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# Predictors of persistence and adherence to deutetrabenazine among patients with Huntington disease or tardive dyskinesia

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## Abstract

**Introduction:** Deutetrabenazine is approved for treatment of Huntington disease (HD)-related chorea and tardive dyskinesia (TD) in adults. Factors associated with deutetrabenazine persistence and adherence are not well understood.

**Methods:** Claims data from the Symphony Health Solutions Integrated Dataverse (2017-2019) were analyzed to identify real-world predictors of deutetrabenazine persistence and adherence in adults with HD or TD in the United States. Predictive models for persistence and adherence that considered patient demographics, payer type, comorbidities, treatment history, and health care resource use were developed.

**Results:** In HD, use of anticonvulsants (HR = 2.00 [95% CI = 1.03, 3.85]; $P < .05$), lipid-lowering agents (2.22 [1.03, 4.76]; $P < .05$), and Medicaid versus Medicare insurance (2.27 [1.03, 5.00]; $P < .05$) predicted persistence, whereas only comorbid anxiety disorders predicted discontinuation (0.46 [0.23, 0.93]; $P < .05$). Of these patients, 62.5% were adherent at 6 months. Use of ≤2 treatments for chronic diseases (OR = 0.18 [95% CI = 0.04, 0.81]; $P < .05$) and Medicaid versus Medicare insurance (0.27 [0.09, 0.75]; $P < .05$) was associated with lower odds of adherence. In TD, use of lipid-lowering agents (HR = 4.76 [95% CI = 1.02, 20.00]; $P < .05$) predicted persistence, while comorbid schizoaffective disorder and/or schizophrenia (0.16 [0.14, 0.69]; $P < .05$) and sleep-wake disorders (0.18 [0.04, 0.82]; $P < .05$) predicted discontinuation. Of these patients, 46.7% were adherent at 6 months. Comorbid schizoaffective disorder and/or schizophrenia was associated with lower odds of adherence (OR = 0.26 [0.07, 0.91]; $P < .05$).

**Discussion:** Identifying factors predictive of discontinuation and/or nonadherence to deutetrabenazine may facilitate the development of personalized support programs that seek to improve outcomes in patients with HD or TD.

**Keywords:** deutetrabenazine, adherence, persistence, tardive dyskinesia, chorea, Huntington disease

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## Introduction

Chorea associated with Huntington disease (HD) and tardive dyskinesia (TD) are hyperkinetic movement disorders,

characterized by excessive abnormal involuntary movements, that can greatly diminish patient QoL.[1] Patient surveys have shown that in chorea associated with HD, overall QoL is known to decline as the severity of chorea increases; chorea has also been shown to negatively impact daily functioning.[2,3] Similarly, individuals with severe TD have significantly worse QoL and social withdrawal compared with those with less severe TD and those without TD.[4]

Vesicular monoamine-transporter 2 (VMAT2) inhibitors are the only class of drugs approved by the United States (US) FDA for treatment of chorea associated with HD and TD. Deutetrabenazine, a selective VMAT2 inhibitor, was approved by the US FDA in 2017[5-7] based on phase 3 clinical trials for treatment of chorea associated with HD[8] and treatment of TD.[9,10] Treatment with deutetrabenazine significantly reduced abnormal involuntary movements and improved patient QoL.[11-13]

Despite this, in a study of real-world adherence patterns in patients with TD receiving VMAT2 inhibitors, approximately 50% of patients were found to be nonadherent to treatment.[14] In a second study of adherence and discontinuation rates among patients with chorea associated with HD, patients receiving deutetrabenazine had greater adherence and lower discontinuation rates compared with patients treated with tetrabenazine.[15] Given the demonstrated positive effects of deutetrabenazine on QoL,[13] treatment discontinuation and/or nonadherence may be associated with declines in patient QoL. An understanding of which characteristics (eg, demographics, comorbidities, concomitant medication, insurance type) correlate to treatment patterns and behaviors has the potential to allow for the identification of patients at high risk of discontinuation and nonadherence and subsequent intervention. However, data on predictors of real-world adherence to deutetrabenazine in patients with chorea associated with HD and TD are limited. This retrospective study was designed to identify patient and treatment characteristics associated with deutetrabenazine persistence and adherence among patients with chorea associated with HD or TD, as well as to develop and validate prediction models of persistence and adherence based on the identified characteristics.

# Methods

## Data Source

Patient data were extracted from May 2017 to May 2019 from the Symphony Health Solutions (SHS) Integrated Dataverse, an insurance claims database that captures deidentified medical, hospital, and prescription (>93% of all prescriptions dispensed from US pharmacies) claims data in all stages of processing and from various payment types (eg, cash, Medicaid, Medicare, commercial insurance payments) for approximately 317 million people in the United States.[16]

## Patients

Eligible patients were aged 18 to 65 years at index date (date of first claim for deutetrabenazine) and had ≥1 claim with a diagnosis of HD (ie, International Classification of Diseases, 10th Revision, Clinical Modification[17] [ICD-10-CM] code G10) or TD (ie, ICD-10-CM code G24.01), ≥1 prescription claim for deutetrabenazine, continuous clinical activity (≥1 medical and ≥1 pharmacy claim) during the baseline period (6 months prior to index date), no discontinuation of index deutetrabenazine within 30 days after index date, and ≥1-day supply of deutetrabenazine from 30 days after index date to the earlier date between an additional 6 months and the data cut-off date.

Patients were grouped by disease into cohort 1 (patients with HD) or cohort 3 (patients with TD) for persistence analyses (6-month study period starting from 30 days after index date) (Figure 1). Patients in cohort 1 and cohort 3 who met the additional inclusion criterion of ≥1 pharmacy claim after the 7-month period after index date (1-month stabilization period plus 6-month study period) were selected for adherence analyses and placed into cohort 2 (patients with HD) and cohort 4 (patients with TD) (Figure 1). For each cohort, data were randomly divided into 2 sets, one for model development (modeling set, two-thirds of the data) and another for model validation (validation set, the remaining one-third of the data).

# Outcomes

The outcome for persistence analyses was time to discontinuation of deutetrabenazine, defined as a gap in index treatment use of >30 days from the end of the last observed deutetrabenazine fill and the end of data. Outcomes for the adherence analyses included proportion of days covered (PDC) and adherence rate, defined as the proportion of patients with PDC >80%. All outcomes were assessed during the 6-month study period.

Kaplan-Meyer analyses were used to characterize the proportions of patients who discontinued deutetrabenazine. Means, medians, SDs, and ranges were used to describe the distribution of PDC within each cohort. For patient characteristics, means and SDs were calculated for continuous variables, while counts and proportions were calculated for categorical variables. For cohorts 2 and 4, patient characteristics were compared between those who were adherent (PDC >80%) versus nonadherent (PDC ≤80%). Wilcoxon rank-sum tests were used to compare continuous variables and Fisher exact tests were used to compare categorical variables between the 2 groups.

# Analysis

Multivariable models adjusted for baseline patient characteristics were developed—2 Cox proportional hazards models to

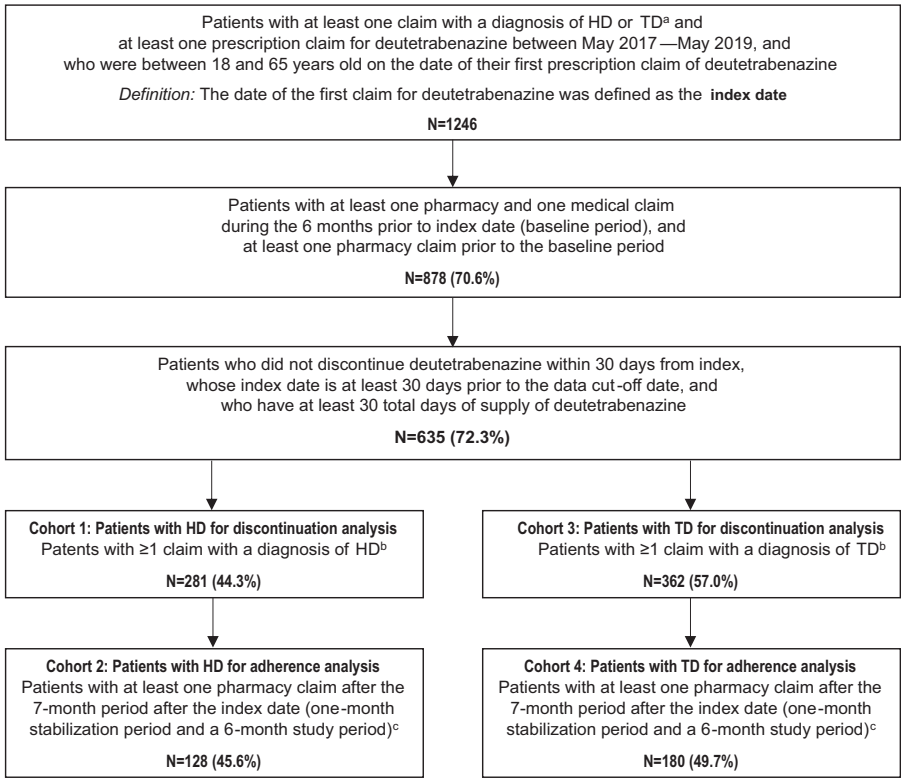


**FIGURE 1: Sample selection**

**HD = Huntington disease; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification; TD = tardive dyskinesia.**
**[a]ICD-10-CM G10 was used to identify HD. ICD-10-CM G24.01 code was used to identify TD.[17]**
**[b]There were 8 patients with both HD and TD diagnoses. These patients were included cohort 1 and cohort 3.**
**[c]There were 5 patients with both HD and TD diagnoses. These patients were included in cohort 2 and cohort 4.**

identify predictors of persistence for each disease cohort separately (cohort 1 and cohort 3) and 2 logistic regression models to identify predictors of adherence for each disease cohort separately (cohort 2 and cohort 4)—using the modeling set. HRs and ORs and the corresponding 95% CIs and *P* values were reported to identify predictors of persistence and adherence, respectively, based on effect size and significance. Grønnesby and Borgan tests and Hosmer—Lemeshow tests were used to evaluate goodness of fit for the persistence and adherence models, respectively. The in-sample predictive performances of the final persistence models were evaluated using the mean of Chambless and Diao's estimates of cumulative or dynamic AUC generated using 10-fold cross validation. The in-sample predictive performances of the final adherence models were evaluated using AUC of receiver operating characteristics curves generated using 5-fold or 10-fold cross-validation, depending on the size of the modeling set.

Each of the 4 models was validated using the data in the corresponding validation sets. The predictive performance was assessed using AUC for all models; AUC $\geq$0.8 was considered an excellent prediction, AUC $\geq$0.70 to $<$0.80 a good prediction, AUC $\geq$0.60 to $<$0.70 a fair prediction, and AUC $\geq$0.50 to $<$0.60 a poor prediction.[18]

# Results

## Patient Population

Of the 635 patients who met the inclusion criteria, 281 patients were categorized into cohort 1 (HD), and 362 were categorized into cohort 3 (TD); these 2 cohorts were used for the analysis of persistence. Of the 635 patients, 8 were diagnosed with both HD and TD and were included in cohort 1 as well as cohort 3. For the analysis of adherence, 128 patients in cohort 1 were further categorized into cohort 2, and 180 patients in cohort 3 were further categorized into cohort 4 (Figure 1). Of these patients, 5 were diagnosed with both HD and TD and were included in cohort 2 as well as cohort 4.

For patients with HD (cohort 1), the majority (89.3%) were aged 38 to 65 years, and 60.9% were female (Table). The majority of patients (90.4%) had a diagnosis of HD before the index date, among whom the mean (SD) observed disease duration between their first diagnosis and index date was

**TABLE: Baseline characteristics in patients with HD and TD**

| | HD | | TD | |
|---|---|---|---|---|
| | 1 (Persistence) n = 281 | 2 (Adherence) n = 128 | 3 (Persistence) n = 362 | 4 (Adherence) n = 180 |
| Age Category, y, n (%) | | | | |
| 18-27 | 10 (3.6) | 8 (6.3) | 6 (1.7) | 3 (1.7) |
| 28-37 | 20 (7.1) | 8 (6.3) | 16 (4.4) | 9 (5.0) |
| 38-47 | 61 (21.7) | 31 (24.2) | 52 (14.4) | 32 (17.8) |
| 48-57 | 87 (31.0) | 37 (28.9) | 129 (35.6) | 62 (34.4) |
| 58-65 | 103 (36.7) | 44 (34.4) | 159 (43.9) | 74 (41.1) |
| Male, n (%) | 110 (39.1) | 46 (35.9) | 111 (30.7) | 64 (35.6) |
| Payer type,[a] n (%) | | | | |
| Medicare | 113 (40.2) | 32 (25.0) | 144 (39.8) | 53 (29.4) |
| Commercial | 53 (18.9) | 35 (27.3) | 101 (27.9) | 65 (36.1) |
| Medicaid | 50 (17.8) | 26 (20.3) | 60 (16.6) | 29 (16.1) |
| Other[b] | 19 (6.8) | 8 (6.3) | 15 (4.1) | 10 (5.6) |
| Unspecified | 46 (16.4) | 27 (21.1) | 42 (11.6) | 23 (12.8) |
| Observed Disease Duration Days, Mean (SD) | n = 254 | n = 109 | n = 287 | n = 133 |
| | 353.4 (214.3) | 244.4 (138.5) | 221.9 (190.1) | 178.5 (138.9) |
| Time From Index Date, d, Mean (SD) | | | | |
| To End of Data | 229.0 (146.1) | 359.2 (79.3) | 229.7 (126.0) | 336.9 (67.5) |
| To Last Observed Medical or Pharmacy Activity | 209.9 (142.0) | 343.3 (79.7) | 218.7 (125.4) | 327.4 (68.3) |
| CCI Score, Mean (SD) | 0.4 (0.8) | 0.4 (0.9) | 0.8 (1.4) | 0.9 (1.5) |
| Selected Comorbidities in the CCI, n (%) | | | | |
| Dementia | 23 (8.2) | 10 (7.8) | 13 (3.6) | 6 (3.3) |
| Chronic Pulmonary Disease | 19 (6.8) | 11 (8.6) | 85 (23.5) | 41 (22.8) |
| Diabetes Without Chronic Complication | 12 (4.3) | 6 (4.7) | 53 (14.6) | 20 (11.1) |
| Diabetes With Chronic Complication | 1 (0.4) | 0 (0.0) | 38 (10.5) | 18 (10.0) |
| Cerebrovascular Disease | 7 (2.5) | 5 (3.9) | 23 (6.4) | 10 (5.6) |
| Mild Liver Disease | 3 (1.1) | 2 (1.6) | 20 (5.5) | 11 (6.1) |
| Renal Disease | 2 (0.7) | 2 (1.6) | 18 (5.0) | 9 (5.0) |
| Congestive Heart Failure | 3 (1.1) | 0 (0.0) | 14 (3.9) | 10 (5.6) |
| Peripheral Vascular Disease | 4 (1.4) | 3 (2.3) | 17 (4.7) | 9 (5.0) |
| Psychiatric Comorbidities, n (%) | | | | |
| Depressive Disorders | 60 (21.4) | 29 (22.7) | 99 (27.3) | 50 (27.8) |
| Anxiety Disorders | 53 (18.9) | 15 (11.7) | 113 (31.2) | 56 (31.1) |
| Substance-Related and Addictive Disorders | 31 (11.0) | 11 (8.6) | 78 (21.5) | 46 (25.6) |
| Bipolar and Related Disorders | 23 (8.2) | 12 (9.4) | 125 (34.5) | 67 (37.2) |
| Schizophrenia | 2 (0.7) | 2 (1.6) | 50 (13.8) | 21 (11.7) |
| Schizoaffective Disorder | 2 (0.7) | 2 (1.6) | 48 (13.3) | 28 (15.6) |
| Trauma-Related and Stress-Related Disorders | 10 (3.6) | 6 (4.7) | 37 (10.2) | 23 (12.8) |
| Nonpsychiatric Comorbidities, n (%) | | | | |
| Hypertension | 42 (14.9) | 14 (10.9) | 140 (38.7) | 68 (37.8) |
| Hyperlipidemia | 42 (14.9) | 15 (11.7) | 128 (35.4) | 59 (32.8) |
| Dysphagia | 42 (14.9) | 21 (16.4) | 26 (7.2) | 10 (5.6) |
| Falls | 37 (13.2) | 16 (12.5) | 38 (10.5) | 23 (12.8) |
| Sleep-Wake Disorders | 29 (10.3) | 14 (10.9) | 87 (24.0) | 42 (23.3) |
| Smoking History | 19 (6.8) | 8 (6.3) | 50 (13.8) | 29 (16.1) |
| Osteoarthritis | 19 (6.8) | 7 (5.5) | 45 (12.4) | 23 (12.8) |

**TABLE: Baseline characteristics in patients with HD and TD** (continued)

| | HD | | TD | |
|---|---|---|---|---|
| | 1 (Persistence) n = 281 | 2 (Adherence) n = 128 | 3 (Persistence) n = 362 | 4 (Adherence) n = 180 |
| EPS (Excluding TD) | 11 (3.9) | 6 (4.7) | 42 (11.6) | 19 (10.6) |
| Dystonia | 10 (3.6) | 6 (4.7) | 250 (69.1) | 125 (69.4) |
| Obesity | 8 (2.8) | 5 (3.9) | 61 (16.9) | 30 (16.7) |
| Treatment History, n (%) | | | | |
| Antidepressants | 185 (65.8) | 80 (62.5) | 246 (68.0) | 125 (69.4) |
| Anticonvulsants | 113 (40.2) | 52 (40.6) | 244 (67.4) | 121 (67.2) |
| Typical or Atypical APs | 105 (37.4) | 49 (38.3) | 210 (58.0) | 110 (61.1) |
| Typical APs | 23 (8.2) | 12 (9.4) | 38 (10.5) | 21 (11.7) |
| Atypical APs | 85 (30.2) | 39 (30.5) | 195 (53.9) | 101 (56.1) |
| Antianxiety Medications | 64 (22.8) | 30 (23.4) | 143 (39.5) | 82 (45.6) |
| Lipid-Lowering Agents | 53 (18.9) | 25 (19.5) | 156 (43.1) | 75 (41.7) |
| VMAT2 Inhibitors | 46 (16.4) | 23 (18.0) | 60 (16.6) | 32 (17.8) |
| Anticholinergics | 44 (15.7) | 22 (17.2) | 141 (39.0) | 81 (45.0) |
| Antihypertensives | 39 (13.9) | 16 (12.5) | 129 (35.6) | 64 (35.6) |
| Antidiabetic Drugs | 15 (5.3) | 5 (3.9) | 95 (26.2) | 38 (21.1) |
| Sedatives and Hypnotics | 14 (5.0) | 8 (6.3) | 61 (16.9) | 32 (17.8) |
| Lithium | 2 (0.7) | 1 (0.8) | 34 (9.4) | 19 (10.6) |
| All-Cause HCRU,[c] Mean (SD) | | | | |
| No. Inpatient Admissions | 0.1 (0.6) | 0.1 (0.4) | 0.4 (1.1) | 0.3 (0.8) |
| Total Hospitalization Days | 0.4 (1.6) | 0.4 (1.3) | 1.0 (3.1) | 0.8 (2.4) |
| No. Outpatient Visits | 4.0 (5.2) | 4.5 (5.6) | 9.4 (11.0) | 9.7 (11.2) |
| No. ED Visits | 0.3 (0.8) | 0.3 (0.9) | 0.7 (1.8) | 0.7 (1.8) |
| No. Other Visits | 4.0 (16.2) | 3.4 (12.7) | 4.6 (15.9) | 6.2 (19.6) |
| No. Unknown Visits | 0.0 (0.5) | 0.1 (0.7) | 0.2 (1.2) | 0.1 (0.6) |

AP = antipsychotic agent; CCI = Charlson Comorbidity Index; EPS = extrapyramidal symptoms; HCRU = health care resource use; HD = Huntington disease; No = number; TD = tardive dyskinesia; VMAT2 = vesicular monoamine transporter 2.

[a]Health plan type was associated with a patient's index claim.

[b]Included cash, employer group, third-party administrator, processors, and workers' compensation.

[c]Outpatient visits include medical office, hospital outpatient, and clinic visits. Other visits include home health, hospital outpatient pharmacy, intermediate care facility, laboratory, long-term care facility, and other facilities. Total hospitalization days were the sum of the lengths of stay for admissions that began during the baseline period.

353.4 (214.3) days (Table). Prior to initiating deutetrabenazine (during the 6-month baseline period), most patients were treated with other agents including antidepressants (65.8%), anticonvulsants (40.2%), and typical or atypical antipsychotic agents (37.4%) (Table).

The majority (93.9%) of patients with TD (cohort 3) were aged 38 to 65 years, and 69.3% were female (Table). Over three-quarters of patients (79.3%) had a TD diagnosis before the index date, among whom the mean (SD) observed disease duration between their first diagnosis and index date was 221.9 (190.1) days (Table). During the baseline period, most patients were treated with other agents including antidepressants (68.0%), anticonvulsants (67.4%), and typical or atypical antipsychotic agents (58.0%) (Table).

## Persistence Analyses

The proportions of patients with HD (cohort 1) who discontinued deutetrabenazine at months 1, 3, and 6 following the 30-day stabilization period were 3.5%, 14.7%, and 25.4%, respectively (Figure 2A); the proportions of patients with TD (cohort 3) were 5.4%, 22.3%, and 36.2%, respectively (Figure 2B).

The prediction models for persistence were fit on two-thirds of the total number of patients in cohort 1 (HD) and cohort 3 (TD), corresponding to 187 and 241 patients, respectively. Four characteristics were identified as significant predictors of persistence in patients with HD (cohort 1). Patients who used Medicaid for their deutetrabenazine claim had a significantly higher likelihood of persistence compared

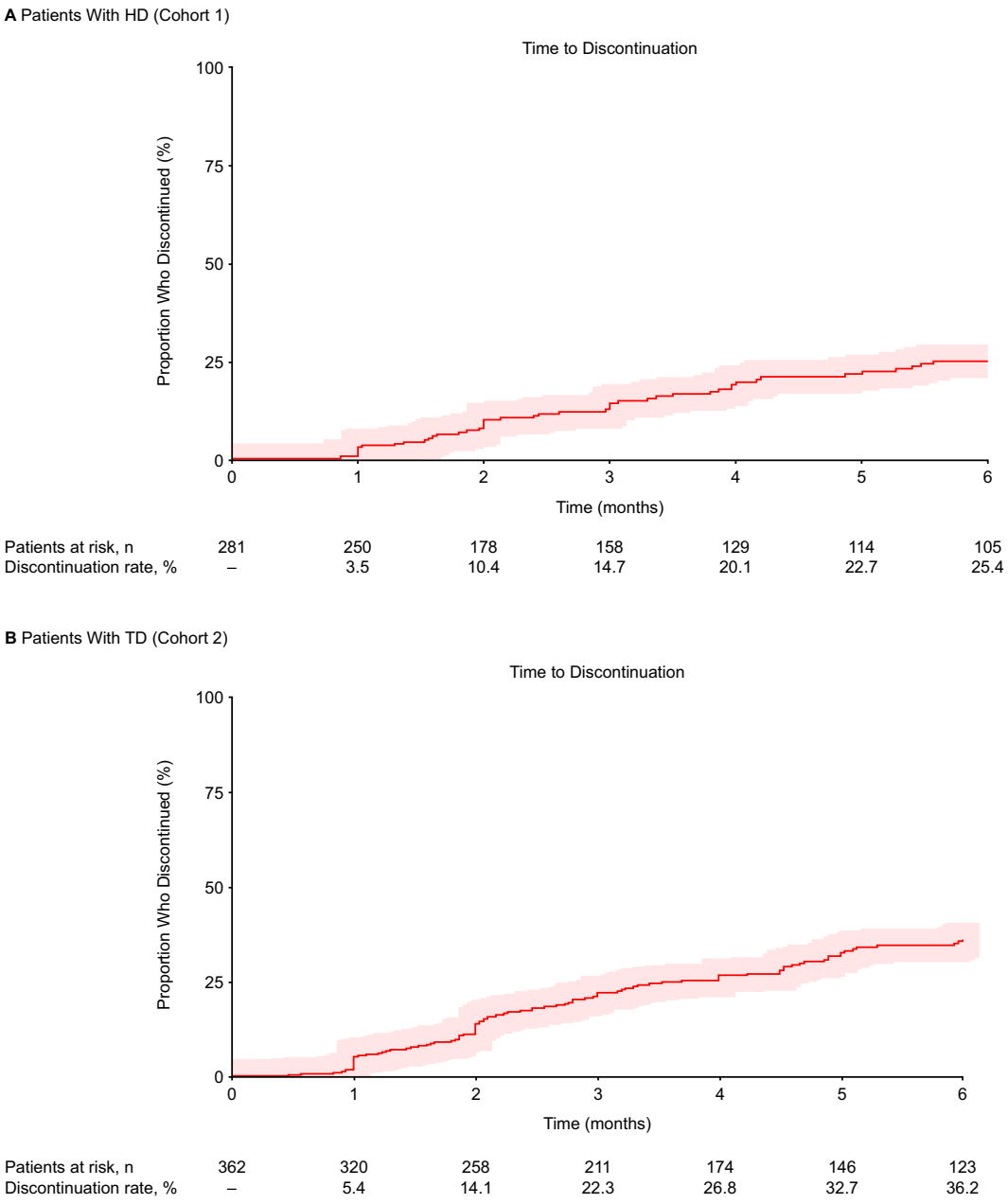


**FIGURE 2: Time to discontinuation of deutetrabenazine. (A) shows patients with HD (cohort 1); (B) shows patients with TD (cohort 3)**

**HD = Huntington disease; TD = tardive dyskinesia.**

with those using Medicare (HR [95% CI], 2.27 [1.030, 5.00]; $P < .05$). Patients with anxiety disorders at baseline were at a significantly higher risk of discontinuation compared with those without (0.46 [0.23, 0.93]; $P < .05$), whereas patients taking anticonvulsants (2.00 [1.03, 3.85]; $P < .05$), or lipid-lowering agents (2.22 [1.03, 4.76]; $P < .05$) during the baseline period had a significantly greater likelihood of persistence compared with those without these treatments (Figure 3). Dysphagia or falls at baseline showed a trend toward increased persistence (2.56 [0.93, 7.14] and 2.78 [0.71, 11.11], respectively), whereas substance abuse disorders (0.54 [0.28, 1.06]) showed a trend toward discontinuation. The model demonstrated strong predictive performances for the modeling set (AUC = 0.7969) and the validation set (AUC = 0.8347). The goodness of fit test indicated no lack of fit of the model ($P = .1021$).

Three baseline characteristics were identified as significant predictors of persistence in patients with TD (cohort 3). Patients with schizoaffective disorder or schizophrenia (HR [95% CI], 0.16 [0.04, 0.69]; $P < .05$) or sleep-wake disorders

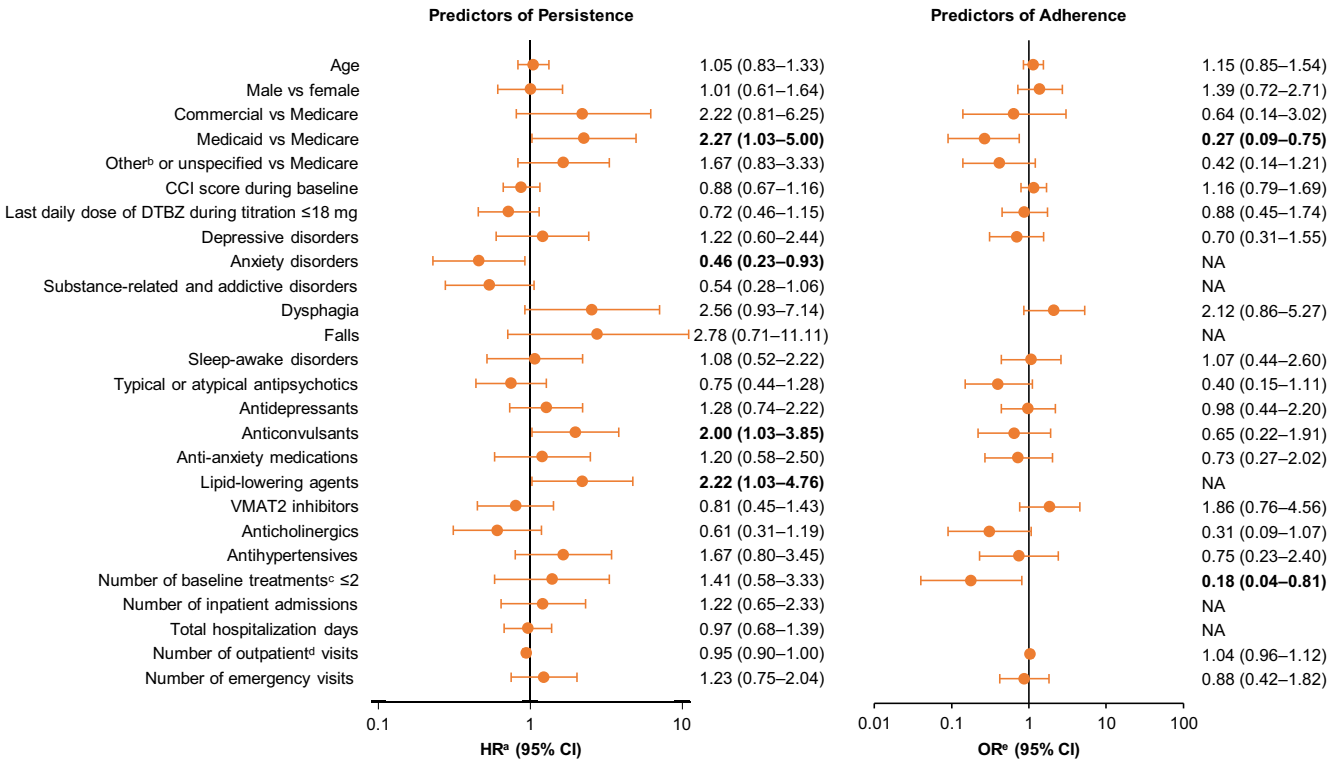


**FIGURE 3: Model predictors for deutetrabenazine persistence (cohort 1, n = 187) and adherence (cohort 2, n = 85) among patients with HD**

**CCI = Charlson Comorbidity Index; DTBZ = deutetrabenazine; HD = Huntington disease; NA = not applicable; VMAT2 = vesicular monoamine transporter 2. Predictors shown in bold were found to be statistically significant ($P < .05$).**

**[a]Health plan type is associated with a patient's index claim. Other health plan types include cash, employer group, third party administrator, processors, and workers' compensation.**

**[b]Number of baseline treatments was calculated as the sum of binary indicators for any baseline use of antidepressants, anticonvulsants, antipsychotic agents, antianxiety medications, anticholinergics, lipid-lowering agents, antihypertensives, antidiabetic drugs, sedatives and hypnotics, lithium, and stimulants or attention deficit or hyperactivity disorder medications.**

**[c]Outpatient visits include medical office, hospital outpatient, and clinic visits. Total hospitalization days were the sum of the lengths of stay for admissions that began during the baseline period.**

**[d]Cox proportional hazards regression without regularization was fit on the modeling set (2/3 of the total number of patients in cohort 1, n = 187), using the above characteristics as predictors. Individual comorbidities and treatments with less than 10% prevalence during the baseline period were excluded and considered as the base-case. In order to avoid potential multicollinearity, hypertension and hyperlipidemia were excluded from the list of predictors, and their related treatments (ie, use of antihypertensives and lipid-lowering agents) were kept instead.**

**[e]Logistic regression without regularization was fit on the modeling set (2/3 of the total number of patients in cohort 2, n = 85), using the listed characteristics as predictors.**

(0.18 [0.14, 0.82]; $P < .05$) at baseline were at a significantly higher risk for discontinuation of deutetrabenazine compared with those without these comorbidities. In contrast, patients taking lipid-lowering agents (4.76 [1.02, 20.00]; $P < .05$) during baseline had a significantly higher likelihood of persistence compared with those without this treatment (Figure 4). Comorbid bipolar disorder showed a trend toward increased persistence (4.55 [1.00, 20.00]), whereas obesity (0.21 [0.04, 1.16]), age (0.64 [0.34, 1.20]), and male gender (0.36 [0.10, 1.25] showed a trend toward discontinuation. The model demonstrated strong predictive performance for the modeling set (AUC = 0.7919) and the validation set (AUC = 0.7715). The goodness of fit test indicated no lack of fit of the model ($P = .7022$).

## Adherence Analyses

For patients with HD (cohort 2), the adherence rate with deutetrabenazine was 62.5%, and the mean PDC during the 6-month study period was 76.7% (SD, 28.2%; median, 92.8%); for patients with TD (cohort 4), the adherence rate was 46.7%, and the mean PDC was 65.7% (SD, 30.2%; median, 72.8%).

The prediction models for adherence were fit on two-thirds of the total number of patients in cohort 2 (HD) and cohort 4 (TD), corresponding to 85 and 120 patients, respectively. Two predictors were found to be significantly associated with adherence in cohort 2 (HD). Patients with ≤2 treatments for chronic diseases (OR [95% CI], 0.18 [0.04, 0.81]; $P < .05$) and those with Medicaid versus Medicare insurance (0.27 [0.09, 0.75]; $P < .05$) had lower odds of

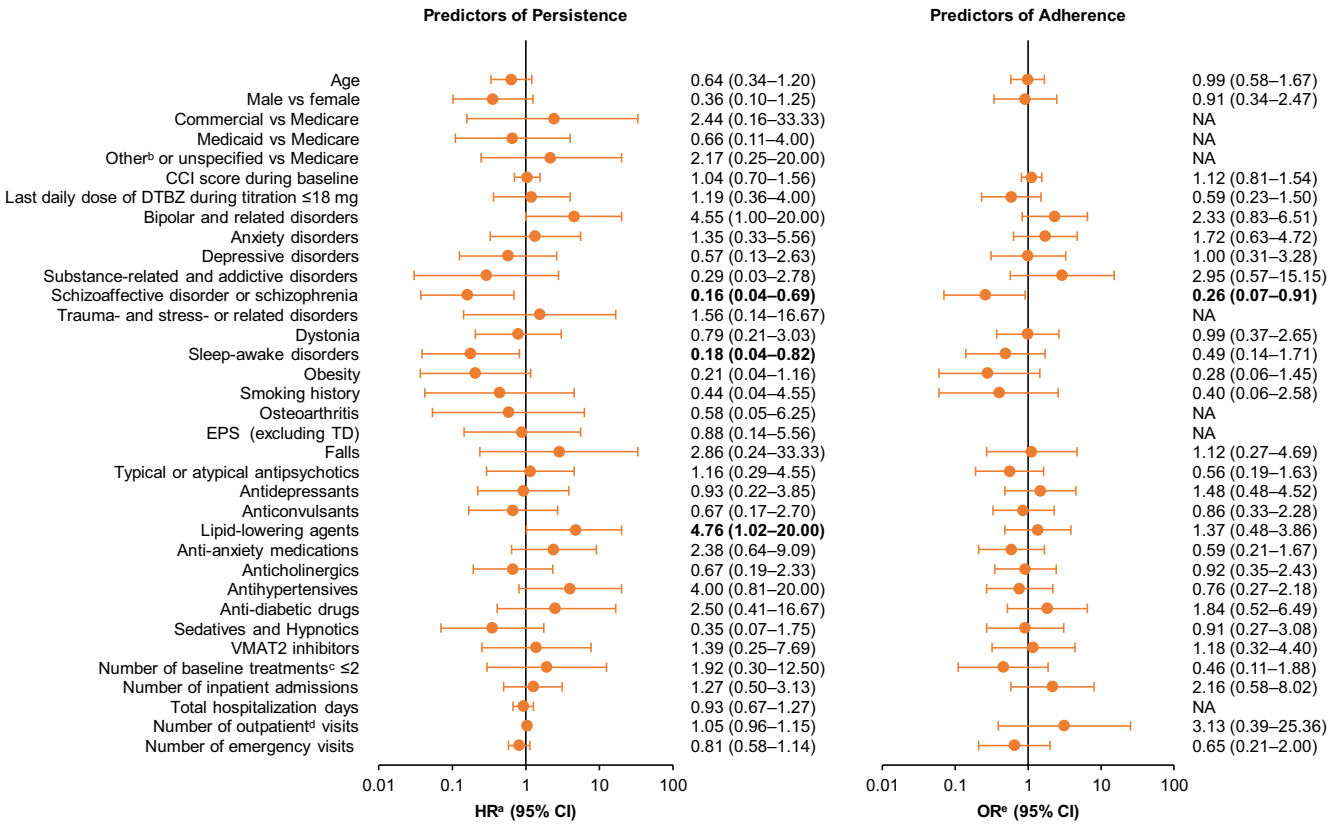


**FIGURE 4: Model predictors for deutetrabenazine persistence (cohort 3, n = 241) and adherence (cohort 4, n = 120) among patients with TD**

**CCI = Charlson Comorbidity Index; DTBZ = deutetrabenazine; EPS = extrapyramidal symptoms; NA = not applicable; TD = tardive dyskinesia; VMAT2 = vesicular monoamine transporter 2. Predictors shown in bold were found to be statistically significant ($P < .05$).**

**[a]Health plan type is associated with a patient's index claim. Other health plan types include cash, employer group, third party administrator, processors, and workers' compensation.**

**[b]Number of baseline treatments was calculated as the sum of binary indicators for any baseline use of antidepressants, anticonvulsants, antipsychotic agents, antianxiety medications, anticholinergics, lipid-lowering agents, antihypertensives, antidiabetic drugs, sedatives and hypnotics, lithium, and stimulants or attention deficit or hyperactivity disorder medications.**

**[c]Outpatient visits include medical office, hospital outpatient, and clinic visits. Total hospitalization days were the sum of the lengths of stay for admissions that began during the baseline period.**

**[d]Cox proportional hazards regression without regularization was fit on the modeling set (2/3 of the total number of patients in cohort 3, n = 241), using the above characteristics as predictors. Individual comorbidities and treatments with less than 10% prevalence during the baseline period were excluded and considered as the base-case. In order to avoid potential multicollinearity, hypertension and hyperlipidemia were excluded from the list of predictors, and their related treatments (ie, use of antihypertensives and lipid-lowering agents) were kept instead.**

**[e]Logistic regression without regularization was fit on the modeling set (2/3 of the total number of patients in cohort 4, n = 120), using the listed characteristics as predictors.**

adherence (Figure 3). Despite no lack of fit ($P = .9075$), the model had limited predictive performance; AUC was 0.6103 and 0.5625 for the modeling and validation sets, respectively.

In cohort 4 (TD), only patients with schizoaffective disorder or schizophrenia were significantly less likely to be adherent to deutetrabenazine than patients without these comorbidities (OR [95% CI], 0.26 [0.07, 0.91]; $P < .05$) (Figure 4). Despite no lack of fit ($P = .6412$), the adherence model had limited predictive performance; AUC was 0.5769 and 0.7011 for the modeling and validation sets, respectively.

## Discussion

This retrospective study used claims data to characterize and identify predictors of real-world persistence and adherence patterns with deutetrabenazine among patients with HD or TD in the United States. In patients with HD (cohort 1), four predictors of persistence were found to be statistically significant ($P < .05$). Patients using Medicaid were more likely to be persistent with deutetrabenazine compared with those using Medicare; similarly, patients using anticonvulsants or lipid-lowering agents were more likely to be persistent with deutetrabenazine compared with patients not on those treatments. In contrast, patients with an anxiety disorder were more likely to discontinue deutetrabenazine than those without

an anxiety disorder diagnosis. For adherence (cohort 2), patients with HD using Medicaid were less likely to be adherent to deutetrabenazine compared with those using Medicare, and patients using ≤2 treatments for chronic diseases also had lower odds of adherence. These results are consistent with the observation that patients with multimorbidity may require more frequent visits with physicians and have better access to health care resources and services, which might be associated with better persistence and adherence to treatment in general.[19]

In TD (cohort 3), 3 predictors of persistence were found to be statistically significant ($P < .05$). Patients treated with lipid-lowering agents were more likely to be persistent with deutetrabenazine therapy, whereas patients with schizoaffective disorder, schizophrenia, or a sleep-wake disorder were more likely to discontinue deutetrabenazine. In cohort 4, patients with schizoaffective disorder or schizophrenia diagnosis were significantly less likely to be adherent to deutetrabenazine. Nonadherence to antipsychotic agents is a common problem in schizophrenia management.[20,21] Lack of patient insight, which manifests as lack of awareness of their own illness and need for treatment, is one factor associated with intentional nonadherence[22] and might precipitate nonadherence to deutetrabenazine.

Whereas both models of persistence demonstrated strong predictive performance, both models of adherence had limited predictive performance. Poor predictive performance could have been driven by the limited sample size of the adherence modeling sets (HD, n = 85; TD, n = 120).

Statistically significant predictors of deutetrabenazine persistence, such as the use of lipid-lowering agents and the presence of comorbid conditions, may reflect more frequent physician visits and/or better access to health care services. Further studies are needed to better understand the reasons for associations between certain variables and treatment persistence or adherence and to investigate the potential association of other variables, such as social determinants of health (eg, educational level, financial status) and health care provider characteristics, with treatment behaviors.

There are a few limitations to this study. Presence of TD, HD, and comorbidities present at baseline were identified by ICD-10-CM codes used for administrative billing purposes and may be underestimated because of lack of coding completeness. This analysis did not capture comorbidities present after treatment initiation, so no conclusions can be drawn regarding treatment side effects. In addition, the SHS Integrated Dataverse does not capture reasons for treatment discontinuation. Continuous health plan enrollment was inferred using medical and pharmacy claims activity, as the SHS Integrated Dataverse database does not include eligibility records. Because the SHS Integrated Dataverse database is based on a large convenience sample, results of this observational study may be confounded by unmeasured characteristics. Additionally, claims that took place outside of the SHS Integrated Dataverse were not captured. Importantly, patient adherence may have been overestimated, as claims for prescription fills may not capture actual use. Moreover, patient sampling did not exclude those who switched from valbenazine or tetrabenazine to deutetrabenazine, which could introduce confounding effects. As deutetrabenazine was only approved by the FDA for use in chorea associated with HD and TD in 2017, sample sizes for patients taking deutetrabenazine were limited. Future studies may benefit from larger sample sizes or a time frame beyond 6 months, which could elucidate additional predictors of persistence and adherence among patients with HD and TD. In addition, future research investigating real-world reasons for treatment discontinuation and side effects is warranted.

In conclusion, these results suggest that underlying psychiatric comorbidities may negatively affect treatment persistence in some patients. Pharmacists and health care providers can leverage these findings to better understand and aid patient populations at the greatest risk for negative treatment use outcomes, as well as implement targeted interventions to maximize adherence to treatment. As deutetrabenazine is often dispensed in a specialty pharmacy setting, there is potential for pharmacists to serve as key personnel in the identification of patients at risk for discontinuation and/or nonadherence, perhaps facilitated by the development of software that flags patients with a risk factor for adverse treatment behavior. Such patients can then be redirected to health care providers, who can provide personalized support designed to improve treatment persistence and adherence.

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