The Association of Oral Stimulant Medication Adherence with Work Productivity among Adults with ADHD

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Abstract

Objective: Examine associations between oral psychostimulant pharmacotherapy adherence, work productivity, and related indirect costs among US adults with ADHD. **Methods**: Medication adherence (Medication Adherence Reasons Scale [MAR-Scale]), work productivity and activity impairment (Work Productivity and Activity Impairment–General Health questionnaire), and ADHD symptom level (Adult ADHD Self-Report Scale version 1.1 Symptom Checklist) were assessed in this noninterventional online survey of adults who self-reported having an ADHD diagnosis and were currently receiving oral psychostimulant treatment for ≥3 months. **Results**: Of 602 respondents, 395 had low/medium adherence (LMA: MAR-Scale total score ≥1) and 207 had high adherence (HA: MAR-Scale total score 0). After adjusting for covariates, the LMA group had significantly greater levels of absenteeism, absenteeism-related indirect costs, and total indirect costs (all $p < .01$) than the HA group. **Conclusion**: In adults with ADHD using oral psychostimulants, lower medication adherence was associated with greater absenteeism and indirect costs. *(J. of Att. Dis. 2022; 26(6) 831-842)*

Keywords

ADHD, indirect costs, medication adherence, psychostimulants, work productivity loss

Introduction

Adult ADHD can be associated with reduced work productivity (Joseph et al., 2019; Murphy & Barkley, 2007). One study reported that US adults diagnosed with ADHD (with unspecified treatment status) compared with adults from a community control group, held jobs for shorter periods (65.9 vs. 97.0 months), were fired or dismissed more frequently (17.4% vs. 3.7%), and had more frequent interpersonal problems in the workplace (32.8% vs. 12.4%) (Murphy & Barkley, 2007). In another study of employed individuals in the United Kingdom who reported receiving an ADHD diagnosis (51.5% of whom were currently receiving medication for ADHD), the mean percentage of time missed from work was 15.7%, and the mean degree of impairment while working due to health problems was 40.6% (Joseph et al., 2019). In analyses based on data from the longitudinal Multimodal Treatment Study of Children with ADHD (MTA), individuals diagnosed with ADHD as children experienced impaired occupational outcomes as adults, including reduced job length, increased number of times fired, lower income, and increased likelihood of using public assistance (Hechtman et al., 2016), with impaired adult occupational outcomes being positively correlated with baseline symptom severity, household income during childhood, and comorbidity burden (Roy et al., 2017).

Studies have also shown that adult ADHD can be associated with excess costs. In one US study, the estimated excess indirect costs due to work productivity loss were $2.6 billion in adults diagnosed with ADHD (including both individuals who were and who were not being treated for their ADHD), relative to matched controls (Birnbaum et al., 2005). In a survey of employees from a large manufacturing firm, adults diagnosed with ADHD (the vast majority of whom were not being treated for ADHD based on medical-pharmacy claims records) had a 4%–5% reduction in work performance, relative to controls without ADHD, which translated to an annual indirect cost of $4336 per worker

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(Kessler et al., 2009). In a systematic review, the annual costs attributed to adult ADHD (including patient- and family member-related costs) in the United States were estimated to range from $105 to $194 billion, with work productivity and income losses accounting for the largest share of these costs (Doshi et al., 2012).

First-line pharmacotherapy for adult ADHD consists of treatment with psychostimulants (Young & Goodman, 2016). The findings of multiple meta-analyses provide support for the efficacy of stimulants for the treatment of the core symptoms of ADHD (Castells et al., 2018; Cortese et al., 2018; Cunill et al., 2016; Faraone & Glatt, 2010). There is also evidence that stimulant therapy improves an array of functional outcomes in adults diagnosed with ADHD, including quality of life and risk for suicidality, substance abuse, and motor vehicle accidents (Adler et al., 2013; Bihlar et al., 2015; Chang et al., 2017; Siffel et al., 2020). Regarding work productivity, a randomized, placebo-controlled study reported significantly greater reductions in Endicott Work Productivity Scale total scores with osmotic-release oral system methylphenidate (OROS-MPH) than with placebo, indicating that OROS-MPH treatment was associated with improvements in work productivity and efficiency compared with placebo (Goodman et al., 2017).

Medication adherence is considered a crucial determinant of treatment efficacy across many psychiatric disorders, including ADHD (Kooij et al., 2013), and studies have reported that adherence to pharmacotherapy is poor in some adults diagnosed with ADHD (Biederman et al., 2019; Bijlenga et al., 2017; Safren et al., 2007). In one study of medication adherence, 22% of adults diagnosed with ADHD reported medication adherence levels <80%, and 44% reported medication adherence levels <90% (Safren et al., 2007). In a long-term naturalistic study, 77.3% of adults diagnosed with ADHD took their medication as directed ≥80% of the time at the start of the study, while only 47.8% were taking their medication as directed ≥80% of the time 3 years later (Bijlenga et al., 2017).

The relationship between treatment adherence to oral psychostimulants and work productivity among US adults diagnosed with ADHD has not yet been well characterized. In this report, the association between oral psychostimulant adherence, work productivity, and related indirect costs among US adults diagnosed with ADHD is examined. In addition, reasons for nonadherence among patients reporting poor adherence are also described.

Methods

Study Design and Procedures

This web-based, cross-sectional, observational online survey was conducted between May 8, 2018 and July 27, 2018 among adults who self-reported having an ADHD diagnosis by a healthcare provider (HCP). Survey respondents were emailed an internet link to the survey, which took approximately 20 minutes to complete and included questions about demographics, health characteristics (e.g., self-report of psychiatric or medical comorbidities diagnosed by an HCP), work productivity, medication adherence, and ADHD symptoms and symptom levels.

The study protocol and questionnaire were reviewed and approved by the Sterling Institutional Review Board (Atlanta, GA). All respondents were required to provide informed consent before participating in the study. No personally-identifying information was stored during data capture, and all data were reported anonymously and analyzed in the aggregate.

Respondents

Respondents were recruited from the US National Health and Wellness Survey (n=73; Kantar, New York, NY) and from additional healthcare ailment panels (n=529; Kantar Profiles/LifePoints [formerly Lightspeed Health], Bridgewater, NJ; Dynata [formerly Research Now], Plano, TX; Survey Sampling International, Plano, TX; Toluna, Dallas, TX; and Disqo [formerly Active Measure], Glendale, CA). All respondents were ≥18 years old, had to self-report being diagnosed with ADHD by an HCP, were currently being treated (for ≥3 months) with oral psychostimulants, had to have access to a computer and the ability to access the survey website, and had to be willing and able to provide informed consent. Respondents who completed the survey were compensated with reward points offered by the panel in which they were a member, with the points reflecting fair market value for the respondents' time.

Measures

The Medication Adherence Reasons Scale (MAR-Scale) is a self-report measure with 19 items that assess reasons for medication nonadherence (see listing of reasons in Table 2) across domains related to logistics, beliefs, forgetfulness, and long-term concerns (Unni et al., 2014, 2019). These 19 items are provided in a "yes/no" format, with "yes" selections followed by a query about how many days in the past week the respondent did not take the medication due to that reason. The MAR-Scale also includes two additional items that assess the frequency of adherence in the past week and the percentage of nonadherence in the past month. For the current analyses, MAR-Scale responses for the overall scale were dichotomized as a score of 0 (perfect adherence across all reasons) or 1 (nonadherence for any reason).

The Adult ADHD Self-Report Scale, version 1.1 (ASRS-v1.1) Symptom Checklist measures ADHD symptom level in adults (Kessler et al., 2005). It includes 18 items derived from the *Diagnostic and Statistical Manual* *of Mental Disorders, 4th Edition* (American Psychiatric Association, 1994). For each item, individuals rate the frequency of ADHD symptoms over the past 6 months on a 5-point scale (0 = never, 1 = rarely, 2 = sometimes, 3 = often, 4 = very often). In the current study, ASRS-v1.1 total score was computed as previously described (Adler et al., 2019), with total score ranging from 0 to 18 (higher scores represent more severe symptoms).

The Work Productivity and Activity Impairment–General Health (WPAI-GH) questionnaire is a 6-item, validated self-report measure (available at www.reillyassociates.net/WPAI_GH.html). It assesses the effect of health on work productivity in terms of absenteeism (absence from work), presenteeism (being unproductive at work because of sickness), and overall work productivity loss (absenteeism plus presenteeism) over the past 7 days in those who are employed, as well as on daily activity impairment (Reilly et al., 1993). It has been utilized to assess work productivity and activity impairment across different medical conditions (Cabeceira et al., 2019; Gajria et al., 2017; Joseph et al., 2019; Rajagopalan & Lee, 2019; Zhang et al., 2010). All measures are reported as percentages, with higher scores representing greater work productivity loss or activity impairment.

Estimated indirect costs were calculated in 2018 US dollars using weekly wage data based on age and sex (Bureau of Labor Statistics, 2018). Wages lost annually as a result of absenteeism or presenteeism were calculated by multiplying the hours missed by the estimated hourly wage (i.e., the weekly wage divided by 40), which was then multiplied by 50 (i.e., the estimated number of work weeks per year). Indirect costs of absenteeism and presenteeism were summed to estimate total indirect costs.

Data Presentation and Analysis

For the current analyses, respondents were dichotomized based on the level of medication adherence (low/medium adherence [LMA], MAR-Scale total score ≥1; high adherence [HA], MAR-Scale total score = 0). Based on prior research indicating that approximately 57% of adults diagnosed with ADHD self-report adherence rates ≥90% (Safren et al., 2007), it was anticipated that recruiting 600 participants would result in HA and LMA groups with approximately 342 and 258 respondents, respectively. Using G*Power 3.1 (Faul et al., 2009), it was anticipated that these sample sizes would yield adequate statistical power (≥80%) to detect differences in work productivity loss, daily activity impairment, and indirect costs as small as Cohen's $d = 0.23$.

Descriptive statistics were calculated for the total sample and for each adherence group. Means with standard deviations (SD) or 95% confidence intervals (CIs) are reported for continuous variables. Frequencies and percentages are reported for categorical variables. Bivariate comparisons between adherence groups were conducted using two-sided independent sample *t* tests for continuous variables and chi-square tests for categorical variables. Statistical significance was set at $p < .05$. No adjustments were made to control for type 1 error associated with conducting multiple comparisons.

Multivariable analyses were conducted for work productivity loss, activity impairment, and related indirect costs using generalized linear models (GLMs) specifying a negative binomial distribution and log link function. One set of GLMs included age, ASRS-v1.1 Symptom Checklist scores (as a continuous variable), comorbidity burden (based on Charlson Comorbidity Index scores), medication use (antidepressants, sleep aids, antipsychotics, antianxiety), and co-occurring psychiatric disorders (bipolar disorder, borderline personality disorder, generalized anxiety disorder, major depressive disorder, and posttraumatic stress disorder) as covariates. A second set of GLMs assessed whether ADHD symptom level moderates the effects of adherence on outcomes. These GLMs included age, comorbidity burden, medication use, and co-occurring illnesses as covariates and ASRS-v1.1 Symptom Checklist scores as a factor/grouping variable (low ADHD symptoms [ASRS-v1.1 Symptom Checklist scores at or below the median] vs. high ADHD symptoms [ASRS-v1.1 Symptom Checklist scores above the median]) and in the interaction term with adherence. Adjusted means, 95% CIs, and *p*-values based on the statistical significance of the regression coefficients were generated for all GLMs. Statistical significance was set at a two-tailed $p < .05$.

Results

Respondent Sociodemographic Characteristics

The LMA and HA groups were generally comparable in terms of sociodemographic characteristics (Table 1). Compared with the HA group, the LMA group was statistically significantly younger ($p < .001$) and had a lower annual income ($p = .006$).

Adherence to ADHD Medication

The mean ± *SD* number of days that respondents took their medication as prescribed in the past week was statistically significantly lower in the LMA group than the HA group (4.56 ± 2.07 vs. 6.86 ± 0.70, $p < .001$). Among respondents in the LMA group, the greatest percentage of respondents reported reasons for nonadherence associated with the forgetfulness domain (68.1% [269/395]), followed by the long-term concerns (52.4% [207/395]),

Table 1. Respondent Sociodemographic Characteristics by Adherence Group.*

Characteristic	HA (*n* = 207)	LMA (*n* = 395)	*p* Value
Mean ± *SD* age, years	44.97 ± 14.64	37.80 ± 13.83	<.001
Sex, *n* (%)			.040
Male	50 (24.2)	85 (21.5)	
Female	154 (74.4)	310 (78.5)	
Prefer not to answer	3 (1.4)	0	
Region, *n* (%)			.670
Northeast	30 (14.5)	64 (16.2)	
Midwest	51 (24.6)	92 (23.3)	
South	97 (46.9)	171 (43.3)	
West	29 (14.0)	68 (17.2)	
Employment, *n* (%)			.246
Unemployed	79 (38.2)	132 (33.4)	
Employed	128 (61.8)	263 (66.6)	
Self-identified race/ethnicity, *n* (%)†			.455‡
White	188 (90.8)	351 (88.9)	
Black or African American	7 (3.4)	17 (4.3)	
American Indian or Alaska Native	3 (1.4)	8 (2.0)	
Asian	5 (2.4)	15 (3.8)	
Hispanic or Latino	7 (3.4)	25 (6.3)	
Other	1 (0.5)	3 (0.8)	
Health insurance, *n* (%)			.221
No insurance	9 (4.3)	27 (6.8)	
Any insurance	198 (95.7)	368 (93.2)	
Education, *n* (%)			.411
Less than a college degree	92 (44.4)	194 (49.1)	
College degree or greater	115 (55.6)	200 (50.6)	
Do not know	0	1 (0.3)	
Annual household income, *n* (%)			.006
<$50,000	84 (40.6)	210 (53.2)	
≥$50,000	114 (55.1)	165 (41.8)	
Do not know	4 (1.9)	3 (0.8)	
Prefer not to answer	5 (2.4)	17 (4.3)	

Note. HA = high adherence; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale; *SD* = standard deviation.
*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).
†Respondents could select multiple options.
‡Based on comparison of those self-identifying as white versus the sum of all who did not self-identify as white.

logistics (47.3% [187/395]), and beliefs (44.8% [177/395]) domains. Specific reasons for not taking medication as directed for ≥3 days in the past week in the LMA group were being unsure how to take the medicine, not having the money to pay for the medicine, not considering taking medicine a high priority in the daily routine, not having a way to get to the pharmacy/provider, and thinking the medicine was not needed anymore (Table 2). Compared with the HA group, a significantly greater percentage of respondents in the LMA group did not take their ADHD medication exactly as prescribed ≥25% of the time (13.9% [55/395] vs. 0.5% [1/207], $p < .05$) over the last 30 days, and a significantly lower percentage never missed taking their medication as prescribed (11.1% [44/395] vs. 75.8% [157/207], $p < .05$).

Medication Use and Health Characteristics

There were no statistically significant differences in the type of ADHD medications used between the LMA and HA groups. In the overall study population, 44.9% (270/602) of respondents used short-acting ADHD medications (LMA, 45.1% [178/395]; HA, 44.4% [92/207]), 40.7% (245/602) used long-acting ADHD medications (LMA, 39.5% [156/395]; HA, 43.0% [89/207]), and 14.5% (87/602) used both short-acting and long-acting medications (LMA, 15.4% [61/395]; HA, 12.6% [26/207]). Medication use for disorders other than ADHD was generally comparable between the LMA and HA groups (Table 3). The only statistically significant difference noted was that a greater percentage of the HA group

Table 2. Mean ± *SD* Number of Days Medication Was Missed Over the Past Week by Reason in the LMA Group.*†

Reason	LMA (n = 395)
Not sure how to take the medicine	4.50 ± 2.12
Did not have money to pay for the medicine	3.74 ± 2.63
Do not consider taking the medicine as a high priority in my daily routine	3.34 ± 2.42
Didn't have the medicine because I didn't have a way to get to the pharmacy/provider	3.17 ± 2.38
Don't think that I need the medicine anymore	3.04 ± 2.01
Don't think that the medicine is working for me	2.89 ± 2.01
Had side-effects from the medicine	2.63 ± 2.04
Didn't have the medicine because the pharmacy/provider was out of this medicine, I was out of refills, or the mail order did not arrive in time	2.47 ± 1.83
Was not comfortable taking it for personal reasons	2.46 ± 2.06
Had difficulty opening the container	2.38 ± 1.06
Have trouble managing all the medicines I have to take	2.34 ± 1.81
Was not comfortable taking it for social reasons	2.33 ± 2.00
Had difficulty swallowing the medicine	2.17 ± 1.95
Would have taken it but have difficulty remembering things in my daily life	2.14 ± 1.70
Sometimes skip the medicine to see if it is still needed	2.01 ± 1.58
Concerned about possible side-effects from the medicine	1.98 ± 1.57
Would have taken it but missed it because of busy schedule/change in routine	1.95 ± 1.48
Concerned about long-term effects from the medicine	1.91 ± 1.53
Would have taken it but simply missed it	1.85 ± 1.51

Note. LMA = low/medium adherence; *SD* = standard deviation.
*LMA group defined by Medication Adherence Reasons Scale (MAR-Scale) total scores ≥1.
†Respondents categorized as high adherence were not asked about the frequency of nonadherence for each of the individual 19 items of the MAR-Scale.

Table 3. Respondent Medication Use by Adherence Group.*

Medication type, *n* (%)	HA (n = 207)	LMA (n = 395)	*p* Value
Antidepressants	107 (51.7)	208 (52.7)	.821
Antianxiety	75 (36.2)	146 (37.0)	.860
Sleep aids	56 (27.1)	111 (28.1)	.785
Antihypertensives	55 (26.6)	66 (16.7)	.004
Other medications	38 (18.4)	51 (12.9)	.074
Antipsychotics	18 (8.7)	53 (13.4)	.088
None of the above	47 (22.7)	95 (24.1)	.712

Note. HA = high adherence; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale.
*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).

compared with the LMA group used antihypertensive medications (p = .004; Table 3).

The most frequently reported co-occurring illnesses were generalized anxiety disorder and major depressive disorder (Table 4). Significantly greater percentages of respondents in the HA group reported hypertension, connective tissue disease, and myocardial infarction, compared with the LMA group (all $p < .05$; Table 4).

ADHD Symptom Levels

Mean (95% CI) ADHD symptom levels, as measured by ASRS-v1.1 Symptom Checklist total scores, were significantly greater in the LMA group than the HA group (10.64 [10.17, 11.12] vs. 8.55 [7.86, 9.24]; $p < .001$).

Work Productivity and Activity Impairment

Based on unadjusted bivariate analyses, respondents in the LMA group had significantly greater mean (95% CI) percentages of absenteeism (10.62% [7.90%, 13.33%] vs. 4.55% [2.15%, 6.94%], p = .001), presenteeism (38.63% [34.99%, 42.26%] vs. 29.66% [24.63%, 34.69%], p = .005), overall work productivity loss (43.35% [39.48%, 47.21%] vs. 32.05% [26.75%, 37.34%], p = .001), and activity impairment (47.29% [44.19%, 50.40%] vs. 40.77% [36.51%, 45.04%], p = .015)

Table 4. Co-occurring Illnesses by Respondent Adherence Group.*

Co-occurring illness, *n* (%)	HA (*n* = 207)	LMA (*n* = 395)	*p* Value
Mental health			
Generalized anxiety disorder	73 (35.3)	161 (40.8)	.189
Major depressive disorder	65 (31.4)	126 (31.9)	.901
Bipolar disorder	35 (16.9)	75 (19.0)	.531
Posttraumatic stress disorder	26 (12.6)	70 (17.7)	.100
Borderline personality disorder	10 (4.8)	25 (6.3)	.456
Autism spectrum disorder	7 (3.4)	8 (2.0)	.311
Tics/Tourette syndrome	1 (0.5)	2 (0.5)	.969
Dementia	0	3 (0.8)	.209
Somatic			
Hypertension	47 (22.7)	60 (15.2)	.022
Diabetes			
With chronic complications	6 (2.9)	4 (1.0)	.085
Without chronic complications	13 (6.3)	19 (4.8)	.445
Chronic pulmonary disease	10 (4.8)	22 (5.6)	.701
Connective tissue disease	12 (5.8)	7 (1.8)	.007
Peptic ulcer disease	7 (3.4)	9 (2.3)	.424
Any tumor	4 (1.9)	10 (2.5)	.643
Congestive heart failure	3 (1.4)	6 (1.5)	.947
AIDS/HIV	3 (1.4)	4 (1.0)	.635
Liver disease			
Mild	4 (1.9)	2 (0.5)	.094
Moderate/severe	0	1 (0.3)	.469
Kidney disease (moderate/severe)	3 (1.4)	4 (1.0)	.635
Atrial fibrillation/DVT/stroke†	3 (1.4)	3 (0.8)	.418
Skin ulcers/cellulitis	1 (0.5)	5 (1.3)	.358
Cerebrovascular disease	2 (1.0)	2 (0.5)	.509
Myocardial infarction	3 (1.4)	0	.016
Hemiplegia	0	2 (0.5)	.305
Peripheral vascular disease	1 (0.5)	1 (0.3)	.641
Leukemia	1 (0.5)	0	.167
Lymphoma	0	1 (0.3)	.469
Unclassified			
Other co-occurring illnesses‡	33 (15.9)	58 (14.7)	.682
None of the above	55 (26.6)	115 (29.1)	.510
"I don't know"	2 (1.0)	5 (1.3)	.745

Note. AIDS = acquired immune deficiency syndrome; DVT = deep vein thrombosis; HA = high adherence; HIV = human immunodeficiency virus; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale.
*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).
†Based on a positive response to use of warfarin as a step to prevent DVT or stroke, plus Coumadin/warfarin for atrial fibrillation or DVT.
‡Respondents could select "other" if they had a co-occurring illness that was not listed in the survey.

than the HA group (Figure 1A). After adjusting for covariates, only absenteeism remained significantly greater in the LMA versus the HA group ($p < .001$; Figure 1B). The interactions between adherence and ADHD symptom level on absenteeism, presenteeism, overall work productivity, and activity impairment were not statistically significant (Table 5).

Indirect Costs Related to Work Productivity and Activity Impairment

Based on unadjusted bivariate analyses, respondents in the LMA group had significantly greater mean (95% CI) absenteeism-related indirect costs ($3669.33 [$2396.50,

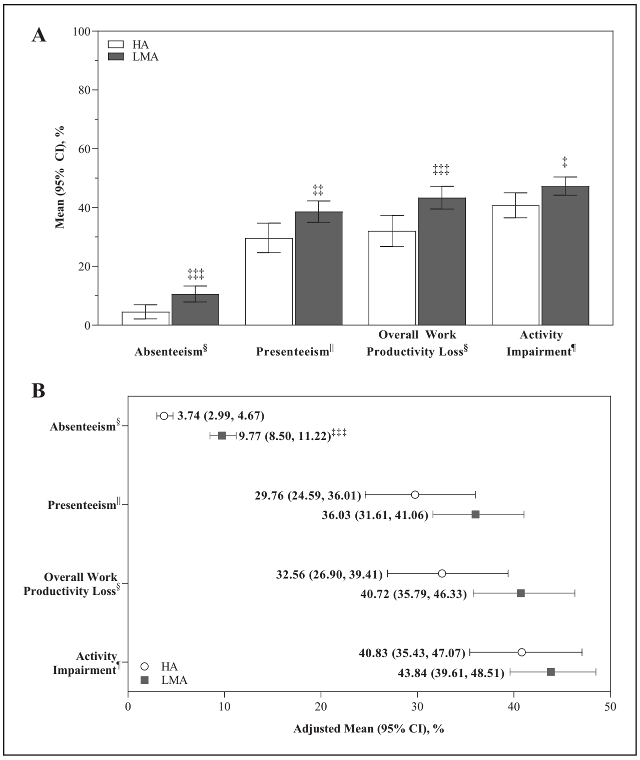

Figure 1. Work productivity and activity impairment by adherence group:* unadjusted bivariate analyses (A) and adjusted multivariable analyses† (B).

Note. ASRS-v1.1 = Adult ADHD Self-Report Scale, version 1.1; CI = confidence interval; HA = high adherence; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale; *SD* = standard deviation.

*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).

†Included age, ASRS-v1.1 Symptom Checklist scores (as continuous variable), comorbidity burden based on Charlson Comorbidity Index scores, medication use, and co-occurring illness as covariates.

§HA (*n* = 119), LMA (*n* = 247).

||HA (*n* = 118), LMA (*n* = 240).

¶HA (*n* = 207), LMA (*n* = 395).

‡$p < .05$. ‡‡$p \leq .01$. ‡‡‡$p \leq .001$ (LMA vs. HA).

$4943.16] vs. $1359.42 [$647.80, $2071.04], $p = .002$) and total indirect costs ($15,401.40 [$13,421.73, 17,381.07] vs. $10,790.17 [$8705.31, $12,875.02], $p = .002$; Figure 2A) than the HA group. Indirect cost differences between adherence groups remained statistically significant after adjusting for covariates for absenteeism-related costs ($p < .001$) and total indirect costs ($p = .005$) (Figure 2B). Examination of the interaction of ADHD symptom level and adherence on indirect costs indicated that the only statistically significant interaction was observed for absenteeism-related indirect costs ($p < .001$; Table 5). The greatest absenteeism-related costs were observed among respondents in the LMA group with low ADHD symptom levels, and the lowest costs were observed among those in the HA group with low ADHD symptom levels.

Discussion

The key findings of this study are that, in adults who self-reported having an ADHD diagnosis from a healthcare provider, lower adherence to oral psychostimulant therapy was associated with a greater level of absenteeism and greater absenteeism-related and total indirect costs after adjusting for potential confounds. The LMA group also had greater ADHD symptom levels, as estimated by ASRS-v1.1 Symptom Checklist scores. To the best of our knowledge, this is the first demonstration of the relationship between adherence to oral psychostimulant therapy and work productivity and related indirect costs in a US population of adults diagnosed with ADHD.

These observations support previous studies that have reported that adults diagnosed with ADHD report high levels of impaired work productivity and incur high indirect costs (Birnbaum et al., 2005; Doshi et al., 2012; Joseph et al., 2019; Murphy & Barkley, 2007). In a study of adults in the United Kingdom diagnosed with ADHD, 15.7% of study participants missed work because of health problems, and 40.6% were impaired while working because of health problems (Joseph et al., 2019). Similarly, US adults diagnosed with ADHD have been reported to hold jobs for shorter periods, to have been fired or dismissed more frequently, and to have had more frequent interpersonal problems in the workplace than adults in a general community sample (Murphy & Barkley, 2007). In a systematic review of the costs of ADHD in the United States, the annual costs attributed to adult ADHD were estimated to range from $105 to $194 billion, with work productivity and income losses accounting for $85 to $138 billion of these costs (Doshi et al., 2012). Taken together, these findings emphasize the negative impact of adult ADHD on work productivity and related indirect costs. Importantly, the current findings were obtained in adults diagnosed with ADHD who were currently prescribed oral psychostimulant therapy. The relatively high levels of presenteeism (29.66%), overall work productivity loss (32.05%), and activity impairment (40.77%) in the HA group suggest the treatment regimens of study respondents may not have been optimal. This possibility is further supported by the overall ADHD symptom level in the HA group (mean ASRS-v1.1 total score of 8.84), which is substantially higher than the mean ASRS-v1.1 score of 2.0 observed in a normative US adult population (Adler et al., 2019).

To the best of our knowledge, this is the first study to demonstrate that higher levels of adherence to oral psychostimulant therapy are associated with lower levels of absenteeism and lower absenteeism-related and total indirect costs. However, these findings are not unexpected. In a randomized, placebo-controlled study of OROS-MPH, significantly greater reductions in Endicott Work Productivity

Table 5. Relationship between Adherence and Work Productivity Loss, Activity Impairment, and Related Indirect Costs, Moderated by ADHD Symptom Level and Adjusted for Covariates,*,† Adjusted Means (95% CIs).

	High adherence		Low/medium adherence		
	Low ADHD symptoms	High ADHD symptoms	Low ADHD symptoms	High ADHD symptoms	*p* Value‡
WPAI-GH outcomes, %					
Absenteeism ($n = 366$)	3.72 (2.70, 5.14)	3.82 (2.81, 5.20)	10.68 (8.57, 13.30)	9.13 (7.63, 10.92)	.495
Presenteeism ($n = 358$)	22.67 (17.39, 29.57)	37.02 (28.23, 48.53)	31.16 (25.35, 38.29)	41.32 (34.75, 49.14)	.376
Overall work productivity impairment ($n = 366$)	26.17 (20.07, 34.11)	38.56 (29.44, 50.51)	35.85 (29.26, 43.93)	45.73 (38.61, 54.16)	.534
Activity impairment ($n = 602$)	32.22 (26.60, 39.02)	48.84 (39.73, 60.02)	36.62 (31.17, 43.01)	51.55 (45.24, 58.74)	.678
Indirect costs, $					
Absenteeism-related ($n = 391$)	541.15 (404.16, 724.57)	1658.58 (1243.46, 2212.29)	4001.97 (3268.54, 4899.97)	2638.69 (2225.33, 3128.82)	<.001
Presenteeism-related ($n = 390$)	6882.28 (5386.14, 8794.00)	12,107.59 (9309.62, 15,746.47)	9268.29 (7635.65, 11,250.02)	13,284.41 (11,297.91, 15,620.18)	.356
Total ($n = 391$)	7807.53 (6115.24, 9968.12)	13,576.24 (10,462.95, 17,615.90)	13,031.31 (10,737.75, 15,814.78)	16,203.04 (13,778.02, 19,054.87)	.126

Note. ASRS-v1.1 = Adult ADHD Self-Report Scale, version 1.1; HA = high adherence; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale; WPAI-GH = Work Productivity and Activity Impairment–General Health.

*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).

†Multivariable models included age, comorbidity burden, medication use, and co-occurring illnesses as covariates; ASRS-v1.1 Symptom Checklist scores were included as a factor/grouping variable (low ADHD symptoms [<median ASRS-v1.1 Symptom Checklist scores] vs. high ADHD symptoms [>median ASRS-v1.1 Symptom Checklist scores]) and in the interaction term with adherence.

‡Based on the regression coefficient for the interaction between adherence and ADHD symptom level.

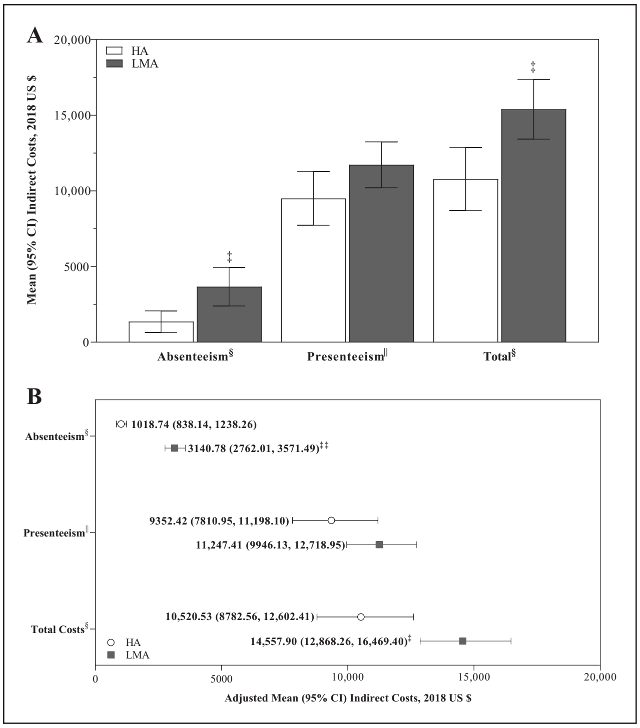

Figure 2. Indirect costs by adherence group:* unadjusted bivariate analyses (A) and adjusted multivariable analyses† (B).
Note. ASRS-v1.1 = Adult ADHD Self-Report Scale, version 1.1; CI = confidence interval; HA = high adherence; LMA = low/medium adherence; MAR-Scale = Medication Adherence Reasons Scale.
*HA (MAR-Scale total score = 0); LMA (MAR-Scale total score ≥1).
†Included age, ASRS-v1.1 Symptom Checklist scores (as continuous variable), comorbidity burden based on Charlson Comorbidity Index scores, medication use, and co-occurring illness as covariates.
§HA (n = 128), LMA (n = 263).
||HA (n = 127), LMA (n = 263).
‡$p \leq .01$. ‡‡$p \leq .001$ (LMA vs. HA).

Scale total scores (i.e., greater improvements in work productivity and efficiency) were reported with OROS-MPH than placebo after 6 weeks of treatment (Goodman et al., 2017). Furthermore, a post hoc analysis of a randomized, double-blind, placebo-controlled study reported that improvements in ADHD symptoms were greater in participants who exhibited greater adherence to OROS-MPH treatment (Kooij et al., 2013). By extension, greater adherence to other oral psychostimulant therapies, such as amphetamine-based formulations, would also be expected to be associated with greater workplace productivity and a lower ADHD symptom level.

A statistically significant interaction between ADHD symptom level and adherence on absenteeism-related indirect costs was observed. As might be expected, poor adherence was associated with higher absenteeism-related indirect costs regardless of symptom level. Yet, in contrast to expectations, this effect was much greater among those with low ADHD symptom levels. The explanation for this finding is not clear. However, when considering the totality of the results, adherence appears most beneficial (and nonadherence most harmful) in individuals with lower ADHD symptom levels.

In this study, the greatest percentage of patients in the LMA group reported reasons for nonadherence associated with the forgetfulness domain. Although these findings are limited to some degree by the options provided to respondents as potential reasons for nonadherence, the MAR-Scale was designed to reflect a comprehensive set of reasons for nonadherence. Furthermore, the results related to forgetfulness align with the nature of ADHD symptoms, especially with the inattentive component of ADHD. For example, diagnostic guidelines for inattention in ADHD based on the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* specifically include a statement related to forgetfulness in relation to daily activities (American Psychiatric Association, 2013).

The most frequently reported individual reasons for nonadherence in the LMA group were being unsure how to take the medicine, not having the money to pay for the medicine, not considering taking the medicine a high priority in the daily routine, not having a way to get to the pharmacy/provider, and thinking the medicine was not needed anymore. In a review of 41 published studies (Frank et al., 2015), the reasons reported most frequently for stopping medication in patients with ADHD included own wish/remission/don't need, withdrawal of consent, adverse effects, and suboptimal effect. Interestingly, in both that review and the current study, thinking medicine was no longer needed was among the most frequently reported reasons for not taking medication. Furthermore, reasons related to efficacy (thought the medicine was not working, suboptimal effect) and tolerability (had side effects, adverse effects) were also observed in both the current study and the review by Frank et al. (2015). Seeming discrepancies between this study and the review by Frank et al. (2015) are likely related to study design. The analysis by Frank et al. (2015) was conducted by focusing on why participants withdrew from clinical studies or terminated treatment. As such, some of the reasons specified in the MAR-Scale that were frequently reported in the current study (i.e., unsure how to take the medicine, not having the money to pay for the medicine, not considering taking medicine a high priority in the daily routine, not having a way to get to the pharmacy/provider) were not relevant to the study by Frank et al. (2015).

The co-occurring medical and psychiatric illnesses reported in this study are consistent with other published reports (Chen et al., 2018; Katzman et al., 2017; Kooij et al., 2012; Mao & Findling, 2014). In the current study, anxiety and depression were the most frequently reported psychiatric illnesses, and hypertension and diabetes were the most frequently reported medical comorbidities. Although there were no differences in psychiatric disorders between adherence groups, some medical comorbidities occurred in significantly greater percentages of respondents in the HA group (hypertension, connective tissue disease, and myocardial infarction) than the LMA group. Reasons for these differences are unclear, in part because the medical histories of the respondents are not known. However, it is worth noting that mean age was significantly greater in the HA than the LMA group. This difference could have contributed to the greater frequency of co-occurring medical illnesses in the HA group. Medication use was generally similar across treatment groups, but a greater percentage of the HA group used antihypertensives. This observation is consistent with higher reporting of hypertension in this group.

These data should be considered in light of several limitations. First, respondents were recruited based on membership in an online market research panel. Therefore, the results may not fully generalize to the adult ADHD population because of potential selection bias. Second, all study data were self-reported. As such, certain study variables (i.e., ADHD diagnosis, medication use and adherence, co-occurring psychiatric and medical illnesses) were not validated in a clinical setting. Although the inability to independently verify respondents' self-reported ADHD diagnosis is a limitation of the current study, using a stimulant for the treatment of ADHD for the last 3 months corroborates an ADHD diagnosis by an HCP because a prescription from an HCP is needed to obtain stimulant medication. Third, detailed information on the ADHD treatment regimens (i.e., the doses used and their frequency of use) was not available, which precluded an assessment of how treatment-related factors might have contributed to the observed differences in ADHD symptoms between adherence groups. Fourth, the demographic analysis only included two annual income categories (<\$50,000 vs. ≥\$50,000). As there could be substantial variability in the ≥\$50,000 grouping, including additional income categories would have allowed for a more detailed analysis of differences in annual income between adherence groups. Fifth, it is unknown how reasons that accounted for the most nonadherent days, such as not knowing how to take the medication or being unable to pay for medication, may have influenced the association of nonadherence with impaired work productivity. Finally, including ASRS-v1.1 Symptom Checklist scores as a covariate in the multivariable analyses may have resulted in conservative estimates of the impact of adherence on work productivity loss, activity impairment, and indirect costs because poor adherence may also be an outcome of ADHD symptoms. In other words, the relationship between adherence and ADHD symptom levels may be bidirectional, such that the increased ADHD symptom levels (e.g., inattentiveness) associated with poor adherence could further exacerbate nonadherence due to their association with forgetfulness.

Conclusion

After adjusting for potential confounders, in adults who self-reported receiving an ADHD diagnosis from a healthcare provider and who were currently using oral psychostimulant therapy, lower medication adherence was associated with greater levels of absenteeism and absenteeism-related and total indirect costs. Although lower medication adherence was also associated with higher ADHD symptom levels, as measured by the ASRS-v1.1 Symptom Checklist, the overall level of ADHD symptoms in the HA group was substantially higher than what has been reported in a normative US adult population (Adler et al., 2019). Further research is warranted to better understand the treatment approaches in adults diagnosed with ADHD that may more effectively optimize treatment and improve adherence, thereby minimizing the effect of ADHD on workplace productivity and its subsequent costs.

Previous Presentations

Portions of these data have been presented at the 2019 meetings of the American Psychiatric Association (May 18–22; San Francisco, CA, USA), US Psychiatric and Mental Health Congress (October 3–6, 2019, San Diego, CA, USA), and International Society for Pharmacoeconomics and Outcomes Research European Congress (November 2–6; Copenhagen, Denmark).

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Declaration of Conflicting Interests

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: William Spalding and Sepehr Farahbakhshian are employees of Shire, a member of the Takeda group of companies, and hold Takeda stock. Martine C. Maculaitis and Eugenia Y. Peck are employees of Kantar, which was funded by Shire, a member of the Takeda group of companies, to conduct this study. Amir Goren was an employee of Kantar at the time this research was conducted, which was funded by Shire, a member of the Takeda group of companies, to conduct this study; he is currently employed by Geisinger (Danville, PA, USA).

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