Heterogeneity of Nonadherent Buprenorphine Patients: Subgroup Characteristics and Outcomes

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ABSTRACT

OBJECTIVES: To examine patient characteristics and outcomes associated with nonadherence to buprenorphine and to identify specific patterns of nonadherent behavior.

STUDY DESIGN: Cross-sectional, retrospective analysis of health claims data.

METHODS: Aetna's administrative claims data were used to categorize incident opioid use disorder (OUD) patients based on buprenorphine medication possession ratio (MPR) into adherent (n = 172) and nonadherent (n = 305) groups. Adherent groups were then divided into 5 subgroups based on level of MPR, as well as 2 a priori–defined groups: intermittent adherent (IA) and early treatment discontinuation—no consequences (ETDNC). Groups were compared on patient characteristics and outcomes.

RESULTS: Nonadherent members incurred significantly greater healthcare costs and were more likely to relapse (P <.05). The use of high-cost healthcare services increased as a function of decreasing MPR (P <.05). Assessment of the a priori groups revealed IA members to have outcomes similar to nonadherent patients, while ETDNC members exhibited outcomes similar to adherent members.

CONCLUSIONS: Administrative claims can be used to define subgroups of buprenorphine-medication assisted treatment (B-MAT) patients. Nonadherence was related to an increased likelihood of relapse, and there is an inverse relationship between MPR and cost. The heterogeneity observed within this sample indicates that treatment regimens effective for 1 subgroup may not be appropriate for all OUD patients. Increased understanding of B-MAT nonadherent subgroups may facilitate development of new interventions and medications specifically designed for nonadherent B-MAT patients, potentially leading to improved outcomes and reduced costs of care.

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The United States is experiencing an opioid abuse epidemic, characterized by increases in the use of illicit drugs and misuse of prescription opioid analgesics.[1,2] Healthcare costs associated with opioid use disorder (OUD) have been estimated at $72 billion annually, with societal costs in excess of $50 billion.[3] In response, the White House issued a mandate to improve access to OUD treatment,[4-7] but significant challenges to the success of treatment remain, including initiation and persistence with treatment.

Medication-assisted treatment (MAT) for OUD includes methadone (M-MAT), naltrexone, and buprenorphine (B-MAT). Approval of B-MAT in 2002 addressed many of the barriers and stigmas associated with M-MAT.[7-11] Yet, fewer than 50% of OUD patients receive MAT of any form,[11-13] and between 40% and 60% of all substance abuse patients relapse within 1 year of discharge.[7,14-16] Therefore, more effective outpatient OUD treatment models, including improved patient–treatment matching are needed.

Nonadherence with buprenorphine and the associated elevated risk of relapse are pervasive challenges in the treatment of OUD. Although OUD is often characterized as a chronic relapsing disorder, treatment nonadherence is likely a contributing factor, as nonadherent patients incur significantly greater healthcare costs and have higher relapse rates than adherent patients.[17,18] Although some patient and treatment characteristics are predictive of lower retention in therapy, treatment characteristics associated with buprenorphine nonadherence remain unclear, as does their possible relationship to relapse.[19-22]

This study extends existing literature on B-MAT treatment failure and explores the factors associated with B-MAT medication nonadherence. An improved understanding of B-MAT adherence patterns could help providers identify early signs of nonadherence and lead to more effective patient–treatment matching. These analyses were designed to examine relationships among buprenorphine utilization, patient characteristics, and patient outcomes within administrative claims data to identify characteristics associated with nonadherent behavior in order to provide the insight

necessary to more effectively manage OUD patient populations.

TAKEAWAY POINTS

- Using administrative claims data, patterns of buprenorphine nonadherence were assessed among individuals in treatment for opioid use disorder.
- Nonadherence was related to increased service utilization, cost, and likelihood of relapse. Use of high-cost venue services increased as a function of decreasing adherence.
- This study confirms previous reports of the relationship between buprenorphine-medication assisted treatment (B-MAT) adherence and costs and advances this line of research by exploring and delineating patterns associated with subgroups of nonadherent B-MAT patients, particularly intermittent adherent and assumed success cases.

METHODS

Data Source

De-identified administrative commercial claims data (Q1 2012-Q1 2015) were supplied by Aetna, and the study was approved by Aetna's human research protection safety committee. The following criteria were imposed (**Table 1**): 1) at least a 28 days' supply of buprenorphine (single ingredient or combination with naloxone) during measurement year; 2) diagnosis of opioid dependence (*International Classification of Diseases, Ninth Revision, Clinical Modification* [*ICD-9-CM*] procedure codes 304.0x; 304.7x), opioid abuse (305.5x), or opioid poisoning (965.0x); 3) 6-month buprenorphine-naïve period preceding earliest buprenorphine fill; 4) continuous eligibility with medical and pharmacy benefits for 6 months prior to (naïve period) and 12 months following (follow-up period) the earliest buprenorphine fill on record (index date); and 5) 18 years or older on the index date.

Patients with serious mental illnesses, neurological disorders, or at the end of life, were excluded from analyses. The following diagnoses (*ICD-9-CM* codes in parenthesis) were the basis for exclusion: adult failure to thrive (783.7); Alzheimer's and other cerebral degenerations (331.x); chronic liver disease and cirrhosis (571.x); end-stage renal disease (585.6); dementias (290.x); debility, not otherwise specified (799.3); heart failure (428.x); Parkinson's disease (332.x); schizophrenia (295.x); and senility without mention of psychosis (797.x).

Study Groups

Members were divided into adherent and nonadherent groups based on their buprenorphine medication possession ratio (MPR). For the current study, adherence was calculated by dividing the total days' supply of medication by the length of the study window (12 months) [23]:

$$\text{MPR} = \frac{\text{total days' supply of buprenorphine}}{\text{1 year post period (365 days)}}$$

An MPR cutoff of 0.80 was used to demarcate adherent from nonadherent members.[24]

B-MAT Subgroups

MPR subgroups. B-MAT subgroups were identified by patterns of buprenorphine fills during the post period. Two methodologies were used to divide cases into subgroups. The first method stratified nonadherent members based on postperiod MPR. The nonadherent MPR subgroups were based on equal increments of 0.20: 1) 0.00-0.19, 2) 0.20-0.39, 3) 0.40-0.59, 4) 0.60-0.79.

Clinical subgroups. The second methodology was based on buprenorphine fill patterns consistent with 2 hypothesized groups described during communication with Aetna medical and psychiatric leadership. The first group, intermittent adherence (IA), included members exhibiting a series of treatment initiations and discontinuations without moving toward sobriety, characteristic of drug holidays. The IA group was operationally defined as evidencing multiple episodes of B-MAT (1 episode includes 2 or more consecutive fills) separated by intermittent periods of medication discontinuation (gap in fills ≥30 days). Assignment to this group required at least 2 episodes of buprenorphine treatment separated by medication discontinuation.

A small number of B-MAT patients completed treatment during a brief period of time (ie, less than 9 months) without evidencing any of the negative consequences normally associated with early discontinuation (ie, relapse). These members were placed in the early treatment discontinuation—no consequences (ETDNC) group, which was defined as demonstrating an MPR of at least 0.80 during their specific treatment period with B-MAT (minimum of 90 days) and showing an absence of relapse indicators

TABLE 1. Sample Attrition

Reason for Inclusion	Patients Excluded		Patients Remaining	
	N	%	N	%
Members with a B-MAT fill[a]	0	0.0%	5349	100.0%
Members with an OUD diagnosis anywhere on record	852	15.9%	4497	84.1%
Member has at least 6 months of pre- and 11 months of postindex eligibility[b]	3889	72.7%	608	11.4%
Absence of exclusionary diagnosis	43	0.8%	565	10.6%
Age ≥18 on index date	2	0.0%	563	10.5%
Minimum of 28 days' supply of B-MAT	73	1.4%	490	9.2%
Does not solely show OUD in remission diagnosis	13	0.2%	477	8.9%

B-MAT indicates buprenorphine-medication assisted treatment; OUD, opioid use disorder.
[a]Earliest B-MAT fill is the index date.
[b]Continuous medical and pharmacy rider present.

following cessation of B-MAT. Given that the ETDNC subgroup exhibited characteristics of both the nonadherent group (briefer treatment window, <0.80 1-year MPR) and adherent group (short-term adherence ≥0.80, absence of relapse), exploratory analyses of this subgroup alone and with both adherent and nonadherent groups were performed.

Outcomes

Demographics. Demographic variables of age, gender, region of residence, and member type were aggregated from the summary membership table. Health statuses during the pre- and post periods were estimated using the Charlson Comorbidity Index (CCI).[25]

Relapse indicators. Four relapse proxies based on procedure codes associated with relapse were identified during the post period[26,27]: 1) OUD status change: change in diagnosis code from opioid dependence in remission (*ICD-9-CM* codes: 304.03, 304.73) to continuous or episodic opioid dependence (304.01, 304.02, 304.71, 304.72); 2) OUD inpatient: presence of an inpatient admission with a primary diagnosis of OUD; 3) OUD emergency department (ED): presence of an ED visit with any OUD diagnosis; and 4) OUD detox: presence of a detoxification claim with any OUD diagnosis.

Healthcare service utilization and costs. Specific healthcare service utilization and costs were measured during both the pre- and post periods: physician office visits and costs, proportion of members with at least 1 inpatient admission, inpatient hospital costs, proportion of members with at least 1 ED visit, ED costs, total medical costs, total prescription fills and costs, and total healthcare costs (medical + pharmacy costs).

Analyses

Overall adherence analysis. Overall adherence groups based on an MPR cutoff of 0.80 were compared on relapse, MPR subgrouping, and healthcare costs during the post period. Means and standard deviations were computed for continuous variables, and counts were presented as frequencies and percentages. Statistically significant differences among cost outcomes were assessed via Mann-Whitney *U* tests, as the distribution of cost data were skewed positive, while χ^2 tests of equality of proportions were used for the relapse indicators. Linear trends between postperiod healthcare costs and B-MAT adherence were examined using the 5-way MPR grouping variable. Costs were log transformed to normalize the distributions and were entered into 1-way analyses of variance examining linear contrasts.

Clinical subgroup exploratory analysis. The ETDNC group was compared with both the adherent group and the balance of the nonadherent groups on demographics and cost. The distribution of MPR groupings within the IA group was also examined. Results of these analyses confirmed that the IA group was appropriately categorized as being nonadherent, while the ETDNC group more closely resembled the adherent cases. Therefore, the primary analyses were conducted with the ETDNC cases moved from the nonadherent group to the adherent group. This updated grouping made up the enhanced adherence analysis.

Enhanced adherence analysis. The adherent group, now including the ETDNC cases, was compared with the nonadherent group on all demographic, service use, cost, and relapse measures during the post period. Descriptive and bivariate analyses were conducted similar to the overall adherence analysis. In addition, multivariate models were also constructed for select cost measures. For pharmacy, total medical, and total healthcare costs variables, gamma models with a log-link were estimated, controlling for age, gender, member type, and preperiod CCI score. Only those cases with nonzero values were included in these models.

MPR-based analysis. MPR subgroups were compared on demographic and relapse indicators via χ^2 tests of equality of proportions. Linear trends (contrasts) between postperiod healthcare costs and B-MAT adherence were examined using the 5-way MPR grouping scheme as the independent variable. Relationships between raw cost means at each of the 5 adherence levels were plotted. Costs were then log transformed to normalize the distributions and were entered into 1-way analyses of variance.

Relapse group analysis. Relapse groups were compared on postperiod costs. Additionally, the associations between relapse status and adherence were calculated for the overall nonadherent, IA, and MPR groups. All data management and analyses were conducted in SPSS version 20 (SPSS Inc; Chicago, Illinois).

RESULTS

Overall Adherence Results

A total of 477 members qualified for the current study, with 172 (36%) categorized as adherent and the balance of 305 (64%) categorized as nonadherent. Results for costs, relapse, and MPR grouping analyses may be viewed in **Table 2**. Nonadherent members were significantly more likely than adherent members to evidence relapse by an OUD inpatient hospitalization or OUD ED visit (P <.05) and were significantly more likely to show any relapse (30.5% vs 15.7%; P <.001). Further, nonadherent members incurred significantly higher office, outpatient hospital, ED, inpatient, and total medical costs compared with adherent members (P <.05).

Regarding specific levels of adherence within the nonadherent group, the MPR 0.00 to 0.19 subgroup (n = 92) was the largest, followed by the 0.20 to 0.39 group (n = 80). Although not presented in Table 2, the relapse rate among the nonadherent MPR subgroups revealed a steady decrease with increased adherence to B-MAT: the 0.00 to 0.19 group had the highest relapse rate at 46.7%, followed by the 0.20 to 0.39 (32.5%), 0.40 to 0.59 (27.9%), and 0.60 to 0.79 groups (15.4%). Furthermore, cost analyses using the MPR subgroups revealed significant linear trends for outpatient hospital, inpatient

hospital, and ED costs, with decreased costs associated with greater MPR (P <.05).

Clinical Subgroup Results

The ETDNC (n = 33) and IA (n = 30) subgroups were examined to further characterize the heterogeneity of adherent and nonadherent B-MAT members. **Table 3** displays the relationship among the ETDNC, adherent, and balance of the nonadherent cases on healthcare expenditure, although no statistical testing was performed for lack of power. Relationships were in the expected direction, with the nonadherent cases having greater outpatient hospital, ED, inpatient hospital, and total medical costs compared with ETDNC members. Conversely, ETDNC members had similar or lower costs compared with adherent cases on the same measures.

As expected, both the adherent and ETDNC groups had increased pharmacy costs compared with nonadherent cases. ETDNC cases were also significantly more likely than the balance of the adherence group to be aged 18 to 25 years (45.5% vs 26.7%) and appeared to be in better overall health (CCI score, 0.06 vs 0.33; P <.05; data not shown). The ETDNC group filled fewer prescriptions (11.6 ± 9.6) than all other groups, including both the adherent group (31.2 ± 20.4) and the balance of the nonadherent group (22.9 ± 23.1).

A total of 30 nonadherent members qualified for the IA group, with the majority (53.3%) falling into the 0.60 to 0.79 MPR group. Compared with the balance of the nonadherence group, IA members had a significantly lower CCI score during the pre- (0.07 vs 0.23) and post periods (0.07 vs 0.33; P <.05) and were more likely to experience an OUD status change compared with the balance of the nonadherent group (13.3% vs 4.5%; P <.05). Based on these results, ETNDC members were placed into the overall adherent group for remaining analyses, while IA members remained in the nonadherent group.

TABLE 2. Overall Adherence Analysis

	B-MAT Adherent (n = 172)		B-MAT Nonadherent (n = 305)		P[a]
Paid amounts[b]					
Office	$1734	$3196	$1765	$4485	.010
Outpatient hospital	$2349	$6096	$5594	$18,643	.006
ED	$623	$1875	$1147	$2947	.003
Inpatient hospital	$2224	$10,335	$5657	$16,032	<.001
Total medical	$6987	$14,694	$14,190	$30,662	.006
Pharmacy	$5302	$6757	$2365	$5955	<.001
Total healthcare	$12,289	$17,523	$16,555	$31,502	.069
Any relapse	27	15.7%	93	30.5%	<.001
Specific relapse event[c]					
OUD remission status change	15	8.7%	15	4.9%	.100
OUD hospitalization	5	2.9%	71	23.3%	<.001
OUD ED visit	3	1.7%	28	9.2%	.002
OUD detoxification	1	0.6%	9	3.0%	.830
MPR grouping					
0.00-0.19	–	–	92	30.2%	–
0.20-0.39	–	–	80	26.2%	–
0.40-0.59	–	–	68	22.3%	–
0.60-0.79	–	–	65	21.3%	–

B-MAT indicates buprenorphine-medication assisted treatment; ED, emergency department; MPR, medication possession ratio; OUD, opioid use disorder.
[a]For significance testing, χ^2 tests of equality of proportions were used for categorical variables, Student's t tests were used for continuous variables, and Mann-Whitney U tests were used for cost and service utilization variables.
[b]All means and standard deviations are unadjusted.
[c]A single member may show multiple relapse events.

TABLE 3. Healthcare Costs by Adherent, Nonadherent, and ETDNC[a]

	B-MAT Adherent: MPR ≥0.80 (n = 172)		B-MAT Adherent: ETDNC (n = 33)		B-MAT Nonadherent (n = 272)	
	Mean/F	SD/%	Mean/F	SD/%	Mean/F	SD/%
Paid amounts						
Office	$1734	$3196	$868	$974	$1873	$4727
Outpatient hospital	$2349	$6096	$2489	$4262	$5971	$19,658
ED	$623	$1875	$782	$1392	$1191	$3081
Inpatient hospital	$2224	$10,335	$1388	$4478	$6175	$16,837
Total medical	$6987	$14,694	$5534	$7692	$15,241	$32,209
Pharmacy	$5302	$6757	$4068	$16,075	$2158	$2978
Total healthcare	$12,289	$17,523	$9602	$17,099	$17,399	$32,742

B-MAT indicates buprenorphine-medication assisted treatment; ED, emergency department; ETDNC, early treatment discontinuation—no consequence; F, frequency; MPR, medication possession ratio.
[a]All means and standard deviations are unadjusted.

Enhanced Adherence Results

Demographics. The inclusion of the ETDNC cases into the adherent group resulted in a final sample of 205 (43%) categorized as adherent, with the balance of 272 (57%) categorized as nonadherent. Demographic, service use, cost, and relapse results by the enhanced adherence grouping may be viewed in **Table 4**. Members were predominately males in their early 30s, with the adherent group

TABLE 4. Enhanced Adherence Analysis

	B-MAT Adherent (n = 205)		B-MAT Nonadherent (n = 272)		
	Mean/F	SD/%	Mean/F	SD/%	P[a]
Age, years	34.0	11.8	31.6	12.4	.038
18-25	61	29.8%	130	47.8%	<.001
26-39	87	42.4%	74	27.2%	<.001
40-64	57	27.8%	66	24.3%	.382
≥65	0	0.0%	2	0.7%	.219
Male	134	65.4%	173	63.6%	.691
Preperiod CCI	0.14	0.44	0.21	0.72	.202
Postperiod CCI	0.29	0.59	0.30	0.81	.838
Region					
Central	15	7.3%	18	6.6%	.766
Northeast	109	53.2%	124	45.6%	.101
Southeast	67	32.7%	103	37.9%	.242
West	14	6.8%	27	9.9%	.232
Member type					
Child	59	28.8%	123	45.2%	<.001
Subscriber	115	56.1%	110	40.4%	.001
Domestic partner	0	0.0%	4	1.5%	.081
Spouse	29	14.1%	31	11.4%	.370
Other	2	1.0%	4	1.5%	.631
Adherence subgroups					
Assumed success	33	16.1%	–	–	–
Intermittent adherence	–	–	30	11.0%	–
MPR 0.00-0.19	–	–	92	33.8%	–
MPR 0.20-0.39	–	–	67	24.6%	–
MPR 0.40-0.59	–	–	55	20.2%	–
MPR 0.60-0.79	–	–	58	21.3%	–
Service use					
Office visits	15.0	13.2	12.6	15.4	.002
Outpatient hospital visits	8.6	15.6	12.6	21.2	.030
Prescription fills	28.1	20.4	22.9	23.1	<.001
Proportion with an ED visit	61	29.8%	114	41.9%	.006
Proportion with an IP visit	31	15.1%	106	39.0%	<.001
Paid amounts[b]					
Office	$1594	$2969	$1873	$4727	.088
Outpatient hospital	$2372	$5831	$5971	$19,658	.004
ED	$648	$1804	$1191	$3081	.014
Inpatient hospital	$2090	$9632	$6175	$16,837	<.001
Total medical	$6753	$13,804	$15,241	$32,209	.001
Pharmacy	$5103	$8889	$2158	$2978	<.001
Total healthcare	$11,857	$17,442	$17,399	$32,742	.485

(continued)

being older (34.0 vs 31.6 years; P <.05). A greater proportion of nonadherent members were aged 18 to 25 years (47.8% vs 29.8%; P <.001). Adherent members were significantly more likely to be the primary plan subscriber compared with nonadherent members, who were more likely to be a dependent (P <.01). Within the nonadherent group, the MPR 0.00 to 0.19 subgroup (n = 92) was the largest of the MPR-based subgroups, followed by the 0.20 to 0.39 (n = 67), 0.60 to 0.79 (n = 58), and 0.40 to 0.59 MPR (n = 55) subgroups.

Relapse. The overall nonadherent group was more than 2.5 times more likely to relapse than the adherent group (34.2% vs 13.2%, P <.001). Nonadherent members were significantly more likely than adherent members to evidence 3 of the 4 relapse proxies (P <.05); the exception was OUD status change. The most commonly observed indicator of relapse in the nonadherent group was OUD inpatient hospitalization (25.0%).

Healthcare service use and cost. During the pre-period, healthcare service utilization and total pharmacy, medical, and overall healthcare costs were similar across adherent and nonadherent groups (P >.05). During the post period, adherent members had significantly more office visits, prescriptions, and accrued greater pharmacy costs, whereas the nonadherent group evidenced significantly greater outpatient hospital, ED, and inpatient visits and increased total medical costs (P <.05). Results of the multivariate models revealed that the nonadherent group incurred significantly decreased pharmacy costs (adjusted means $1930 vs $4818) but higher total medical costs ($8148 vs $3723) and total healthcare costs ($10,638 vs $7581; P <.01) compared with the adherent group.

MPR Grouping Results

Compared with the balance of the overall nonadherence group, the 0.00 to 0.19 group was significantly less likely to be the primary subscriber (30.4% vs 45.6%), whereas the 0.60 to 0.79 group was significantly more likely to be the primary subscriber (51.7% vs 37.4%) and was also less likely to be aged 18 to 25 years (34.5% vs 51.4%; P <.05). Those in the 0.00

to 0.19 MPR group were significantly more likely than other nonadherent members to relapse (46.7% vs 27.8%); specifically, they were more likely to evidence OUD hospitalizations (35.9% vs 19.4%) and OUD ED visits (15.2% vs 6.1%; P <.01). In contrast, those in the 0.60 to 0.79 MPR group were significantly less likely to relapse than other nonadherent members (13.8% vs 60.3%). Across the MPR groups, the results of 1-way analyses of variance of logged-transformed costs revealed statistically significant linear contrasts on 4 of 7 cost metrics: pharmacy, outpatient hospital, inpatient hospital, and total medical (P <.05) (**Figure**). Pharmacy costs increased with MPR, but the remaining cost indicators decreased with increasing amounts of medication on hand, with the MPR 0.60 to 0.79 group approximating the adherent group (MPR >0.80).

TABLE 4. Enhanced Adherence Analysis *(continued)*

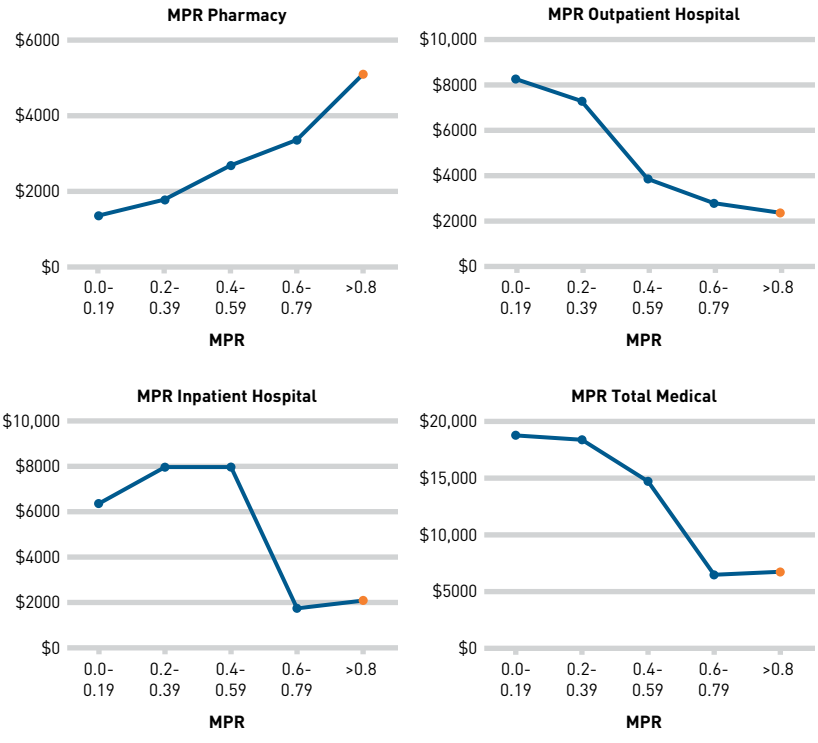
	B-MAT Adherent (n = 205)		B-MAT Nonadherent (n = 272)		
	Mean/F	SD/%	Mean/F	SD/%	*P*[a]
Any relapse	27	13.2%	93	34.2%	<.001
Specific relapse event[c]					
OUD remission status change	15	7.3%	15	5.5%	.422
OUD hospitalization	8	3.9%	68	25.0%	<.001
OUD ED visit	6	2.9%	25	9.2%	.006
OUD detoxification	1	0.5%	9	3.3%	.033

B-MAT indicates buprenorphine-medication assisted treatment; CCI, Charlson Comorbidity Index score; ED, emergency department; F, frequency; IP, inpatient hospital; MPR, medication possession ratio; OUD, opioid use disorder; SD, standard deviation.
[a]For significance testing, χ^2 tests of equality of proportions were used for categorical variables; Student's t tests were used for continuous variables, and Mann-Whitney U tests were used for cost and service utilization variables.
[b]All means and standard deviations are unadjusted.
[c]A single member may show multiple relapse events.

Relapse Grouping Results

Compared with members who did not evidence a relapse (n = 357), members who experienced any type of relapse (n = 120) incurred significantly lower pharmacy costs ($2103 vs $3868) but more than 3 times the medical ($24,866 vs $7132) and twice the total healthcare costs ($26,969 vs $11,000; P <.001). Relapsing members were more likely to be nonadherent with B-MAT compared with those who had not relapsed (77.5% vs 50.1%; P <.001) and were also more likely to be in the MPR 0.00 to 0.19 subgroup (35.8% vs 13.7%; P <.001). By contrast, members who did not experience relapse were significantly more likely to be in the MPR 0.60 to 0.79 subgroup compared with relapsers (14.0% vs 6.7%; P <.001).

FIGURE. Relationship Between Medication Possession Ratio and Costs



MPR indicates medication possession ratio.

DISCUSSION

Member demographics, relapse, healthcare service utilization, and costs associated with B-MAT nonadherence were examined in administrative claims from a commercially insured sample of OUD patients. Nonadherent members were younger and less likely to be employed, consistent with previously published predictors of nonadherence.[19,21,22] Adherent members were more likely to use office- and pharmacy-based services compared with nonadherent members; the latter group incurred significantly greater high-cost healthcare services, consistent with the increased rate of relapse observed within this group. Overall, the nonadherent group demonstrated a 1.5-fold increase in total annual healthcare costs and significantly higher medical costs compared with adherent members. Although the relationship

between B-MAT adherence and healthcare costs has previously been demonstrated,[17] this study extended these findings by further stratifying the nonadherent group based on MPR and examining clinically meaningful subgroups.

A significant linear trend demonstrating a negative relationship between adherence and outpatient, inpatient, and total medical costs was revealed, indicating that incremental increases in B-MAT adherence are associated with healthcare savings. The rate of relapse also decreased as adherence across the MPR subgroups increased. Differences in demographics among the MPR subgroups were also observed; nonadherent members within the 0.00 to 0.59 MPR groups were younger and more likely to be the dependent of the primary subscriber compared with adherent members. These characteristics are in notable contrast to those of the nonadherent 0.60 to 0.79 MPR group, who were older, more likely to be the primary subscriber, and significantly less likely to relapse. Conversely, the 0.00 to 0.19 MPR group was the most likely to evidence a relapse event and exhibited the highest medical and lowest pharmacy costs.

Treatment and demographic characteristics of the sample were also examined within 2 clinical subgroups of the larger adherent and nonadherent populations: the IA and ETDNC groups. Comparison of the demographic and treatment characteristics associated with these groups, as opposed to the MPR subgroups and larger adherence groups, highlighted the heterogeneity within the adherence groups and identified particular patterns of B-MAT utilization that may be associated with nonadherence.

The IA group included members who evidenced multiple starts and stops with B-MAT, which clinically could be indicative of patients either taking drug holidays or forming the belief that they were no longer in need of B-MAT. Members in the IA group predominately fell into the 0.60 to 0.79 MPR group. Despite their relative high rate of adherence, their demographics, relapse rate, and cost of care diverged from the balance of the 0.60 to 0.79 MPR subgroup and more closely resembled the characteristics of members in the other nonadherent MPR subgroups. These results indicate that assessment of MPR alone is insufficient to estimate a patient's risk of relapse and potential success with B-MAT.

The other clinical subgroup, ETDNC, was included to represent a potential subpopulation of B-MAT patients who may not require prolonged use of B-MAT to gain the benefits of treatment. These members were originally placed into the nonadherent group, as their 1-year MPR was less than 0.80 due to their short course of B-MAT. Despite their short period of B-MAT, they exhibited no negative consequences characteristic of active OUD following treatment discontinuation. These members more closely resembled adherent members, as evidenced by their service utilization and cost profiles, along with a high proportion of primary subscribers. Therefore, the ETDNC members were ultimately assigned to the enhanced adherent group on the basis of their short-term adherence to B-MAT and lack of relapse during the follow-up. To assess the potential implications of switching the ETDNC group from nonadherent to adherent, analyses comparing the original adherent and revised enhanced adherence groups were conducted. Findings demonstrated that, although the relapse rate is slightly decreased in the enhanced adherence group due to ETDNC members showing no relapses during their course of B-MAT treatment, the direction and significance of the remaining relationships between the adherent and the nonadherent groups remain unchanged, indicating that the ETDNC members may represent 1 subgroup of adherent B-MAT members.

The findings of this study indicate great variability within the B-MAT population, calling into question whether a strict definition of adherence is fully appropriate for this population. Although an 80% cutoff has been widely accepted as an indicator of acceptable adherence in various therapeutic areas,[24] the 0.60 to 0.79 MPR group exhibited a cost profile similar to the adherent group, suggesting that this level of nonadherence may be adequate for some OUD patients to avoid the consequences characteristic of active OUD. The authors are not suggesting that this lower tier of adherence should be the target for all cases; however, in some cases, there may be a therapeutic benefit to instituting an intermediate adherence goal of 0.60 or above. Further, it may be appropriate to consider interventions that effectively raise adherence to 0.60 or above as successful, even if the intervention is not able to move the patient to the optimal level of adherence of 0.80.

Limitations

Administrative claims are known to include administrative coding errors,[28] and they lack the clinical data necessary to provide insight into treatment. For instance, it may be difficult to determine with certainty whether buprenorphine was prescribed to primarily treat OUD or pain, as buprenorphine is indicated for both conditions. Requiring an OUD diagnosis largely alleviated the issue in this study, although the possibility of pain being the reason for buprenorphine cannot be discounted. Also, claims-based proxies used to estimate relapse in this study returned slightly lower levels of relapse compared with a prior study that used clinically based endpoints for relapse.[18] Alternative data sources, such as urine drug screen results, are needed to confirm the relapse proxies used here, and to define clinical indicators of success with treatment. Additionally, the small sample size of the IA and ETDNC groups prohibited statistical testing. Replication of this study in larger commercial or public sector data sets is warranted, as this study may not generalize to other populations. Additionally, although OUD is common within severely mentally ill populations, this study excluded these members, as the primary outcome was adherence. The final limitation is the potential endogeneity of B-MAT adherence, as factors unmeasured in the claims may drive these outcomes.

CONCLUSIONS

This study confirms the burden of B-MAT nonadherence on the healthcare system through an analysis of service utilization and healthcare expenditure and extends these findings to relapse rates. Furthermore, specific patterns of adherence were examined through the construction of the adherence-based MPR subgroups and the clinically-focused ETDNC and IA subgroups. Although larger samples of OUD patients are needed to replicate and validate the findings of this study, the definition of various subgroups provides initial insight into patterns of B-MAT use. These groups could be essential to developing more effective methods for case finding in support of adherence-enhancing programs. Improved methods, such as those initiated here, to identify members in need of alternative interventions and to assess success with treatment are required to promote improved management of the OUD population, which stands to benefit both health plans and OUD patients by improving outcomes and containing healthcare costs. ■

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