

# Real-World Benztropine Use in DRBA-Induced Movement Disorders



# DRBA-Induced Movement Disorders

- Dopamine Receptor Blocking Agent (DRBA)-induced movement disorders are movement disorders associated with the use certain medications, such as antipsychotics<sup>1</sup>
- Movements can include<sup>1</sup>
  - Acute dystonia
  - Acute akathisia
  - Tardive dystonia
  - Tardive dyskinesia (TD)
  - Drug-induced parkinsonism
- TD is a persistent and potentially disabling movement disorder associated with prolonged exposure to DRBAs<sup>2,3</sup>
  - TD is often underdiagnosed due to overlap between DRBA-induced movement disorders, historic categorization of TD as extrapyramidal symptoms (EPS), and limited awareness of the number of drugs that can cause TD<sup>4</sup>

## DRBAs can include:<sup>1</sup>

- First-generation antipsychotics
- Second-generation antipsychotics
- Gastrointestinal medications, such as metoclopramide

DRBA, dopamine receptor blocking agent; TD, tardive dyskinesia.

1. American Psychiatric Association: Diagnostic and Stat Diagnostic and Statistical Manual of Mental Disorders. Fifth Edition – Text Revision. American Psychiatric Association: Washington, DC; 2022. 2. Lerner PP, et al. Psychiatry Clin Neurosci. 2015;69(6):321-334. 3. Waln O, et al.. Tremor Other Hyperkinet Mov (N Y). 2013;3. 4. Hauser RA, Meyer JM, Factor SA, et al. CNS Spectr. 2022;27(2):208-217.

# Benzotropine in Guidelines

- Benzotropine is a medication with anticholinergic properties FDA-approved as adjunct therapy for all forms of Parkinsonism and the control of extrapyramidal disorders\* (**except tardive dyskinesia**) due to neuroleptic drugs<sup>1</sup>
- Use of multiple treatment options may be necessary in patients with multiple DRBA-induced movement disorders<sup>2</sup>

## American Academy of Neurology (AAN)

### 2013 AAN Evidence-Based Guidelines<sup>3</sup>:

- No controlled trials examining the efficacy of **benztropine**, biperiden, chlorprothixene, and trihexyphenidyl in treating TD
- Insufficient data to determine the effectiveness of anticholinergics for the treatment of TD ([Level U](#))

## American Psychiatric Association (APA)

### 2022 APA DSM-5-TR: Medication Induced Movement Disorders<sup>4</sup>:

- The symptoms of tardive dyskinesia tend to be **worsened** by stimulants, antipsychotic medication withdrawal, and **anticholinergic medications (such as benztropine**, commonly used to manage medication-induced parkinsonism) and may be transiently worsened by emotional arousal, stress, and distraction during voluntary movements in unaffected parts of the body

**Not recommended for the treatment of TD<sup>1,3-5</sup>**

AAN, American Academy of Neurology; APA, American Psychiatric Association; DRBA, dopamine receptor blocking agent; DSM-5-TR, Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision; FDA, US Food and Drug Administration; TD, tardive dyskinesia; US, United States. \*Previously described as extrapyramidal symptoms (EPS). EPS is an obsolete umbrella term that has been used to describe a collection of DRBA-induced movement disorders despite each having a distinct presentation, pathophysiology, and treatment<sup>6</sup>

1. Benztropine mesylate [package insert]. Warren, NJ: Cipla USA, Inc.; 2020. 2. Hauser RA, et al. *CNS Spectr*. 2020;1-10. 3. Bhidayasiri R, et al. *Neurology*. 2013;81(5):463-469. 4. APA: DSM-5-TR. Washington, DC. 2022. 5. Bergman H, et al. *Cochrane Database Syst Rev*. 2018;1(1):CD00020. 6. Dilks S, et al. *Nurs Clin North Am*. 2019;54(4):595-608.

# Benztropine Prescribing Information States:

“TD may appear in some patients on long-term therapy with phenothiazines<sup>a</sup> and related agents, or may occur after therapy when these drugs have been discontinued”

“In treating acute drug-induced extrapyramidal disorders, after one or two weeks the drug should be withdrawn to determine continued need for it”

“Antiparkinsonism agents<sup>b</sup> do not alleviate the symptoms of TD and in some instances may aggravate them”

**“Benztropine is not recommended for use in patients with TD”**

TD, tardive dyskinesia.

<sup>a</sup>Examples of phenothiazines include fluphenazine, chlorpromazine, and perphenazine (all first-generation antipsychotics). <sup>b</sup>Refers to anticholinergics such as benztropine or trihexyphenidyl.

Benztropine mesylate [package insert]. Warren, NJ: Cipla USA, Inc.; 2020.

# Beers Criteria

Benztropine (oral) and trihexyphenidyl are not recommended in older adults for prevention or treatment of extrapyramidal symptoms associated with antipsychotics according to the [AGS Beers Criteria®](#)

## What are the AGS Beers Criteria?

**Explicit list of potentially inappropriate medications** that are best avoided by older adults in most circumstances/specific situations, including certain diseases or conditions

### **Adults aged ≥65 years**

in all ambulatory, acute, and institutionalized settings of care, except for the hospice and palliative care settings

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## What is the Purpose of the AGS Beers Criteria?

**Improve** medication selection

**Educate** clinicians and patients

**Reduce** adverse drug events

**Serve as a tool** for evaluating quality of care, cost, and patterns of drug use of older adults

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# Anticholinergic Burden



- The Anticholinergic Cognitive Burden (**ACB**) scale is a clinical tool that identifies the severity of negative anticholinergic effects on cognition<sup>1-3</sup>
  - There are several different ACB scales cited in the literature
  - Benztropine is listed in the strongest/highest anticholinergic burden category
- A medication with the highest ACB score in healthy, older adults is associated with cognitive dysfunction and a **50% increase in risk for developing dementia**<sup>4</sup>
- High anticholinergic burden in the elderly is associated with increases in<sup>5</sup>
  - Delirium
  - Falls
  - Functional and cognitive deficits





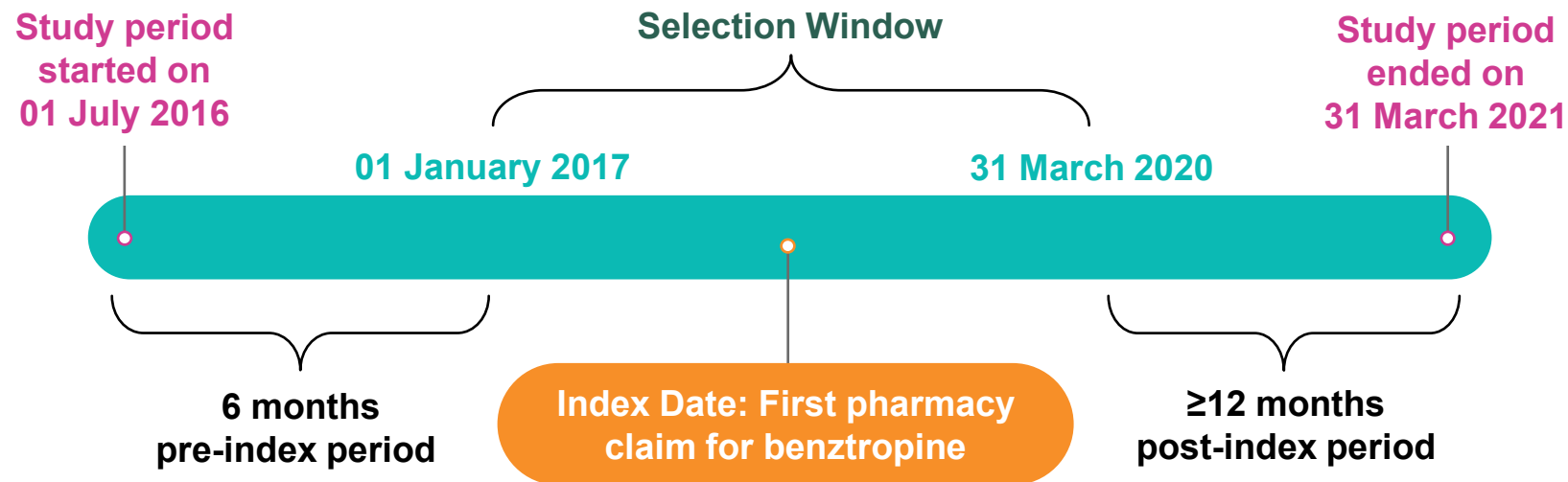
# Real-World Treatment Patterns in Patients Prescribed Benzotropine

A Claims Analysis From 2017-2020

# Claims Analysis: Methods

- A real-world, retrospective claims analysis was conducted among patients receiving an antipsychotic and newly initiating benzotropine in the US to
  - Describe patient characteristics and evaluate benzotropine treatment patterns

- Adult patients  $\geq 18$  years were included if they had  $\geq 1$  pharmacy claim for an antipsychotic and no use of benzotropine before the index date



US, United States.

Chepke C. et al. NEI 2022; Colorado Springs, CO.



# Claims Analysis: Patient Characteristics

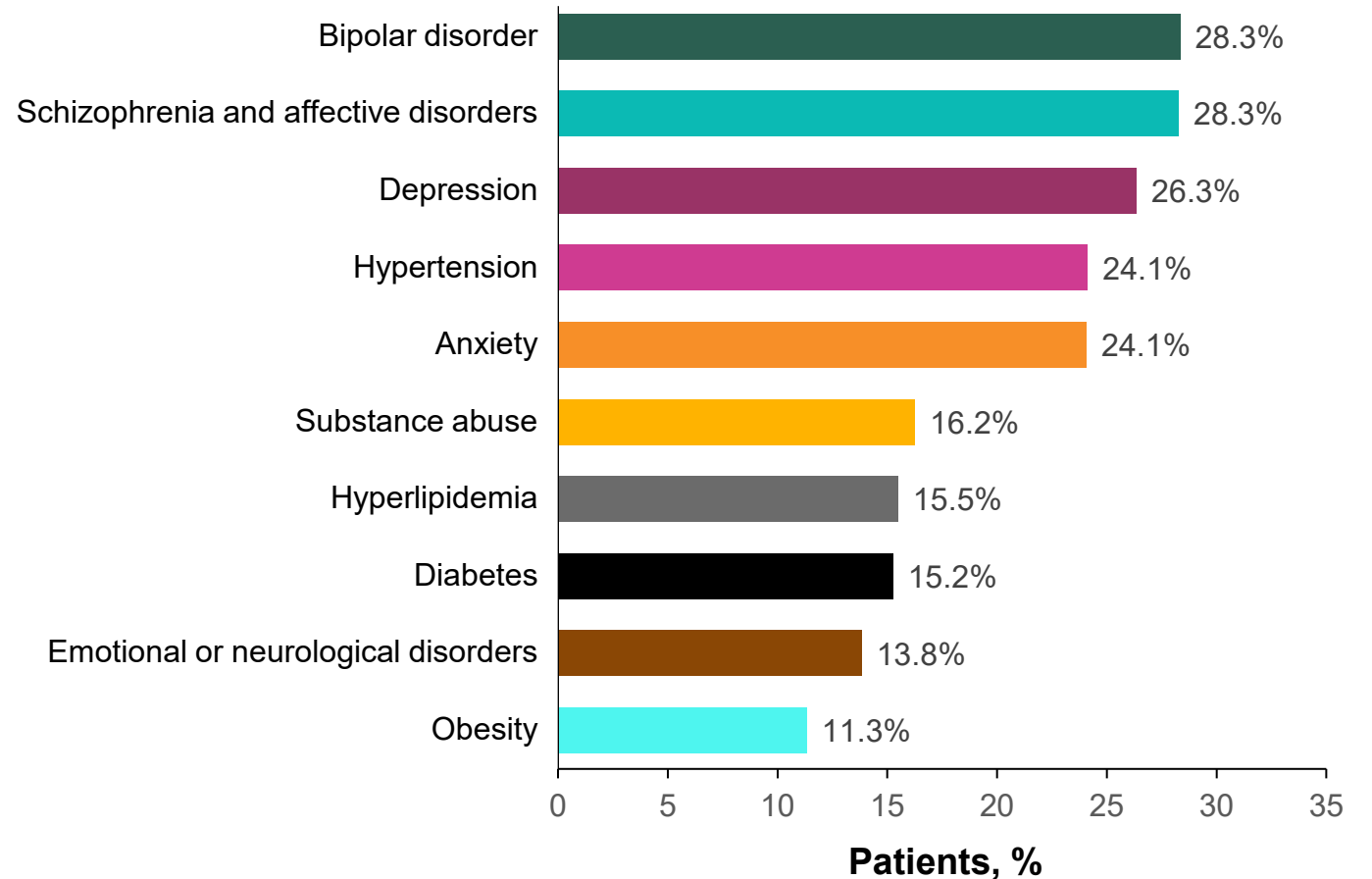
Of 112,542 patients included in the analysis:

59% female

Mean age, 46 years

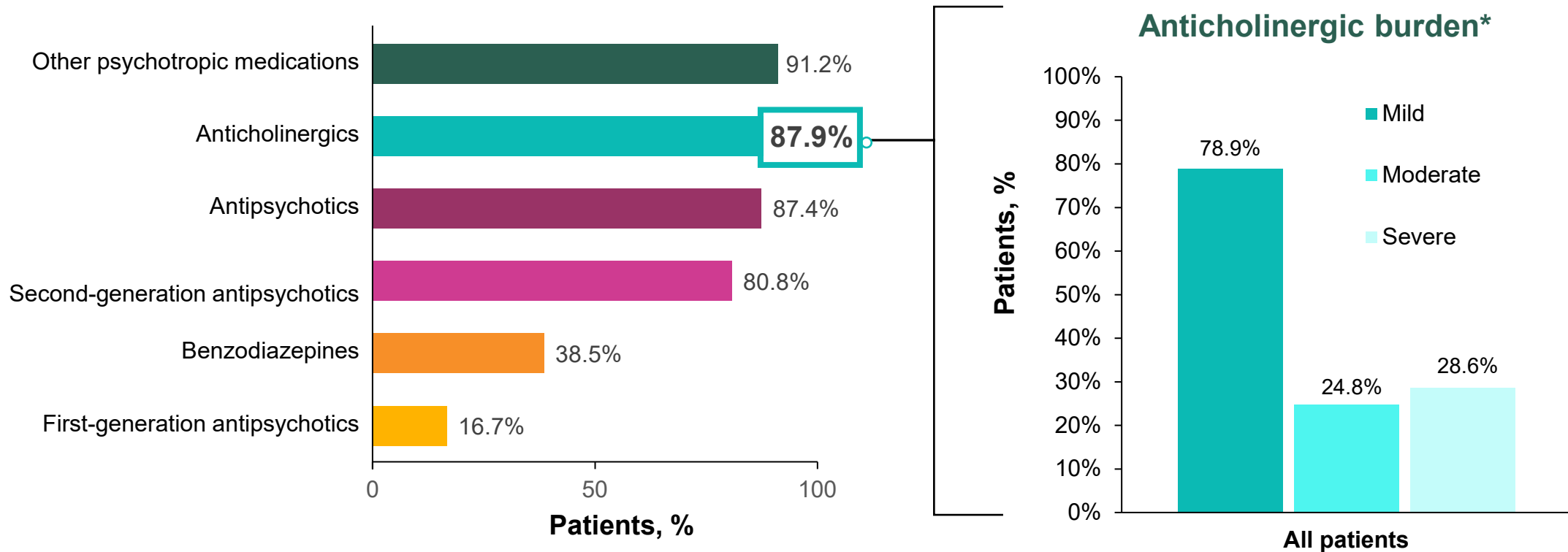
54% had  $\geq 2$  comorbid conditions

Baseline comorbidities occurring in >10% of the population (N=112,542)



# Claims Analysis: Polypharmacy and Anticholinergic Burden

Medication use and anticholinergic burden in post-index period (N=112,542)

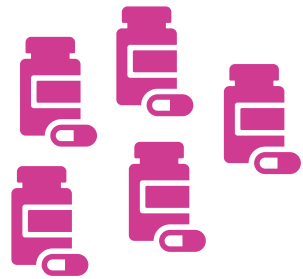


- 59.1% of patients experienced polypharmacy with claims for  $\geq 10$  medications
- 87.9% were receiving  $\geq 1$  medication with anticholinergic properties at baseline

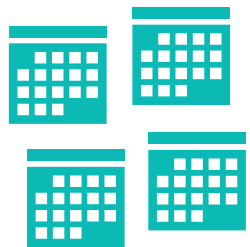
\*Mild, moderate, and severe categories adapted from acbcalc.com accessed June 2021. Mild includes "minimal" and "mild" anticholinergic burden medications from acbcalc.com.

Chepke C. et al. NEI 2022; Colorado Springs, CO.

# Claims Analysis: Bzotropine Utilization



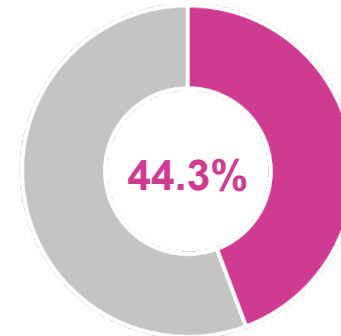
Median of  
**5 prescription fills**  
for bzotropine over 12  
months (N=112,542)



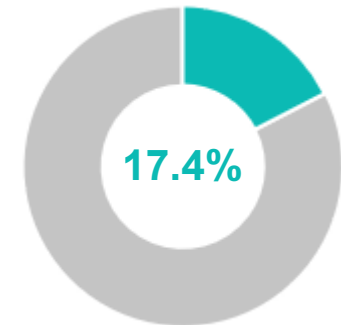
Median time to  
discontinuation  
**85 days**

## Bzotropine Utilization (N=112,542)

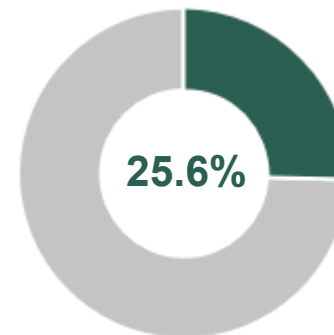
Up to 3 months



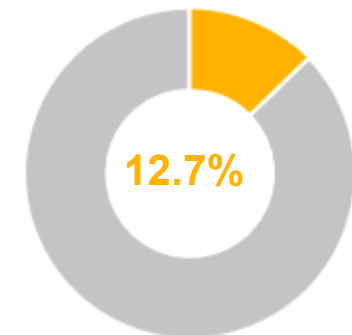
>3 to 6 months



>6 to 12 months



>12 to 24 months



# Claims Analysis: Summary<sup>1</sup>

Findings of polypharmacy, high anticholinergic burden, and long duration of benztropine use in this analysis demonstrates the need for appropriate evaluation and use of anticholinergics

**54% had  $\geq 2$  comorbid conditions**  
Most common:



- Bipolar disorder
- Schizophrenia
- Depression

**Polypharmacy and anticholinergic burden were frequent**



- Average 5 refills for benztropine
- 61.7% used benztropine up to 6 months before discontinuing



# Healthcare Provider Perspective of Benztropine Use in Drug-Induced Movement Disorders, Including Tardive Dyskinesia

A Real-World Healthcare Provider Survey (2021-2022)

# HCP Survey of Benztropine Use in DIMD

An HCP survey was conducted from December 2021 to January 2022 to understand the management of patients who present with benztropine as part of their medication regimen

The survey consisted of the following HCPs\* (N=349):



## Psychiatry

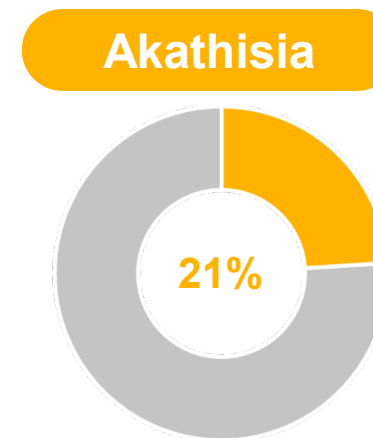
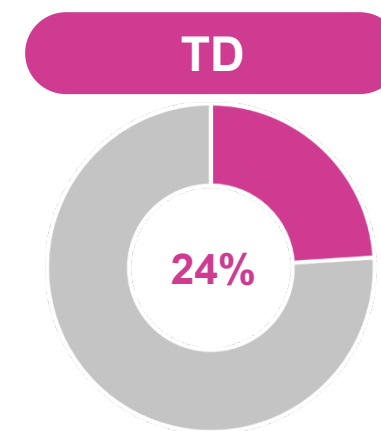
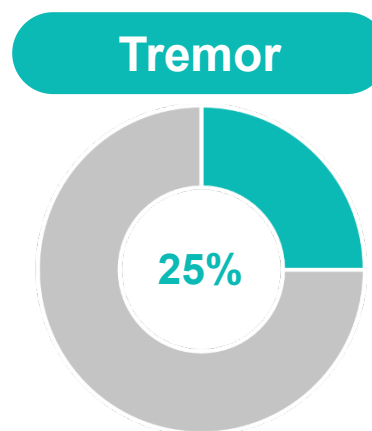
- 151 physicians
- 98 NP/PAs



## Primary Care

- 75 physicians
- 25 NP/PAs

Most common diagnoses in patients with a DIMD included:



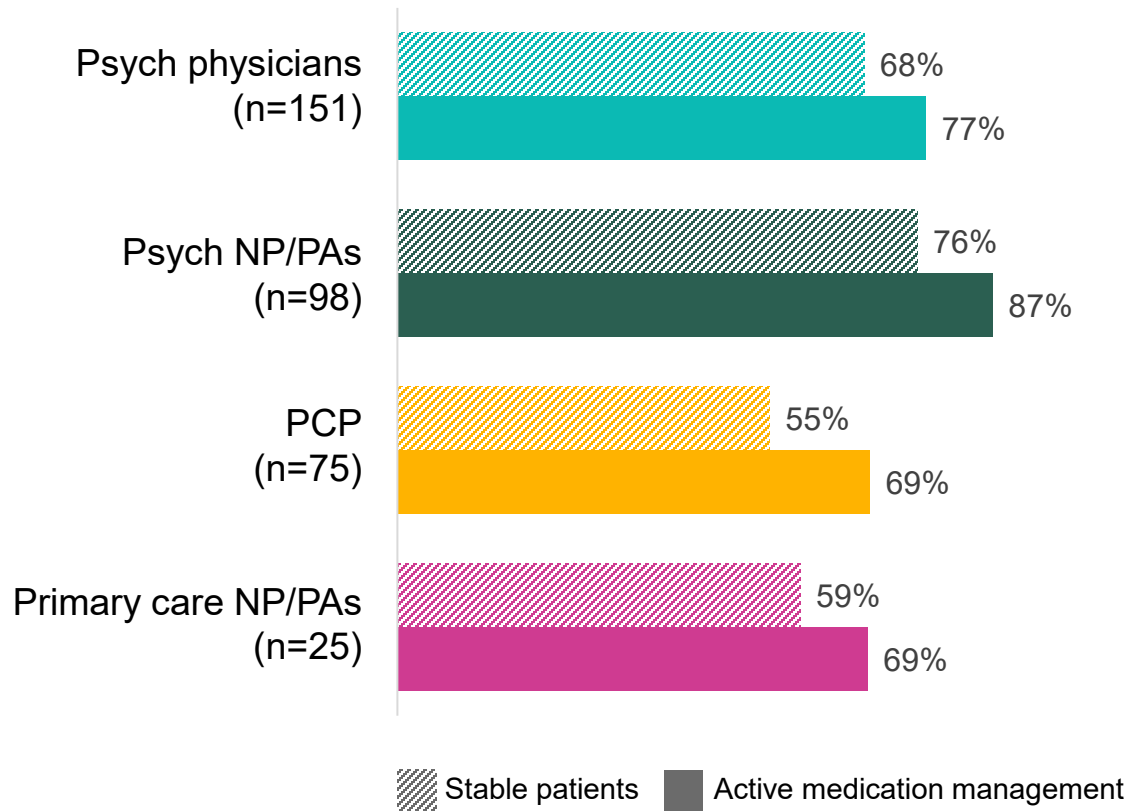
DIMD, Drug-induced movement disorders; HCP, healthcare provider; NP/PA, nurse practitioner/physician's assistant; TD, tardive dyskinesia.

\*HCPs were included if they treated  $\geq 2$  patients with DIMD (primary care physicians) or  $\geq 3$  patients with DIMD (psychiatric physicians and all NPs/PAs) in the past 6 months and prescribed benztropine. Each practice must have treated  $\geq 70\%$  adults, with  $\geq 60\%$  of time dedicated to direct patient interaction in outpatient or telehealth setting.

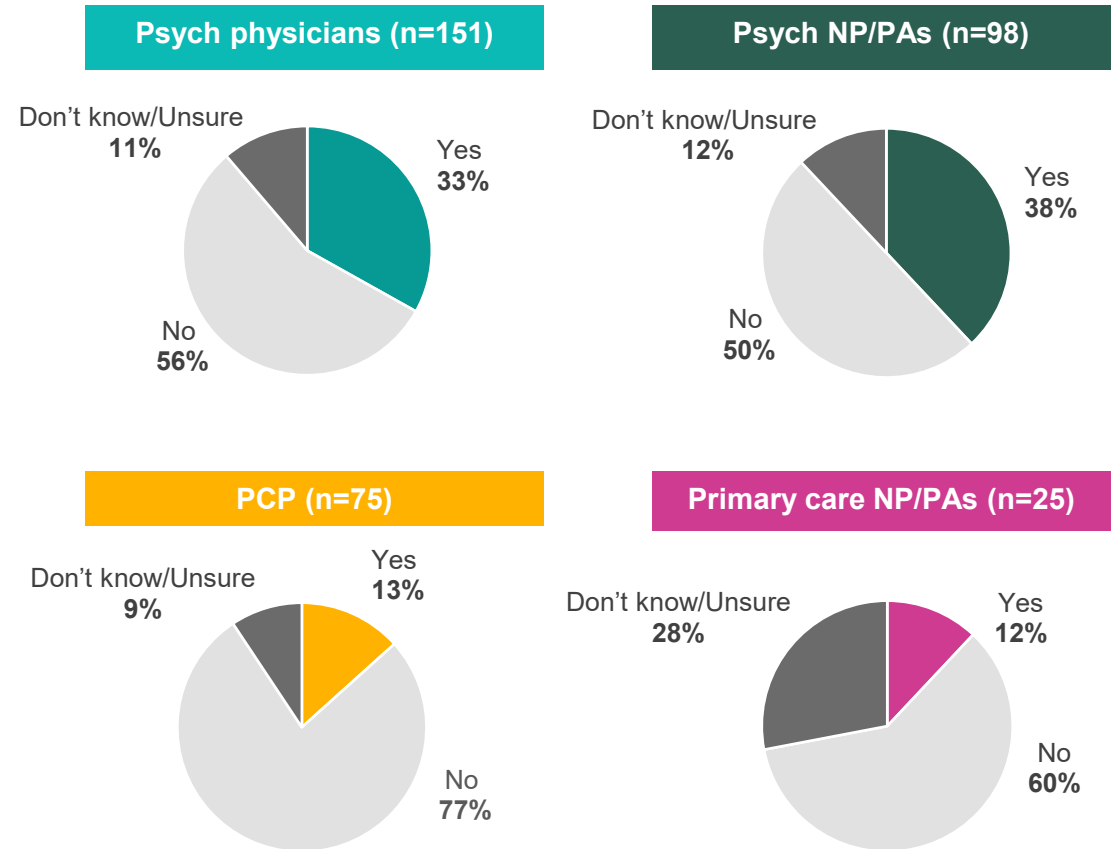
Chepke C, et al. Psych Congress 2022; New Orleans, LA.

# HCP Survey: DIMD Evaluation

Frequency of DIMD Evaluation and/or Monitoring, % of Visits, Mean



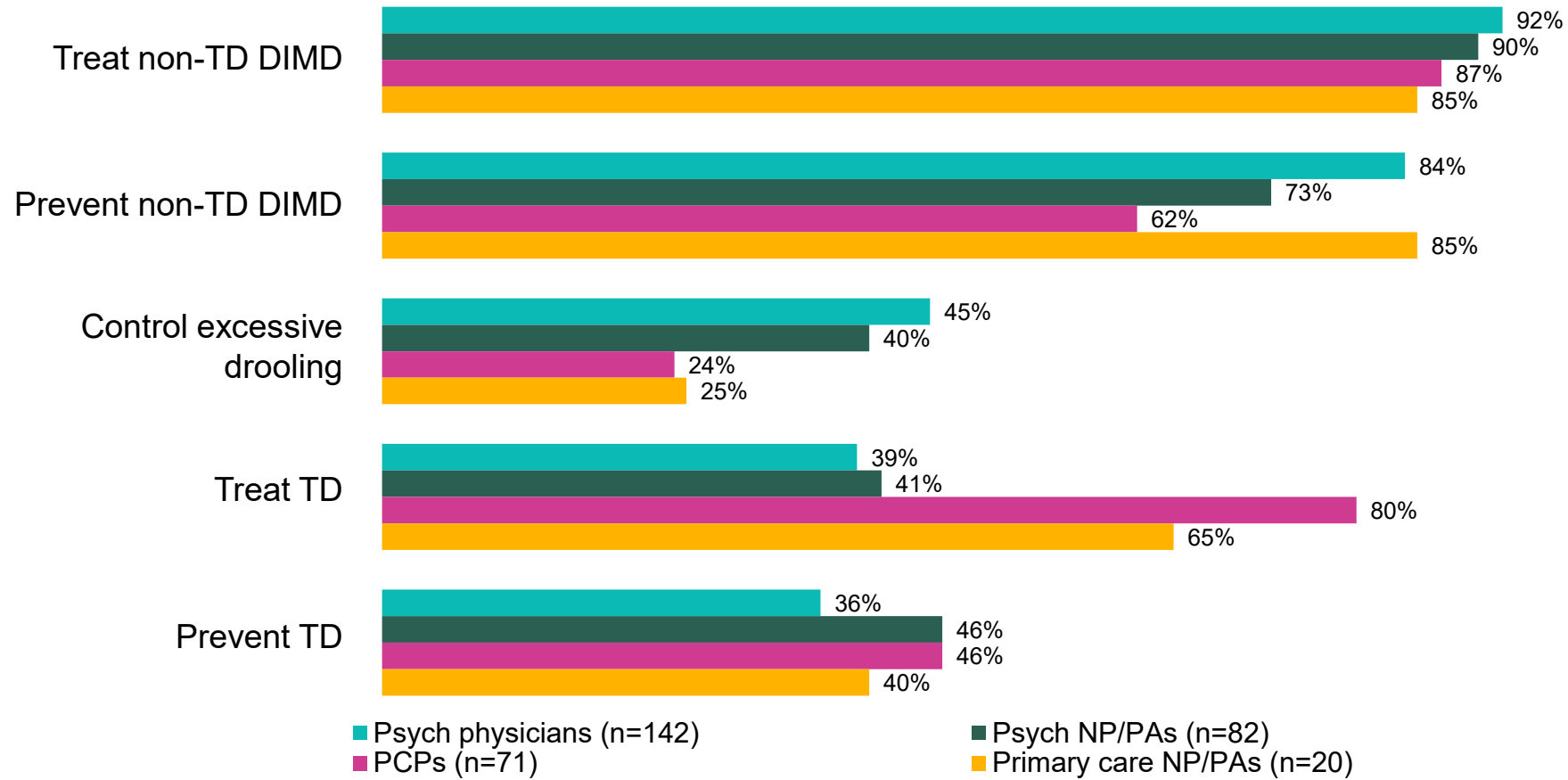
Policy in Place for Recommended Frequency for DIMD Evaluation, % of HCPs



DIMD, drug-induced movement disorder; HCP, healthcare provider; NP/PA, nurse practitioner/physician's assistant; PCP, primary care provider.  
 Chepke C, et al. Psych Congress 2022; New Orleans, LA.

# HCP Survey: Benztropine Initiation

Top 3 reasons to **initiate** benztropine, % of HCPs\*



AEs, adverse events; DIMD, drug-induced movement disorder; HCP, healthcare provider; NP/PA, nurse practitioner/physician's assistant; PCP, primary care provider; TD, tardive dyskinesia.

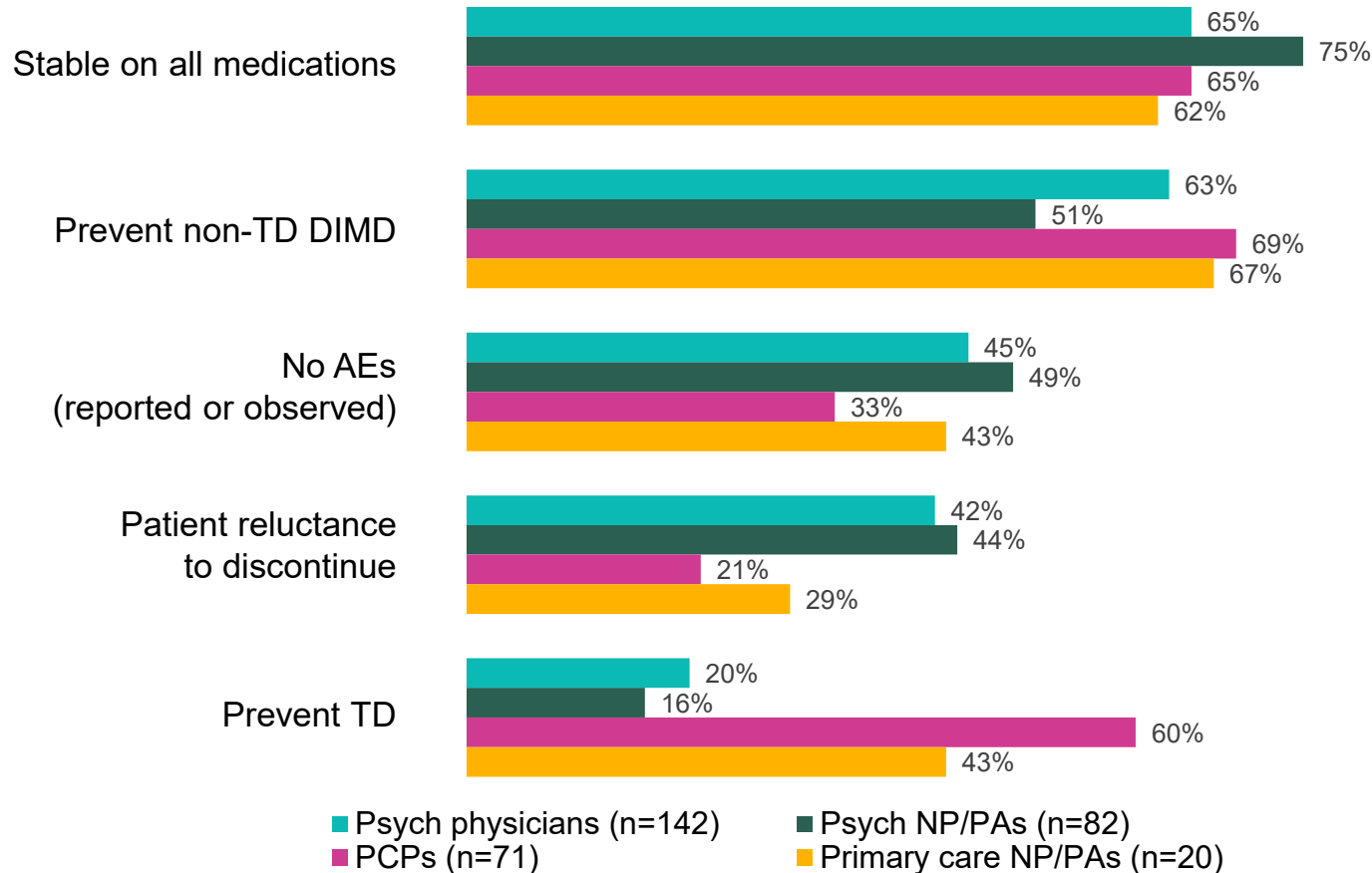
\*When asked to rank from a list, the top 3 factors that influence initiation of benztropine. 1 indicates the option with most influence.

Chepke C, et al. Psych Congress 2022; New Orleans, LA.



# HCP Survey: Benztropine Continuation and Discontinuation

Top 3 reasons to **continue** benztropine for >3 months, % of HCPs\*



## Benztropine Discontinuation†

- Common reasons to discontinue benztropine:
  - Comorbid conditions being exacerbated by the anticholinergic burden (65%–77%)
  - High anticholinergic burden (46%–62%)
- <15% of all HCPs reported that their practice had a standard protocol or guidelines for discontinuing benztropine

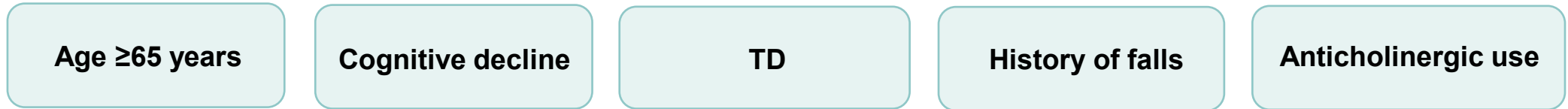
AEs, adverse events; DIMD, drug-induced movement disorder; HCP, healthcare provider; NP/PA, nurse practitioner/physician's assistant; PCP, primary care provider; TD, tardive dyskinesia.

\*When asked to rank from a list, the top 3 factors that influence the decision to continue benztropine in patients who have been taking benztropine for more than 3 months. 1 indicates the option with the most influence. †When asked to rank from a list, the top 3 factors that influence discontinuation of benztropine. 1 indicates the option with most influence.

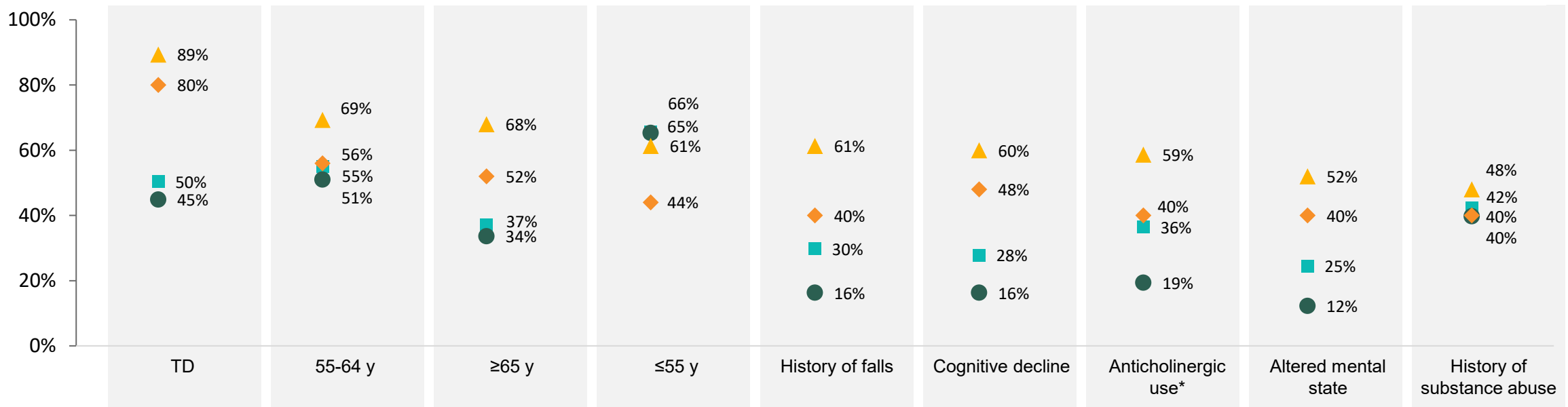
Chepke C, et al. Psych Congress 2022; New Orleans, LA.

# HCP Survey: Benztropine Use and Patient Characteristics

>50% of primary care HCPs responded they would use benzotropine in patients with any of the following characteristics\*:



## HCPs “somewhat” or “extremely” likely to treat various types of patients with benzotropine



\*When asked about specific patient characteristics and the use of benzotropine. Five-point scale from “extremely unlikely” to “extremely likely”.

DIMD, drug-induced movement disorder; HCP, healthcare provider; NP/PA, nurse practitioner/physician’s assistant; PCP, primary care provider; TD, tardive dyskinesia.

Chepke C, et al. Psych Congress 2022; New Orleans, LA.

■ Psych physicians (n=151)

● Psych NP/PAs (n=98)

▲ PCPs (n=75)

◆ Primary care NP/PAs (n=25)

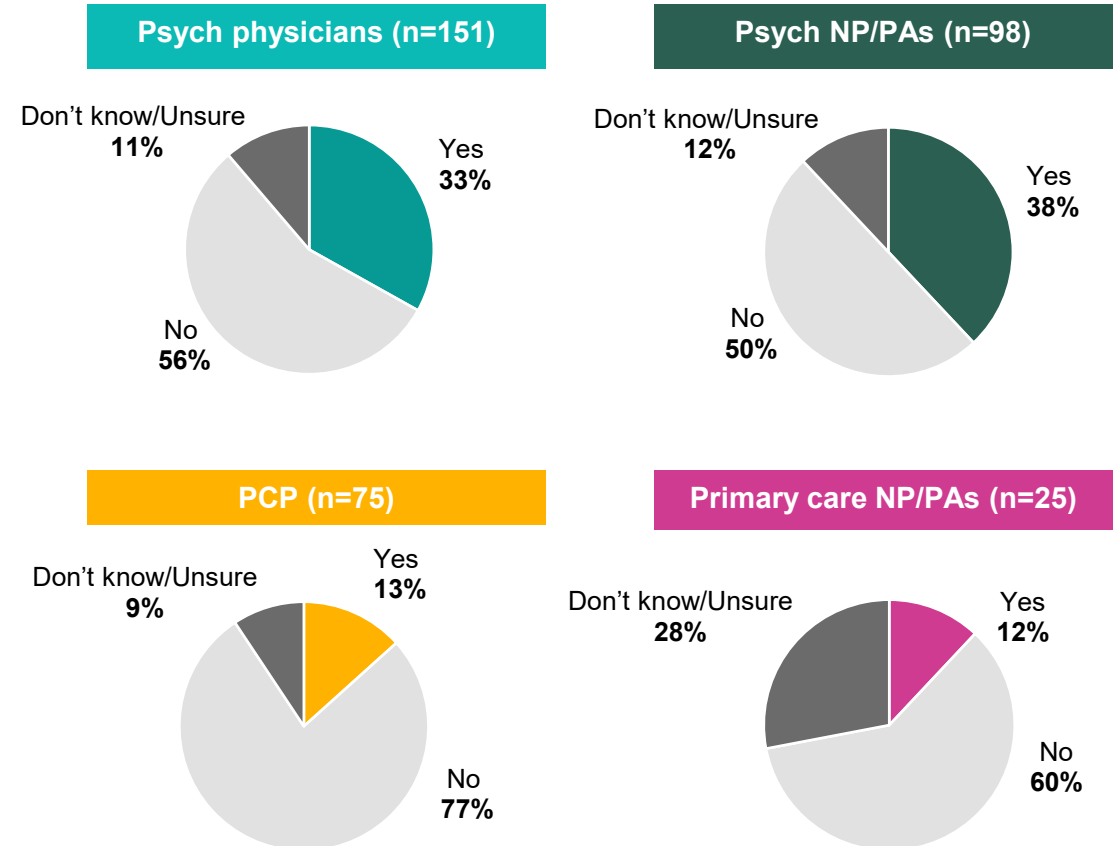
# HCP Survey: Policies

For all HCPs, **<40% had policies** at their workplace to guide the frequency of evaluating patients for DIMD

More **psychiatric HCPs** reported these policies were present compared to primary care HCPs

**<15% of all HCPs** reported their practice had a **standard protocol or guidelines** for discontinuing benztropine

## Policy in Place for Recommended Frequency for DIMD Evaluation, % of HCPs



DIMD, drug-induced movement disorder; HCP, healthcare provider; NP/PA, nurse practitioner/physician's assistant; PCP, primary care provider.  
Chepke C, et al. Psych Congress 2022; New Orleans, LA.

# HCP Survey: Use of Guidelines

Familiarity with the 2020 APA guidelines for the treatment of schizophrenia was low

<40% indicated familiarity when prompted



39% of psychiatric HCPs

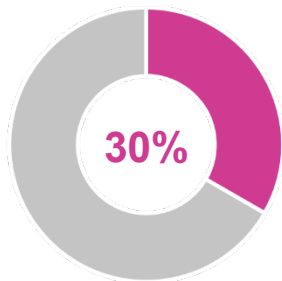
29% of primary care HCPs

○ were “somewhat” or “very” familiar with the recommendations

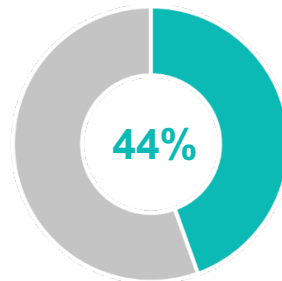


80% of those agreed that following the guidelines led to optimal treatment of DIMDs

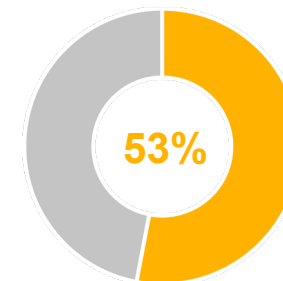
HCPs were interested in learning more about several topics related to DIMD:



Rationale for discontinuing benztropine



Guidance on dose tapering of medications with anticholinergic properties




Differential diagnosis of DIMD via telehealth

APA, American Psychiatric Association; DIMD, drug-induced movement disorder; HCP, healthcare provider.

Chepke C, et al. Psych Congress 2022; New Orleans, LA.


# HCP Survey Summary

Results indicate benztropine is often used appropriately for DIMDs, but long-term use or use for the treatment of TD counter to label recommendations, and the lack of policies to evaluate and monitor DIMDs may necessitate additional education on appropriate benztropine use



Most psychiatric visits included evaluation/monitoring for DIMD

Which was significantly higher compared to primary care visits



Main reasons to adjust benztropine therapy:

**Initiate or continue > 3 months:** Prevention and treatment of non-TD DIMD

**Discontinue:** comorbid conditions exacerbated by anticholinergic burden

>50% of Primary Care HCPs

Would use benztropine in patients

- With TD
- Aged  $\geq 65$  years
- Cognitive decline
- Anticholinergic use
- History of falls



<40% of all HCPs had policies at their workplace to guide the frequency of evaluating patients for DIMD

But 80% of those agreed that following guidelines led to optimal treatment of DIMDs