements while maintaining necessary antipsychotic therapy

Q&A

