



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.

Faculty

Desiree Matthews, MSN, PMHNP-BC

Different Mental Health Program

Charlotte, NC

Ashley Walters

Paralegal

Charleston, SC

Rakesh Jain, MD, MPH

Clinical Professor

Texas Tech – Permian Basin

Odessa, TX

Elizabeth Walters

Administrative Assistant

Charleston, SC

Faculty Disclosures

Desiree Matthews, MSN, PMHNP-BC: Advisory Board—AbbVie, Alkermes, Biogen/Sage, Bristol Myers Squibb, Definium Therapeutics, Johnson & Johnson, Teva Pharmaceuticals; Consultant—AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Indivior, Johnson & Johnson, Neurocrine Biosciences, Otsuka Pharmaceuticals; Speakers Bureau—AbbVie, Alkermes, Axsome, Bristol Myers Squibb, Johnson & Johnson, Lundbeck, Luye, Neurocrine Biosciences, Otsuka Precision Health, Otsuka Pharmaceuticals, Teva Pharmaceuticals

Rakesh Jain, MD, MPH: Advisory Board—Adamas, Alkermes, Corium, Eisai, Indivior, Intra-Cellular Therapies, Ironshore Pharmaceuticals, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka Pharmaceuticals, PamLab, Pfizer, Shire, Sunovion, Supernus, Takeda, Teva, Tris Pharmaceuticals; Consultant—AbbVie (Allergan), Acadia, Adamas, Alfasigma USA, Inc., Axsome, Corium, Cingulate Therapeutics, Eisai, Evidera, Impel NeuroPharma, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Osmotica, Otsuka Pharmaceuticals, PamLab, Pfizer, Sage Therapeutics, Shire, Sunovion, Supernus, Takeda, Teva; Grant/Research Support—AbbVie (Allergan), Lilly, Lundbeck, Otsuka Pharmaceuticals, Pfizer, Shire, Takeda; Speakers Bureau—AbbVie (Allergan), Alkermes, Axsome, Corium, Eisai, Indivior, Intracellular Therapies, Ironshore Pharmaceuticals, Janssen, Lilly, Lundbeck, Merck, Neos Therapeutics, Neurocrine Biosciences, Otsuka Pharmaceuticals, PamLab, Pfizer, Shire, Sunovion, Takeda, Teva, Tris Pharmaceuticals

Ashley Walters: Has disclosed no relevant financial relationship with any ineligible company (commercial interest).

Elizabeth Walters: Has disclosed no relevant financial relationship with any ineligible company (commercial interest).

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

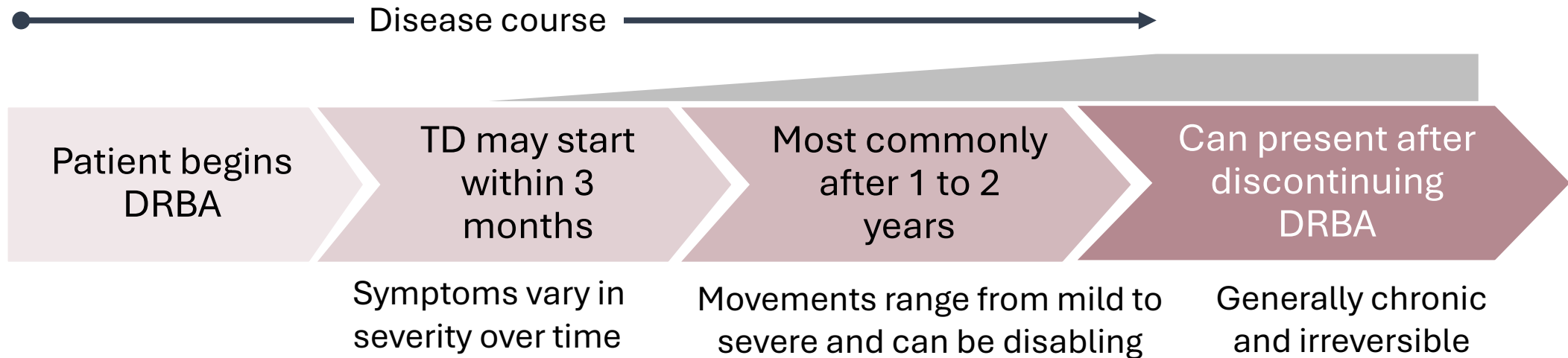
- Define and describe the importance of functional and QoL restoration as long-term treatment goals for patients with TD as well as their caregivers
- Identify subtle manifestations of TD, differentiate it from other movement disorders, and utilize validated tools to assess its functional and QoL impacts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

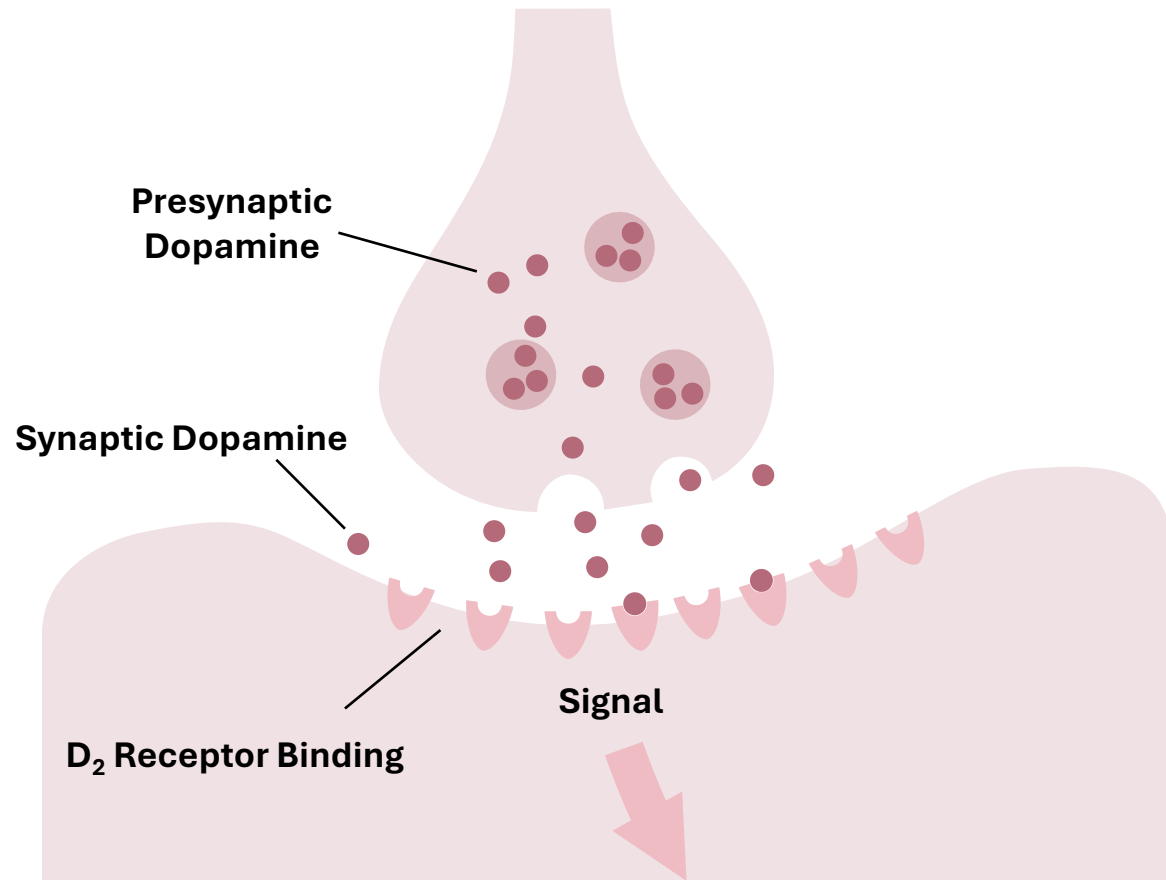


DRBA = Dopamine receptor blocking agent.

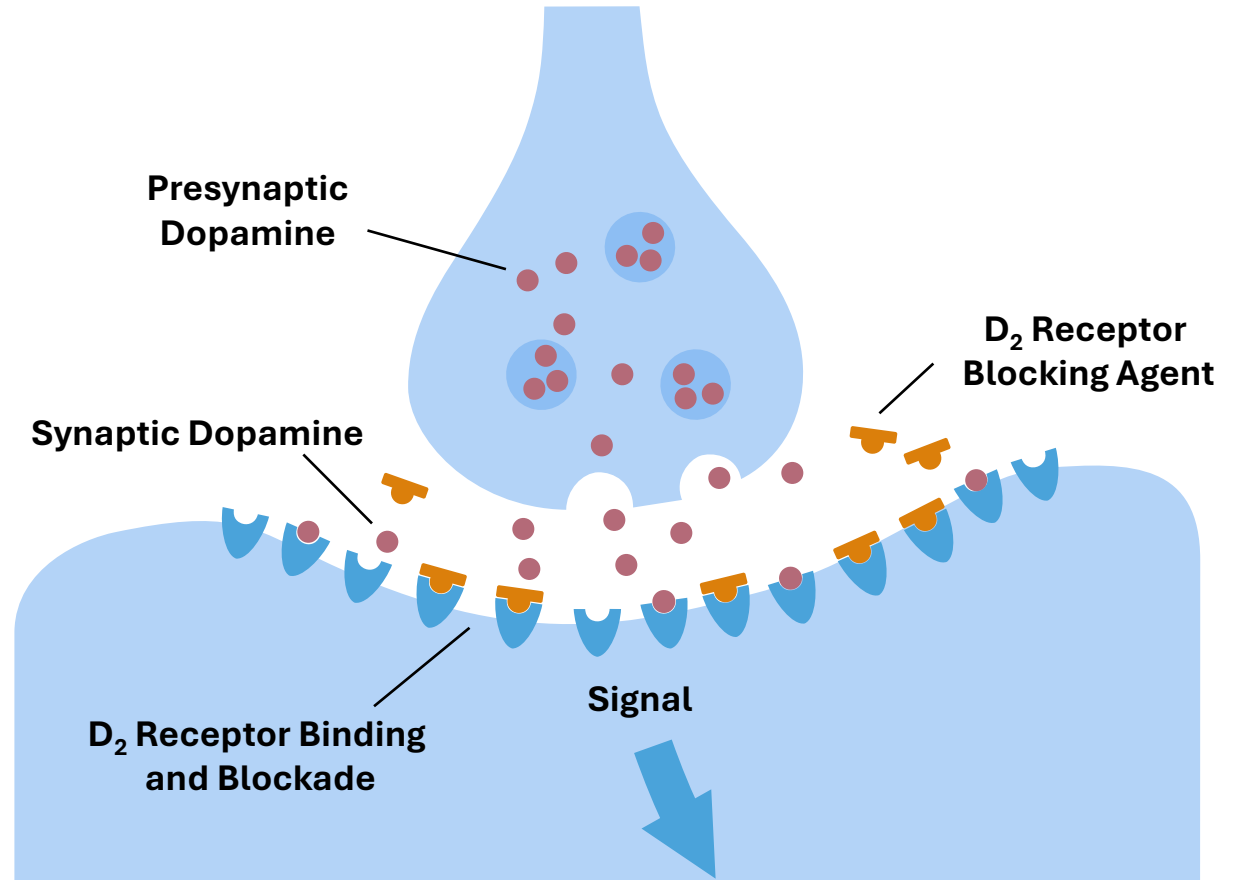
Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-78. Lerner PP, et al. *Psychiatry Clin Neurosci*. 2015;69(6):321-34. Merriam-Webster Medical Dictionary. Accessed May 12, 2025. <https://www.merriam-webster.com/medical/tardive>. O'Brian A. *Int J Geriatr Psychiatry*. 2016;31(7):683-93.

Receptor-Level Changes in Tardive Dyskinesia

Homeostatic Dopamine Signaling



Impact of Chronic DRBA Exposure



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

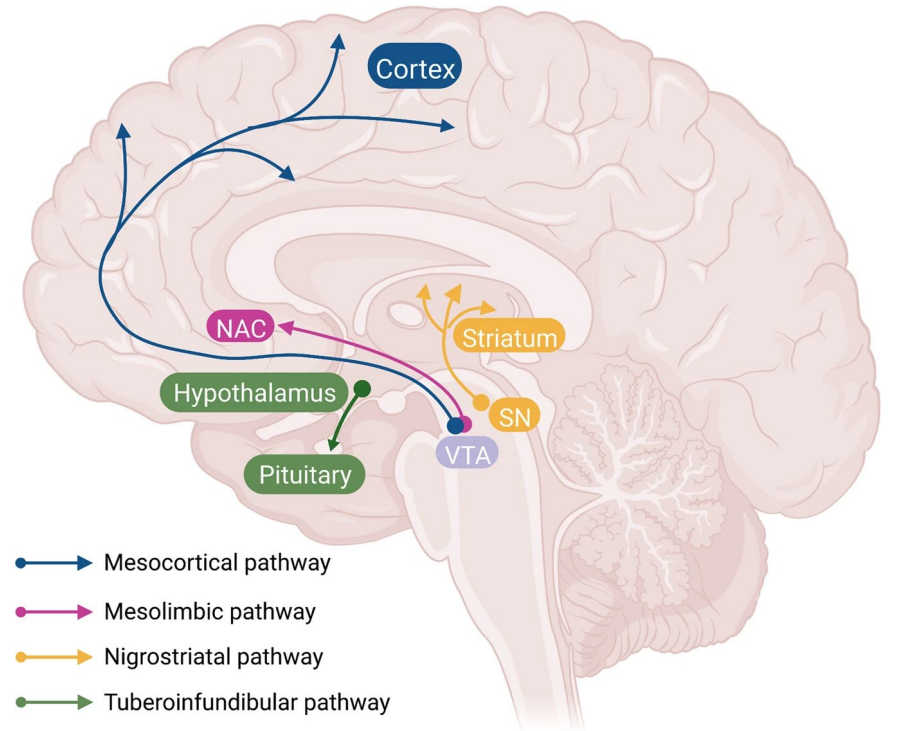
↑ in D₂ Receptor
Number and Density

↑ in Receptor
Sensitivity

Altered downstream
signaling

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**

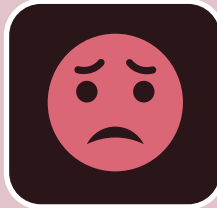


TD Is More Than a Movement Disorder



Physical and Functional Impact

- Trouble walking/gait instability
- Pain and discomfort to muscles
- Dental damage/pain
- Trouble swallowing
- Gaspings/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



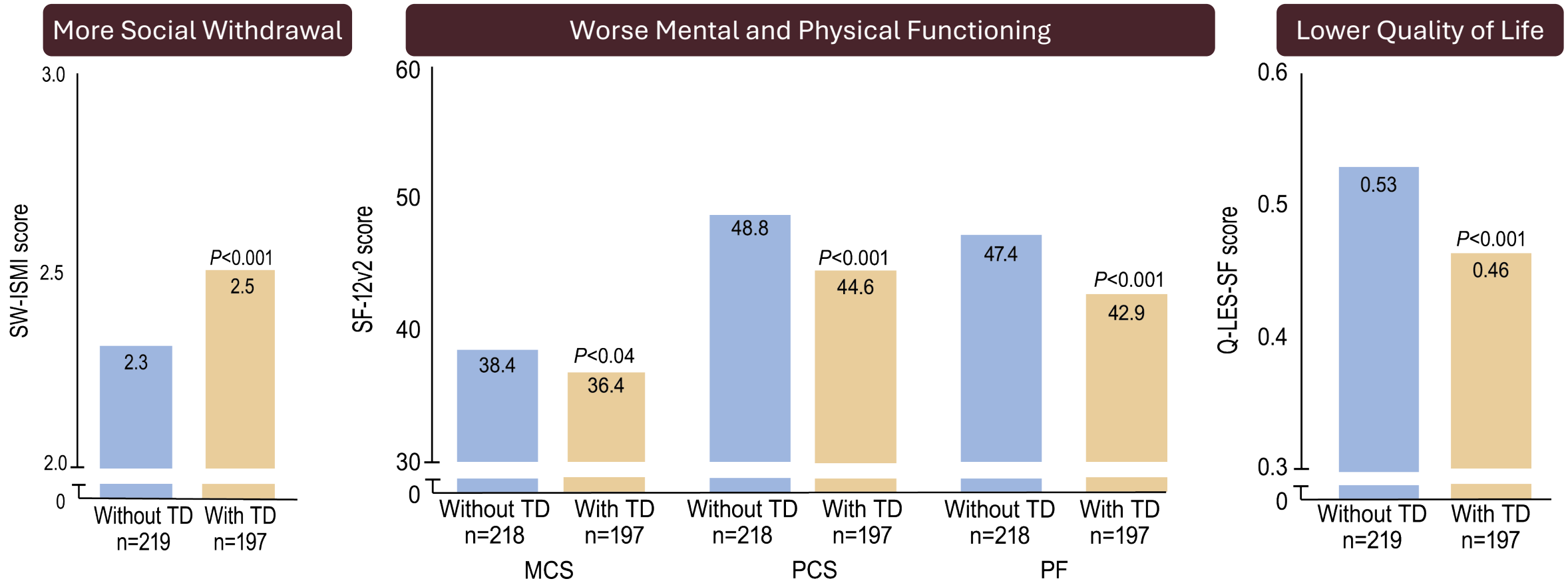
Psychological and Therapeutic Impact

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

TD Negatively Impacts Life No Matter the Underlying Diagnosis



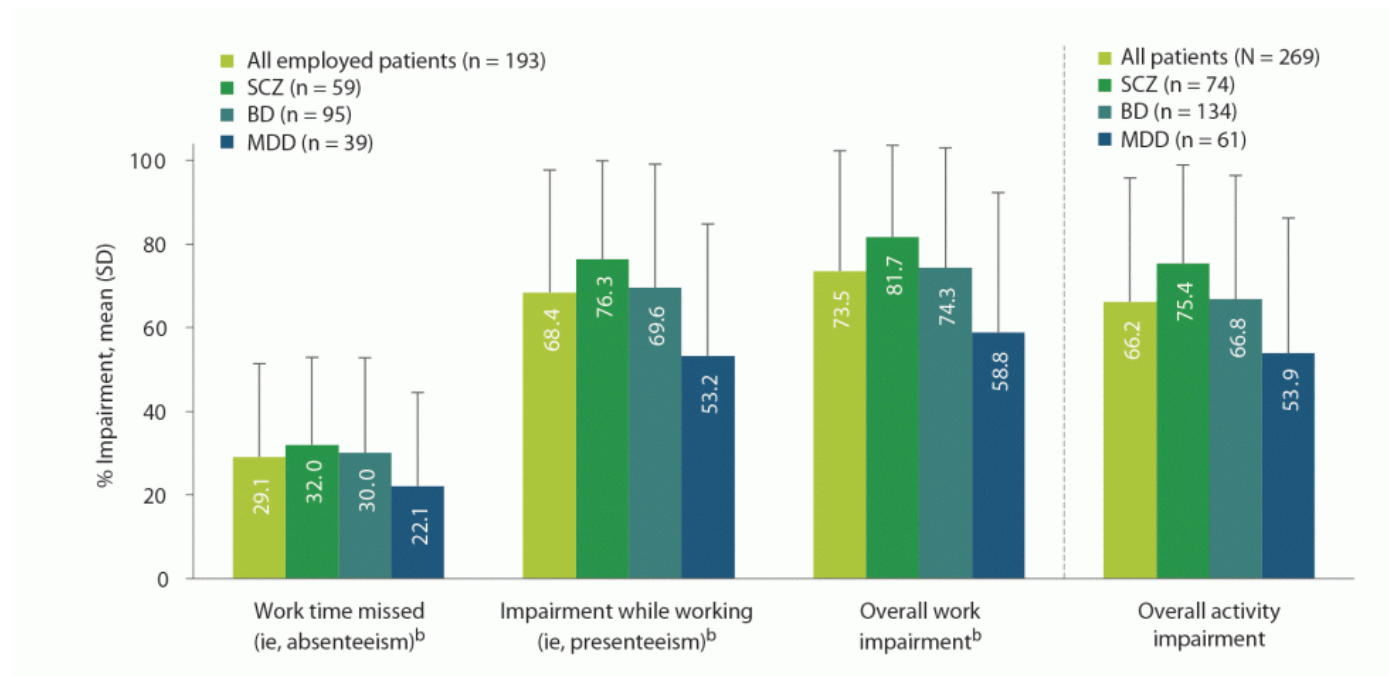
Survey of patients with clinician-confirmed diagnosis of BD, MDD, or SCZ shows those with TD have significantly:



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

Patient Advocate:
Living with TD
Before Effective Treatment



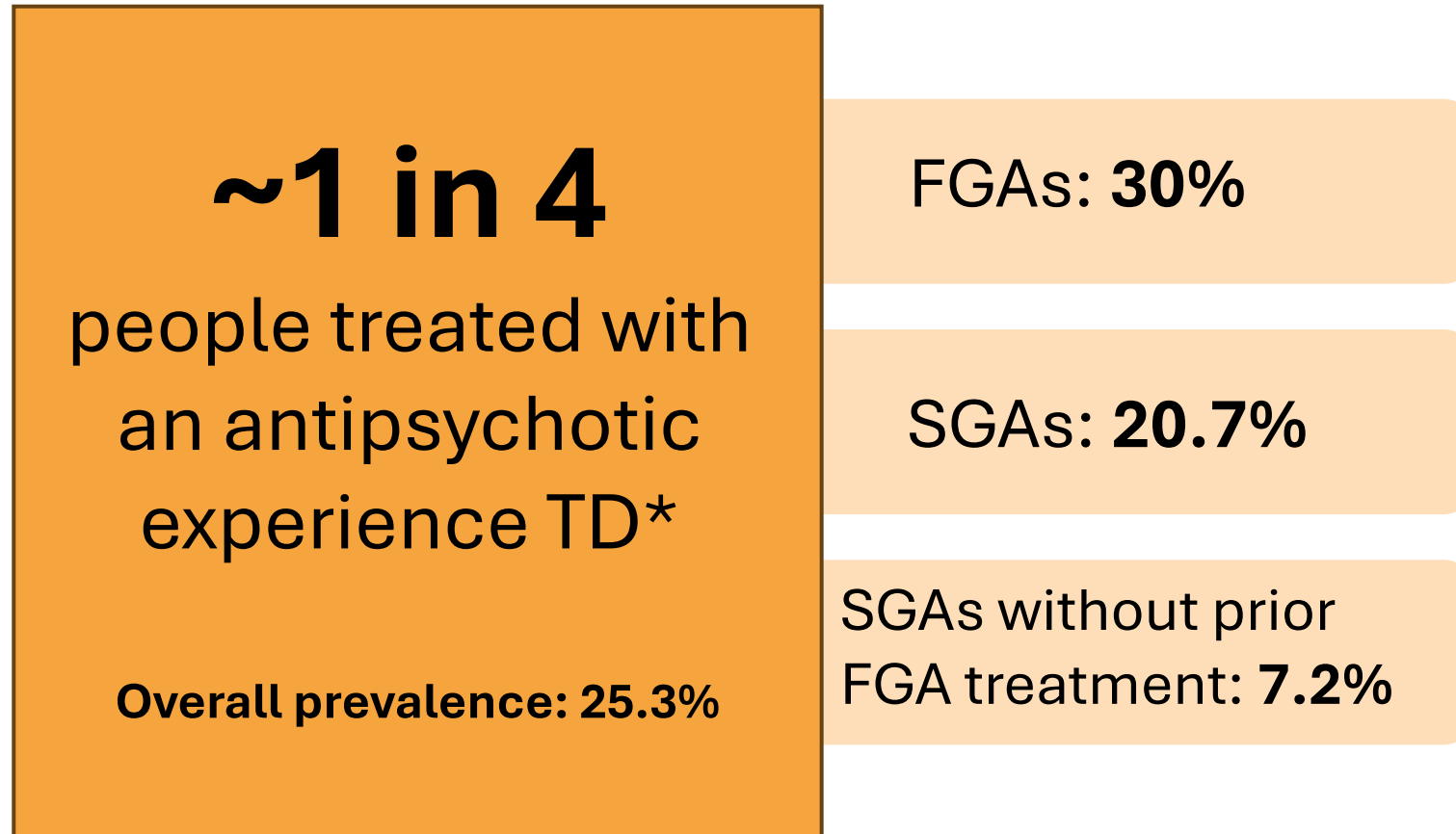
Key Learning Points



- 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?

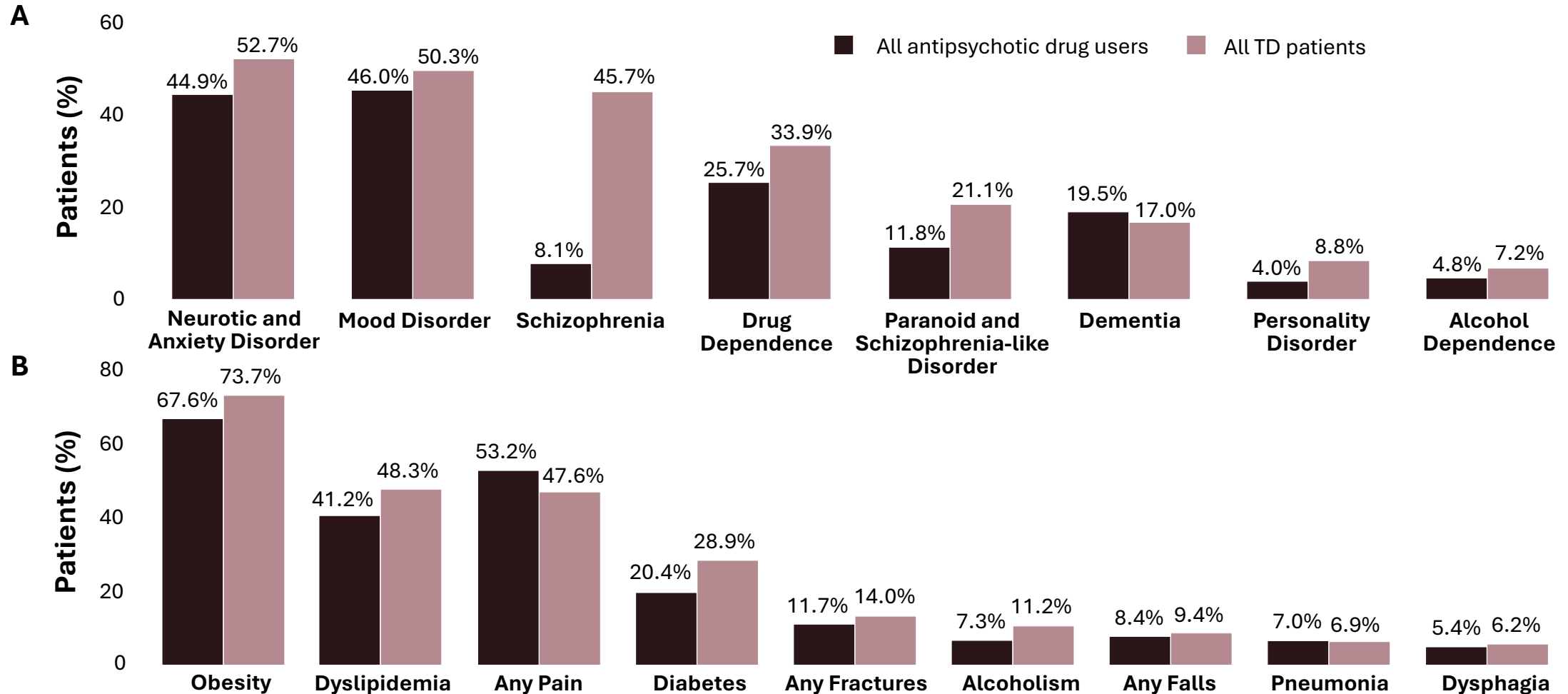


*Based on a meta-analysis of 41 studies (N=11,493; mean age=42.8 years, 66.4% male, 77.1% schizophrenia spectrum).

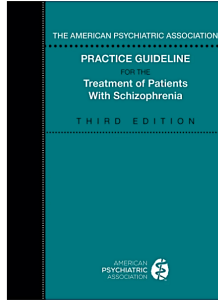
EPS=Extrapyramidal symptoms.

Carbon M, et al. *J Clin Psychiatry*. 2017;78(3):e264-e278.

Psychiatric and Physical Diagnoses in Patients With/Without TD



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	VMAT2 inhibitors (tetrabenazine, valbenazine, deutetabenazine), Ginkgo biloba, clonazepam, amantadine	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

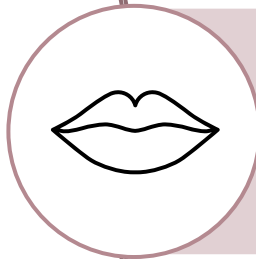
0=None 1=Minimal 2=Mild
3=Moderate 4=Severe

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 difficult 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**

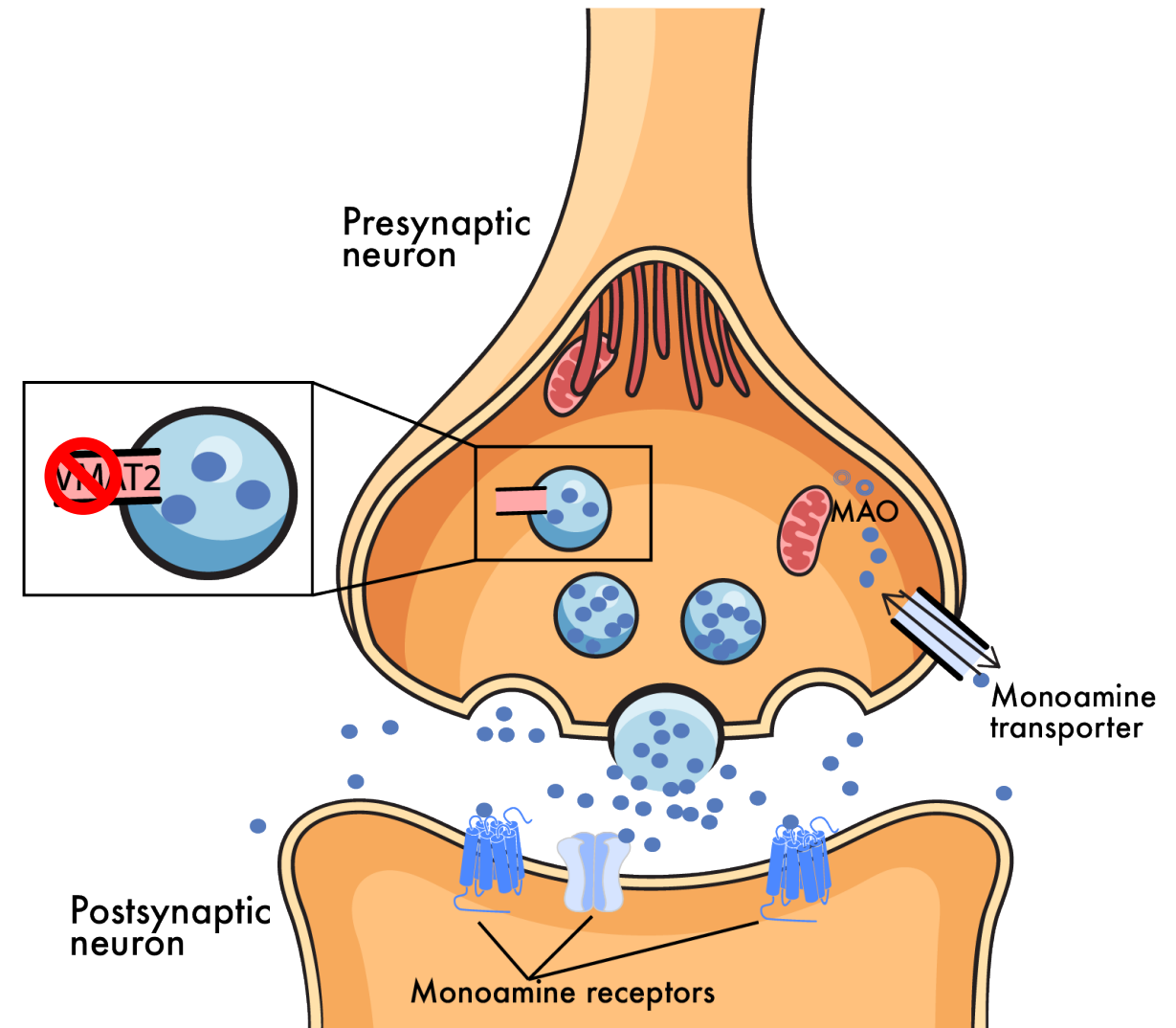
Consider **amantadine as an alternative to anticholinergic medication** to manage DIP

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.

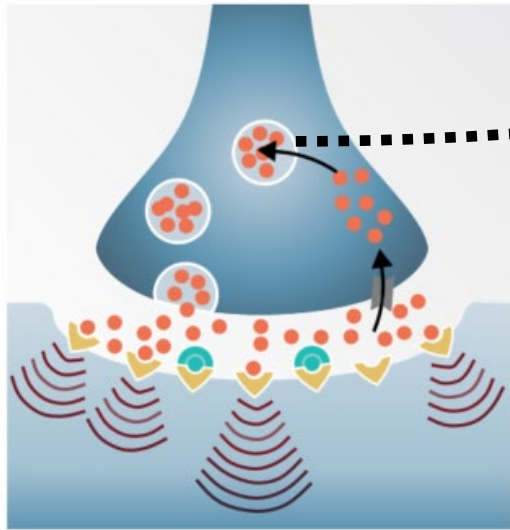
What Are VMAT-2 Inhibitors?





- 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 **hyperdopaminergic** state of TD

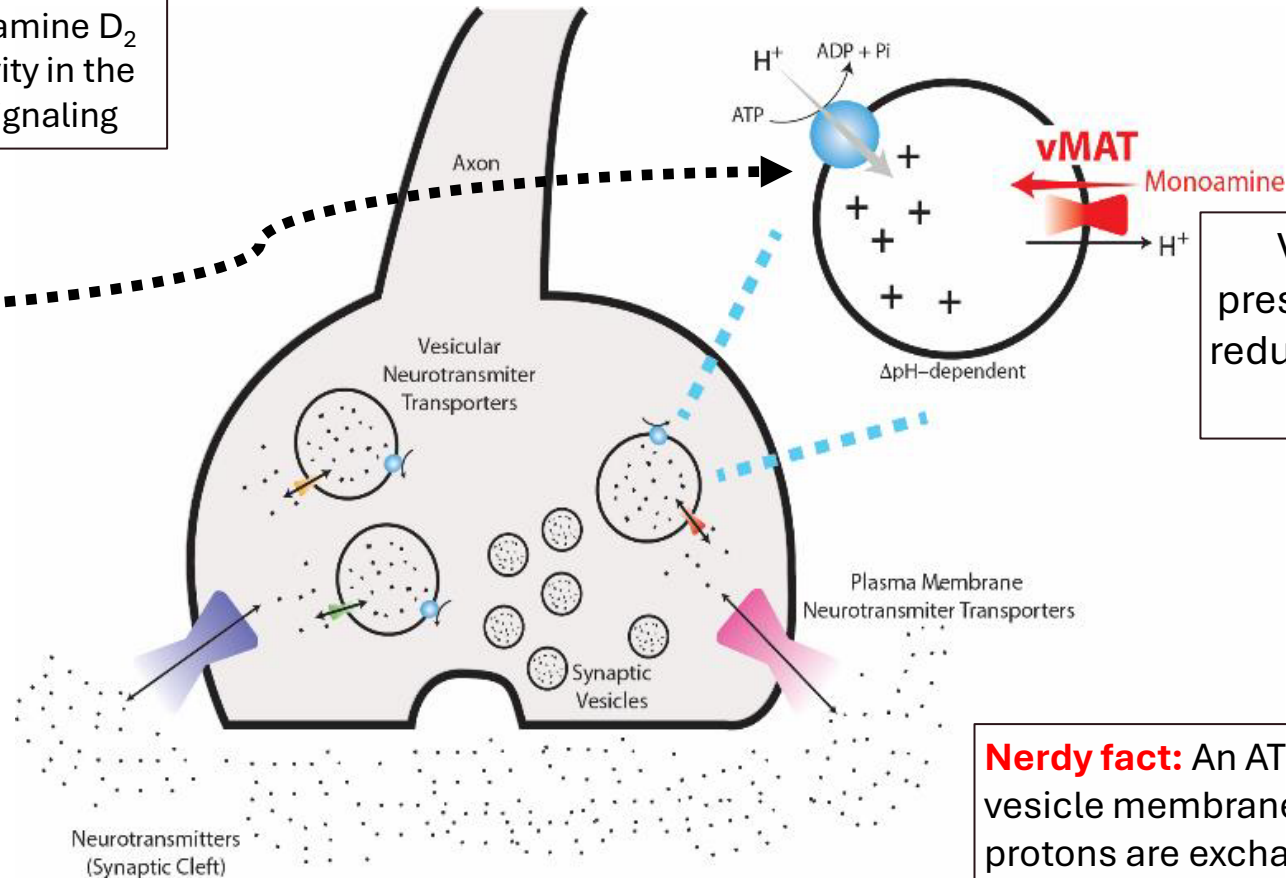


Reversible VMAT-2 Inhibitor: Mechanism of Action

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.

Overview of VMAT-2 Inhibitors Approved for TD

	Valbenazine	Deutetrabenazine Extended-Release
Dosage	40 to 80 mg, once daily with or without food	12 to 48 mg, once daily with or without food
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
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

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.

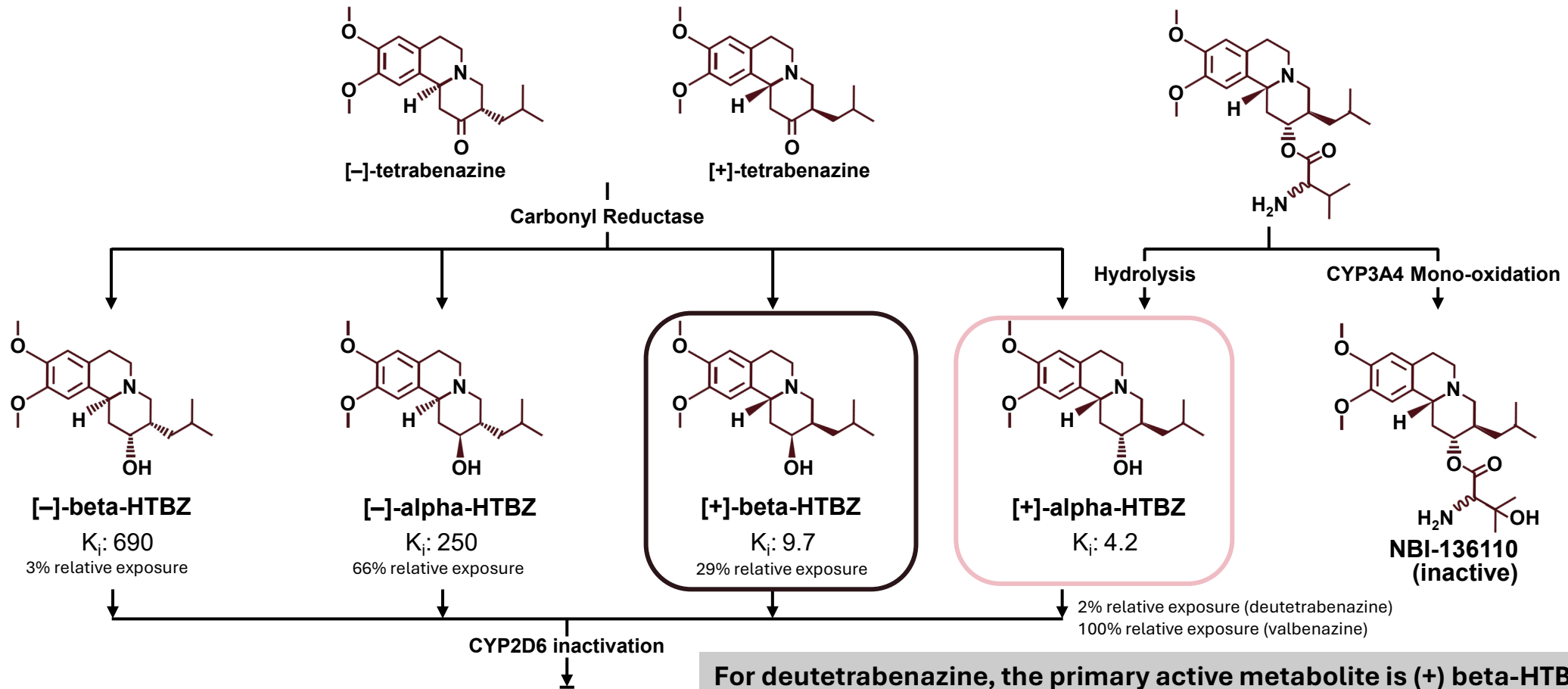
https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/209241s029lbl.pdf. Deutetrabenazine PI. US Food and Drug Administration. Drugs@FDA: FDA Approved

Drugs. Accessed February 2025. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/208082s016s017lbl.pdf.

Differences in Metabolism of Valbenazine and Tetrabenazine/Deutetetrabenazine

Tetrabenazine or Deutetetrabenazine

Valbenazine



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

**Valbenazine:
Clinical and Real-World
Evidence in TD**

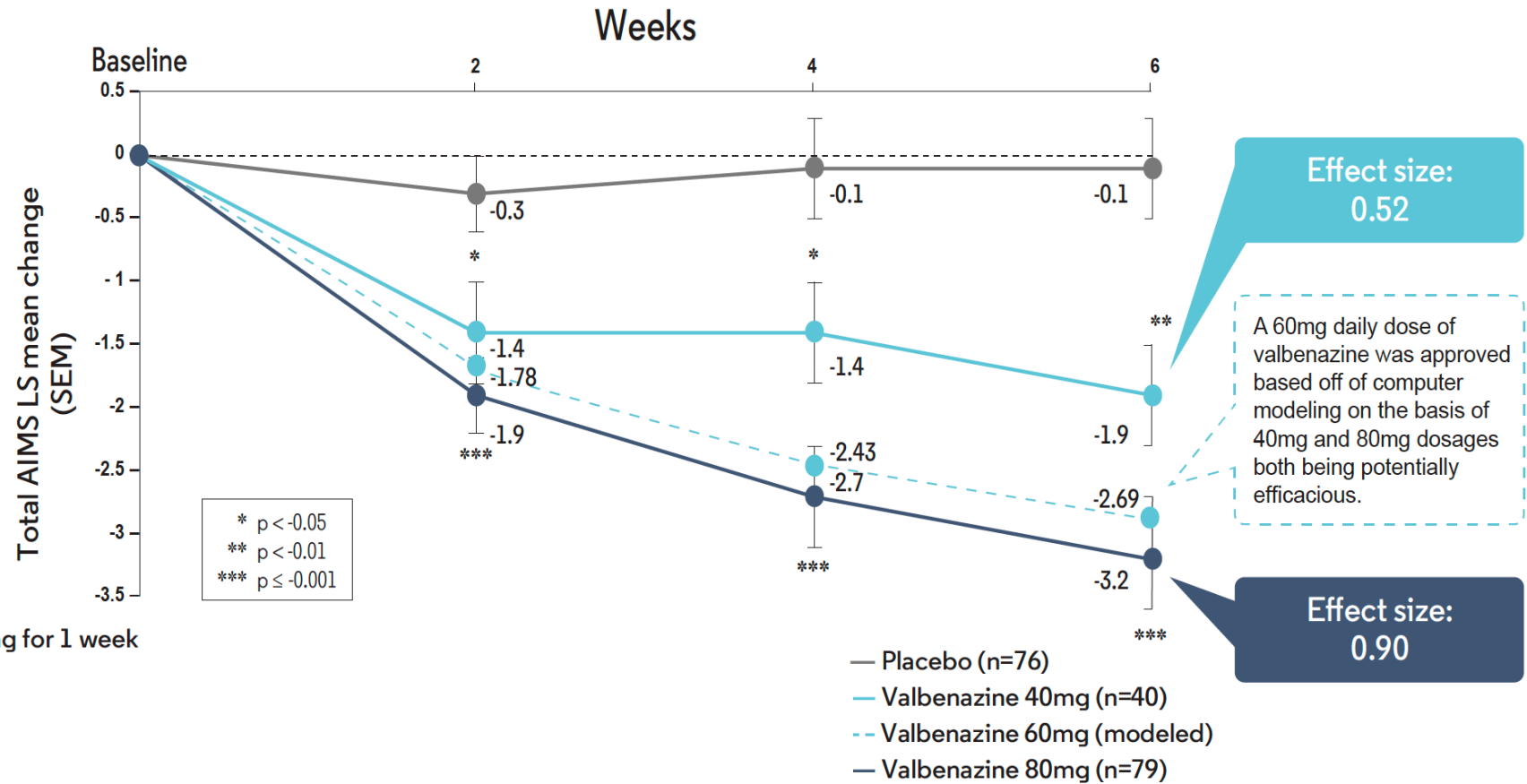
6-Week Placebo-Controlled Fixed-Dose Study of Valbenazine (KINECT-3)

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

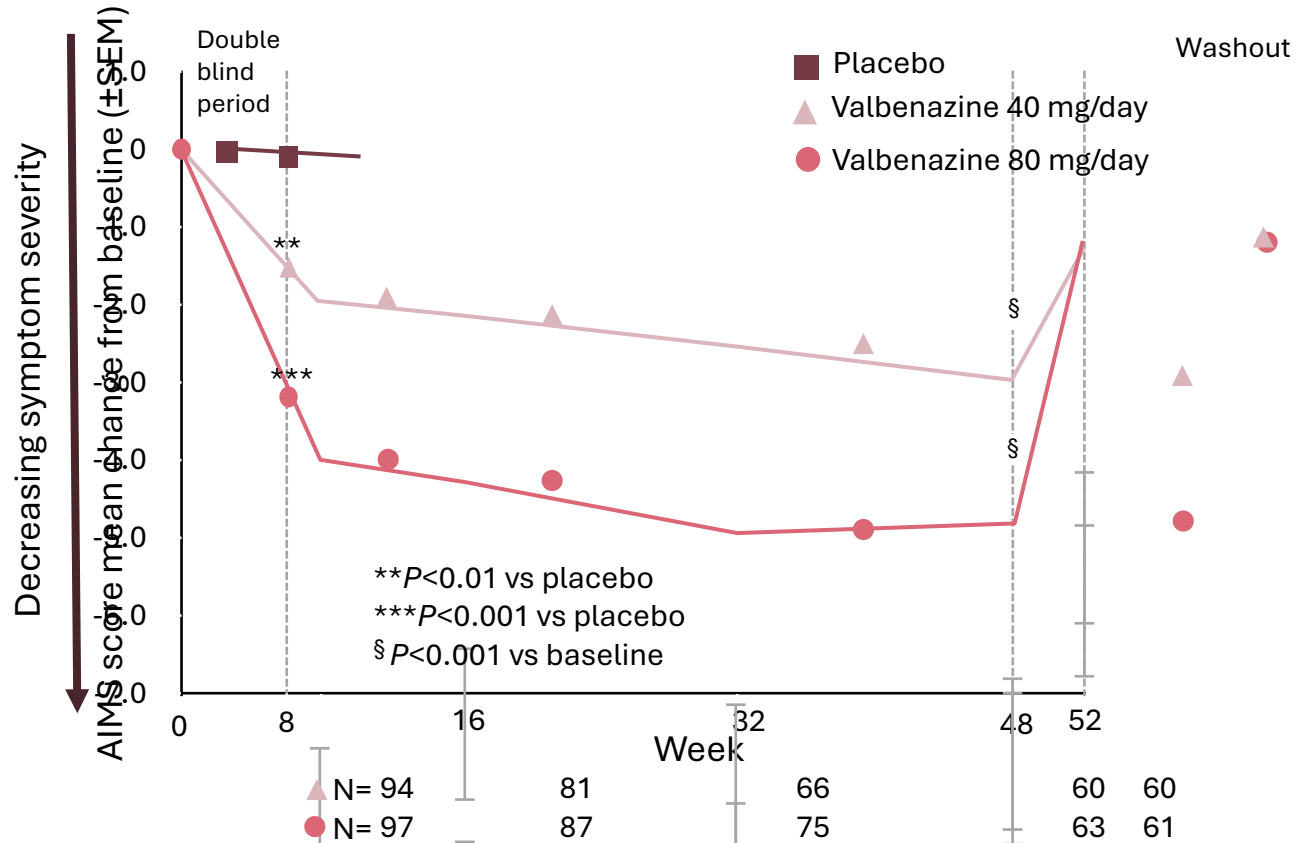
Adverse Events in 6-Week Valbenazine DBPC Studies in North America Reported at $\geq 2\%$ and Greater Than Placebo

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%

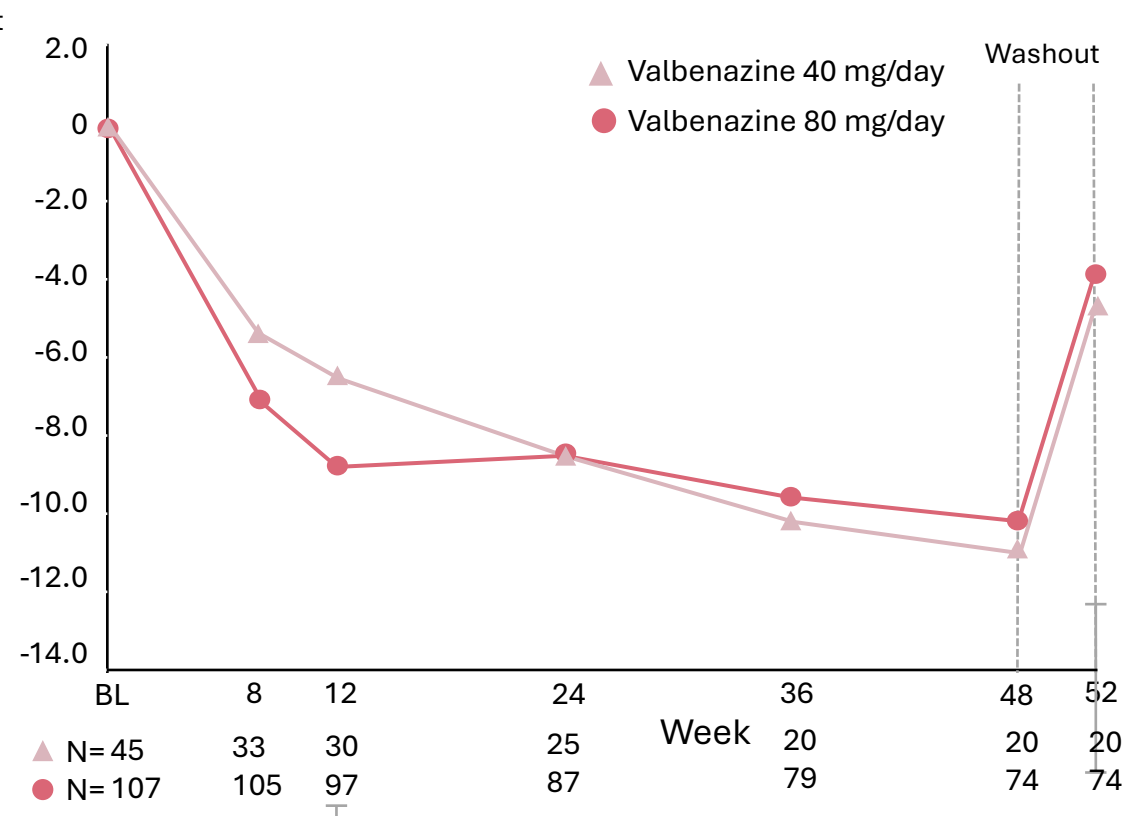
Discontinuation due to AEs occurred in 3% of patients taking valbenazine vs 2% of patients taking placebo

Long-Term Studies of Valbenazine

KINECT-3 Open Label Extension Study



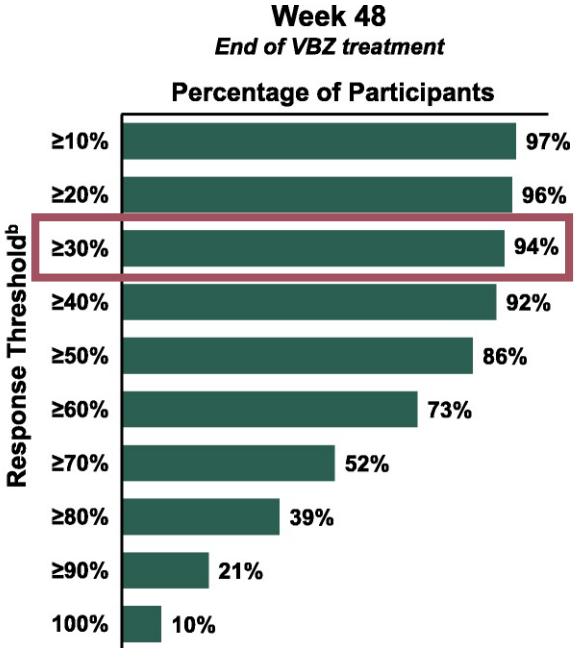
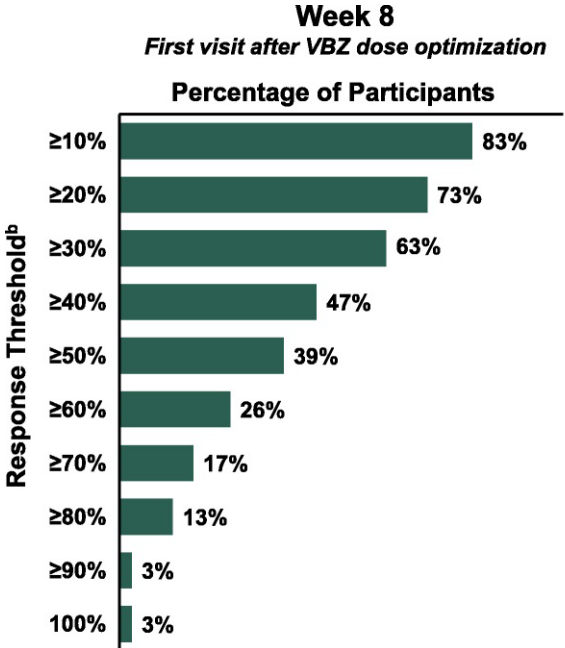
KINECT-4 Study



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

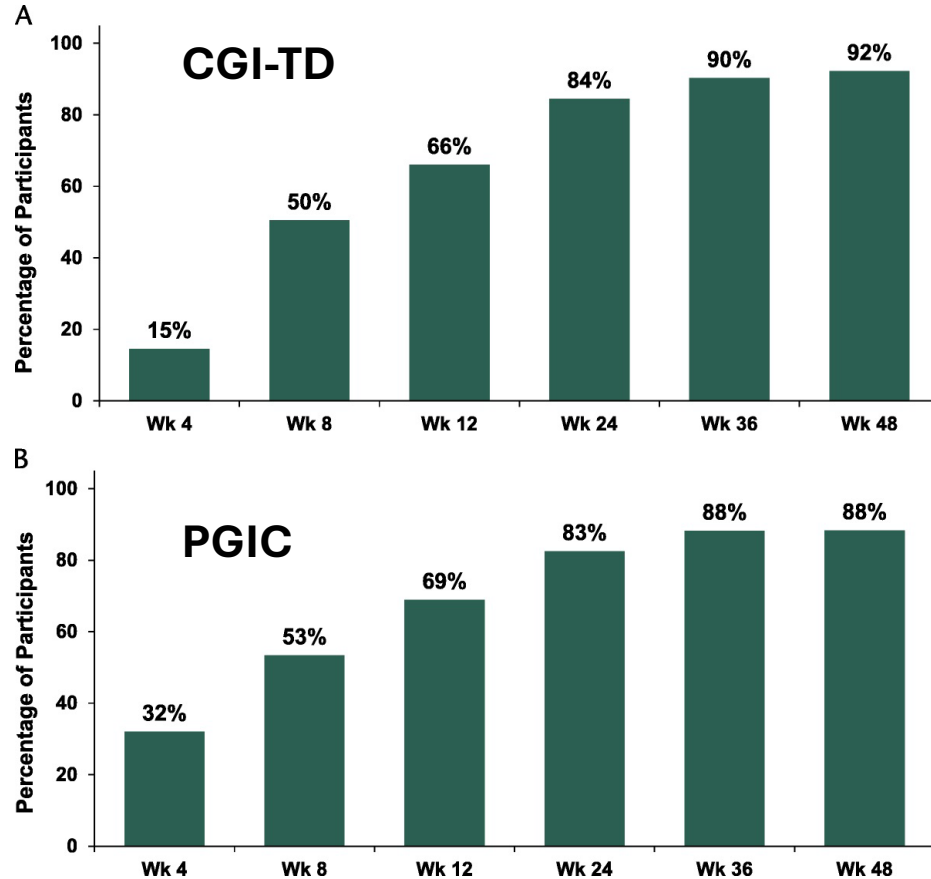
94% treatment completers met the response threshold of $\geq 30\%$ AIMS improvement at week 48



Sustained Response with Valbenazine Treatment

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

Valbenazine Demonstrates Sustained Global and AIMS Improvement Through 48 Weeks



Response was defined as “much improved” or “very much improved” (score ≤ 2).

By 48 weeks, most patients with moderate-to-severe TD improved to mild or better across nearly all AIMS body regions with valbenazine treatment.

AIMS Item	Participants With AIMS Item Shifts (Score ≥ 3 to ≤ 2 [†]), % (n/N)
1. Face	98 (40/41)
2. Lips	100 (63/63)
3. Jaw	98 (50/51)
4. Tongue	98 (58/59)
5. Upper extremities	100 (50/50)
6. Lower extremities	100 (29/29)
7. Trunk	89 (23/26)
8. Global (site-rater judgment) [‡]	96 (94/98)
8. Global (highest score from items 1–7) [§]	94 (93/99)

* Total number of participants who completed 48 weeks of open-label, once-daily treatment with valbenazine (40 or 80 mg).

[†] Shift from “moderate” or “severe” to “mild” or better (based on AIMS scoring by site raters).

[‡] Based on investigators' ratings of item 8 (based on clinical judgment regarding the entire examination as a whole).

[§] Based on investigators' highest single score from items 1–7 (ie, determined algorithmically from the investigator's individual ratings).

N, number of participants with item score ≥ 3 at baseline; n, number of participants with item score ≤ 2 at Week 48.

AIMS, Abnormal Involuntary Movement Scale.

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

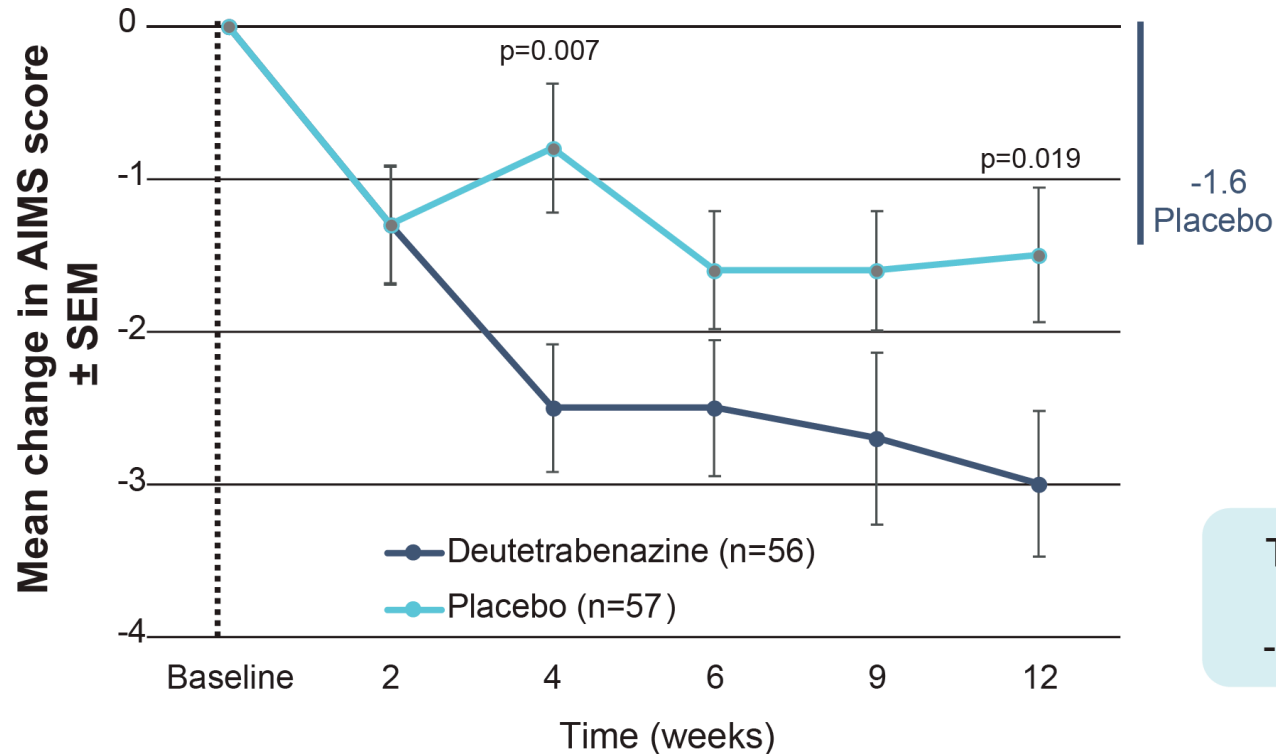


pudding

**Deutetrabenazine:
Clinical and Real-World
Evidence in TD**

Flexible-Dose Study of Deutetrabenazine (ARM-TD)

Change in Abnormal Involuntary Movement Scale (AIMS) from Baseline to Week 12



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

-3.0
Deutetrabenazine

Treatment effect of -1.4 points

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

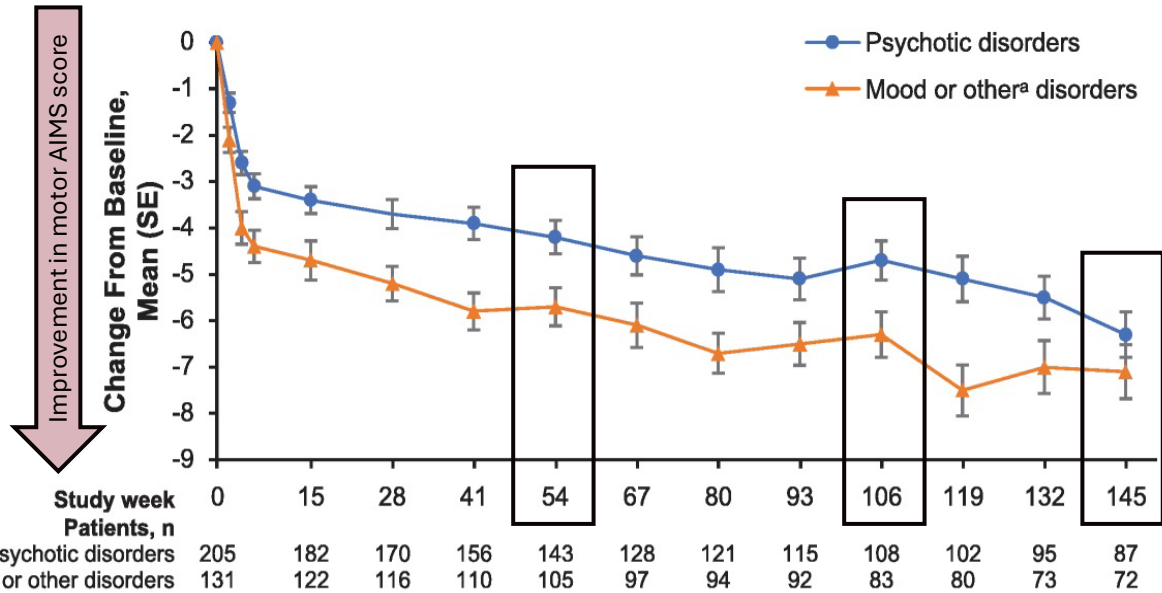
Discontinuation due to AEs occurred in 4% of patients taking deutetrabenazine vs 3% of patients taking placebo

AE = adverse effect.

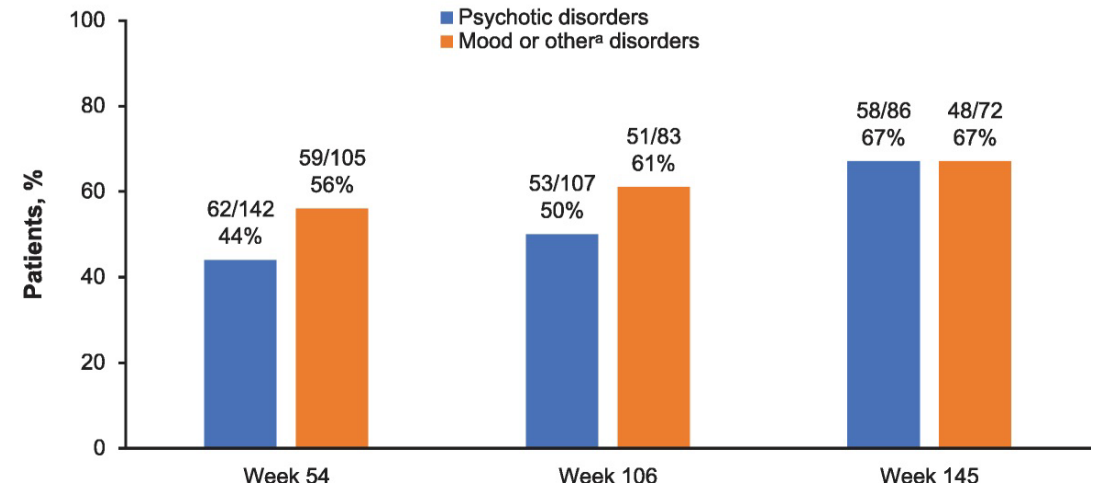
Anderson KE, et al. *Lancet Psychiatry*. 2017;4(8):595-604. Fernandez HH, et al. *J Neurol Neurosurg Psychiatry*. 2019;90(12):1317-1323.

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

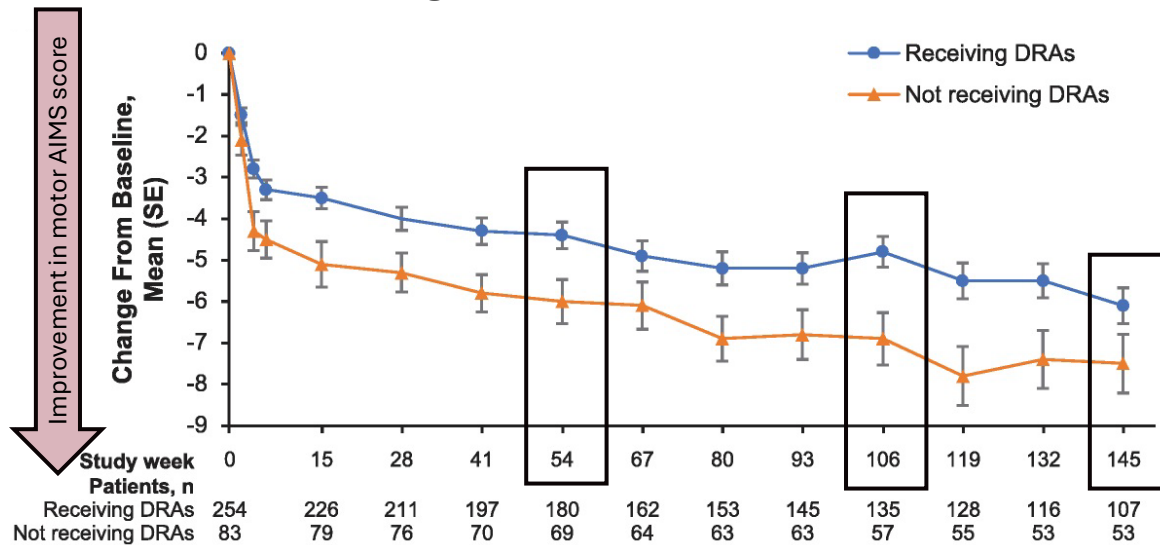


Deutetrabenazine produced **sustained, clinically meaningful reductions in AIMS scores over 3 years**, with similar long-term benefits across both psychotic and mood/other disorder populations.

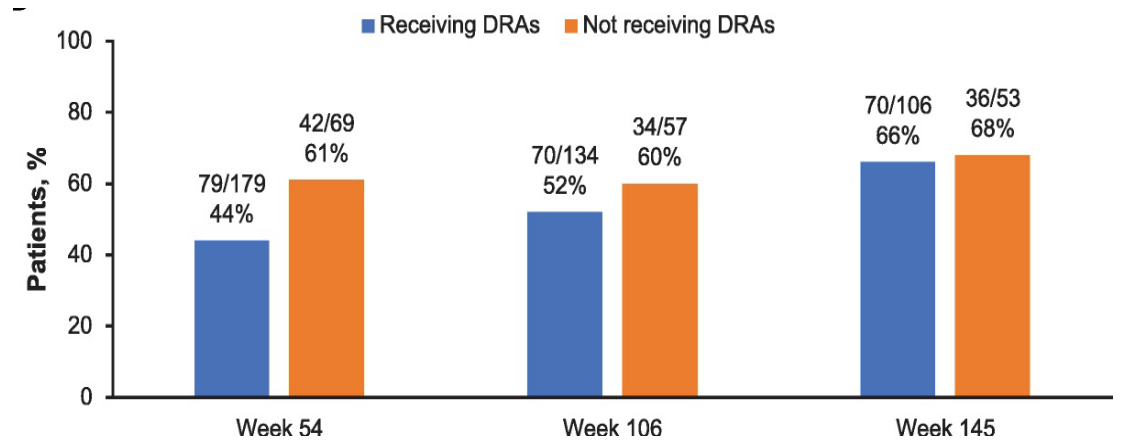
^aExamples of other disorders include abdominal discomfort, alcohol withdrawal syndrome, gastroesophageal reflux disease, insomnia, neurosis, and tic.
Hauser RA, et al. *J Clin Psychopharmacol*. 2024;44(4):386-396.

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

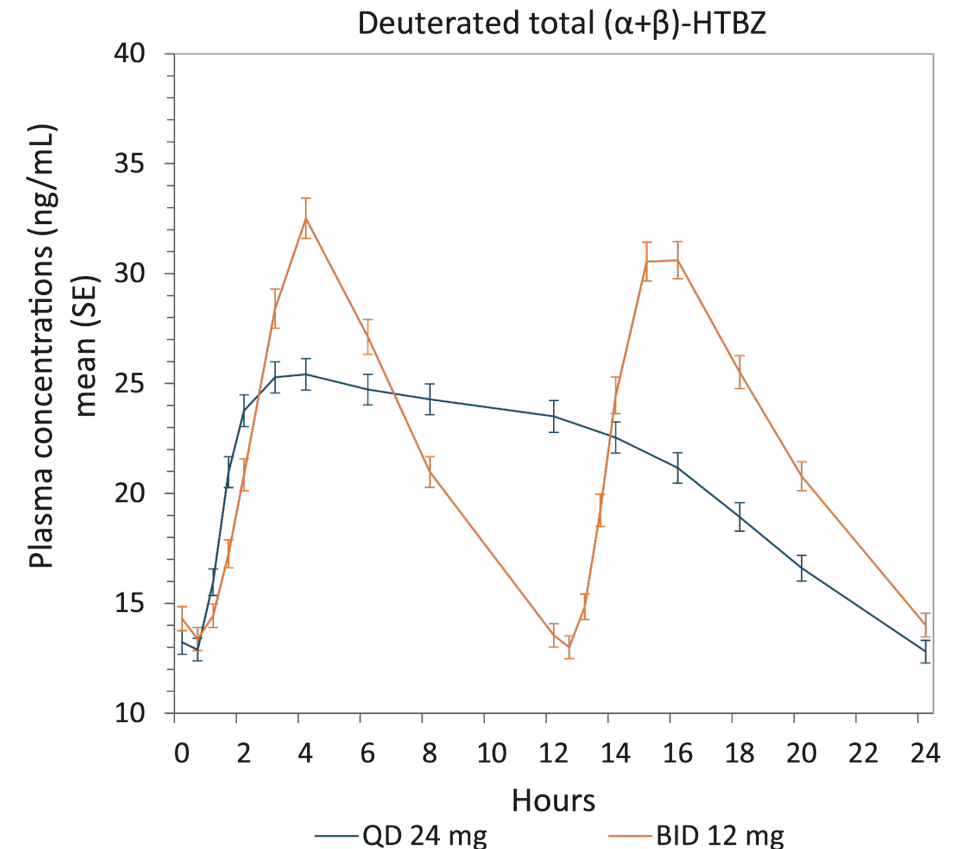
DRA=Dopamine Receptor Antagonist.

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

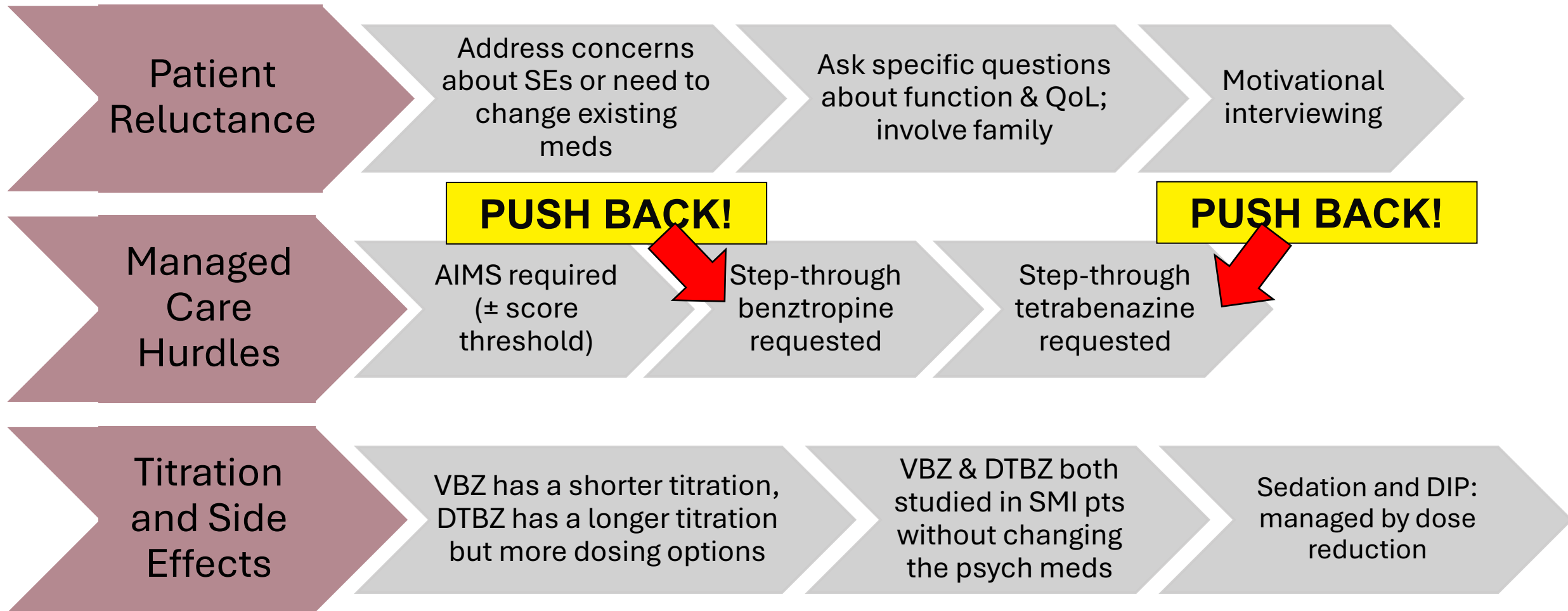


XR = extended release; BID = twice daily; QD = once daily; PM = poor metabolizer; MAOI = monoamine oxidase inhibitor.

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.

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)

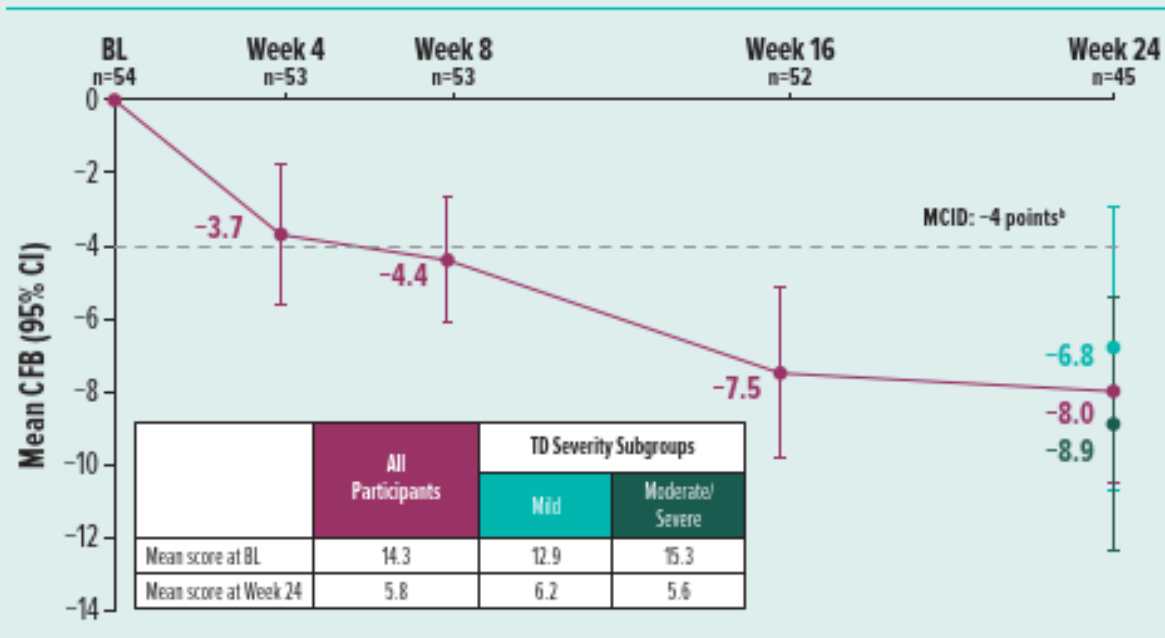
Domain	TDIS item	Corresponding TDRS item
Mouth/throat function	1. Speech	Item 2. Speech
	2. Mouth noises	Not applicable
	3. Swallowing	Item 3. Chewing and swallowing
Dexterity	4. Gripping	Item 4. Eating tasks Item 5. Dressing Item 6. Hygiene Item 8. Hobbies
	5. Writing	Item 7. Handwriting
Mobility	6. 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

Figure 2. TDIS Total Score^a

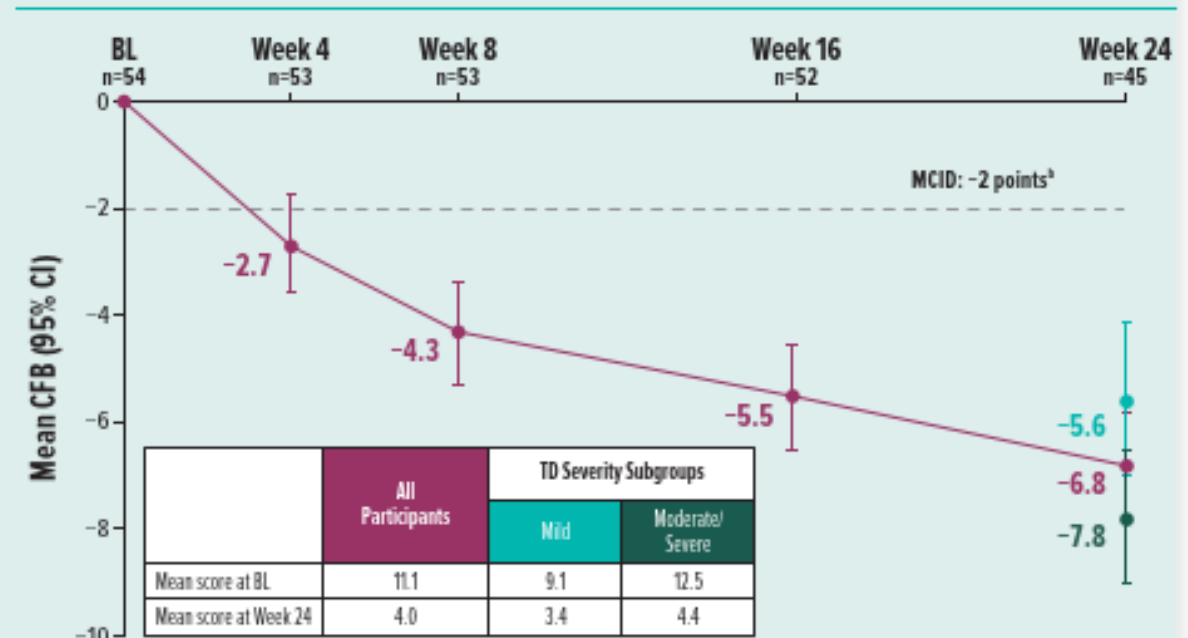


^aTDIS total score ranges from 0 to 44, with higher scores indicating worse impact. The total score is summed from the 11 item scores, each of which range from 0 (no impact) to 4 (extreme impact).

^bFrom: Farber RH, et al. *Neurology*. 2023;26:5462.

BL, baseline; CFB, change from baseline; CI, confidence interval; MCID, minimum clinically important difference; TD, tardive dyskinesia; TDIS, Tardive Dyskinesia Impact Scale.

Figure 3. AIMS Total Score^a



^aAIMS 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).

^bFrom: Stacy M, et al. *Mov Disord*. 2019;34:1203-9.

AIMS, Abnormal Involuntary Movement Scale; BL, baseline; CFB, change from baseline; CI, confidence interval; MCID, minimum clinically important difference.

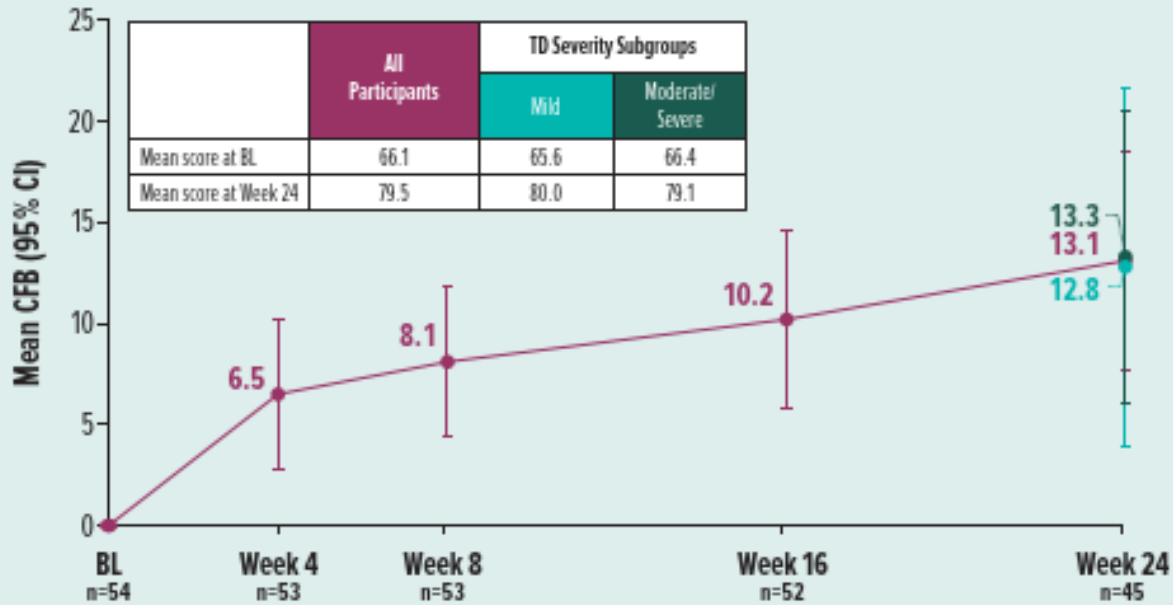
Valbenazine significantly reduced TDIS and AIMS Total Scores from baseline (MCID=-4 and -2, respectively)

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.

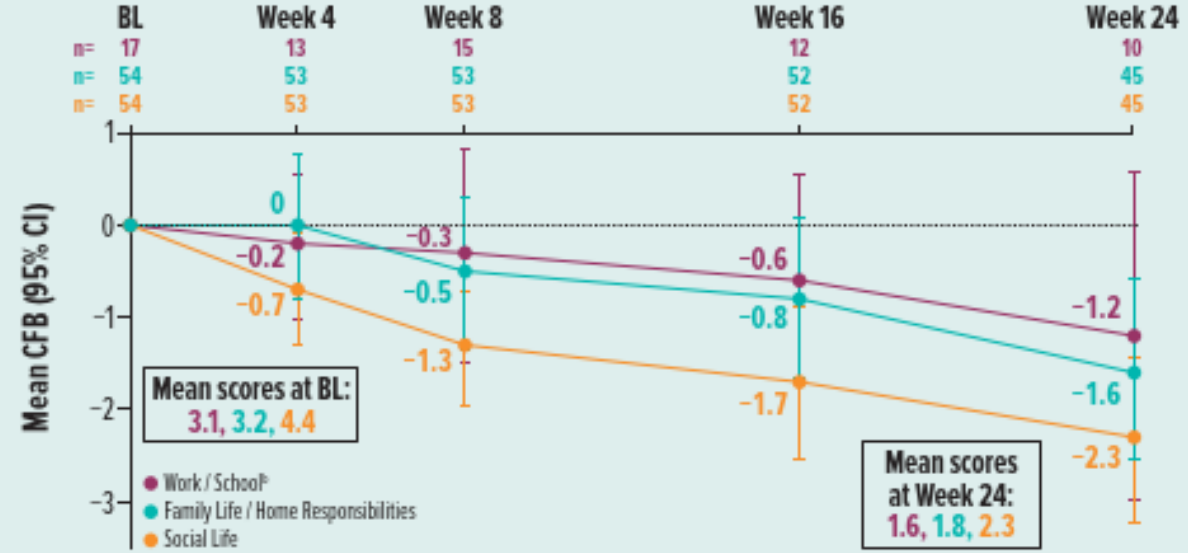
Valbenazine Improves the Impacts and Symptoms of TD: Results From the Phase 4 KINECT-PRO™ Study

Figure 4. EQ-VAS Score^a



^aEQ-VAS ranges from 0 ("worst health you can imagine") to 100 ("best health you can imagine").
BL, baseline; CFB, change from baseline; CI, confidence interval; EQ-VAS, EuroQol Group's EQ-5D-5L visual analog scale.

Figure 5. SDS Domain Scores^a



^aSDS domain scores each rate functional impairment from from 0 (none at all) to 10 (extremely). Subgroup data is available on request to medinfo@neurocrine.com.
^bFew study participants were working or attending school during the study (n=17 at BL). Therefore, interpretation of these results is limited.
BL, baseline; CFB, change from baseline; CI, confidence interval; SDS, Sheehan Disability Scale.

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

SOCIAL IMPACTS

- Difficulty participating in events with family and others (e.g., holiday gatherings, religious services)
- Self-consciousness/embarrassment about movements or being seen/asked about them by others (i.e., stigma, rejection)
- Avoidance of interaction with others (e.g., declines invitations, avoids leaving home, isolation)
- Reduced quality of interpersonal communication (e.g., distraction from conversation problems, interpreting body language)



PSYCHOLOGICAL IMPACTS

- Feelings of sadness, depression, anxiety, worry, concern, low self-esteem, hopelessness, loss of sense of purpose
- Poor concentration, attention, and memory
- Worsening or recurrence of previous symptoms/disorder (e.g., depressed mood, anxiety, psychosis)
- Difficulty with appropriate treatment of mental disorder (e.g., reduced adherence with medication regimens, discontinuation of treatment)
- Unhealthy coping strategies (e.g., substance use/abuse)

PHYSICAL IMPACTS

- Difficulty using utensils, writing, typing, dressing
- Difficulty speaking, chewing, or swallowing
- Difficulty walking or maintaining balance (e.g., stumbling, need for assistive device)
- Problems breathing (e.g., shortness of breath, gasping for air)
- Pain due to TD (e.g., biting inside of mouth, jaw clenching)
- Difficulty sitting still, falling asleep

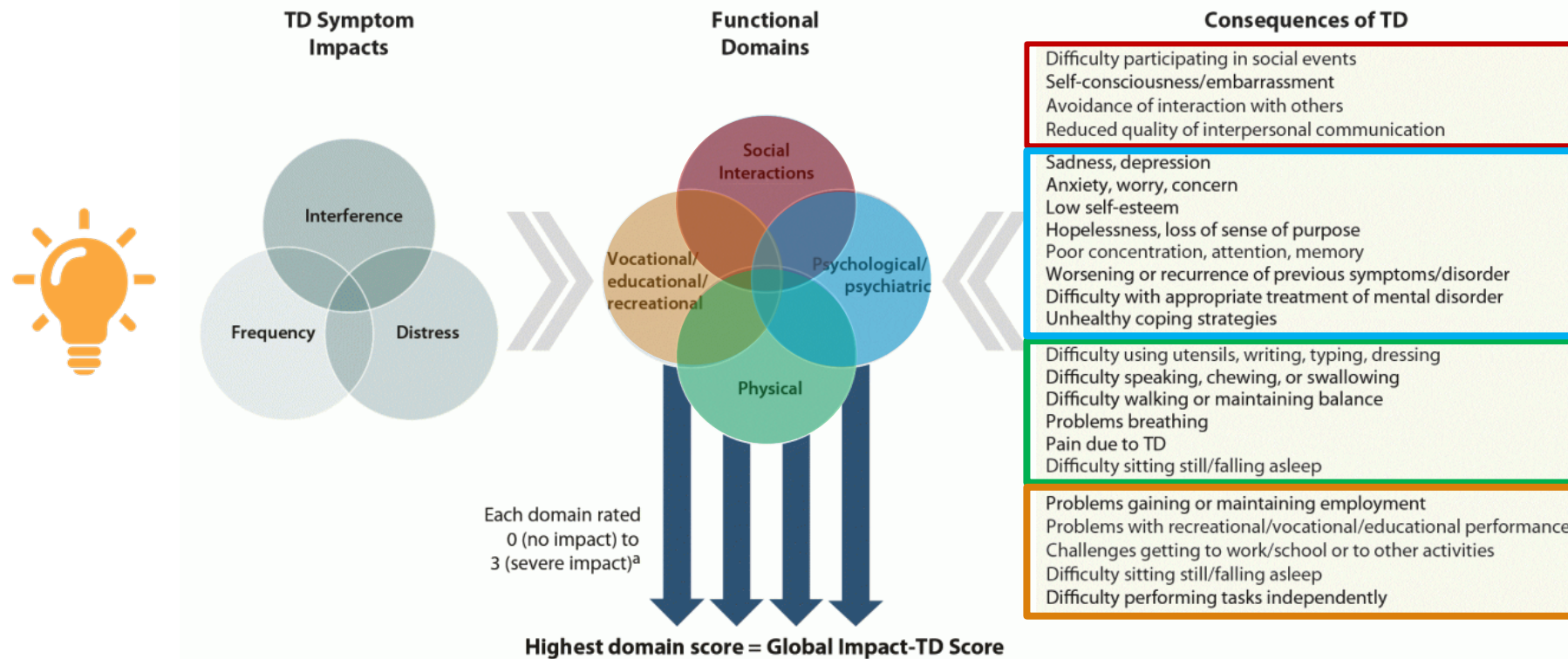
**Mild score
on AIMS
may not =
mild impact**

VOCATIONAL/EDUCATIONAL/ RECREATIONAL IMPACTS

- Problems gaining or maintaining employment
- Problems with recreational or vocational/educational performance (e.g., poor concentration, trouble communicating, physical limitations)
- Challenges getting to work/school, or other activities
- Difficulty with colleague/classmate/customer interactions
- Difficulty performing tasks independently

IMPACT-TD Scale: Design and Real-World Validation

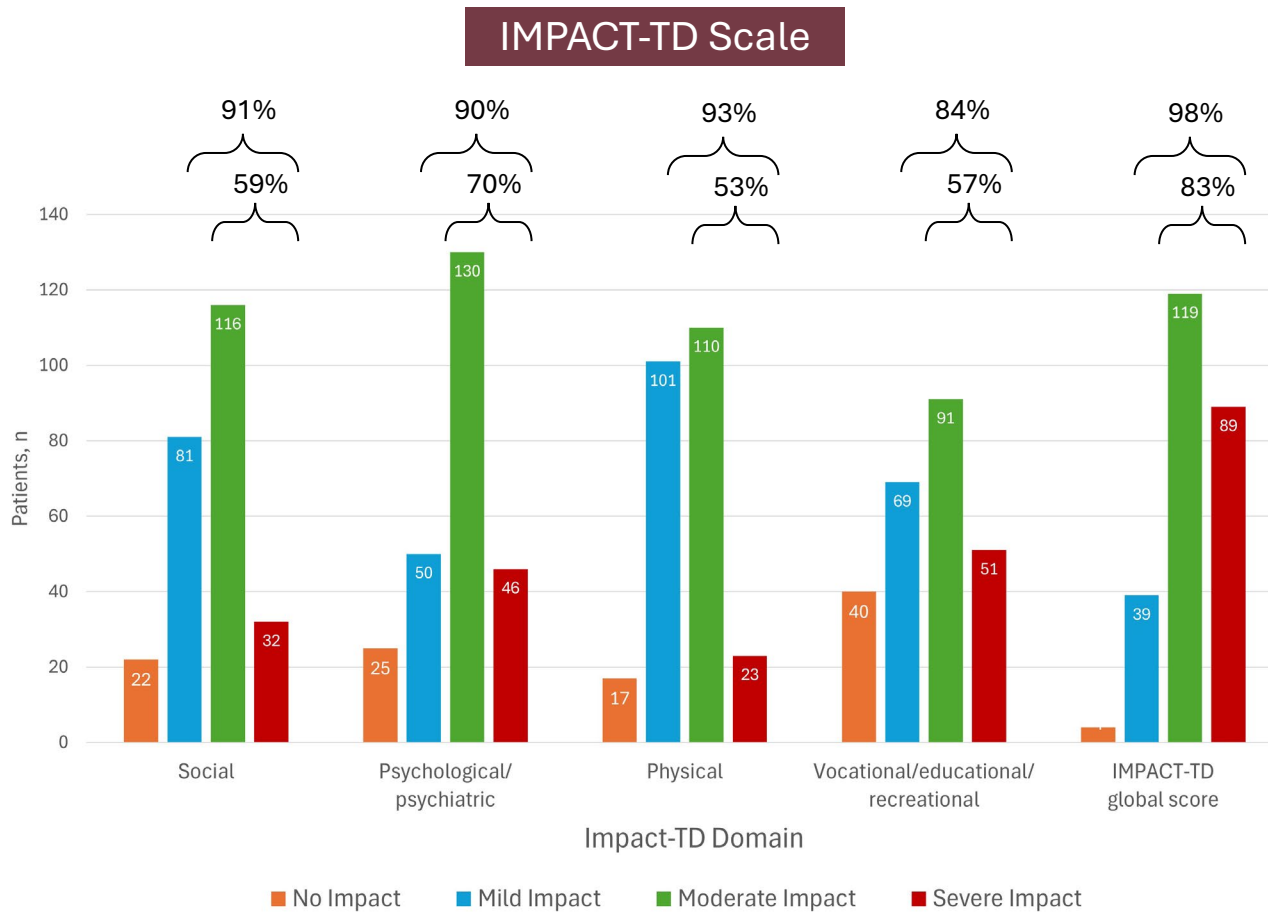
Figure 1. Components of the Impact-TD Scale



^aWhen rating the overall impact of a functional domain, the rater should consider the degree of interference, distress, and/or frequency for that domain.
Abbreviation: TD = tardive dyskinesia.

Each domain rated: 0 = No impact; 1 = Mild impact; 2 = Moderate impact; 3 = Severe impact

IMPACT-TD Registry: Ongoing Phase 4 Longitudinal Study

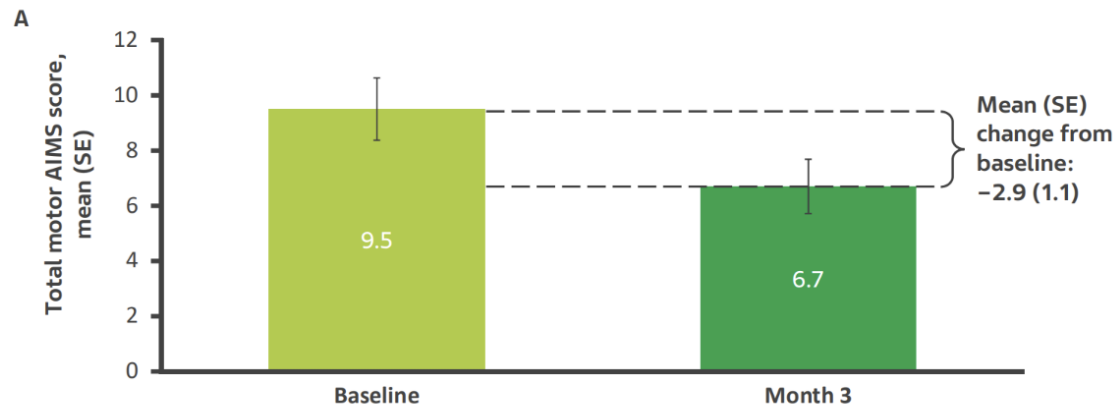


Most patients experience **moderate to severe impact** across QoL domains:

- social (59%)
- psychological/psychiatric (70%)
- physical (53%)
- vocational/educational/recreational (57%)

IMPACT-TD Registry: Ongoing Phase 4 Longitudinal Study

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



*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

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 Advocate:
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 tens of millions of family caregivers. These Americans care for loved ones with chronic conditions, disabilities, or diseases, including **TARDIVE DYSKINESIA**.

Visit their website for **helpful tools and resources** to share with patients and their caregivers, including:

- Risk Factors
- Early Symptoms
- Screening Standards
- Treatment Options
- Importance of Early Intervention
- And additional helpful resources

Scan this
QR code



Visit: <https://www.caregiveraction.org/understanding-tardive-dyskinesia/>

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 dyskinesic movements while maintaining necessary antipsychotic therapy