VALUE IN HEALTH 17 (2014) 661–668

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/jval

ORIGINAL ARTICLES
Economic Evaluation

Impact of Mental Health Comorbidities on Health Care Utilization and Expenditure in a Large US Managed Care Adult Population with ADHD

Aniket A. Kawatkar, PhD[1,], Tara K. Knight, PhD[2], Robert A. Moss, MD[3], Vanja Sikirica, PharmD[4], Li-Hao Chu, MPH[1], Paul Hodgkins, PhD[4], M. Haim Erder, PhD[4], Michael B. Nichol, PhD[2]*

[1]*Kaiser Permanente Southern California, Pasadena, CA, USA;* [2]*Leonard D. Schaeffer Center for Health Policy and Economics, University of Southern California, Los Angeles, CA, USA;* [3]*Southern California Permanente Medical Group, Woodland Hills, CA;* [4]*Shire, Development LLC Wayne, PA, USA*

ABSTRACT

Objective: To estimate the health resource use (HRU) and expenditure of adult patients with attention deficit/hyperactivity disorder (ADHD) subsequently diagnosed with one or more mental health (MH) comorbidities. **Methods:** Using Kaiser Permanente Southern California electronic medical records (January 1, 2006, to December 31, 2009), we identified adults with *at least one* ADHD diagnosis and *at least two* subsequent prescriptions fills for ADHD medication. The date of first MH comorbidity diagnosis after the index ADHD diagnosis was defined as the *index transition date*. Continuous eligibility 12 months before and after the index transition date was required. For patients with multiple transitions (≥2), the post-transition period reflected the 12 months after the second transition. HRU for all-cause inpatient, outpatient, emergency department, behavioral therapy, overall prescription fill counts, and ADHD-specific prescription fill counts and mean patient expenditure (2010 US $) were estimated. Generalized estimating equations were used to evaluate differences in HRU and expenditure between the pre- and post-transition periods, respectively. **Results:** Of the 3809 patients with ADHD identified, 989 (26%) had at least one transition (n = 357 single and n = 632 multiple). From the pre- to the post-transition period, for single transition cohort, all HRU increased significantly except for behavioral therapy. In the multiple transition cohort, all HRU increased significantly. Total expenditure increased by mean ± SE of $1822 ± $306 and $4432 ± $301 (both $P < 0.0001$) in the single and multiple transition cohorts, respectively. **Conclusions:** Twenty-six percent of patients with ADHD transitioned to MH comorbid diagnoses. Increased HRU and expenditure were associated with MH transitions. Identifying of patients with ADHD at risk for MH comorbidities may help to improve their outcomes.

Keywords: ADHD, comorbidity, expenditure, mental health, utilization.

Introduction

Attention deficit/hyperactivity disorder (ADHD) is generally considered a childhood condition, although it may clearly persist into adulthood. Persistence rates into adulthood have been reported to be as high as 50% to 60% of childhood-diagnosed cases [1,2]. In addition, although approximately half of ADHD cases are diagnosed before the age of 13 years, an estimated 35% are not diagnosed until after age 18 years [3]. Even with this knowledge, ADHD in adults has only recently become a focus of the medical community [4,5]. The National Comorbidity Survey Replication tracked the prevalence of attention deficit/hyperactivity symptoms and found that an estimated 4.4% of adults aged 18 to 44 years experienced symptoms and some associated disability [6], raising awareness about the longevity of ADHD and the need for more research in the area of ADHD in adults. Although there is increasing awareness of the significant psychosocial outcomes associated with ADHD in adults, only a few studies have evaluated ADHD expenditure in adults and its economic burden on the health care system [2–7]. ADHD contributes to rising costs for payers, employers, and patients in both direct and indirect costs [8]. Of the limited research available, studies demonstrate significantly higher annual medical costs among adults with ADHD (ranging from $4929 to $5651, in 2005 US $) than among matched controls (ranging from $1473 to $2771, in 2005 US $) when controlling for comorbidities [8,9]. Hodgkins et al. [10] have reported that annual productivity losses of $4403 (2006 US $) (including absences, short-term disability leave, and

* *Address correspondence to:* Aniket A. Kawatkar, Kaiser Permanente Southern California, 100 S. Los Robles, 2nd Floor, Pasadena, CA 91101.

E-mail: aniket.a.kawatkar@kp.org.

1098-3015$36.00 – see front matter

http://dx.doi.org/10.1016/j.jval.2014.06.002

worker's compensation claims) were nearly as high as direct health care costs of $4306 (including inpatient, emergency department visit, outpatient visit, other outpatient services, and outpatient prescriptions expenditure) in adult patients with ADHD [10].

Independent of ADHD, psychiatric comorbidities may have an even more profound effect on costs, with annual estimates totaling $58.3 billion for drug abuse, $85.8 billion for alcohol abuse, and $43.7 billion for depression [11,12]. A study estimating treatment costs for children with ADHD plus comorbidities versus ADHD alone found that comorbid psychiatric disorders substantially increased the costs of treatment [13]. Indirect costs of ADHD also contribute significantly to the burden of disease, particularly for patients and employers [9,14]. The symptoms of ADHD can lead to decreased academic and workplace performance, increased absenteeism, short-term disability, worker's compensation claims, and subsequent loss of income or even employment [15,16].

Currently, little is known about the health care resource utilization and cost impact of adult patients with ADHD subsequently diagnosed with one or more comorbid mental health (MH) conditions. Because ADHD in adults often coexists with other comorbidities [6], including conduct disorder, obsessive compulsive disorder, and depression, diagnosis and treatment are often compromised. These MH comorbid conditions may potentially amplify the use of health care resources and raise the risk of adverse long-term outcomes for patients, including violence and substance abuse [7,8]. Before exploring cost-effective approaches that can reduce the effect of future MH comorbidities in adult patients with ADHD, we first need to understand whether the associations of mental disorders with subsequent expenditure are strong enough and their magnitude justifies the introduction of such interventions. The objective of this study was to estimate the incremental expenditure in adult patients with ADHD who were subsequently diagnosed with predefined comorbid MH conditions.

Methods

Study Population

The study population included members from the Kaiser Permanente Southern California (KPSC) managed care population who were diagnosed and treated for ADHD. The KPSC is an integrated health care system that provides comprehensive health services to approximately 3.5 million residents of Southern California. The population served by the KPSC is socioeconomically diverse and broadly representative of the racial/ethnic groups living in Southern California [17]. Members enroll through the Kaiser Foundation Health Plan for prepaid health care insurance, including pharmaceutical benefits. The KPSC region includes 14 hospitals and more than 198 medical offices by a partnership of more than 5700 physicians who comprise the entire range of medical specialists.

Data Source

The primary data source was KPSC electronic medical records, which contain detailed accounts of interactions of members with the health care system. Data on resource utilization were extracted from research data sets created from the electronic medical records that included comprehensive information on inpatient and outpatient utilization, emergency department visits, diagnoses, procedures, vital signs, laboratory, and pharmacy. Information from external medical claims was also extracted to include services and care provided outside of the KPSC. Patients' demographic and health plan enrollment information was obtained from KPSC membership databases and augmented by mapping geocoded income and education-level information by census tract.

Study Design

This was a retrospective cohort study among members of the KPSC health plan identified as those diagnosed and treated for ADHD between January 1, 2006, and December 31, 2009. Health care and prescription utilization data were obtained from KPSC electronic medical records and external claims, whereas direct medical expenditure data were obtained by weighting the utilization counts with nationally representative reimbursement scales [18]. The study was approved by the KPSC Institutional Review Board.

Patient Inclusion

Using KPSC electronic medical records from January 1, 2005, to December 31, 2009, we identified adult patients (aged 18–100 years) with *at least one* ADHD diagnosis (using *International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] codes 314.0, 314.00, 314.01, and 314.9) and *at least two* dispensing records for Food and Drug Administration–approved ADHD medications prescribed after the diagnosis. The requirement of active pharmacological treatment for ADHD was imposed to identify the subset of adult patients with ADHD who were not only diagnosed with ADHD but also treated with a pharmacologic agent as confirmatory. The first medical record satisfying the diagnosis and prescription criteria for ADHD was identified as the index ADHD diagnosis (Fig. 1). Continuous health plan eligibility was required for the entire 4-year duration of the study.

Exclusions

To avoid the inclusion of patients using stimulants for non-ADHD conditions, individuals with evidence of the following conditions within the 12-month preindex period were excluded from the analysis: narcolepsy (*ICD-9-CM* code 347.X), poststroke (*ICD-9-CM* codes 430.xx, 431.xx, 432.xx, 433.01, 433.11, 433.21, 433.31, 433.81, 433.91, 434.xx, and 436.xx), and early dementia (*ICD-9-CM* codes 290.xx, 294.1x, 294.8x, 331.0, 331.1x-9x, and 797.xx). If a patient with ADHD had any MH comorbidity diagnosis in the 12-month period before the ADHD index diagnosis, they were excluded so that the cohort represented patients with ADHD with subsequent (predefined) MH comorbidity, as opposed to patients with MH conditions who may develop ADHD as comorbidity. Last, patients who did not have any transition during the follow-up period were also excluded.

MH Transition

MH transition was defined as the occurrence of one or more predefined MH condition diagnosed after the index ADHD diagnosis. The date of the first MH comorbidity diagnosis code (oppositional defiant disorder, generalized anxiety disorder, conduct disorder, major depressive disorder, bipolar disorder, antisocial personality disorder, social phobia disorder, or substance abuse disorder) was defined as the *index transition date* (ITD) (Fig. 1). Depending on the number of additional predefined MH conditions experienced during follow-up, two mutually exclusive cohorts were created. Patients with ADHD diagnosed with only one predefined MH condition were categorized in the single transition cohort, whereas those experiencing two or more different MH conditions were categorized in the multiple transition cohort. The pretransition period was defined as the 12 months before ITD, whereas the posttransition period included the 12 months after the ITD if a patient had a single MH comorbidity. For patients with two or more different transitions, the

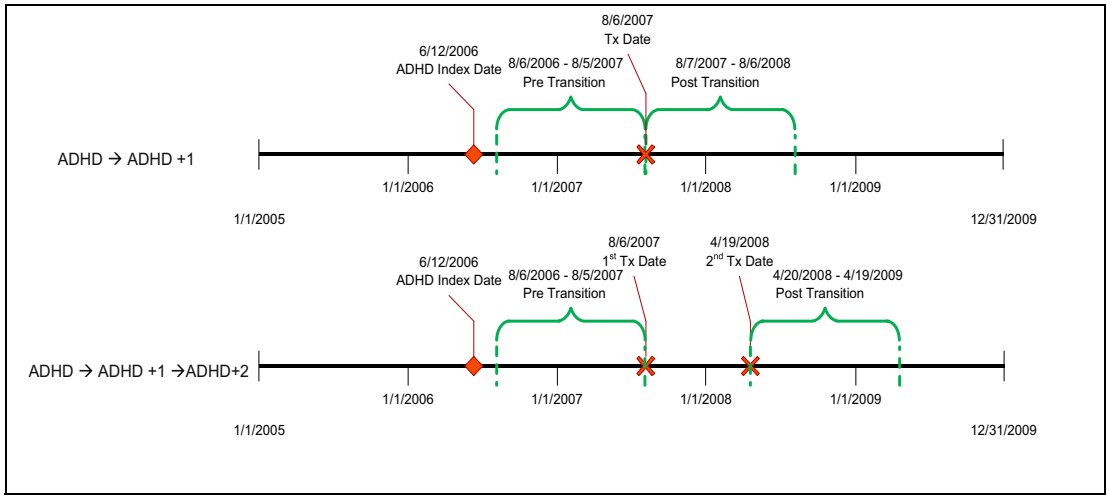

Fig. 1 – Illustration of mental health transitions in patients with ADHD. ADHD, attention deficit/hyperactivity disorder; ADHD +1, patients with ADHD with single mental health transition after the index date; ADHD +2, patients with ADHD with multiple mental health transitions after the index date; Tx date, transition index date.

post-transition period reflected the 12 months after the addition of the second comorbidity diagnosis. The single MH comorbidity cohort and the cohort experiencing two or more MH conditions were mutually exclusive. The time period until the MH transition occurred could vary. In addition, patients were required to have at least 1-year post-transition follow-up data before the end of the study so that utilization and expenditures for the entire 1-year post-transition period were accounted. Hence, the last transition date for any patient was December 31, 2008, or earlier.

Outcomes

Utilization

All-cause health care resource utilization and expenditure were estimated in the pre- and post-transition periods to evaluate change after a transition to MH comorbidity. All-cause health care resource utilization included counts of outpatient visits, behavior therapy visits, emergency department visits, inpatient visits, length of inpatient stay (in days), and pharmacy fills (ADHD-specific and all-cause prescription fills). The duration of both pre- and post-transition periods was 12 months.

Expenditure

For enhanced generalizability, costs were assigned to health care services by using the Medicare Resource Based Relative Value Scale multipliers for medical utilization [18], average wholesale price for prescription utilization, and per diem amounts for inpatient stays. Resource-based relative value multipliers are based on Current Procedural Terminology codes and are published under the Physician Fee Schedule in the *Federal Register* [19]. Drug costs were estimated by matching average wholesale drug prices to pharmacy National Drug Codes. Inpatient hospitalizations included one or more days stay from KPSC's hospitalization data and further classified as stays with surgery and without surgery. The median per day hospitalization expenditure was calculated from the expenditure data (paid cost) reported in the 2007 Medical Expenditure Panel Survey inpatient encounter data for those who had surgery during an inpatient stay ($3402.25 per day) and for those who did not have surgery ($1814.86 per day) during an inpatient stay. An aggregate total expenditure variable was created as summation of all-cause expenditure associated with outpatient visits, emergency department visits, inpatient visits, and pharmacy utilization. All expenditures were inflated to the 2010 US $ using the medical component of the consumer price index [20].

Statistical Analysis

Descriptive statistics including mean, and standard errors for continuous variables and frequencies and percentages for categorical variables, were calculated. Negative binomial models were used to evaluate differences in utilization counts, whereas generalized linear models with log-link function and gamma distribution were used to compare expenditure differences during the pre- and post-transition periods. The study design compared the incremental difference between the pre- and post-transition period for the same patient. This paired matching mitigated time invariant sources of selection bias. Essentially, each subject served as his or her own control, allowing us to identify unbiased incremental differences in expenditures and utilization. To address the effects of possible correlation caused by nonindependent samples, generalized estimating equations were used to solve outcome models. The generalized estimating equation uses a working correlation matrix to correct the bias in standard errors caused by correlated observations on same subjects. All data management and analyses were conducted using the Statistical Analysis System (SAS, version 9.1).

Results

During the study period from 2006 to 2009, a total of 6014 incident adult patients with ADHD were identified. Of these, 3809 adult patients with ADHD met the eligibility criteria and 989 (26%) had at least one transition to a subsequent MH condition after ADHD diagnosis within our study time frame. Among the 989 patients, 357 had a single transition and 632 had multiple transitions during follow-up. Table 1 provides descriptive statistics of patients' demographic characteristics for the transition cohorts. The mean age was similar for those with a single transition (34.5 ± 14.4 years) and for those with multiple transitions (34.7 ± 14.4 years). The single transition cohort was comprised predominantly of men (60.8%); however, there were slightly more women (50.6%) in the multiple transition cohort. Differences in racial composition were evident where the group with multiple MH transitions had a slightly higher number of Caucasians (57.3%)

Table 1 – Patient characteristics by transition cohort.

Characteristic	Total with transitions	Single transition	Multiple transitions
Total	989 (100.0)	357 (100.0)	632 (100.0)
Age (y)			
18–21	298 (30.1)	114 (31.9)	184 (29.1)
22–24	82 (8.3)	36 (10.1)	46 (7.3)
25–34	143 (14.5)	41 (11.5)	102 (16.1)
35–44	161 (16.3)	58 (16.3)	103 (16.3)
45–54	203 (20.5)	76 (21.3)	127 (20.1)
55–64	89 (9.0)	27 (7.6)	62 (9.8)
65+	13 (1.3)	5 (1.4)	8 (1.3)
Sex			
Female	460 (46.5)	140 (39.2)	320 (50.6)
Male	529 (53.5)	217 (60.8)	312 (49.4)
Race			
White	535 (54.1)	173 (48.5)	362 (57.3)
Hispanic	311 (31.5)	127 (35.6)	184 (29.1)
Black	31 (3.1)	15 (4.2)	16 (2.5)
Asian/Pacific Islander	24 (2.4)	9 (2.5)	15 (2.4)
Others	45 (4.5)	16 (4.5)	29 (4.6)
Unknown	43 (4.4)	17 (4.8)	26 (4.1)
Insurance type			
Employer paid	837 (84.6)	307 (86.0)	530 (83.9)
Government paid*	45 (4.6)	16 (4.5)	29 (4.6)
Other	107 (10.8)	34 (9.5)	73 (11.6)
Income†			
0–24,999	15 (1.5)	9 (2.5)	6 (1.0)
25,000–49,999	166 (16.8)	59 (16.5)	107 (16.9)
50,000–74,999	312 (31.6)	105 (29.4)	207 (32.8)
75,000–99,999	238 (24.1)	79 (22.1)	159 (25.2)
100,000 and up	258 (26.1)	105 (29.4)	153 (24.2)
Charlson comorbidity index			
0	839 (84.8)	302 (84.6)	537 (85.0)
1	114 (11.5)	45 (12.6)	69 (10.9)
≥2	36 (3.6)	10 (2.8)	26 (4.1)
Mental health conditions			
Oppositional defiant disorder	6 (0.6)	3 (0.8)	3 (5.1)
Conduct disorder	4 (0.4)	2 (0.6)	2 (0.3)
Antisocial personality disorder	2 (0.2)	0 (0)	2 (0.3)
Social phobia	42 (4.6)	4 (1.1)	38 (6)
Bipolar disorder	60 (6.1)	10 (2.8)	50 (7.9)
Major depressive disorder	475 (48.0)	114 (31.9)	361 (57.1)
General anxiety disorder	513 (51.9)	126 (35.3)	387 (61.2)
Substance abuse disorder	336 (34.0)	98 (27.5)	238 (37.7)

Note. Values are n (%).

* Government-paid insurance includes Medicare, Medicaid, or both Medicare/Medicaid.

† Income refers to annual household income (US $) in the census tract where the subject resided.

and a lower number of Hispanics (29.1%) as compared with the single transition group (Caucasians, 48.5%; Hispanics, 35.6%). There were no marked differences between insurance type, income, or the number of Charlson comorbidities [21,22] between the single and multiple transition cohorts.

Pre-Post Transition Changes for Patients with a Single Transition

Among patients with a single transition, the mean number of annual visits increased significantly from the pre- to the post-transition period for most of the utilization types with the exception of behavioral therapy and inpatient length of stay (Table 2). Although behavioral therapy visits (mean ± standard error) decreased from 2.15 ± 0.38 to 0.79 ± 0.17 ($P = 0.0006$), the length of stay for inpatient visits did not change significantly (1.05 ±0.45 to 2.07 ± 0.37 ; $P = 0.18$).

Similar trends were observed for all-cause health care expenditures, again with the exception of behavioral therapy visits. Average outpatient expenditure did not change significantly from the pre-transition period ($1006 ± $53) to the post-transition period ($1147 ± $69) ($P = 0.08$). Emergency department expenditure ($142 ± $17 to $254 ± $22), inpatient expenditure ($1900 ± $814 to $3757 ± $668), all-cause prescription expenditure ($2928 ± $255 to $4345 ± $381), and ADHD-specific prescription expenditure ($881 ± $58 to $1057 ± $64) increased significantly (all $P < 0.05$) (Table 3). Behavioral therapy expenditure decreased significantly from $163 ± $29 to $57 ± $13 ($P < 0.0001$). Overall total expenditure ($4177 ± $298 to $5981 ± $436) increased by $1822 ± $306 and was statistically significant ($P < 0.0001$) (Table 3).

Table 2 – All-cause health care utilization pre- and post-transition (single transition).

Resource utilization	N	Mean ± SE			P* for post-pre difference
		Pretransition	Post-Transition	Post-pre difference	
Outpatient visits	357	8.21 ± 0.42	9.28 ± 0.54	1.07 ± 0.54	0.0451
Emergency department visits	121	0.57 ± 0.07	1.01 ± 0.08	0.45 ± 0.13	0.0003
Behavioral therapy visits	52	2.15 ± 0.38	0.79 ± 0.17	−1.48 ± 0.43	0.0006
Inpatient visits	43	0.44 ± 0.11	0.91 ± 0.13	0.48 ± 0.23	0.032
Length of stay	43	1.05 ± 0.45	2.07 ± 0.37	1.06 ± 0.79	0.1793
ADHD medications	321	2.38 ± 0.12	2.85 ± 0.14	0.47 ± 0.16	0.0042
All medications	353	10.79 ± 0.62	12.28 ± 0.61	1.49 ± 0.40	0.0002

ADHD, attention deficit/hyperactivity disorder; SE, standard error.
* P value for difference between pre- and post-transition utilization counts assuming negative binomial family distribution and log link in a generalized linear model.

Pre-Post Transition Changes for Patients with Multiple Transitions

Among patients with multiple transitions (where the *post-transition period* was defined as the period after the diagnosis of a different second MH condition), the mean number of visits also increased significantly from the pre- to the post-transition period within all utilization categories including behavioral therapy (all $P < 0.05$) (Table 4). The magnitude of increase was quite large in case of outpatient visits (64% increase), all-cause prescription utilization (46% increase), and length of hospital stay (nearly five times higher) from the pre- to the post-transition period.

This higher utilization resulted in a significantly higher expenditure in all categories of utilization including behavioral therapy. Average outpatient expenditure increased significantly from $1059 ± $44 in the pretransition period to $1778 ± $73 post-transition ($P < 0.001$). Similarly, emergency department expenditure ($191 ± $15 to $306 ± $23), inpatient expenditure ($1367 ± $336 to $8058 ± $1511), all-cause prescription expenditure ($2750 ± $174 to $5348 ± $257), and ADHD-specific prescription expenditure ($762 ± $48 to $1224 ± $59) increased significantly (all $P < 0.05$) (Table 5). Total expenditure ($4061 ± $196 to $8313 ± $397) increased by $4432 ± $301 and was statistically significant ($P < 0.0001$).

Discussion

The objective of this study was to estimate the incremental direct medical expenditure in adult patients with ADHD who were subsequently diagnosed with comorbid MH conditions. Of the 3809 adult patients with ADHD identified in this study, 989 (26%) were subsequently diagnosed with at least one MH comorbidity, with the large majority (64%) among these 989 patients having two or more MH transitions. In this cohort with multiple transitions, behavioral therapy expenditure increased by 40%, ADHD medications expenditure increased by 61%, while total expenditure as well as all-cause medications expenditure nearly doubled in the post-transition period. In addition, in the same cohort, post-transition outpatient expenditure increased by 68%, emergency department expenditure increased by 60%, while inpatient expenditure was nearly five times higher as compared with that in the pretransition period. These findings indicate that subsequent diagnosis of MH comorbidities in adult patients with ADHD resulted in a significant increase in overall health care utilization and expenditure that will substantially increase the overall burden of ADHD. They also provide a strong economic justification to explore cost-effective interventions that can reduce the effect of future MH comorbidities in adult patients with ADHD. Furthermore, physicians treating adults diagnosed with ADHD should carefully screen for other MH comorbidities.

These findings are consistent with published studies that have reported higher utilization and expenditure associated with patients with ADHD with MH comorbidities [8,23–28]. Previous studies comparing patients with ADHD with control populations in both pediatrics [29,30] and adults[8,9,31] suggest that patients with ADHD yield higher expenditure than do non-ADHD controls, even after controlling for patient comorbidities [8]. To our knowledge, this is the first study in adult patients with ADHD to confirm the magnitude and effect of additional MH disorders on utilization and expenditures. Subsequent comorbid MH diagnoses may be

Table 3 – All-cause health care expenditure ($) pretransition and post-transition (single transition).

Expenditure	N	Mean ± SE			P* for post-pre difference
		Pretransition	Posttransition	Post-pre difference	
Outpatient	357	1006 ± 53	1147 ± 69	141 ± 68	0.08
Emergency department	121	142 ± 17	254 ± 22	115 ± 34	<0.0001
Behavioral therapy	52	163 ± 29	57 ± 13	−117 ± 32	<0.0001
Inpatient	43	1900 ± 814	3757 ± 668	1929 ± 1436	0.002
ADHD medications	321	881 ± 58	1057 ± 64	176 ± 67	0.02
All medications	353	2928 ± 255	4345 ± 381	1435 ± 223	<0.0001
Overall expenditure†	357	4177 ± 298	5981 ± 436	1822 ± 306	<0.0001

ADHD, attention deficit/hyperactivity disorder; SE, standard error.
* P value for difference between pre- and post-transition expenditure assuming gamma distribution and log link in a generalized linear model.
† Overall expenditure is the sum of total cost from outpatient, inpatient, and emergency department visits and all-cause medications.

Table 4 – All-cause health care utilization pretransition and post-transition (multiple transitions).

Resource utilization	N	Mean ± SE			P* for post-pre difference
		Pretransition	Posttransition	Post-pre difference	
Outpatient visits	632	8.83 ± 0.36	14.50 ± 0.58	5.79 ± 0.57	<0.0001
Emergency visits	268	0.73 ± 0.05	1.19 ± 0.08	0.47 ± 0.10	<0.0001
Behavioral therapy visits	182	1.46 ± 0.12	2.03 ± 0.27	0.57 ± 0.28	0.0403
Inpatient visits	85	0.35 ± 0.06	1.21 ± 0.16	0.96 ± 0.20	<0.0001
Length of stay	85	0.75 ± 0.19	4.39 ± 0.84	4.53 ± 0.87	<0.0001
ADHD medications	564	1.98 ± 0.09	3.12 ± 0.10	1.16 ± 0.12	<0.0001
All medications	629	12.03 ± 0.44	17.65 ± 0.61	5.68 ± 0.42	<0.0001

ADHD, attention deficit/hyperactivity disorder; SE, standard error.
* P value for difference between pre- and post-transition utilization counts assuming negative binomial family distribution and log link in a generalized linear model.

especially noteworthy in adults when considering the increase for substance abuse and other at-risk health behaviors, which may lead to further medical expenditures.

As compared with other utilization categories, behavioral therapy utilization counts declined significantly in the single transition cohort but increased significantly in the multiple transition cohort. In the single transition cohort, this finding may be indicative of satisfaction with pharmacotherapy treatment options and consequently, there may be less focus on behavior therapy. If medications are working well and keeping symptoms under control, the patient and/or physician may not feel that behavioral therapy is necessary. Because this is a population also afflicted with one or more comorbid disorders, however, one may expect that behavioral therapy would be an important component of treatment. Behavioral therapy may be underutilized in this population because presently, no nationally recognized treatment guidelines exist for ADHD in adults. Another plausible explanation may be that patients are seeking behavioral therapy outside of the KPSC health plan and therefore this information may not be accurately accounted within our data. This explanation is consistent with a study that found that a significant number of commercially insured individuals received outpatient MH care out of network, particularly those receiving psychotherapy [32]. In the multiple transition cohort though, utilization counts of behavior therapy increased by 40% on average. Further research on the use of behavior therapy within adult populations with ADHD is important in understanding how it relates to treatment outcomes.

Utilization and expenditure were significantly higher, on average, for patients with two or more MH transitions than for those with a single transition, suggesting incremental economic burden with the addition of psychiatric comorbid conditions. As compared with the pretransition period, most utilization in the post-transition period for the multiple transition cohort increased by more than 60%; however, in the single transition cohort, only emergency visits and inpatient expenditure increased by more than 50%. Nevertheless, the trend in increases in resource use and expenditure in pre- to post-MH transition change was similar in direction (though not in magnitude) across both the single and multiple transition cohorts, except for behavioral therapy, inpatient length of stay, and outpatient expenditures. Our findings support the previous literature in other chronic conditions, which suggests that patients with comorbid psychiatric conditions were more likely to have emergency care and high primary care utilization [33]. This study expands on the previous literature by quantifying the incremental expenditure of MH comorbidities in adult patients with ADHD.

From a health policy perspective, these findings underscore the need for resource allocation toward cost-effective and efficient preventive interventions, management, and pharmacological treatment for the cohort of patients with ADHD who are more likely to experience additional MH comorbidities. This may not only potentially save downstream costs but also positively affect the quality of life and productivity of these patients [34]. The incremental expenditures identified in our study provide the lower bounds of expected future cost-savings associated with such interventions if they allow affected individuals to lead a normal life. Future research should identify which preventive interventions not limited to behavioral and medical therapies can provide cost-effective outcomes for this population. Private and public payers may want to consider such research or the creation of algorithms to help identify patients who may be at risk to

Table 5 – All-cause health care expenditure ($) pretransition and post-transition (multiple transition).

Expenditure	N	Mean ± SE			P* for post-pre difference
		Pretransition	Post-transition	Post-pre difference	
Outpatient	632	1059 ± 44	1778 ± 73	734 ± 70	<0.0001
Emergency department	268	191 ± 15	306 ± 23	118 ± 27	<0.0001
Behavioral therapy	182	109 ± 10	153 ± 20	44 ± 21	0.001
Inpatient	85	1367 ± 336	8058 ± 1511	8359 ± 1583	<0.0001
ADHD medications	564	762 ± 48	1224 ± 59	470 ± 60	<0.0001
All medications	629	2750 ± 174	5348 ± 257	2693 ± 185	<0.0001
Overall expenditure†	632	4061 ± 196	8313 ± 397	4432 ± 301	<0.0001

ADHD, attention deficit/hyperactivity disorder; SE, standard error.
* P value for difference between pre- and post-transition expenditure assuming gamma distribution and log link in a generalized linear model.
† Overall expenditure is the sum of total expenditure from outpatient, inpatient, and emergency department visits and all-cause medications.

develop a comorbid MH to potentially intervene earlier and prevent downstream costs. Because the cost-effectiveness of interventions may differ between patients with single transitions and patients with multiple transitions, an initial first step may be to identify and/or develop screening tools or predictive models to identify those patients with ADHD who are most likely to transition to additional MH comorbidities.

Study limitations

Indirect costs were not assessed as part of this study. We hypothesize that the burden due to work loss, or other indirect costs of comorbid disorders, would add incremental expenditure to the overall cost of illness, and future research could evaluate these effects. Our findings may have limited generalizability beyond the KPSC population if adult patients with ADHD are treated differently in fee-for-service health plans, or if significant variations exist because of patient or plan characteristics. In addition, by excluding patients with ADHD who did not use pharmacological treatment, our findings of incremental resource use are more generalizable to the diagnosed and treated population and may not be representative of the entire ADHD diagnosed population if such patients experience differential utilization patterns. Conversely, we are also ensuring that these patients were more likely to tolerate their ADHD medication and/or respond to their medications, because if they were not, they may have discontinued the treatment.

In terms of study design, we had required a limited 12-month period before the index ADHD diagnosis where MH comorbidities diagnosis codes were not observed. MH conditions, however, may have been present before this 12-month preindex period. Also, a matched control group that did not transition to MH comorbidity for comparison between groups could have further reinforced our inferences. In regard to the follow-up period, because the time to second (or higher) transition was not restricted, the multiple transition cohort may have experienced the second transition significantly later than the first transition. Thus, by not controlling for time effects, we may have introduced bias, if health technologies, treatment, or diagnostic guidelines changed significantly between the pre-post transition periods.

Our approach of applying standardized costing weights poses additional limitations. Standardized resource assignment is unlikely to reflect a specific provider's cost of producing health services because it does not capture the resources used in a specific setting (e.g., specific to the KPSC) but reflects a broader assessment of the relative resources required to deliver health care services. Thus, relative value–based approaches capture expected, standardized resource use rather than the actual costs experienced within KPSC's specific setting. The use of per-diem reimbursement for inpatient stay and discounted average wholesale price for pharmaceuticals has similar consequences although these are common approaches used in health services research.

Last, this study is subject to the traditional limitations of retrospective research including the lack of physician charts to confirm diagnoses of ADHD, as well as the use of *ICD-9* codes, which could be prone to errors in the coding of diagnosis [35].

Conclusions

In adult patients with ADHD, the increase in MH comorbidities was associated with an increase in health care utilization and expenditure as compared with the period with no MH comorbidities. From a value assessment perspective, adult patients with ADHD may need to be monitored routinely for the presence of other MH comorbidities with the goal of reducing future expenditures through early interventions. Clinicians and health care decision makers should be aware of the effect that comorbid MH conditions have on utilization and expenditure in adult patients with ADHD. We also need to better understand the relationship between current management approaches and health outcomes and look for more effective and efficient ways to treat adult patients with ADHD to reduce the chances of future MH transitions. Further research is necessary to improve the understanding of the long-term relationship between adults with ADHD and comorbid conditions.

Acknowledgments

We thank Miwa Takayanagi for statistical analysis and Amanda Bruno for reviewing the article.

Source of financial support: This study was funded by a subaward from the University of Southern California. The University of Southern California was funded for this study through a research grant from Shire Development LLC.

REFERENCES

[1] Adler L, Cohen J. Diagnosis and evaluation of adults with attention-deficit/hyperactivity disorder. Psychiatr Clin North Am 2004;27:187–201.
[2] Biederman J. Impact of comorbidity in adults with attention-deficit/hyperactivity disorder. J Clin Psychiatry 2004;65(Suppl. 3):3–7.
[3] Mannuzza S, Klein RG, Bessler A, et al. Adult psychiatric status of hyperactive boys grown up. Am J Psychiatry 1998;155:493–8.
[4] Wilens TE, Faraone SV, Biederman J. Attention-deficit/hyperactivity disorder in adults. JAMA 2004;292:619–23.
[5] Pary R, Lewis S, Matuschka PR, et al. Attention deficit disorder in adults. Ann Clin Psychiatry 2002;14:105–11.
[6] Kessler RC, Adler L, Barkley R, et al. The prevalence and correlates of adult ADHD in the United States: results from the National Comorbidity Survey Replication. Am J Psychiatry 2006;163:716–23.
[7] Arseneault L, Moffitt TE, Caspi A, et al. Mental disorders and violence in a total birth cohort: results from the Dunedin Study. Arch Gen Psychiatry 2000;57:979–86.
[8] Secnik K, Swensen A, Lage MJ. Comorbidities and costs of adult patients diagnosed with attention-deficit hyperactivity disorder. Pharmacoeconomics 2005;23:93–102.
[9] Birnbaum HG, Kessler RC, Lowe SW, et al. Costs of attention deficit-hyperactivity disorder (ADHD) in the US: excess costs of persons with ADHD and their family members in 2000. Curr Med Res Opin 2005;21:195–206.
[10] Hodgkins P, Montejano L, Sasane R, et al. Cost of illness and comorbidities in adults diagnosed with attention-deficit/hyperactivity disorder: a retrospective analysis. Prim Care Companion CNS Disord 2011;13: PCC.10M01030.
[11] Greenberg PE, Stiglin LE, Finkelstein SN, et al. The economic burden of depression in 1990. J Clin Psychiatry 1993;54:405–18.
[12] Rice DP, Kelman S, Miller LS. Estimates of economic costs of alcohol and drug abuse and mental illness, 1985 and 1988. Public Health Rep 1991;106:280–92.
[13] Burd L, Klug MG, Coumbe MJ, et al. The attention-deficit hyperactivity disorder paradox, 2: phenotypic variability in prevalence and cost of comorbidity. J Child Neurol 2003;18:653–60.
[14] Swensen AR, Birnbaum HG, Secnik K, et al. Attention-deficit/hyperactivity disorder: increased costs for patients and their families. J Am Acad Child Adolesc Psychiatry 2003;42:1415–23.
[15] Seidman LJ, Biederman J, Weber W, et al. Neuropsychological function in adults with attention-deficit hyperactivity disorder. Biol Psychiatry 1998;44:260–8.
[16] Murphy K, Barkley RA. Attention deficit hyperactivity disorder adults: comorbidities and adaptive impairments. Compr Psychiatry 1996;37:393–401.
[17] Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. Permanente J 2012;16:37–41.
[18] Hsiao WC, Braun P, Becker ER, et al. The Resource-Based Relative Value Scale: toward the development of an alternative physician payment system. JAMA 1987;258:799–802.
[19] CMS. Federal Register Rules and Regulations. In: Services CfMM, ed. Washington, DC: Government Printing Office, 2008.

[20] Bureau of Labor Statistics. Consumer Price Index 2010.
[21] Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. J Clin Epidemiol 1992;45:613–9.
[22] Quan H, Sundararajan V, Halfon P, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care 2005;43:1130–9.
[23] Leibson CL, Barbaresi WJ, Ransom J, et al. Emergency department use and costs for youth with attention-deficit/hyperactivity disorder: associations with stimulant treatment. Ambul Pediatr 2006;6:45–53.
[24] Leibson CL, Katusic SK, Barbaresi WJ, et al. Use and costs of medical care for children and adolescents with and without attention-deficit/hyperactivity disorder. JAMA 2001;285:60–6.
[25] American Academy of Pediatrics. Subcommittee on Attention-Deficit/Hyperactivity Disorder and Committee on Quality Improvement. Clinical practice guideline: treatment of the school-aged child with attention-deficit/hyperactivity disorder. Pediatrics 2001;108:1033–44.
[26] Leibson CL, Long KH. Economic implications of attention-deficit hyperactivity disorder for healthcare systems. Pharmacoeconomics 2003;21:1239–62.
[27] Fishman PA, Stang PE, Hogue SL. Impact of comorbid attention deficit disorder on the direct medical costs of treating adults with depression in managed care. J Clin Psychiatry 2007;68:248–53.
[28] Hinnenthal JA, Perwien AR, Sterling KL. A comparison of service use and costs among adults with ADHD and adults with other chronic diseases. Psychiatr Serv 2005;56:1593–9.
[29] Chan E, Zhan C, Homer CJ. Health care use and costs for children with attention-deficit/hyperactivity disorder: national estimates from the medical expenditure panel survey. Arch Pediatr Adolesc Med 2002;156:504–11.
[30] Guevara J, Lozano P, Wickizer T, et al. Utilization and cost of health care services for children with attention-deficit/hyperactivity disorder. Pediatrics 2001;108:71–8.
[31] Swensen A, Birnbaum HG, Ben Hamadi R, et al. Incidence and costs of accidents among attention-deficit/hyperactivity disorder patients. J Adolesc Health 2004;35(346):e1–9.
[32] Stein BD, Meili R, Tanielian TL, et al. Outpatient mental health utilization among commercially insured individuals: in- and out-of-network care. Med Care 2007;45:183–6.
[33] Pugh MJ, Zeber JE, Copeland LA, et al. Psychiatric disease burden profiles among veterans with epilepsy: the association with health services utilization. Psychiatr Serv 2008;59:925–8.
[34] Fletcher JM. The effects of childhood ADHD on adult labor market outcomes. Health Econ 2014;23:159–81.
[35] Zuvekas SH, Fleishman JA. Self-rated mental health and racial/ethnic disparities in mental health service use. Med Care 2008;46:915–23.