Increased Health Care Utilization in Children and Adolescents With Tourette Syndrome Treated With Dopamine D2 Receptor Antagonists/Partial Agonists: An Electronic Health Records Database Analysis

POSTER NUMBER: 179

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BACKGROUND

- Tourette syndrome (TS) is a neurodevelopmental disorder characterized by motor and vocal tics of varying frequency, intensity, and complexity that begin in childhood and have a duration of ≥1 year[1,2]
- The dopamine D2 receptor antagonists/partial agonists (D2RAs) aripiprazole, haloperidol, and pimozide are indicated in the United States for treatment of TS; however, these medications are associated with multiple adverse effects (eg, weight gain, lipid abnormalities, hyperglycemia, hyperprolactinemia) that can limit long-term use[2-5]
- Data on health care resource utilization (HCRU) for children and adolescents with TS prescribed D2RAs are lacking

OBJECTIVE

- To compare HCRU in D2RA-exposed versus D2RA-nonexposed children and adolescents with TS

METHODS

- Data were analyzed from an electronic health records (EHR) database (TriNetX Dataworks-USA Network) containing information for >119 million unique individuals
- The D2RA-exposed cohort was indexed on first record for a D2RA (2011-2021) with TS diagnosis (ICD-9-CM diagnosis: 307.23 or ICD-10-CM: F952) during a baseline period (18 months before and including index date), and the non-D2RA cohort was indexed on a randomly selected record with TS diagnosis (2011-2021)
- Additional criteria were age 6 to 17 years at index date and ≥1 provider encounter during baseline and during a follow-up period (18 months after index)
- Individuals in each cohort were 1:1 matched based on age group, index year, region, and sex
- Incidence rates (per 100 patient-years; allowing multiple events per patient) and incidence rate ratios (IRRs) for all-cause and TS-related HCRU (emergency, inpatient, and outpatient health care encounters) were calculated for the 18-month follow-up period
- All-cause HCRU was defined as health care encounters in any of the following settings: emergency, inpatient (hospital, non-acute, or short stay), and outpatient (ambulatory, home health, observation, pre-admission, or virtual)
  - TS-related HCRU was defined as health care encounters (noted above) with a TS diagnosis code (ICD-9-CM diagnosis: 307.23 or ICD-10-CM: F952)

RESULTS

- 1684 individuals aged 6 to 17 years with TS were included in each of the matched D2RA and non-D2RA cohorts (**Table**)
  - In the D2RA cohort, the first-month (index) D2RAs identified were risperidone (42.0%), aripiprazole (33.1%), haloperidol (7.6%), quetiapine (7.4%), pimozide (6.7%), olanzapine (3.4%), and ziprasidone (2.1%)

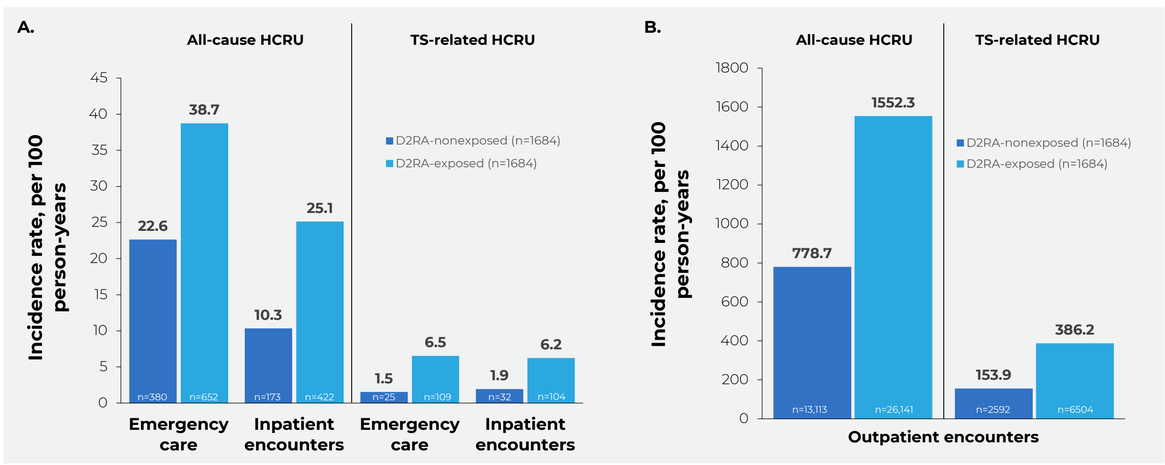
Table. Patient Demographic* and Baseline Characteristics† After Matching

Parameter	D2RA-Exposed Cohort (n=1684)	D2RA-Nonexposed Cohort (n=1684)
Age		
Median, y	13	13
6-11 y, n (%)	576 (34.2)	576 (34.2)
12-17 y, n (%)	1108 (65.8)	1108 (65.8)
Male, n (%)	1245 (73.9)	1245 (73.9)
Race, n (%)		
White	1290 (76.6)	1225 (72.7)
Black	87 (5.2)	105 (6.2)
Asian	27 (1.6)	29 (1.7)
Other	15 (0.9)	11 (0.6)
Missing	265 (15.7)	314 (18.6)
BMI category,‡ n (%)		
Underweight/normal weight§	706 (41.9)	610 (36.2)
Overweight/obesity¶	388 (23.0)	286 (17.0)
Missing	590 (35.0)	788 (46.8)
Neuropsychiatric comorbidities, n (%)		
Anxiety	998 (59.3)	680 (40.4)
ADHD	960 (57.0)	637 (37.8)
OCD	432 (25.7)	242 (14.4)
Depression/mood disorder	276 (16.4)	111 (6.6)
Autism spectrum disorder	256 (15.2)	135 (8.0)
Sleep disorder	200 (11.9)	137 (8.1)
Headache/migraine	147 (8.7)	150 (8.9)
Suicidality/suicide attempt	134 (8.0)	24 (1.4)
Abnormal involuntary movements	81 (4.8)	82 (4.9)
Non-D2RA TS-related medications, n (%)		
Guanfacine	669 (39.7)	386 (22.9)
Clonidine	422 (25.1)	194 (11.5)
Topiramate	147 (8.7)	75 (4.5)
Botulinum toxin A	2 (0.1)	2 (0.1)
Other medications, n (%)		
Antidepressant	922 (54.8)	346 (20.5)
ADHD medication	621 (36.9)	331 (19.7)
Antianxiety#	340 (20.2)	122 (7.2)
Antiseizure**	222 (13.2)	81 (4.8)

*Age, sex, and race reported at index. †BMI category, neuropsychiatric comorbidities, and medication records during the baseline period (18 months before and including index). ‡Based on BMI Z score (calculated per age and sex using US Centers for Disease Control and Prevention growth charts). §BMI Z score <1.0. ¶BMI Z score ≥1.0. #Benzodiazepine (excluding clonazepam) or buspirone. **Did not include topiramate.
ADHD = attention-deficit/hyperactivity disorder; BMI = body mass index; D2RA = dopamine D2 receptor antagonist/partial agonist; OCD = obsessive-compulsive disorder; TS = Tourette syndrome.

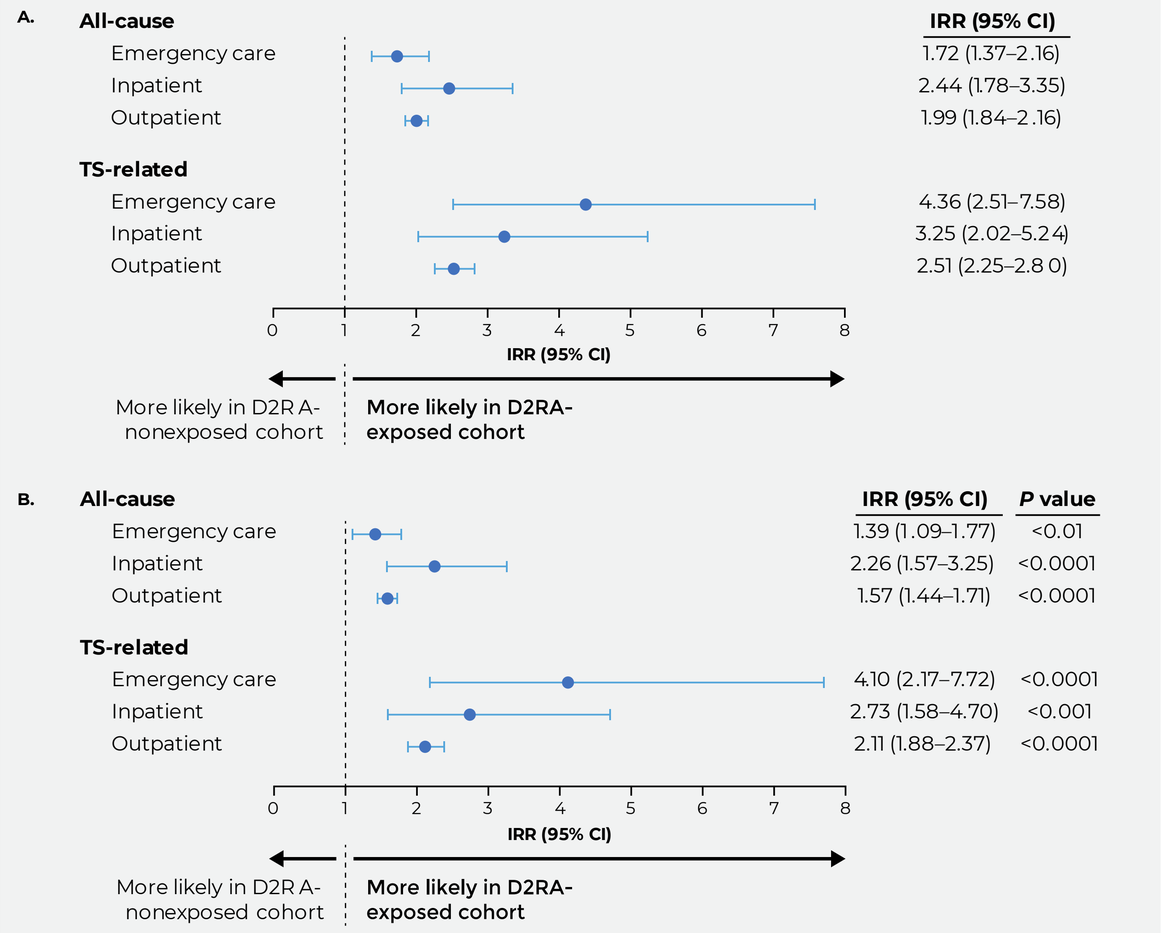
- The D2RA-exposed TS cohort had a higher rate of all-cause HCRU compared with the non-D2RA exposed TS cohort during the 18-month follow-up period (**Figures 1A and 1B**), with 1.7-fold higher emergency care, 2.4-fold higher inpatient encounters, and 2.0-fold higher outpatient encounters (**Figure 2A**)
  - The D2RA-exposed TS cohort also had a higher rate of TS-related HCRU compared with the non-D2RA exposed TS cohort (**Figures 1A and 1B**), with 4.4-fold higher emergency care, 3.3-fold higher inpatient encounters, and 2.5-fold higher outpatient encounters (**Figure 2A**)
- Similar results were observed after multivariable adjustment for demographics and clinical characteristics, with significantly greater increase (IRR) in the D2RA-exposed versus non-D2RA cohort for all-cause and TS-related emergency, inpatient, and outpatient health care encounters (IRR range, 1.4-4.1; *P*<0.01 for all; **Figure 2B**)

Figure 1. All Cause and TS-Related (A) Emergency and Inpatient and (B) Outpatient Health Care Resource Utilization During an 18-Month Follow-Up Period in Children and Adolescents With TS



D2RA = dopamine D2 receptor antagonist/partial agonist; HCRU = health care resource utilization; TS = Tourette syndrome.

Figure 2. Health Care Resource Utilization in Children and Adolescents With TS During an 18-Month Follow-Up Period (A) Before and (B) After Multivariable Adjustment



D2RA = dopamine D2 receptor antagonist/partial agonist; IRR = incidence rate ratio; TS = Tourette syndrome.

CONCLUSIONS

- These retrospective EHR-based results suggest that children/adolescents with TS and treated with D2RAs experienced a higher HCRU burden during an 18-month period following D2RA initiation than those not treated with D2RAs
- Although analyses included multivariable adjustment for demographics and clinical characteristics, higher utilization may reflect underlying TS severity/complexity, drug-related adverse effects, and/or coding and attribution artifacts
- Further studies should investigate TS severity and medication-related effects, potentially leveraging episode-based methods and multiple sources of evidence, including integrated claims data and chart reviews

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ACKNOWLEDGMENTS:
This study was funded by Emalex Biosciences, Inc. Editorial and medical writing assistance were provided under the direction of the authors by Mary Beth Moncrief, PhD, Synchrony Medical Communications, LLC, West Chester, PA. Funding for this assistance was provided by Emalex Biosciences, Inc., Chicago, IL.

DISCLOSURES:
DAI is a clinical trial site investigator for Emalex Biosciences, Inc. and receives funding from the National Institute of Neurological Disorders and Stroke and Teva Branded Pharmaceutical Products, R&D, Inc. JPS, FMD, FM, and CAP are employees of Thermo Fisher Scientific, a company that received funding from Emalex Biosciences, Inc., to conduct the analyses. DLG is a clinical trial site investigator for Emalex Biosciences, Inc., Quince Therapeutics, and PTC Therapeutics; and has received consulting fees and/or travel support from Emalex Biosciences, Inc., PTC Therapeutics, and Vima Therapeutics. GBK, SDA, and FEM are employees of Emalex Biosciences, Inc. SPW and TMC are employees of Paragon Biosciences, LLC, a company that founded Emalex Biosciences, Inc. KKT has been a clinical trial site investigator for Emalex Biosciences, Inc.; received travel support from Emalex Biosciences, Inc.; and received consulting fees from Jazz Pharmaceuticals.

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