tardive dyskinesia360

AIMS Is Nothing but a Number:

Focusing on Function and Family in Tardive Dyskinesia

MasterClass

Supported by independent educational grants from Neurocrine Biosciences, Inc and Teva Pharmaceuticals.

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Faculty Disclosures

- **Kristian Dambrino, DNP, PMHNP-BC:** Advisory Board—Alkermes, Axsome Therapeutics Inc., Johnson & Johnson, Neurocrine Biosciences; Consultant—AbbVie Inc., Axsome Therapeutics Inc., Neurocrine Biosciences; Speaker Bureau—Alkermes, Axsome Therapeutics Inc., Bristol-Myers Squibb, Intra-Cellular Therapies (Johnson & Johnson), Luye Pharma Group, Neurocrine Biosciences
- **Greg Mattingly, MD:** Consultant – AbbVie, Acadia, Akilli, Alkermes, Angelini, Axsome, Biogen, Boehringer Ingelheim, Cerevel, Colegium, Corium, Eisai, Intracellular, Johnson & Johnson, Liva Nova, Lumos Labs, Lundbeck, Neurocrine, Noven, Otsuka, Redax, Relmada, Revibe, Roche, Sage, Sirona, Sunovion, Supernus, Takeda, Teva, and Tris Pharma; Research – AbbVie, Acadia, Alkermes, Akilli, Alto Therapeutics, Avanir, Axsome, Boehringer Ingelheim, Cingulate, Click Therapeutics, Corium, Emalex, Idorsia, Intracellular, Johnson & Johnson, Lumos Labs, Medgenics, Neurocrine, NLS Pharma, Redax, Relmada, Roche, Sage, Sirtsei, Sumitomo, Sunovion, Supernus, Takeda, and Teva; Speakers Bureau – AbbVie, Alkermes, Angelini, Axsome, Corium, Intracellular, Ironshore, Johnson & Johnson, Lundbeck, Neurocrine, Noven, Otsuka, Sunovion, Supernus, Takeda, Teva and Tris Pharma

Disclosure

- 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).

- Applicable CME staff have no relationships to disclose relating to the subject matter of this activity.

- This activity has been independently reviewed for balance.

Learning Objectives

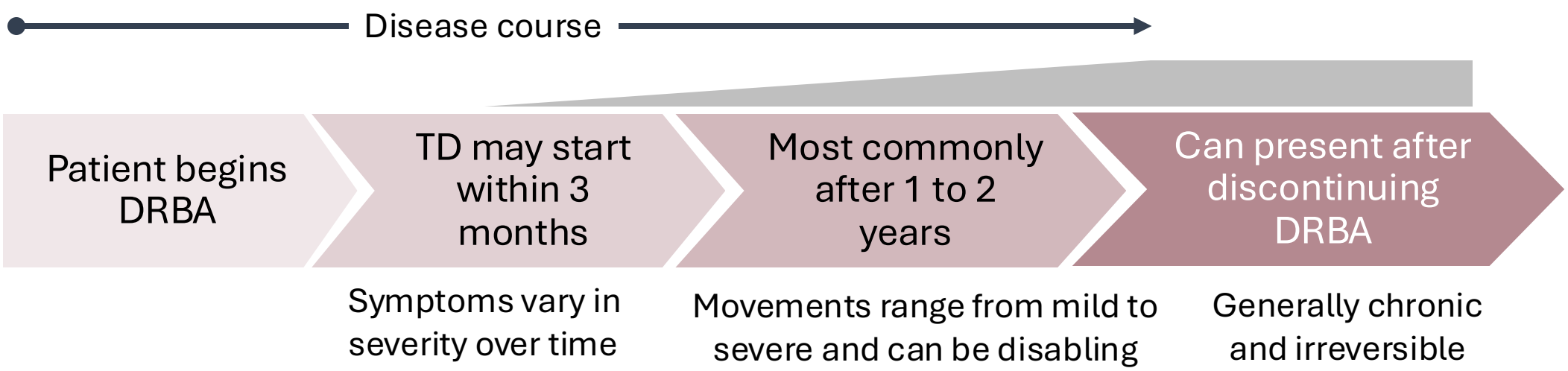
- Define and describe the importance of functional and QoL restoration as long-term treatment goals for patients with TD as well as their caregivers
- Identify subtle manifestations of TD, differentiate it from other movement disorders, and utilize validated tools to assess its functional and QoL impacts 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

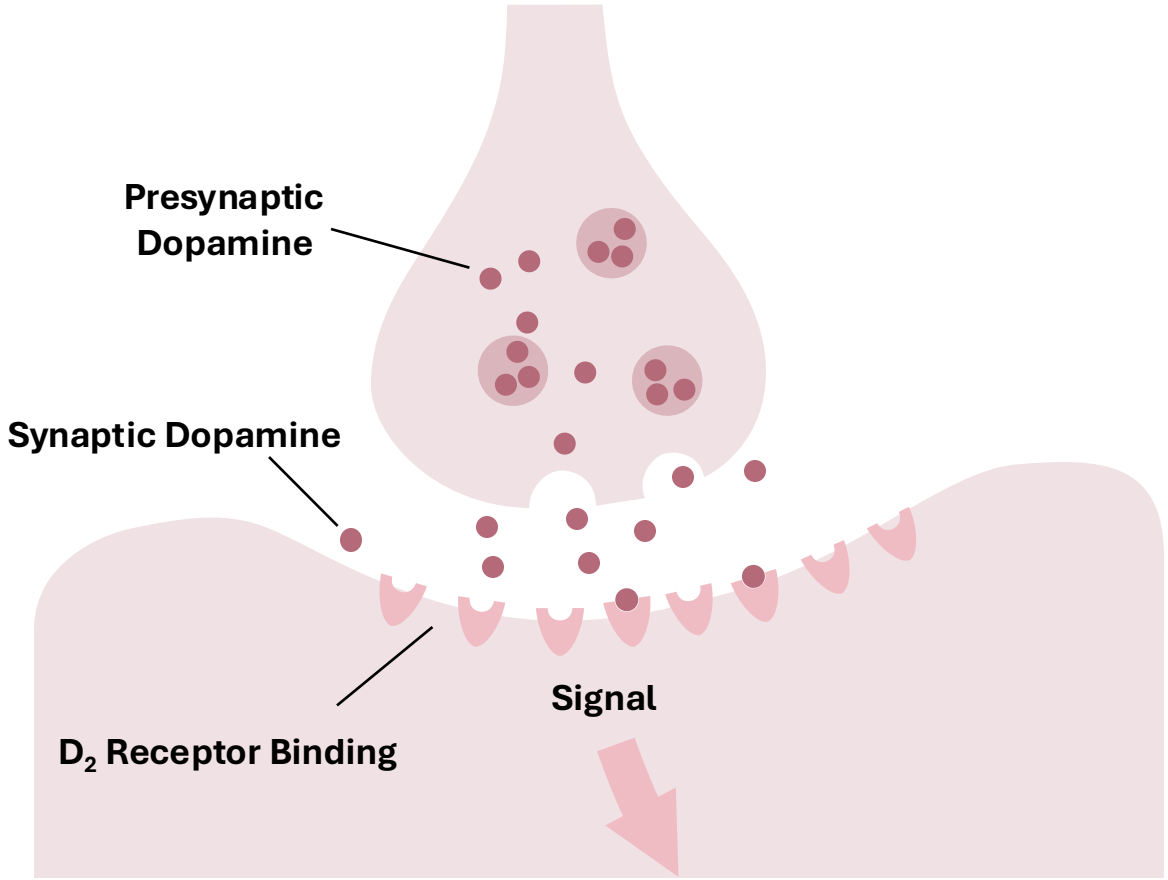


DRBA = Dopamine receptor blocking agent.

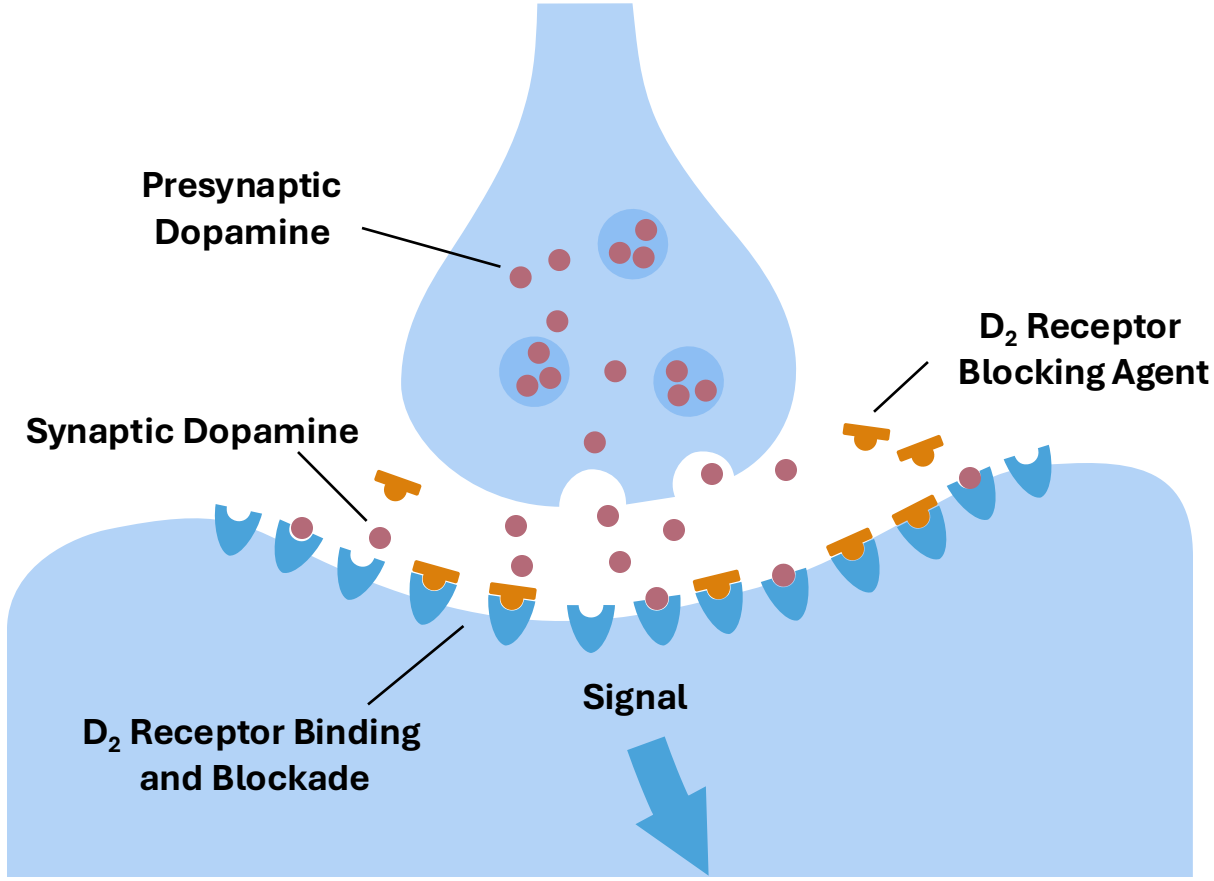
Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-78. Lerner PP, et al. *Psychiatry Clin Neurosci*. 2015;69(6):321-34. Merriam-Webster Medical Dictionary. Accessed May 12, 2025. https://www.merriam-webster.com/medical/tardive. O'Brian A. *Int J Geriatr Psychiatry*. 2016;31(7):683-93.

Receptor-Level Changes in Tardive Dyskinesia

Homeostatic Dopamine Signaling



Impact of Chronic DRBA Exposure



↑ in D_2 Receptor Number and Density	↑ in Receptor Sensitivity	Altered downstream signaling

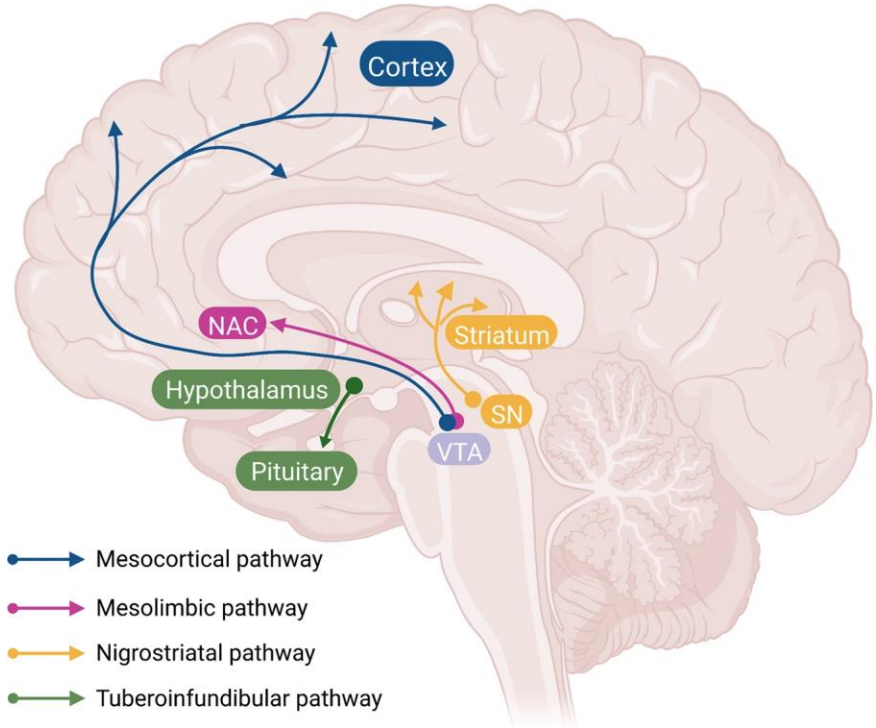
DRBA=Dopamine Receptor Blocking Agent

Stahl SM. *CNS Spectr.* 2018;23(4):239-247.

Nigrostriatal Pathway Alterations in TD

- **Substantia Nigra → Dorsal Striatum**
  - Involved in motor planning
  - High density of D2 receptors

- Chronic blockade of post-synaptic receptors and an increase in receptor hypersensitivity can lead to **extrapyramidal symptoms**



Ward KM, Citrome L. Neurol Ther. 2018;7(2):233-248. Xu H, Yang F. Transl Psychiatry. 2022;12(1):464.

TD Is More Than a Movement Disorder

Physical and Functional Impact

- Trouble walking/gait instability
- Pain and discomfort to muscles
- Dental damage/pain
- Trouble swallowing
  Gasping/grunting with respirations
- Ulcerations/bite marks on tongue and inside of mouth

Social and Emotional Impact

- Embarrassment
- Social isolation
- Trouble maintaining friendships/relationships
- Decrease in enjoyment of leisure activities

Psychological and Therapeutic Impact

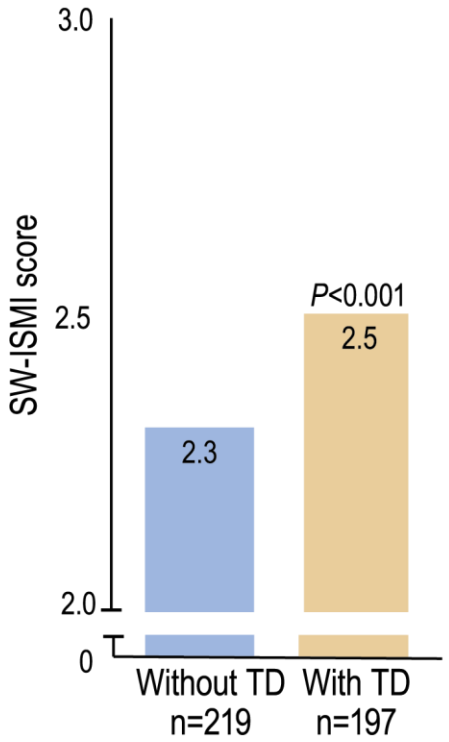
- Feeling hopeless
- Increase in depression and anxiety
- Noncompliance with medications
- Harder to treat the underlying condition

Zutshi D, et al. *Tremor Other Hyperkinet Mov (N Y)*. 2014;4:266. Jackson R et al. *Neuropsychiatr Dis Treat*. 2021;17:1589-1597. Jackson R, et al. *J Clin Psychiatry*. 2022;84(1):22cs14563.

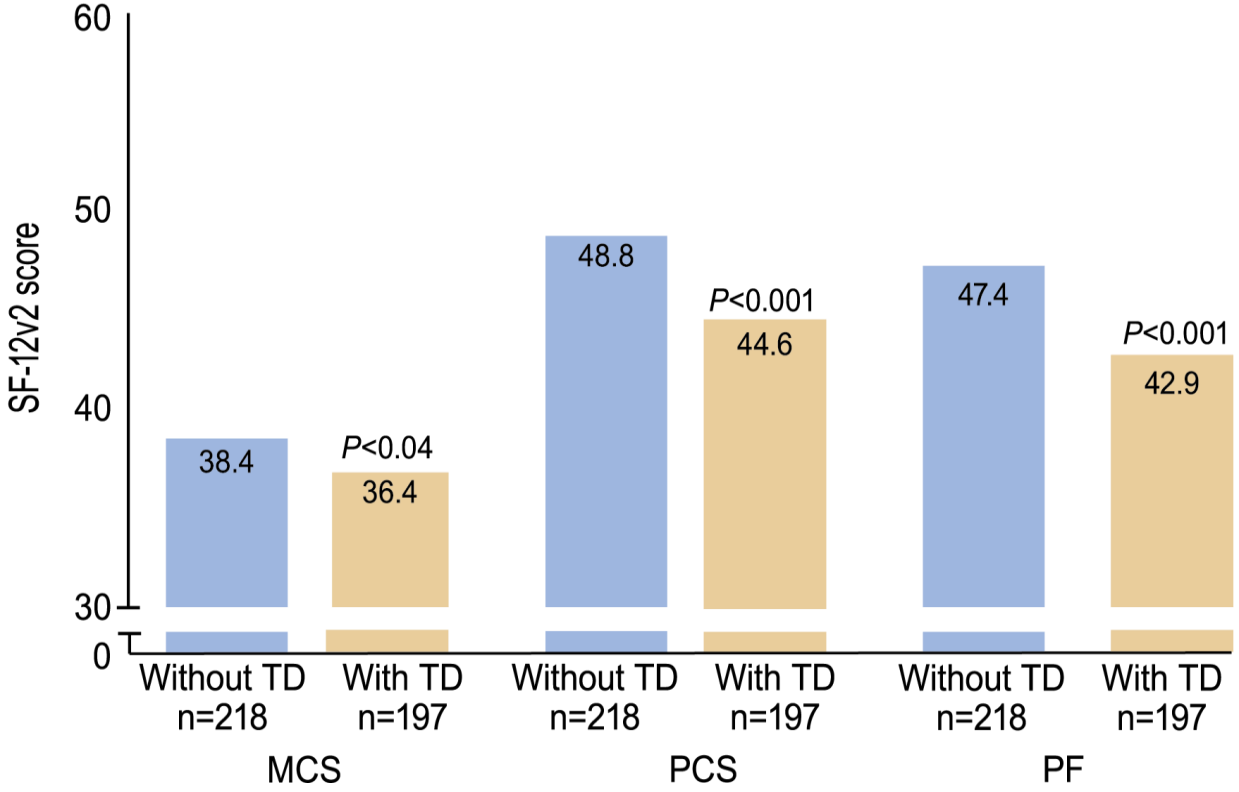
TD Negatively Impacts Life No Matter the Underlying Diagnosis

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

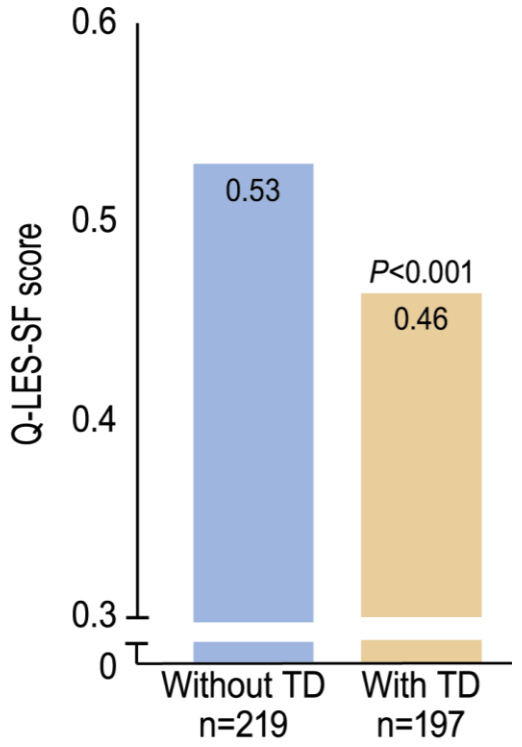
More Social Withdrawal



Worse Mental and Physical Functioning



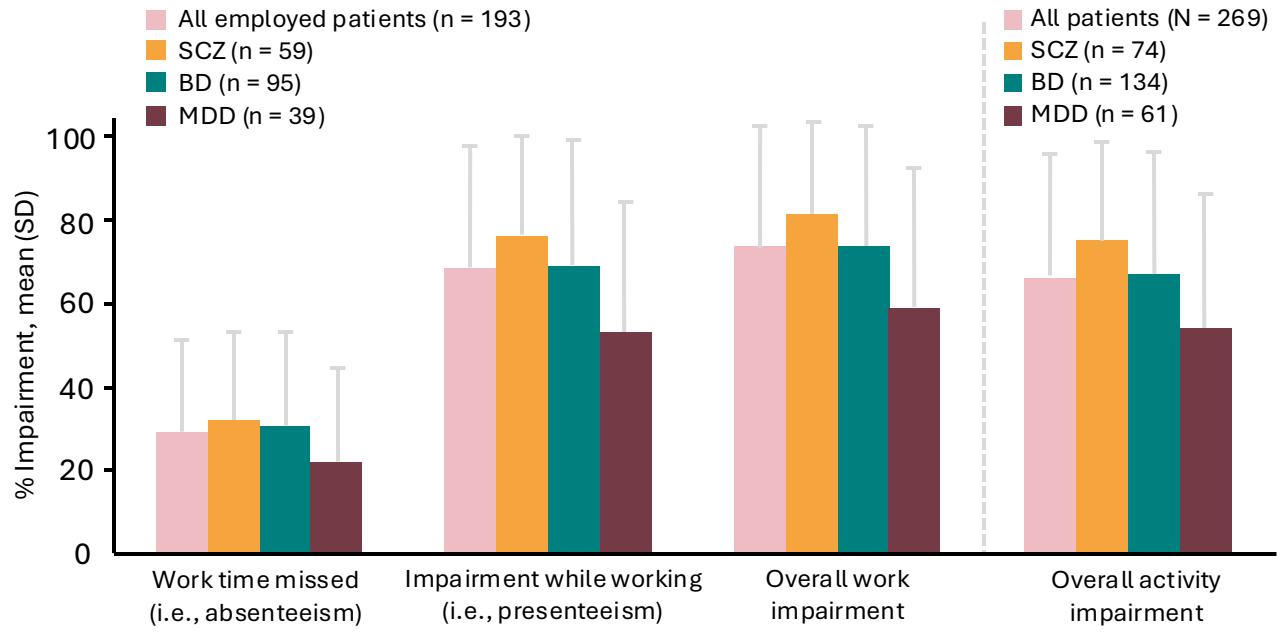
Lower Quality of Life



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

Patient & Caregiver Advocate:
Living with TD
Before Effective Treatment

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%

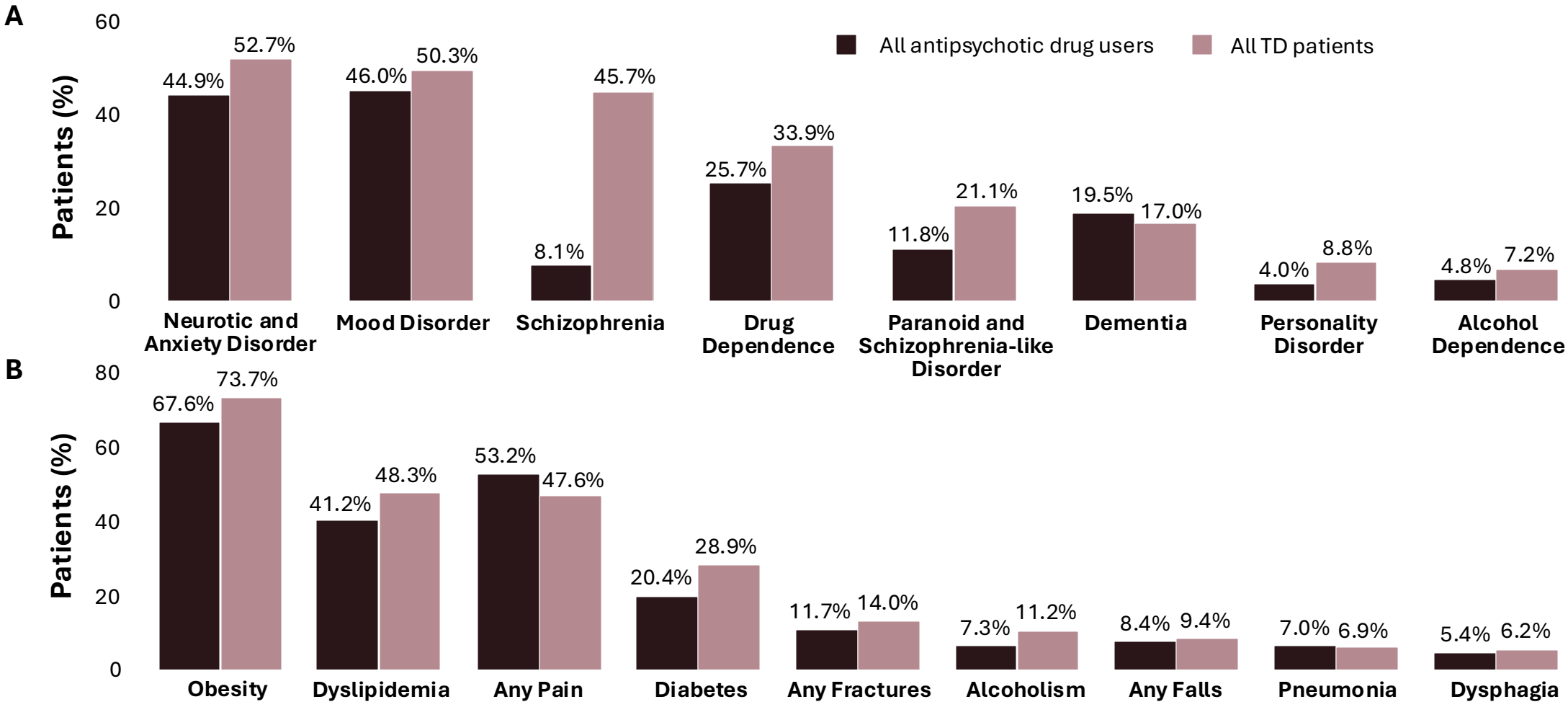
FGAs: **30%**

SGAs: **20.7%**

SGAs without prior FGA treatment: **7.2%**

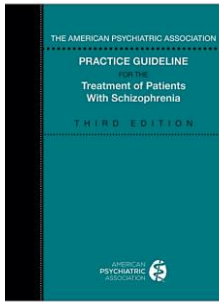
***Based on a meta-analysis of 41 studies (N=11,493; mean age=42.8 years, 66.4% male, 77.1% schizophrenia spectrum).**
EPS=Extrapyramidal symptoms.
Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-e278.

Psychiatric and Physical Diagnoses in Patients With/Without TD



Loughlin AM, et al. *PLoS One*. 2019;14(6):e0216044.

Structured Screening Is Standard of Care: APA Guideline Recommendations



Before AP
All patients

Q3 months
High risk + FGA

Q6 months
FGA or high risk + SGA

Q12 months
SGA

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	FDA Approved: VMAT2 inhibitors (deutetrabenazine and valbenazine) Off-Label: amantadine, clonazepam, gingko 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

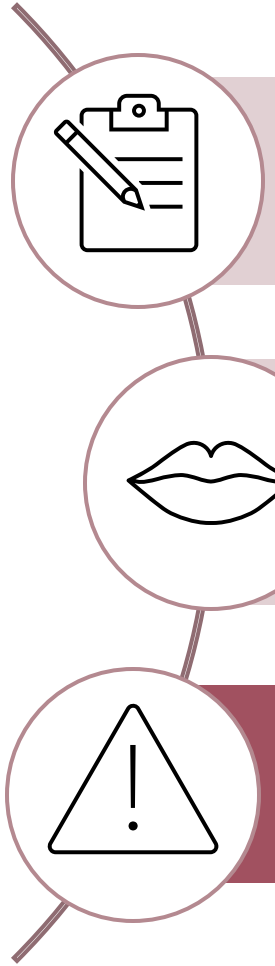
Movement Ratings		Score
Facial & Oral Movements	1. Muscles of facial expression	0 1 2 3 4
	2. Lips and perioral area	0 1 2 3 4
	3. Jaw	0 1 2 3 4
	4. Tongue	0 1 2 3 4
Extremity Movements	5. Upper (arms, wrists, hands, fingers)	0 1 2 3 4
	6. Lower (legs, knees, ankles, toes)	0 1 2 3 4
Trunk Movements	7. 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

American Psychiatric Association. *Practice Guideline for the Treatment of Patients with Schizophrenia*. 3rd ed. APA Publishing; 2021. Caroff SN, et al. *J Clin Psychiatry*. 2020;81(2):19cs12983.

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 carefully 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**

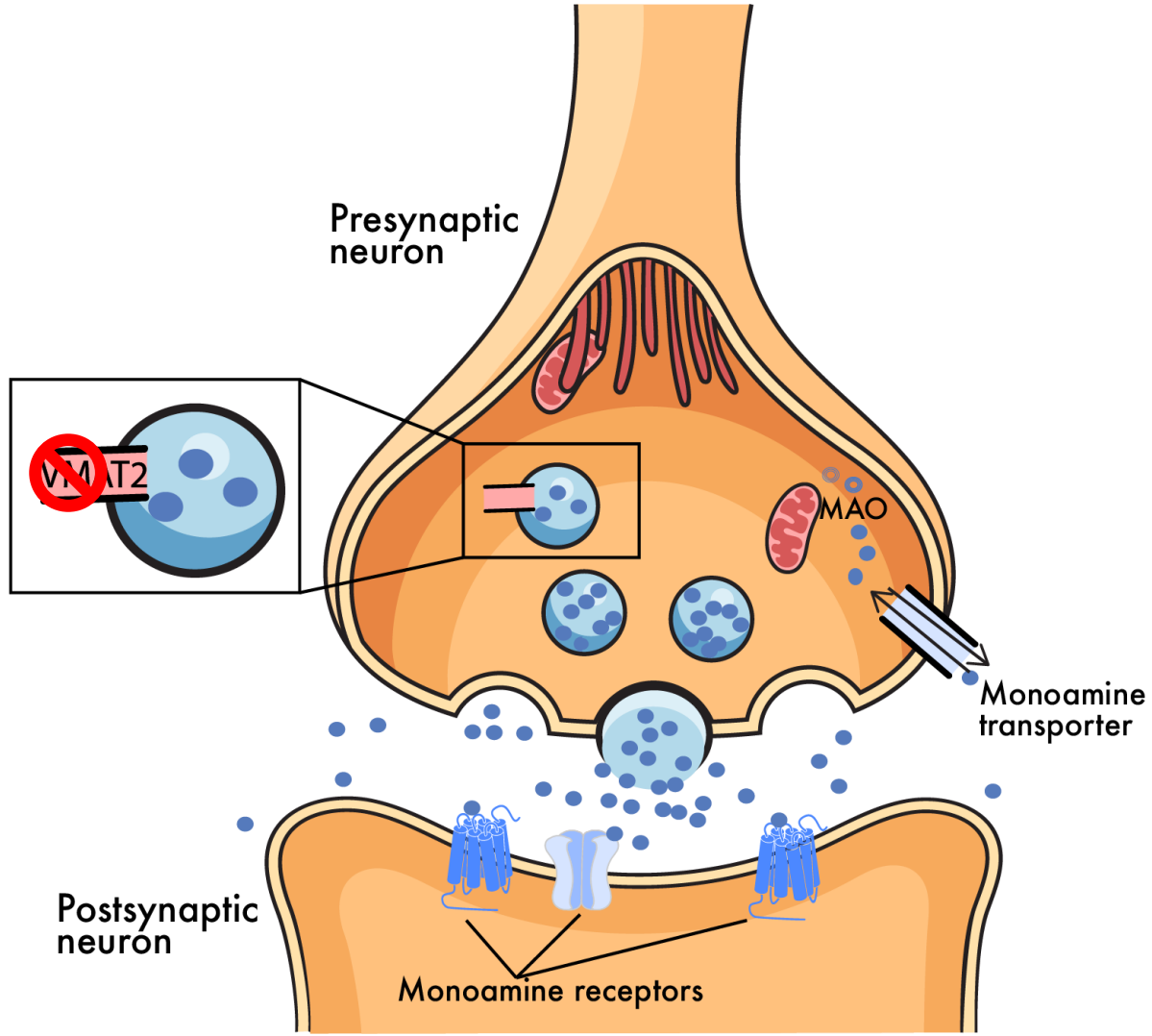
Consider **amantadine as an alternative to anticholinergic medication** to manage DIP

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?

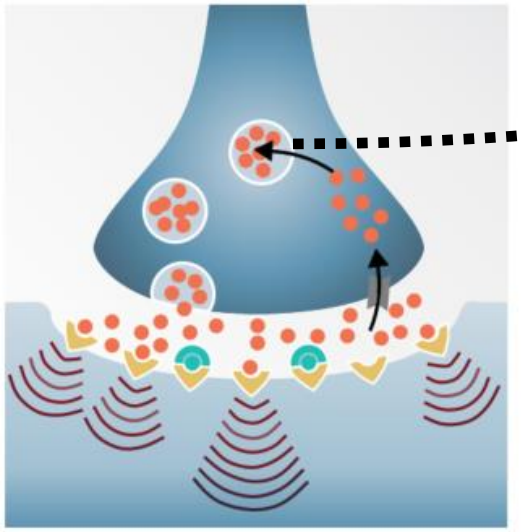
- VMAT-2 packages and transports monoamine neurotransmitters into synaptic vesicles
  - Serotonin
  - Dopamine
  - Histamine
  - Norepinephrine
- Inhibiting VMAT-2 decreases the amount of neurotransmitter released when a neuron fires
- VMAT-2 inhibitors
  - Reduce dopamine release in the dorsal striatum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

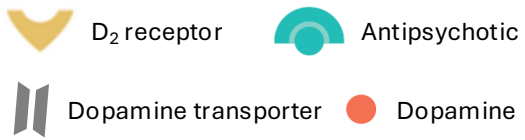


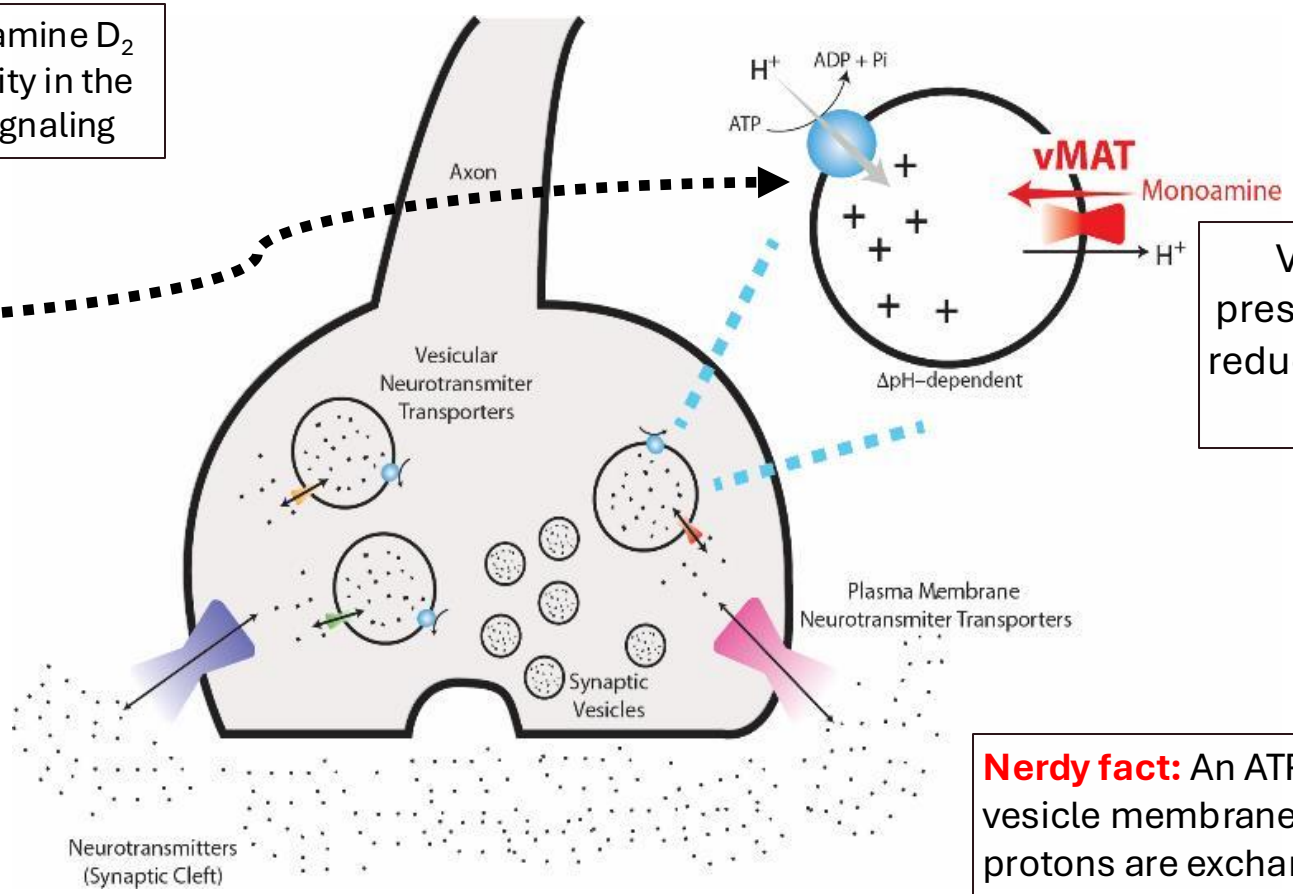
Citrome L. *Expert Rev Neurother*. 2018;18(4):323-332.

Reversible VMAT-2 Inhibitor: Mechanism of Action

TD Pathophysiology: Postsynaptic dopamine D_2 receptor upregulation and supersensitivity in the indirect pathway – not enough "stop" signaling





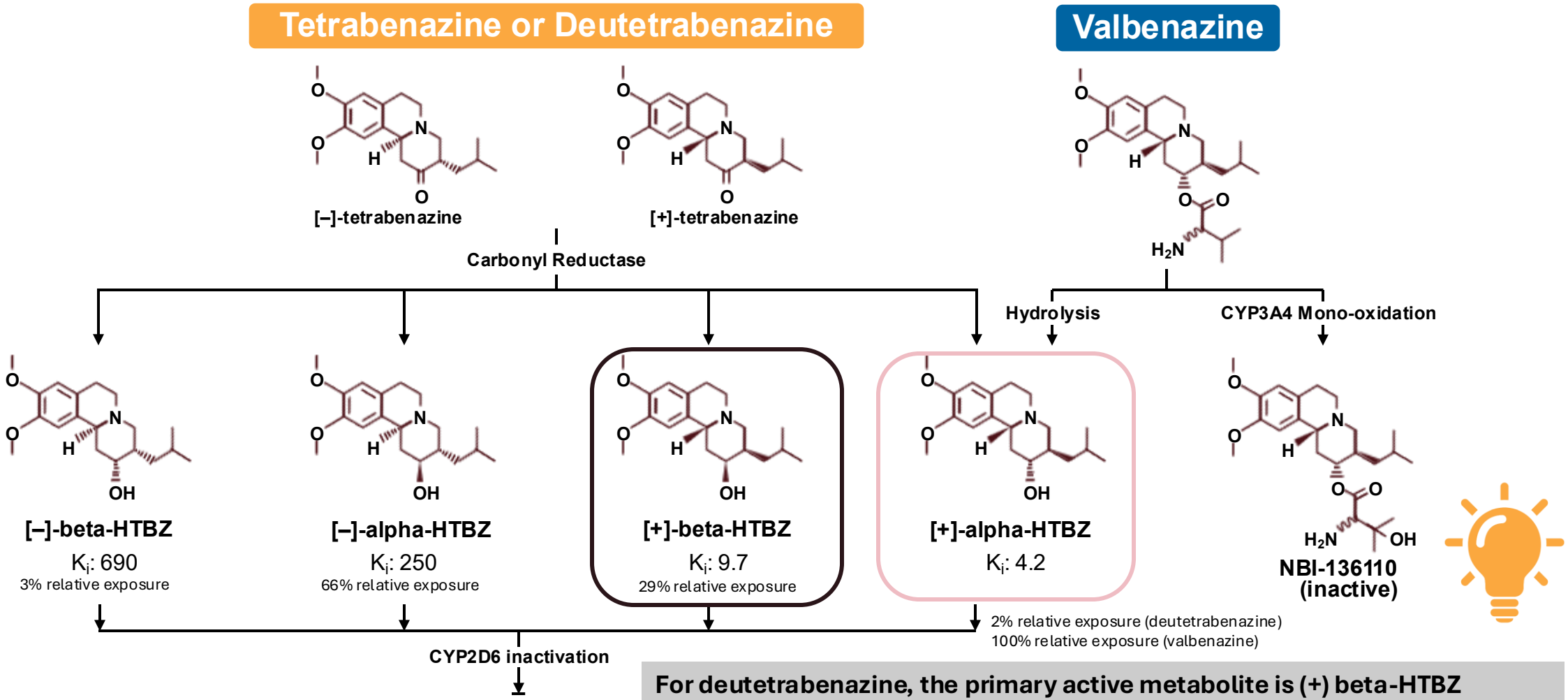


VMAT2 inhibitors decrease presynaptic dopamine release by reducing the amount of dopamine packaged into vesicles.

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/Deutetrabenazine



For deutetrabenazine, the primary active metabolite is (+) beta-HTBZ
For valbenazine, the primary active metabolite is (+) alpha-HTBZ.

Grigoriadis DE, et al. *J Pharmacol Exp Ther*. 2017;361(3):454-461. Skor H, et al. *Drugs R D*. 2017;17(3):449-459. Brar S, et al. *Clin Pharmacol Drug Dev*. 2023;12(4):447-456.

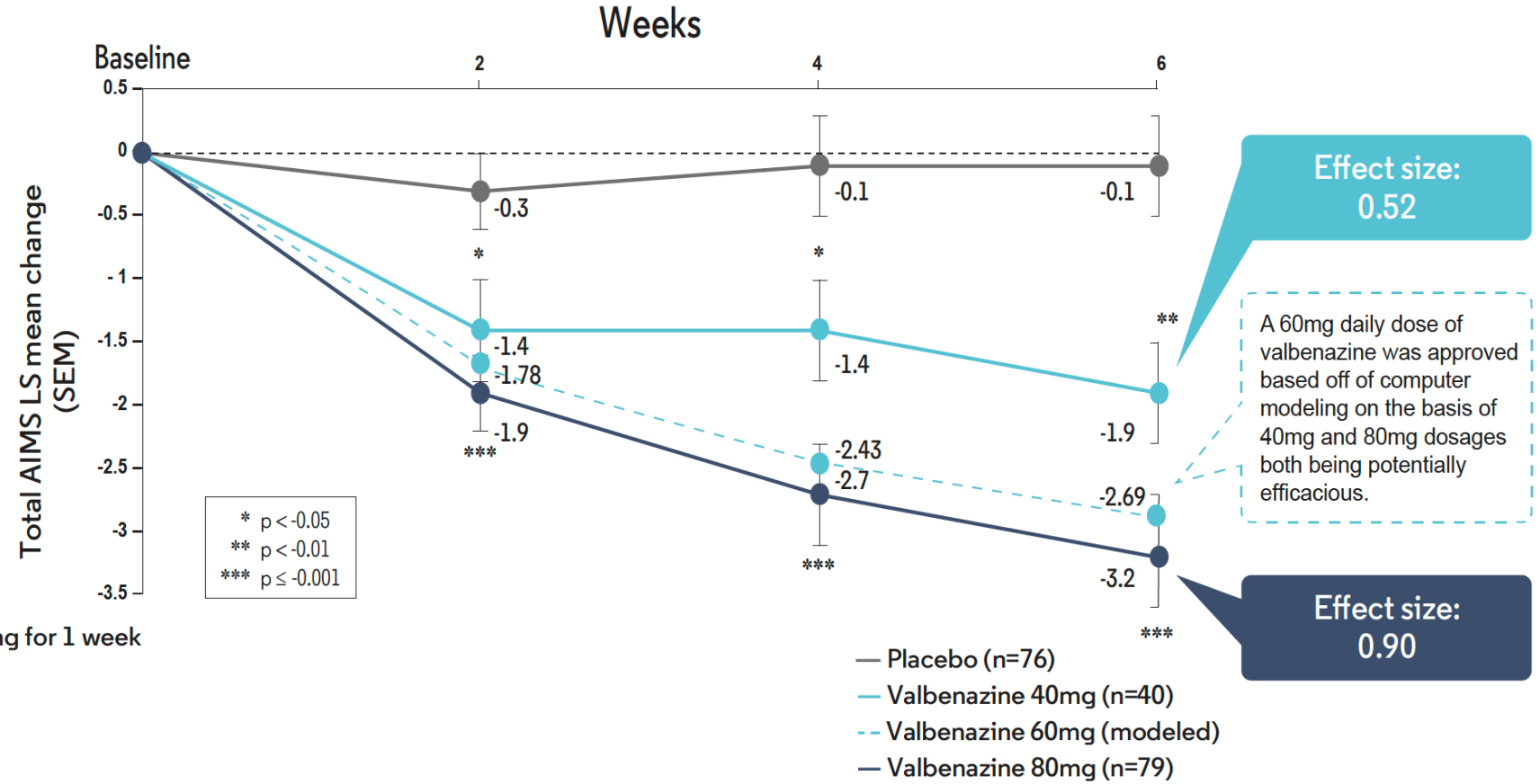
Valbenazine: Clinical and Real-World Evidence in TD

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

Mean baseline AIMS total score: 10.0± 4.0

Placebo Subtracted Change from Baseline

VBZ 80 mg: -3.2 ***
VBZ 40 mg: -1.9 **
Placebo: -0.1



All participants received valbenazine 40mg for 1 week

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

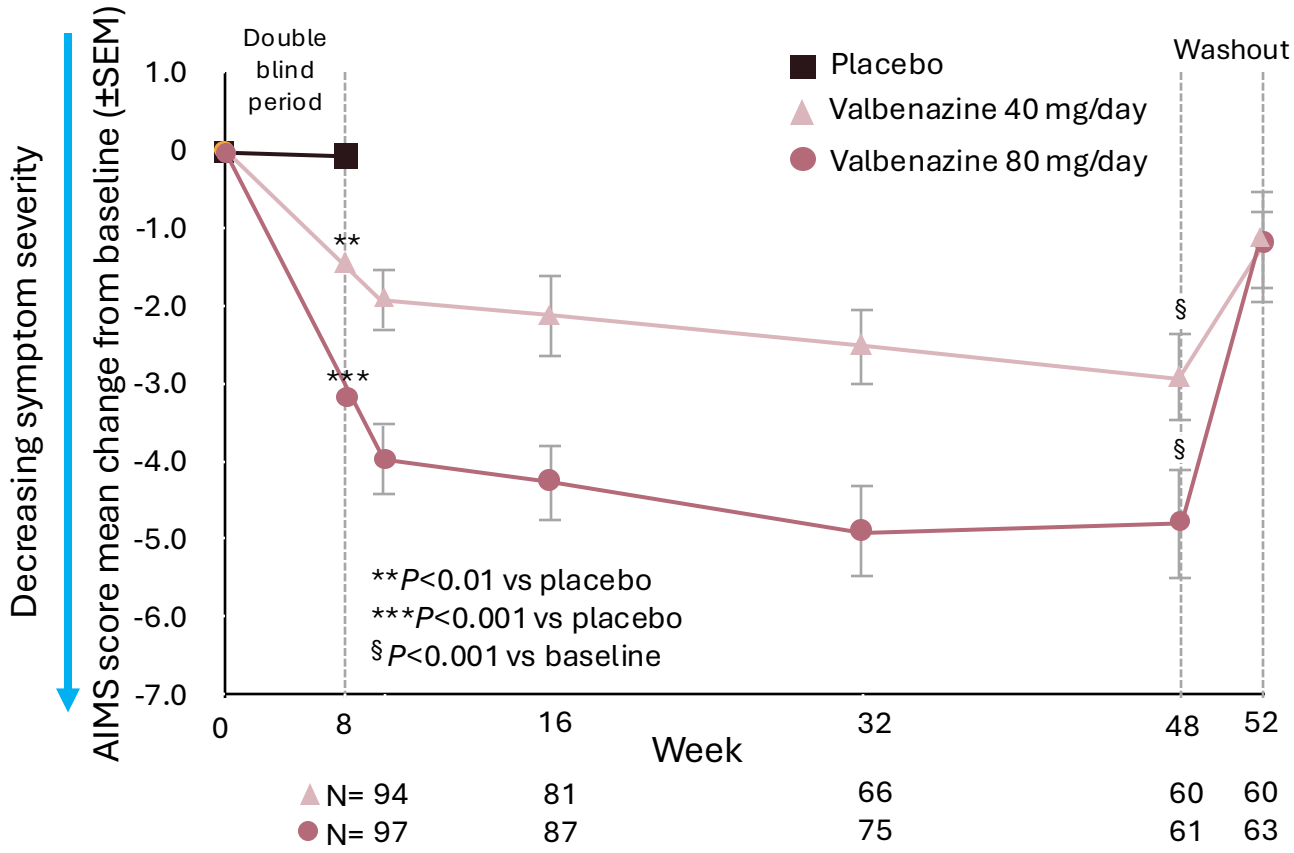
Adverse Event	Valbenazine (n=262) (%)	Placebo (n=183) (%)
Somnolence	10.9%	4.2%
Anticholinergic effects	5.4%	4.9%
Balance disorders/fall	4.1%	2.2%
Headache	3.4%	2.7%
Akathisia (akathisia, restlessness)	2.7%	0.5%
Vomiting	2.6%	0.6%
Nausea	2.3%	2.1%
Arthralgia	2.3%	0.5%

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

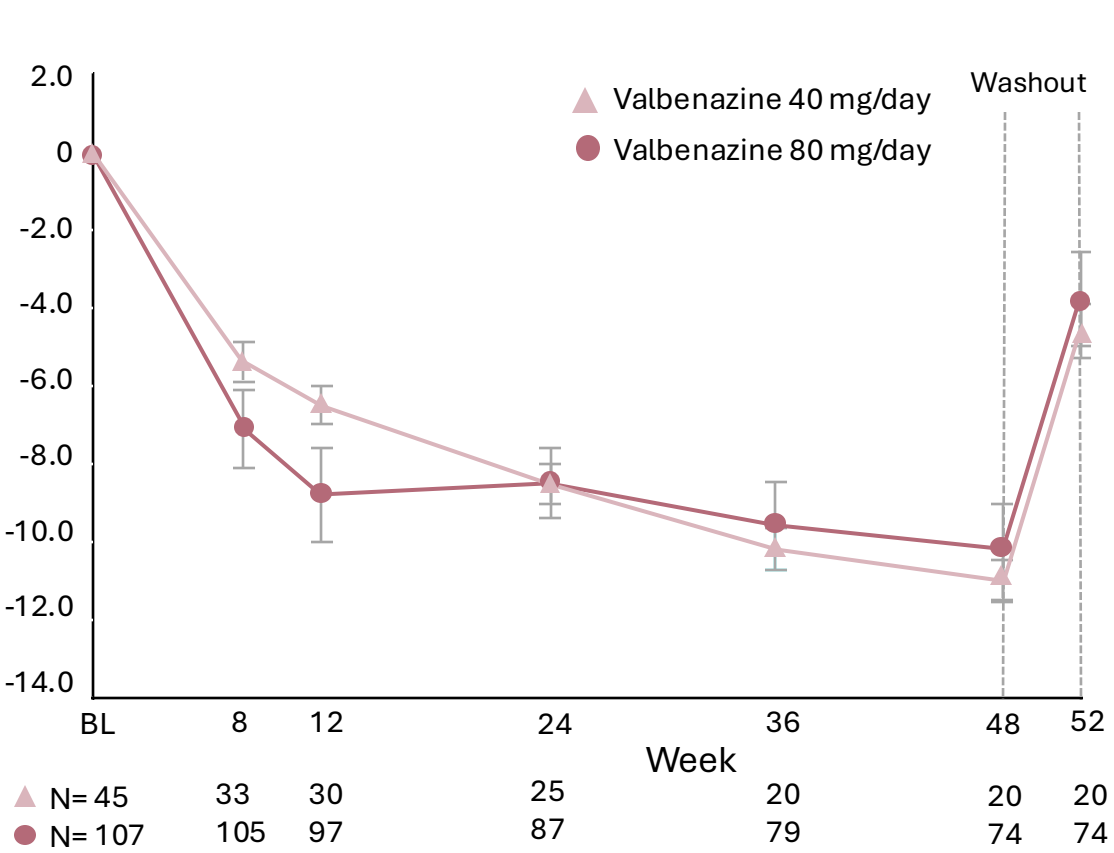
Valbenazine PI. Drugs@FDA: FDA-Approved Drugs. Accessed February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209241s029lbl.pdf. Horiguchi J, et al. *Psychiatry Clin. Neurosci*. 2022;76(11):560-569.

Long-Term Studies of Valbenazine

KINECT-3 Open Label Extension Study



KINECT-4 Study

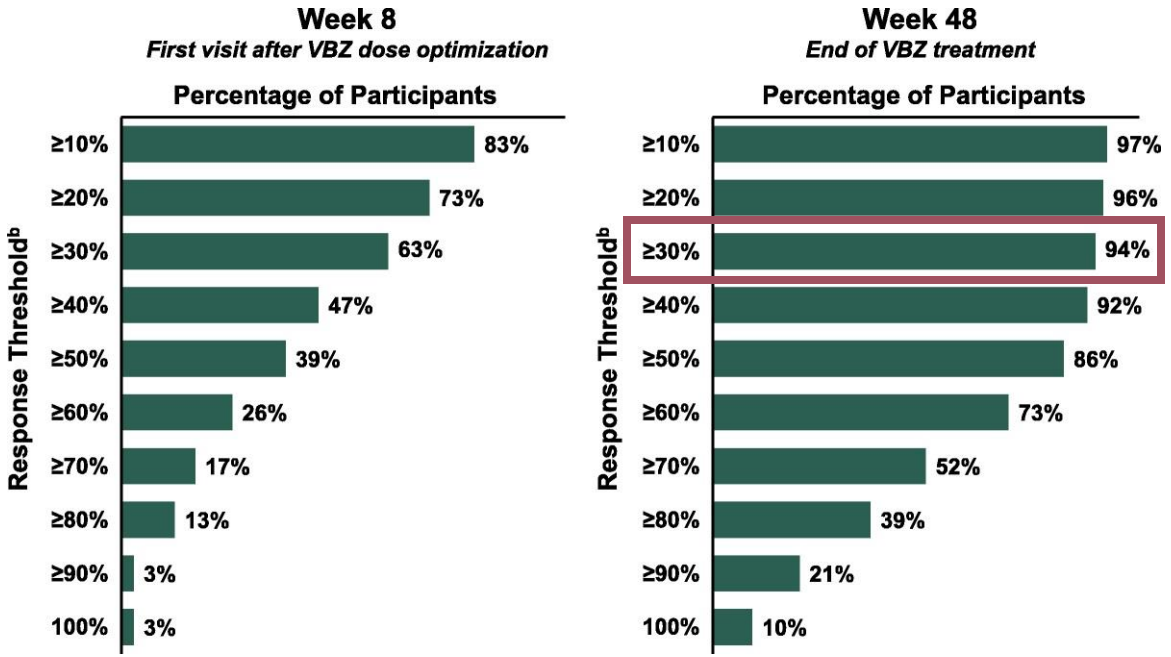


No new safety signals or concerns emerged in either study

Factor SA, et al. *J Clin Psychiatry*. 2017;78(9):1344-1350. Marder SR, et al. *J Clin Psychopharmacol*. 2019;39(6):620-627.

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 ≥30% AIMS improvement at week 48



Sustained Response with Valbenazine Treatment

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

Correll CU, et al. *J Clin Psychopharmacol*. 2024;44(4):353-361.

Formulations and Administration of Valbenazine

Valbenazine	
Dosage forms	• 40, 60, 80 mg capsules • 40, 60, 80 mg sprinkle capsules
Dosing	• 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	• MAOIs • Strong CYP3A4 inducers • Maximum dose 40 mg with strong CYP2D6 or strong CYP34A
Contraindications	• Known hypersensitivity to valbenazine or any components of capsule

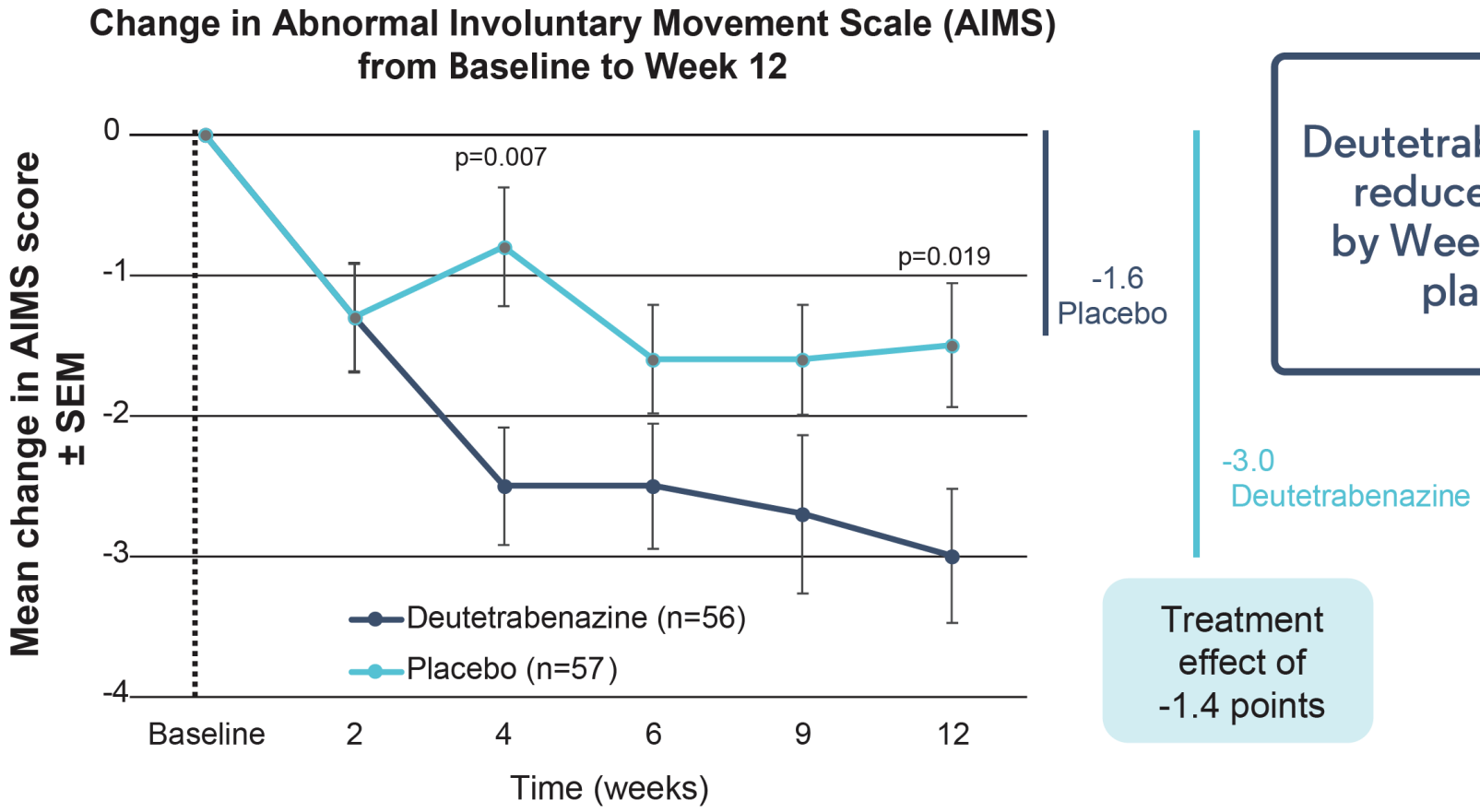
The valbenazine sprinkle capsule is bioequivalent to the original formulation and may be sprinkled onto soft foods such as:

apple sauce yogurt pudding

Jimenez, et al. Presented at: 37th Annual Psych Congress; Oct 29 – Nov 2, 2024; Boston, MA. Valbenazine PI. Drugs@FDA: FDA-Approved Drugs. Accessed February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209241s029lbl.pdf.

Deutetrabenazine: Clinical and Real-World Evidence in TD

Flexible-Dose Study of Deutetrabenazine (ARM-TD)



-1.6
Placebo

-3.0
Deutetrabenazine

Treatment effect of -1.4 points

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

SEM = standard error of the mean.

Fernandez HH, et al. *Neurology*. 2017;88(21):2003-2010.

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

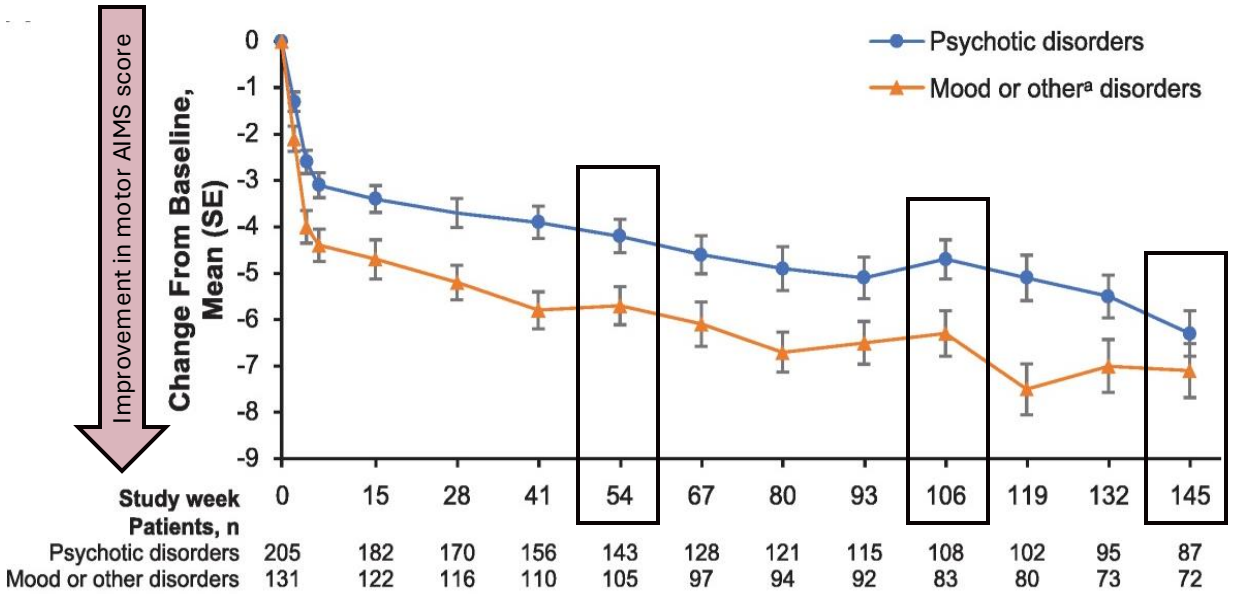
Discontinuation due to AEs occurred in 4% of patients taking deutetrabenazine vs 3% of patients taking placebo

AE = adverse effect.

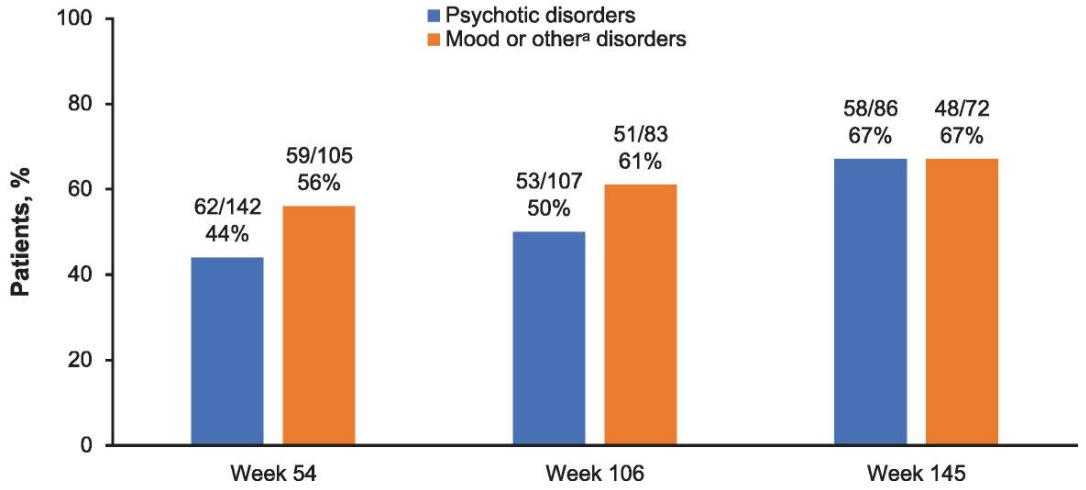
Anderson KE, et al. *Lancet Psychiatry*. 2017;4(8):595-604. Fernandez HH, et al. *J Neurol Neurosurg Psychiatry*. 2019;90(12):1317-1323.

Deutetrabenazine Improves TD Over 3 Years Independent of Diagnosis…

Change in Total Motor AIMS Score



Proportion of Patients Achieving ≥50% Improvement in Total Motor AIMS Score



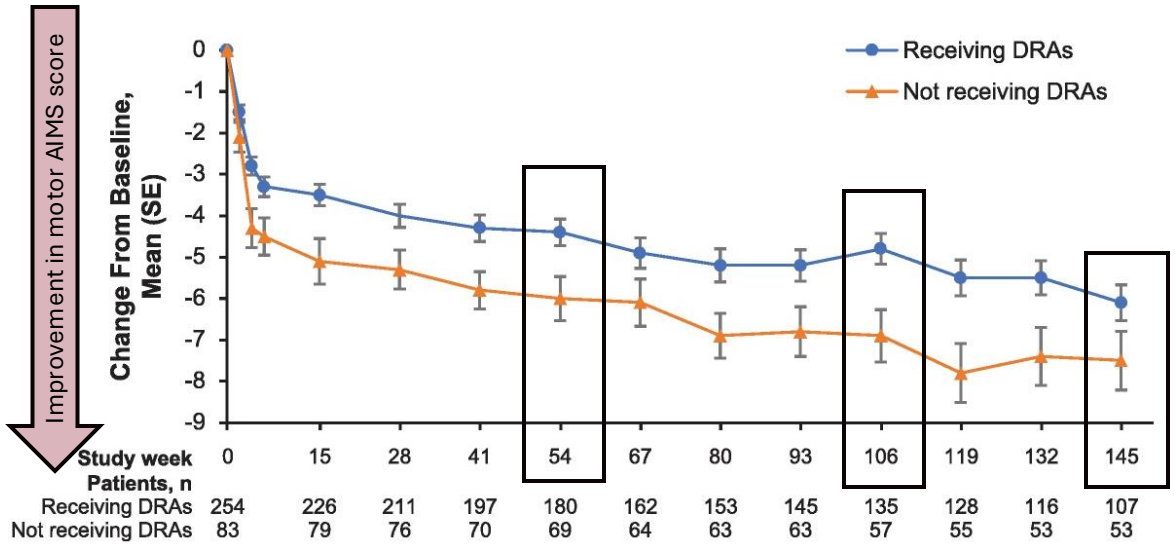
Deutetrabenazine produced **sustained, clinically meaningful reductions in AIMS scores over 3 years**, with similar long-term benefits across both psychotic and mood/other disorder populations.

[a]Examples of other disorders include abdominal discomfort, alcohol withdrawal syndrome, gastroesophageal reflux disease, insomnia, neurosis, and tic.

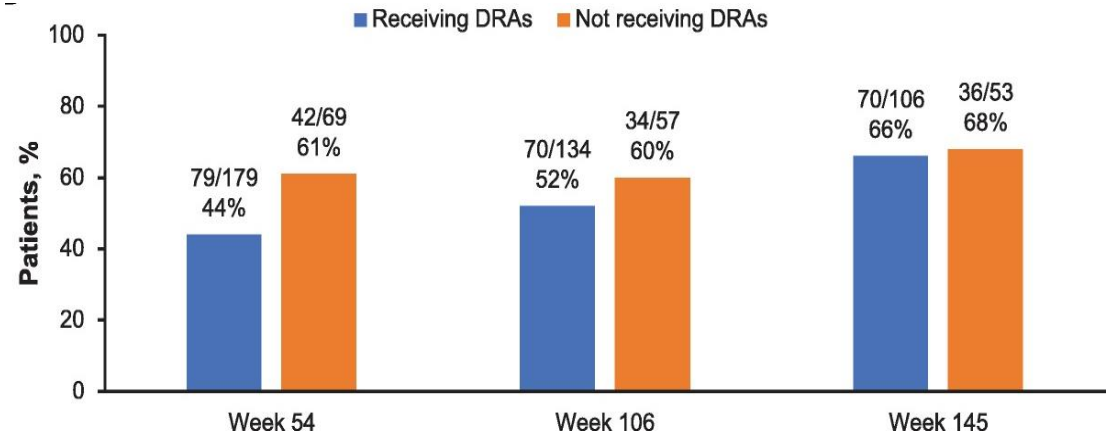
Hauser RA, et al. *J Clin Psychopharmacol*. 2024;44(4):386-396.

...And Independent of DBRA Use

Change in Total Motor AIMS Score



Proportion of Patients Achieving ≥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.

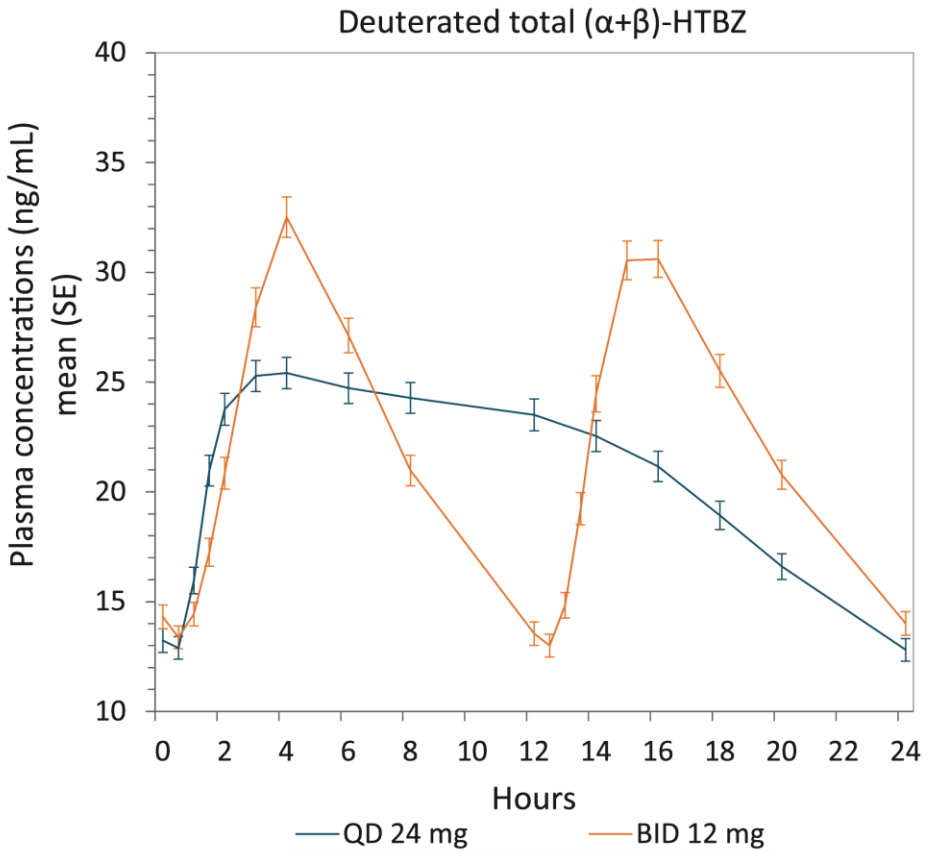
DRA=Dopamine Receptor Antagonist.

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

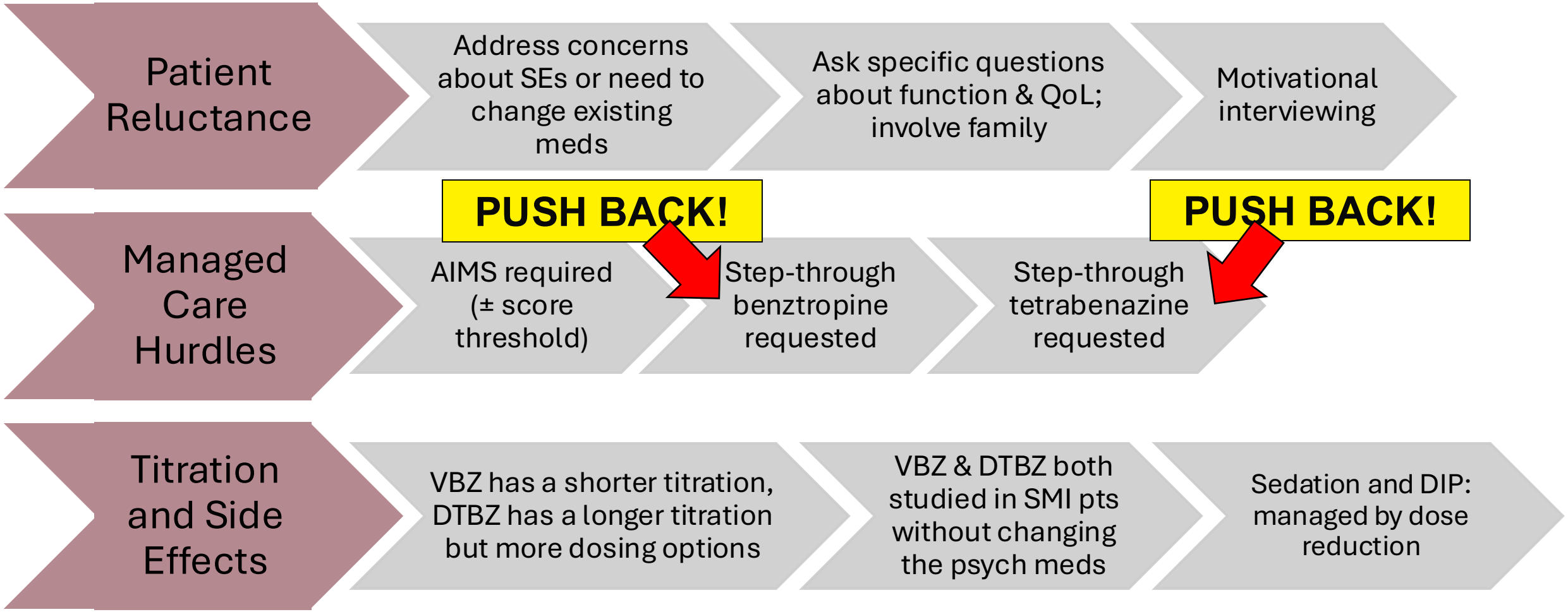
Both deutetrabenazine and valbenazine are efficacious and well-tolerated in treating TD regardless of psychiatric diagnosis

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

Valbenazine PI. US Food and Drug Administration. Drugs@FDA: FDA Approved Drugs. Accessed February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209241s029lbl.pdf. Deutetrabenazine PI. US Food and Drug Administration. Drugs@FDA: FDA Approved Drugs. Accessed February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208082s016s017lbl.pdf.

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)

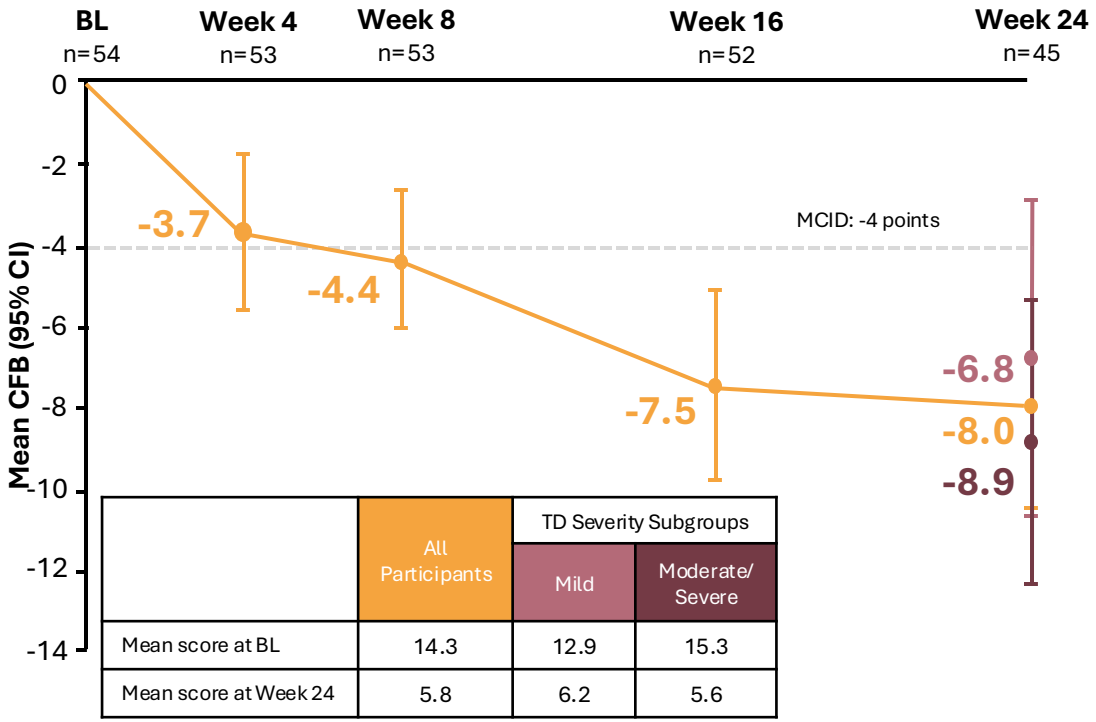
Domain	TDIS item	Corresponding TDRS item
Mouth/throat function	1. Speech	Item 2. Speech
	2. Mouth noises	Not applicable
	3. Swallowing	Item 3. Chewing and swallowing
Dexterity	4. Gripping	Item 4. Eating tasks Item 5. Dressing Item 6. Hygiene Item 8. Hobbies
	5. Writing	Item 7. Handwriting
Mobility	6.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

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

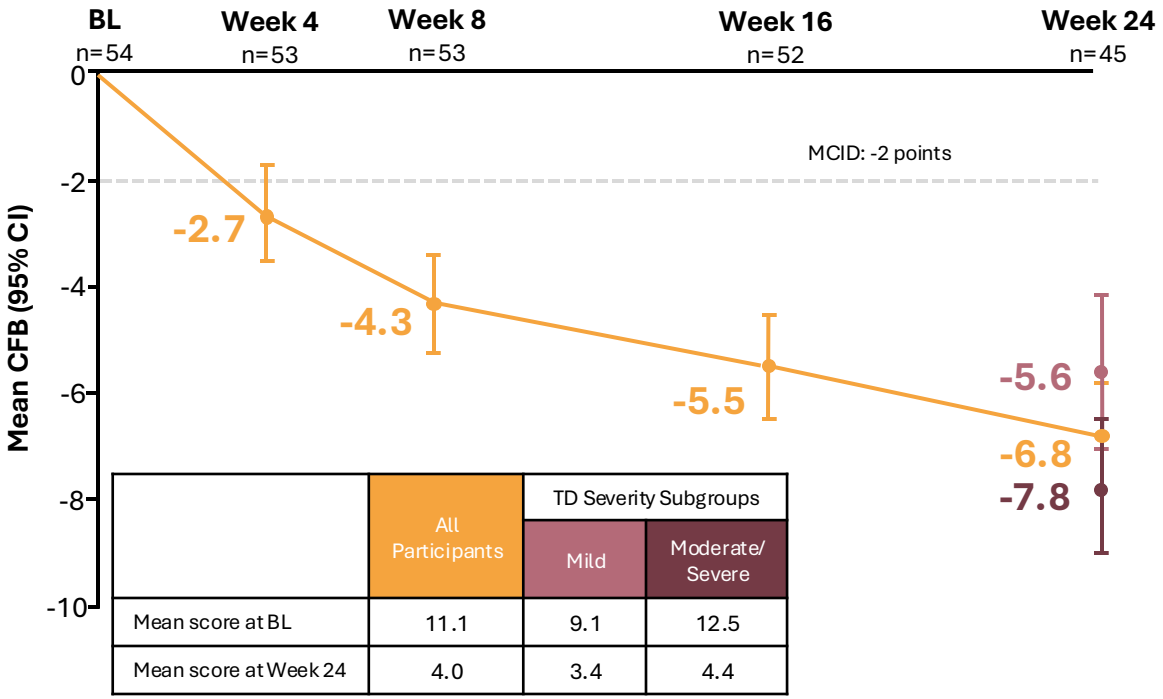
TDIS Total Score



	All Participants	TD Severity Subgroups	
		Mild	Moderate/ Severe
Mean score at BL	14.3	12.9	15.3
Mean score at Week 24	5.8	6.2	5.6

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



	All Participants	TD Severity Subgroups	
		Mild	Moderate/ Severe
Mean score at BL	11.1	9.1	12.5
Mean score at Week 24	4.0	3.4	4.4

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)

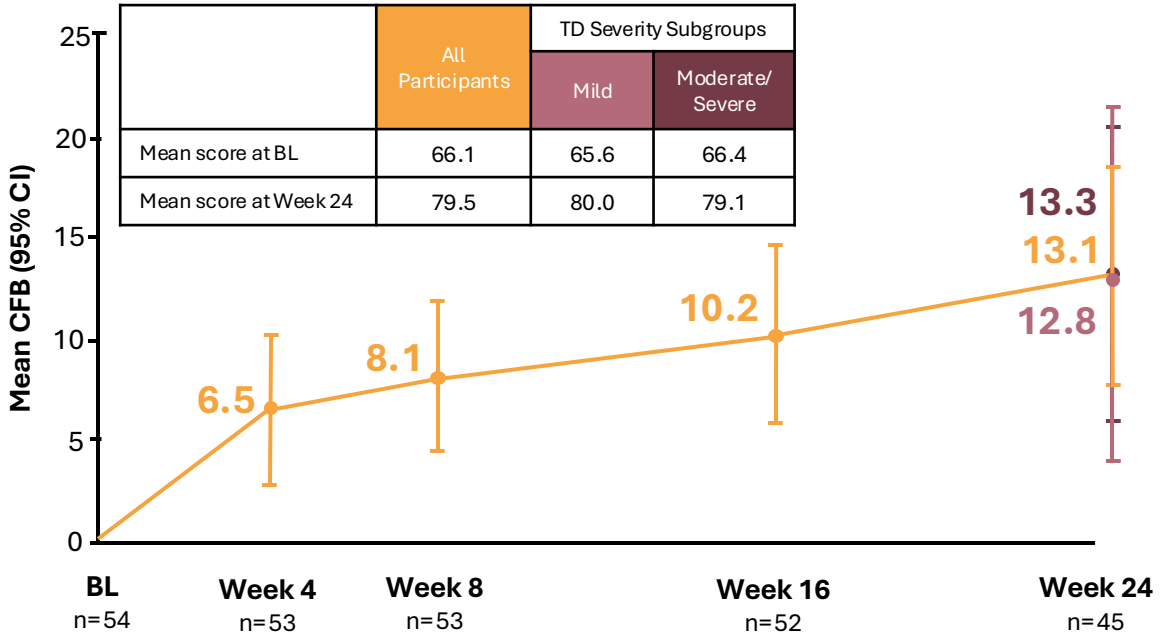
BL = baseline, CI = confidence interval; CFB = change from baseline; MCID = minimal clinically important difference

Dunayevich E, et al. Poster presented at: Psych Congress Elevate; May 28-31, 2025; Las Vegas, NV.

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

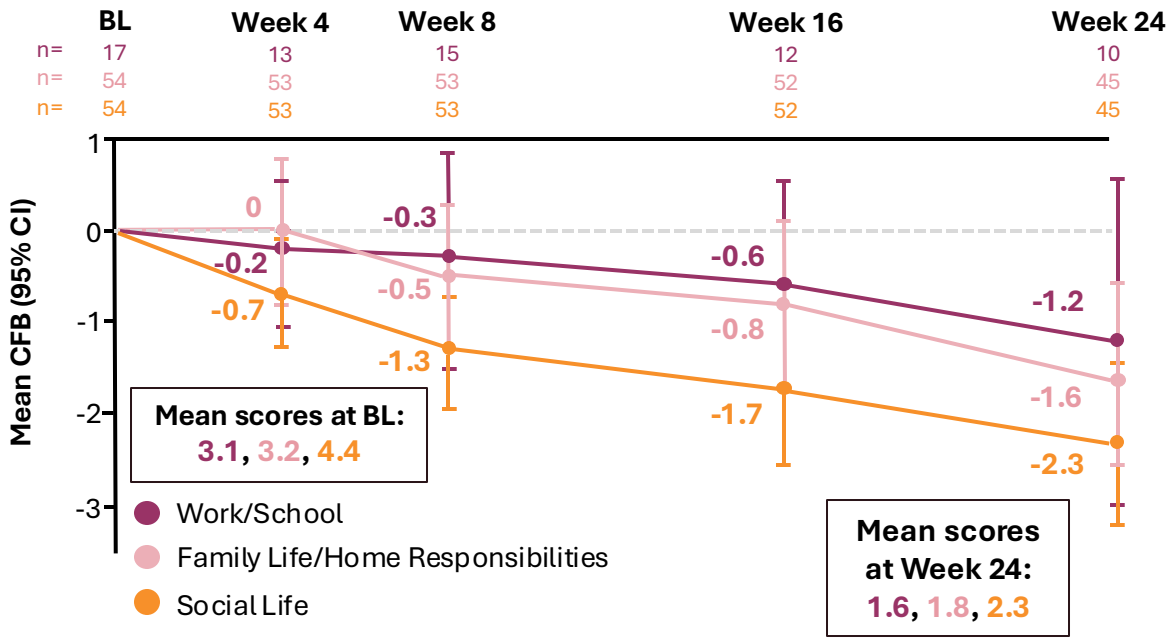
EQ-VAS Score

	All Participants	TD Severity Subgroups	
		Mild	Moderate/ Severe
Mean score at BL	66.1	65.6	66.4
Mean score at Week 24	79.5	80.0	79.1



EQ-VAS ranges from 0 ("worst health you can imagine" to 100 ("best health you can imagine")

SDS Domain Score



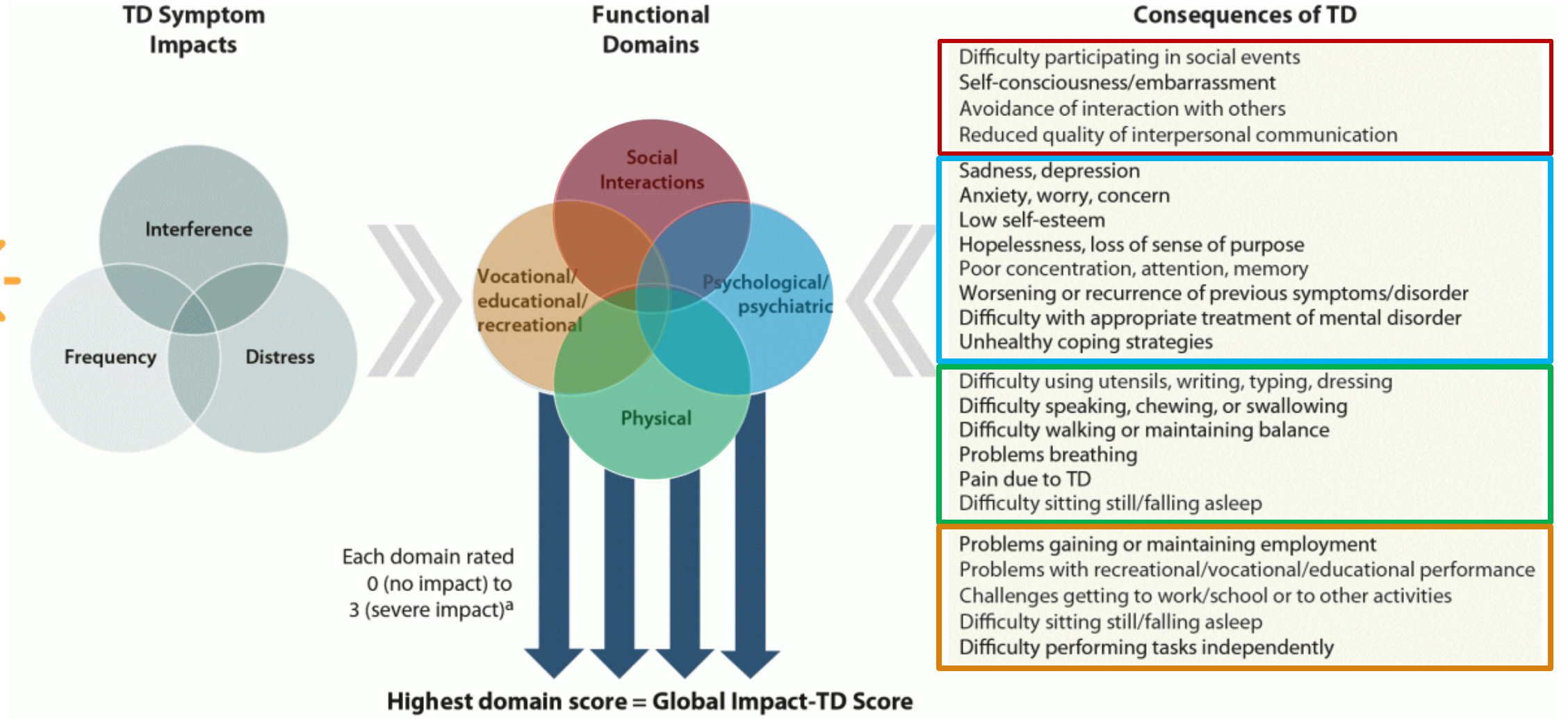
SDS domain scores each rate functional impairment from 0 (none at all) to 10 (extremely)
*Few study participants were working or attending school during the study (n=17 at BL). Therefore, the interpretation of these results is limited.

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

EQ-VAS = EuroQol Visual Analogue Scale; SDS = Sheehan Disability Scale

Dunayevich E, et al. Poster presented at: Psych Congress Elevate; May 28-31, 2025; Las Vegas, NV.

IMPACT-TD Scale: Design and Real-World Validation



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

Jackson R, et al. *J Clin Psychiatry*. 2023;84(1):22cs14563.

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)

	IMPACT-TD ClinRO domains				
Body region AIMS score, 1 or 2	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

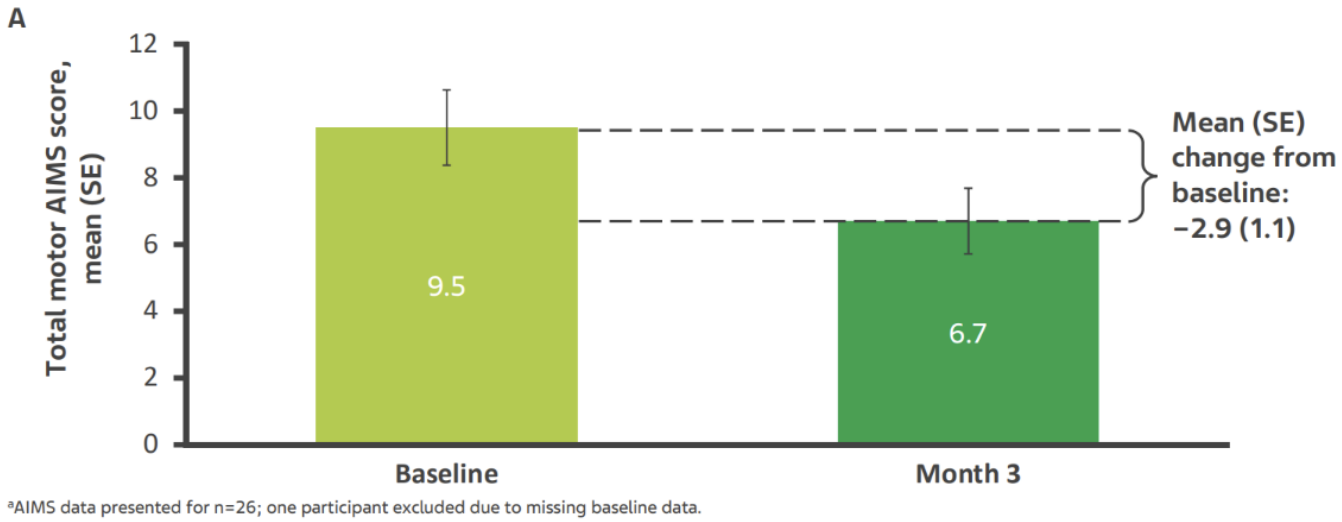
The percentages of patients shown in the table cells are coded from green (0%) to red (100%)

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**.

Chepke C, et al. ***Anatomical Distribution of Involuntary Movements and Clinician-Reported Impact of Tardive Dyskinesia: A Real-World Analysis of the IMPACT-TD Registry.*** **Poster presented at the Annual Psych Congress; September 17–21, 2025; San Diego, CA.**

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**



[a]AIMS 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

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

- 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
- TD has impacts across physical, psychological, social, and vocational/educational/recreational domains
- 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

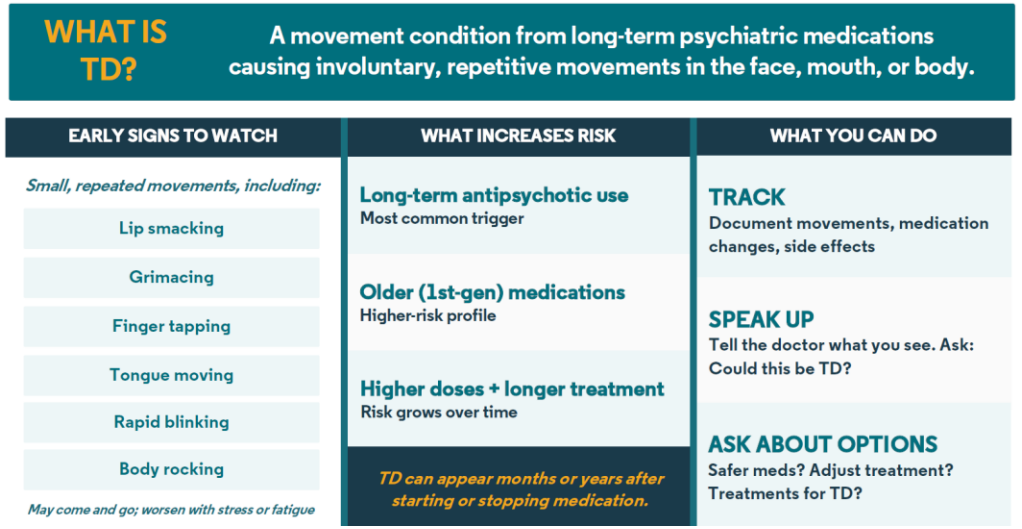
Shared-Decision-Making with Patients and Caregivers

Patient & Cargiver:
Living with TD
After Effective Treatment

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**.

CAREGIVER ACTION NETWORK CAN™



KEY RESOURCES

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

Patient Advocate Foundation patientadvocate.org	**National Alliance on Mental Illness (NAMI)** nami.org
Movement Disorder Policy Coalition movementdisorderspolicy.org	**Depression and Bipolar Support Alliance** dbsalliance.org
Treatment Advocacy Center treatmentadvocacycenter.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