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ORIGINAL INVESTIGATION

Further evidence of low adherence to stimulant treatment in adult ADHD: an electronic medical record study examining timely renewal of a stimulant prescription

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Abstract

Rationale ADHD is a prevalent and morbid neurobiological disorder affecting up to 5% of adults. While stimulants have been documented to be safe and effective in adults with ADHD, uncertainties remain about adherence to these treatments.

Objectives The main aim of this article was to evaluate contemporaneous rates and correlates of adherence to stimulants in adults with ADHD using data from electronic medical records from a large healthcare organization focusing on timely renewal of an initial prescription.

Methods Subjects were patients 18 to 44 years of age who had been prescribed a stimulant between January 1, 2015, and December 31, 2016. Prescription and sociodemographic data were extracted from the Partners HealthCare Research Patient Data Registry (RPDR). Our outcome metric was renewal of the index stimulant prescription defined as the first prescription recorded in the electronic record for the period under investigation.

Results We identified 2689 patients with an index prescription for a stimulant medication. Results showed that only 42% of patients renewed their prescriptions in a timely enough fashion to be considered consistently medicated.

Conclusions Results indicate that adults with ADHD have a low rate of renewal of their initial stimulant prescription indicating poor patient engagement in their treatment for ADHD.

Keywords Adult ADHD · Attention-deficit/hyperactivity disorder · Stimulants · Medication adherence · Electronic health records · Non-renewal

Introduction

Attention-deficit/hyperactivity disorder (ADHD) is a prevalent and morbid neurobiological disorder estimated to afflict up to 5% of adults in the USA (Kessler et al. 2006; Fayyad et al. 2007). Its morbidity has been documented in studies showing high levels of psychiatric comorbidity (Biederman et al. 2006c); addictions to cigarettes, drugs, and alcohol (Kollins et al. 2005; Biederman et al. 2006b); educational and occupational under-attainment (Biederman et al. 2008; Biederman et al. 1996); automobile accidents (Biederman et al. 2007; Jerome et al. 2006); traumatic brain injury (Segalowitz and Lawson 1995; Max et al. 2004); PTSD (Biederman et al. 2006c); criminality (Lichtenstein et al. 2012); and suicide (Barbaresi et al. 2013; Dalsgaard et al. 2015), among many others.

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At the same time, ADHD is among the most treatable psychiatric disorders due to the well-documented safety and efficacy of stimulants (Spencer et al. 2005; Spencer et al. 2007; Spencer et al. 2013; Biederman et al. 2006a; Medori et al. 2008; Faraone and Glatt 2009; Canadian ADHD Resource Alliance 2008; Kendall et al. 2008; Kooij et al. 2010; Faraone and Glatt 2010; Faraone and Buitelaar 2010). Moreover, an emerging literature documents that during periods on stimulant medication, patients with ADHD were at significantly decreased risk for many of the negative ADHD-associated adverse functional outcomes including suicide-related events (Chen et al. 2014), depression (Chang et al. 2016), substance-related events (Quinn et al. 2017), criminality (Lichtenstein et al. 2012), motor vehicle collisions (Chang et al. 2017), and accidents and injuries (Lam 2002; Lam 2005; Mikolajczyk et al. 2015) compared with periods off stimulant medication.

While these studies stress the critical importance of adherence to stimulant treatment in ADHD, uncertainties remain as to the magnitude of this problem in clinical practice (Adler and Nierenberg 2010; Gajria et al. 2014) (Ahmed and Aslani 2013; Gajria et al. 2014). A limited literature suggests that non-adherence to stimulants in ADHD may be high in pediatric ADHD (Adler and Nierenberg 2010; Gajria et al. 2014). In one of the few studies on adults with ADHD, Perwien et al. found that 88% of adults with ADHD were non-compliant with their stimulant treatment after 2 months of treatment (Perwien et al. 2004). This finding suggests that non-adherence may be prevalent in adults with ADHD and it can be observed shortly after initiation of stimulant treatment. Considering the adverse impact of untreated ADHD, improved efforts to better quantify rates of adherence to stimulants in adults with ADHD are a critical step towards developing appropriate measures to offset this problem.

One opportunity to assess adherence to stimulant treatment in adults with ADHD is through mining data from electronic medical records (EMR). This approach can be most informative since it incorporates actual clinical practice data within a large representative population, which yields greater ecological validity than clinical trials or select subpopulations.

We recently used data derived from electronic medical records (EMR) to assess rates of stimulant medication adherence in pediatric ADHD (Biederman et al. In Press). Findings revealed that out of more than 2206 pediatric patients with prescriptions for a stimulant medication identified in the EMR, only 46% refilled their index prescriptions within a timeframe to be considered consistently medicated. Poor adherence could not be linked to sociodemographic or clinical factors. While these findings provide compelling new evidence of low rates of medication adherence in children with ADHD, whether similar findings are operant in adults with ADHD remain unknown.

The main aim of the present study was to extend to adults efforts to quantify rates and correlates of initial stimulant renewal in adults with ADHD. To this end, we conducted a systematic search of EMR from a large healthcare organization for patients 18–44 years of age who had been prescribed an amphetamine or methylphenidate product between January 1, 2015, and December 31, 2016. We used the rate of renewal of the initial stimulant prescription as our outcome metric. Based on the literature, and our previous work in pediatrics, we hypothesized that the rate of renewal of the initial stimulant prescription in adults with ADHD would be low.

Methods and materials

Sample

Prescription and sociodemographic data were extracted from the Partners HealthCare Research Patient Data Registry (RPDR) for patients 18–44 years of age who had been prescribed a stimulant between January 1, 2015, and December 31, 2016. This period was based on the time when the newest EMR system from Epic Systems Corporation (EPIC) was implemented. EPIC is one of the largest providers of health information technology used to access, organize, store, and share EMRs. Prescription information in EPIC prior to January 1, 2015, was considered incomplete. This study was approved by the Institutional Review Board at Massachusetts General Hospital.

Patients were included in the study sample if they had been prescribed any of the following formulations of stimulants (short- or long-acting): amphetamine/dextroamphetamine, dextroamphetamine or lisdexamphetamine, dexmethylphenidate or methylphenidate. We included medications with single prescriptions (30-day supply) or post-dated prescriptions up to 3 months (60- or 90-day supply). Patients with stimulant prescriptions were excluded from the study sample if they had no endorsed ADHD diagnosis in the EMR and had either (1) an endorsed cancer, obesity, or narcolepsy diagnosis in the EMR or (2) their index prescription from a cancer, weight loss, or sleep center. Patients with ADHD diagnoses endorsed in the EMR were included regardless of the department from which they received their prescription.

Definitions and variable derivation

Defining the index prescription

We defined a patient's index prescription as the first stimulant prescription during the study period of January 1, 2015, to December 31, 2016. As prescription data prior to January 1, 2015, were incomplete in the system, we were unable to

differentiate between newly treated patients and patients who received any treatment before the study period.

Defining prescription refills and initial stimulant renewal

We defined a stimulant prescription refill as receiving another prescription for any stimulant medication regardless of the medication type (amphetamine or methylphenidate), dose, or formulation (short- versus long-acting). We defined the renewal of an index stimulant prescription in the following three ways: (1) Single index prescriptions needed to have a second one issued within 90 days; (2) index prescriptions post-dated 2 months (i.e., two prescriptions in the system with the same prescribing date for medications of the same dose, formulation, and type) needed to have a third one > 30 days and ≤ 120 days after the date of the index prescription; and (3) index prescriptions post-dated 3 months (i.e., three prescriptions in the system with the same prescribing date for medications of the same dose, formulation, and type) needed to have a fourth prescription > 60 days and ≤ 150 days after the date of the index prescription. If patients had more than one medication prescribed on the date of the index prescription (i.e., medications with different doses or formulations), they only had to renew one of the medications. Additionally, if patients had more than one medication prescribed on the date of the index prescription and one was post-dated, we followed the rules for post-dated prescriptions. Patients were excluded if the window of time to refill their prescriptions extended beyond the endpoint of our study.

Variable derivation for correlates and prediction analysis

We used patients' zip codes to identify the median incomes for the towns in which they lived using the US Census Bureau's 2015 American Community Survey 5-Year Estimates (U.S. Census Bureau. American Community Survey 2011). We used a tercile split of the median income to classify patients as lower (median income < $72z837), middle ($72,837 ≤ median income < $90,077), or upper class (median income ≥ $90,077). We categorized index prescriptions as prescribed from a psychiatry or non-psychiatry clinic based on the clinic reported in the EMR. Non-psychiatry clinics mainly consisted of primary care clinics (83%) followed by neurology clinics (8%), weight and cancer clinics with an endorsed ADHD diagnosis (2%), and then other clinics not falling the in aforementioned categories (7%). If patients had more than one medication prescribed on the date of the index prescription and at least one was from a non-psychiatry clinic, we categorized that patient as having a non-psychiatry source.

Statistical methods

Of the available pool of 2689 participants, a minority (N = 926, 34%) had unspecified data for at least one of the following demographic or treatment characteristics: race (n = 70 [3%] missing), clinic source (n = 871 [32%] missing), primary language (n = 29 [1%] missing), and economic status (n = 2 [< 1%] missing). Therefore, we used multivariate imputation using chained equations to impute the missing data for these independent variables. Using Stata's *mi impute* command with 20 imputations, we implemented logistic regression imputation methods for race, clinic source, and primary language, and ordered logistic regression imputation methods for economic status. In addition to the imputed variables, we included the following predictors in our imputation models: sex, age, medication formulation (long- versus short-acting), medication type (methylphenidate versus amphetamine), and medication renewal.

We analyzed our data using a discovery and replication set approach which allowed us to build a model to predict initial stimulant renewal in one dataset and evaluate how well the model worked in a separate, unbiased dataset. To do this, we randomly selected 75% of the subjects to be in a discovery set and 25% of the subjects to be in a replication set. We performed all analyses in the discovery set and then assessed the accuracy of prediction in the replication set. First, using the discovery set, we compared rates of initial stimulant renewal between patients with different demographic (e.g., males versus females) and treatment (e.g., short- versus long-acting formulation) characteristics using logistic regression models. We then ran a multivariable logistic regression model predicting initial stimulant renewal from the demographic characteristics with $p \leq 0.10$ in the bivariate analyses and all treatment characteristics. We generated an area under the curve (AUC) statistic for the multivariable model to see how well these characteristics predicted initial stimulant renewal. An AUC of 0.5 means the combined characteristics do not exceed chance in predicting initial stimulant renewal and an AUC of 1.0 means the combined characteristics predict initial stimulant renewal perfectly. Next, using the replication set, we again compared initial stimulant renewal between patients with different demographic and treatment characteristics and then ran the multivariable logistic regression model that was developed in the discovery set to see how well it predicted initial stimulant renewal in the replication set. This approach is used routinely in predictive analytics to protect against drawing conclusions from false positive results.

To assess the robustness of the findings in our primary analysis, we performed five sensitivity analyses: (1) excluding patients who had an unspecified prescribing clinic; (2) excluding patients with an unclear ADHD diagnosis; (3) excluding patients who had index prescriptions prior to January 1, 2016, ensuring 1-year of lead-in time without stimulant medication

for all included patients; (4) using a 45-day window to define initial stimulant renewal; and (5) using a 37-day window to define initial stimulant renewal.

For all analyses, standard errors were adjusted by Stata's *mi* estimate command to account for the variability between imputations. All tests were two-tailed and performed at the 0.05 alpha level using Stata (Version 15.1) (StataCorp 2017).

Results

Sample

We identified 2689 patients with prescriptions for stimulant medication in the EMR. Forty-nine percent of patients were male, 86% were Caucasian, and the average age was 29.0 ± 7.2 years. Of the 2689 patients with prescriptions for stimulant medication identified, 95% had a *single* index prescription (as opposed to prescriptions that were post-dated 2 months [4.6%] or 3 months [0.3%]). Fifty-three percent of patients had methylphenidate prescribed as their index prescription and 63% had a long-acting formulation. Of the available pool of stimulant-treated patients, we randomly assigned 75% (N = 2010 patients) to the discovery or model development set and the other 25% (N = 679) patients to the replication set.

Discovery set results

Initial stimulant renewal

Only 42% (N = 854) of patients in the discovery set met our a priori definition of initial stimulant renewal, indicating that they renewed their stimulant prescriptions in a timely fashion to be considered consistently medicated.

Sociodemographic correlates of initial stimulant renewal

As shown in Table 1, there were statistically significant differences in the rates of initial stimulant renewal when examining stimulant formulation (higher in patients receiving long-acting versus short-acting formulations) and prescription source (higher in psychiatry versus non-psychiatry clinics). There were no meaningful differences in demographic characteristics or any other treatment characteristics.

Predictors of initial stimulant renewal

To examine predictors of initial stimulant renewal, we ran a multivariate logistic regression model using demographic characteristics with $p \leq 0.10$ in the bivariate analyses and all treatment characteristics (Table 2). Only treatment characteristics were included in this model because none of the demographic characteristics had even marginal significance ($p \leq 0.10$). After controlling for all other variables, only prescription source remained significantly associated with initial stimulant renewal. Patients who got their prescriptions from a psychiatry clinic were at significantly increased odds of renewing their initial stimulant prescription. However, this model yielded an AUC statistic of 0.61, indicating that the ability of treatment characteristics to predict initial stimulant renewal was poor and only modestly better than chance.

Replication set results

Initial stimulant renewal

Consistent with results in the discovery set, only 39% (N = 266) of patients in the replication set met our definition of initial stimulant renewal, indicating that they renewed their stimulant prescriptions in a timely fashion to be considered consistently medicated.

Sociodemographic correlates of initial stimulant renewal

As shown in Table 3, here too there were some small but statistically significant differences in the rates of initial stimulant renewal when examining prescription source and race. Like in the discovery set, patients who received their prescriptions from psychiatry clinics had a small but significantly greater percentage of patients who renewed their initial stimulant prescriptions when compared with those from non-psychiatry clinics. Caucasian patients were significantly less likely to renew their initial stimulant prescriptions compared with non-Caucasians (Table 3). There were no other meaningful differences.

Predictors of initial stimulant renewal

We applied the multivariable logistic regression model estimated from the discovery set data to predict initial stimulant renewal in the replication set. The model yielded an AUC statistic of 0.60, indicating an absence of over fitting in the initial model but again suggesting that treatment characteristics were poor predictors of initial stimulant renewal in this population.

Sensitivity analysis results

We re-ran our analyses excluding 1638 patients with no endorsed ADHD diagnoses in the EMR as a sensitivity analysis to assess the robustness of the results in our primary analysis. Initial stimulant renewal remained low (60% in discovery set, 61% in replication set) and our model predicting initial stimulant renewal from age, medication formulation, medication type, and prescribing clinic yielded a low AUC statistic of 0.59 in both the discovery and replication sets.

Table 1 Bivariate analyses comparing rates of initial stimulant renewal between patients with different demographic and treatment characteristics in the discovery set ($N = 2010$)

Characteristic	Did not renew initial stimulant prescription $N = 1156$		Renewed initial stimulant prescription $N = 854$		p value
	N	Row %	N	Row %	
Age (mean ± SD)	29.0 ± 7.3		29.1 ± 7.1		0.72
Sex					0.14
Male ($N = 1004$)	561	56	443	44	
Female ($N = 1006$)	595	59	411	41	
Race					0.18
Caucasian ($N = 1761$)	1,023	58	738	42	
Not Caucasian ($N = 249$)	133	53	116	47	
Primary language					0.23
English ($N = 1995$)	1,145	57	850	43	
Not English ($N = 15$)	11	73	4	27	
Economic Status					0.92
Lower ($N = 669$)	385	58	284	42	
Middle ($N = 681$)	388	57	293	43	
Upper ($N = 660$)	383	58	277	42	
Medication formulation					0.009
Long-acting ($N = 1246$)	699	55	565	45	
Short-acting ($N = 746$)	457	61	289	39	
Medication type					0.47
Methylphenidate ($N = 1052$)	597	57	455	43	
Amphetamine ($N = 958$)	559	58	399	42	
Prescription source					< 0.001
Psychiatry clinic ($N = 1061$)	514	48	547	52	
Non-psychiatry clinic ($N = 949$)	642	68	307	32	

We also re-ran our analyses excluding 871 patients with unspecified prescribing clinics as a second sensitivity analysis. Initial stimulant renewal remained low (53% in discovery set, 49% in replication set) and our model predicting initial stimulant renewal from medication formulation, medication type, and prescribing clinic yielded a low AUC statistic of 0.61 in the discovery set and 0.60 in the replication set.

As a third sensitivity analysis, we excluded 1493 patients with index prescriptions prescribed prior to January 1, 2016, to help mitigate the problem of being unable to differentiate between newly treated patients and patients who received treatment before the study period. This ensured that all patients included in the analysis had at least 1 year of lead-in time without stimulant prescriptions. Again, initial stimulant renewal remained low (61% in discovery set, 56% in replication set) and our model predicting initial stimulant renewal from economic status, medication formulation, medication type, and prescribing clinic yielded a low AUC statistic of 0.64 in the discovery set and 0.65 in the replication set.

In the fourth sensitivity analysis, we narrowed the prescription refill window from 90 days to within 7 to 45 days, making an additional assumption that prescriptions refilled within the

Table 2 Multivariable logistic regression in the discovery set predicting initial stimulant renewal from demographic characteristics with p values ≤ 0.10 in the bivariate analyses and all treatment characteristics ($N = 2010$)

Variable	Renewed initial stimulant prescription versus did not renew initial stimulant prescription		p value
	OR	95% CI	
Long-acting formulation (reference: short-acting formulation)	1.39	1.03–1.87	0.38
Methylphenidate (reference: amphetamine)	0.78	0.59–1.04	0.16
Prescription from psychiatry clinic (reference: non-psychiatry clinic)	2.18	1.74–2.73	< 0.001

OR, odds ratio; *CI*, confidence interval

Table 3 Bivariate analyses comparing rates of initial stimulant renewal between patients with different demographic and treatment characteristics in the replication set ($N = 679$)

Characteristic	Did not renew initial stimulant prescription $N = 413$		Renewed initial stimulant prescription $N = 266$		p value
	N	Row %	N	Row %	
Age (mean ± SD)	28.8 ± 6.7		29.1 ± 7.4		0.62
Sex					0.65
Male ($N = 322$)	193	60	129	40	
Female ($N = 357$)	220	61	137	38	
Race					0.01
Caucasian ($N = 604$)	378	63	226	37	
Not Caucasian ($N = 75$)	35	47	40	54	
Primary language					0.32
English ($N = 670$)	409	61	261	39	
Not English ($N = 9$)	4	44	5	56	
Economic status					0.06
Lower ($N = 229$)	128	56	101	44	
Middle ($N = 214$)	128	60	86	40	
Upper ($N = 236$)	157	67	79	33	
Medication formulation					0.05
Long-acting ($N = 431$)	250	58	181	42	
Short-acting ($N = 248$)	163	66	85	34	
Medication type					0.10
Methylphenidate ($N = 361$)	209	58	152	42	
Amphetamine ($N = 318$)	204	64	114	36	
Prescription source					< 0.001
Psychiatry clinic ($N = 343$)	177	52	166	48	
Non-psychiatry clinic ($N = 336$)	236	70	100	30	

first 7 days were not actually refills, but likely reprints of lost prescriptions, for example. We decided to give a 15-day window beyond the date the medication ran out to allow some margin of error for any minor delays or problems refilling exactly when the medication ran out. With this new definition, initial stimulant renewal dropped to 26% in the discovery set (25% in replication set) and our model predicting initial stimulant renewal from race, medication formulation, medication type, and prescribing clinic yielded a low AUC statistic of 0.55 in the discovery set and 0.57 in the replication set.

In our last sensitivity analysis, we narrowed the prescription refill window even more from 90 days to within 7 to 37 days. Initial stimulant renewal was the lowest using this definition (22% in discovery set and 20% in replication set) and our model predicting initial stimulant renewal from race, medication formulation, medication type, and prescribing clinic yielded a low AUC statistic of 0.54 in the discovery set and 0.58 in the replication set. As in the primary analysis, the low AUC statistics in all sensitivity analyses indicate that these demographic and treatment characteristics were only modestly better than chance at predicting initial stimulant renewal.

Discussion

Two years of recent EMR data from a large healthcare organization in a major urban area showed that only 42% of 2689 adult patients prescribed stimulant medications renewed their initial prescriptions. These findings extend to adults' similar findings reported in pediatric samples and provide new estimates of low rates of initial stimulant renewal in clinical practice.

Strengths of this study include the reliance on data from a large EMR dataset that contains information on a well-defined, representative population of adult patients seen at a large healthcare organization in a large urban area representing a diverse group of patients representing a range of socioeconomic and ethnic strata. Also, a strength is the reliance on an objective measure of initial stimulant renewal based on the issuance of a dated prescription for a stimulant as documented in the EMR. Additionally, data were analyzed using different definitions of initial stimulant renewal (sensitivity analyses) as well as using a discovery and replication set analysis with all analyses leading to similar results showing low rates of initial stimulant renewal.

There were no statistically significant demographic or clinical differences between adult patients who did and did not renew their initial stimulant prescriptions. These results suggest that poor initial stimulant renewal afflicts all ages, sexes, and social class strata.

Our result showing small but statistically significant higher rates of initial stimulant renewal in patients receiving long-acting versus short-acting formulations (45% versus 39%) is consistent with the literature showing better initial stimulant renewal of long-acting versus short-acting stimulants (Olfson et al. 2007). However, it is noteworthy that initial stimulant renewal was still quite low in patients taking long-acting formulations, indicating that the problem of low initial stimulant renewal affects all stimulant formulations. If confirmed however, this finding would suggest that efforts to improve initial stimulant renewal for ADHD may benefit from using preferentially long-acting formulations when prescribing stimulants to adult patients with ADHD.

Similarly, although statistically significantly higher rates of initial stimulant renewal were seen in patients seen in psychiatric than in primary care settings (52% versus 32%), initial stimulant renewal rates were quite low in both settings. However, if this novel finding were to be confirmed, it would suggest that efforts to improve initial stimulant renewal for adults with ADHD may be most needed in a primary care setting.

Although the reasons for the low rate of initial stimulant renewal remain unclear, it is possible to postulate that it may be due at least in part to the symptoms of ADHD themselves such as forgetfulness, difficulties in follow through, and deficits in planning and organization could play an important role. Also likely to play an important role is the complexity of the treatment itself with a Schedule II medicine that requires monthly recontact with the prescriber for renewal of the prescription. While post-dating stimulant prescriptions is a possibility, it was only seen in 5% of our sample and the same symptoms of ADHD that might play a role in a patient with a single prescription forgetting to contact their prescriber for a renewal likely also play a role in a patient with post-dated prescriptions losing the post-dated prescriptions or forgetting to refill them. Equally potent in inhibiting initial stimulant renewal could be the ongoing misconceptions and biases about ADHD and stimulant treatments that could also influence initial stimulant renewal. Clearly, more research is needed to clarify the causes of poor initial stimulant renewal in order to develop appropriate measures to mitigate them.

Our results should be seen in the context of methodological limitations. Large data sets include limited diagnostic information. Although we relied on sensitivity analysis, in cases where diagnostic information was lacking, we used stimulant treatment as a proxy for a diagnosis of ADHD considering that ADHD is the main FDA-approved indication for the use of stimulants. However, it is certainly possible that a subset of patients was receiving stimulant treatment for some other indication. Additionally, we did not examine how commonly stimulants were co-prescribed with benzos or opiates or if patients had a comorbid substance use diagnosis. Future studies could benefit from examining whether these affect initial stimulant renewal. Although the index medication was the first one coded in the EMR, it is unclear whether any patients had been on stimulants prior to 2015. Our sensitivity analyses examined rates of initial stimulant renewal with the assumption that prescriptions refilled within the first seven days were likely reprints of lost prescriptions. Future studies could benefit from looking at different lead-in times for refills, such as starting the refill window 14 or 21 days from the index prescription.

Additionally, we do not know whether non-renewal of stimulants was due to other reasons such as poor tolerability, lack of efficacy, use of the stimulants on as needed basis, diversion, changing healthcare systems, or geographical relocation. Future studies could benefit from examining the reasons for non-renewal of stimulant medications and whether there is a relationship between dosing and initial stimulant renewal. Moreover, for patients who discontinued due to lack of efficacy or adverse effects, it would be useful to examine if there was an effort to titrate the medication and if follow-up appointments were offered and attended once the prescription was not renewed.

Laws regarding the maximum dispensing quantity of Schedule II medications vary by state. In Massachusetts, Schedule II prescriptions can only be issued for a 30-day supply, except for methylphenidate which can be issued for a 60-day supply if used to treat ADHD. Additionally, clinicians may issue post-dated prescriptions for up to a 90-day supply of Schedule II medications and each of those prescriptions can be no more than a 30-day supply. Patients' prescription history of Schedule II prescriptions is tracked in the state's Prescription Monitoring Program. We do not know if these regulations had an impact on initial stimulant renewal. Future studies could benefit from examining rates of initial stimulant renewal in states with stricter laws and states with more lenient laws.

Also, because our sample derived from a single New England healthcare organization (albeit one serving a large catchment area and broad range of socioeconomic status and racial/ethnic groups), the extent to which they would generalize to other regions or countries merits further investigation.

Notwithstanding these caveats, these data indicate that only 42% of 2689 adult patients renewed their initial stimulant medication prescription. These findings provide strong contemporaneous and ecologically informative evidence of low rates of initial stimulant renewal in adult patients, underscoring the need for active efforts to better understand the problem and develop approaches to help mitigate it, especially in the primary care settings.

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Compliance with ethical standards

This study was approved by the Institutional Review Board at Massachusetts General Hospital.

Conflict of interest Dr. Biederman's program has received departmental royalties from a copyrighted rating scale used for ADHD diagnoses, paid by Ingenix, Prophase, Shire, Bracket Global, Sunovion, and Theravance; these royalties were paid to the Department of Psychiatry at MGH. Through MGH corporate licensing, he has a US patent (#14/027,676) for a non-stimulant treatment for ADHD, and a patent pending (#61/233,686) on a method to prevent stimulant abuse.

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Dr. Perlis reports personal fees from Psy Therapeutics, personal fees from Genomind, and personal fees from RID Ventures, outside the submitted work.

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