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Buprenorphine Treatment for Opioid Use Disorder in Community-Based Settings: Outcome Related to Intensity of Services and Urine Drug Test Results

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Background and Objectives: Variables contributing to the outcome of buprenorphine treatment for opiate use disorder have been studied, including patient characteristics and the treatment approach applied. It is also valuable to study the types of clinical facilities that can affect outcome.
Methods: We evaluated patients (N = 20 993) in 573 facilities where buprenorphine was prescribed. Urine drug test results were analyzed for those (N = 13 281) who had buprenorphine prescribed at least twice in the period January 2015 through June 2017. Facilities were divided into three categories: medication management (MM) only, limited psychosocial (LP) therapy, and recovery-oriented (with more extensive counseling and a 12-step orientation) (RO).
Results: Urine drug tests negative for other opioids at the time of the second buprenorphine prescription were 34% for MM, 56% for LP, and 62% for RO ($P < .001$). A comparison was made between the most recent and the established patients at the facilities. The decrement in urinalyses positive for other opioids in this latter comparison was 3% for MM, 7% for LP, and 23% for RO ($P < .001$).
Discussion and Conclusions: In a large sample of community settings, buprenorphine patients' urinalyses positive for opioids can vary considerably across treatment facilities, and more intensive recovery orientation may yield a better outcome in terms of secondary opioid use.
Scientific Significance: The majority of buprenorphine patients are treated in community facilities. It is important that research be done by facility type in such settings in order to plan for optimal treatment. (© 2020 The Authors. *The American Journal on Addictions* published by Wiley Periodicals, Inc. on behalf of The American Academy of Addiction Psychiatry (AAAP);29:271–278)

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INTRODUCTION

Studies have been published on how the outcome of buprenorphine-based medication-assisted treatment can vary in relation to settings for treatment, such as individual private offices[1]; health maintenance organizations[2]; and home induction.[3] When psychosocial adjunctive treatments are applied, such as group counseling and cognitive behavioral therapy,[4] outcomes may vary as well. The effectiveness of buprenorphine treatment has also been studied in terms of prescriptions for secondary opioids both before and after treatment.[5]

Another option for evaluating outcome in the assessment of misuse of other opioids when buprenorphine is prescribed is the examination of the results of urine drug testing during treatment, and this can be done relative to different community-based programs. We present data here on urinalyses for ongoing opioid use among buprenorphine patients in a large sample of community-based facilities, relative to the nature of the adjunctive counseling provided.

MATERIALS AND METHODS

Data Source

Dominion Diagnostics, LLC, of North Kingstown, RI, is a national toxicology laboratory serving treatment programs and practitioners in 41 US states, specializing in the treatment of substance use disorders and pain management. The institutional review board of Dominion Diagnostics reviewed and approved the use of anonymized urine drug test data for this outcome study without the approval of the original patients. Informed consent of patients was therefore not required. Urine drug testing data are maintained in a database that contains clinical information related to patients' adherence to the prescribed treatment. Laboratory results are

combined with clinical information obtained at the time of urine collection. Prior to the analysis for this study, the data from the records studied were de-identified and anonymized. Anonymized results were then analyzed for those patients (N = 20 993) who had buprenorphine prescribed during the calendar year 2015. All data, including laboratory results and clinical information, were fully anonymized prior to being accessed by any of the authors of this study.

Inclusion Criteria

Facilities (N = 573) where buprenorphine was prescribed for the treatment of opioid use disorder were studied. The number of patients in the settings where treatment was carried out is given in Table 1. The treatment approach in the facilities selected was characterized on the basis of clinical descriptions given by facilities' staff and on reports of on-site visits by the laboratory's clinical staff at each respective facility. These reports are then reviewed with the laboratory's clinical research staff.

The facilities studied were then divided into three categories defined by the laboratory's clinical research staff, headed by two of the authors (MH and JF). This allows for determining the relative role of counseling in three facility types. The three facility types are: (a) medication management (MM) facilities (138 facilities and 6103 patients) where buprenorphine is prescribed with periodic medication checks, but without an onsite counseling program; (b) limited psychosocial (LP) facilities (9 facilities and 2557 patients), where case management is limited to periodic individual counseling sessions; (c) and recovery-oriented (RO) facilities (109 facilities and 11 589 patients), with case management, and individual therapy takes place along with more extensive counseling (such as family and group treatment), and an orientation towards 12-step referral. The two facility types not included in this study were, therefore, (a) those solely conducting opioid detoxification (5 facilities and 244 patients), and (b) those prescribing medications upon referral from other facilities where counseling was carried out (8 facilities and 586 patients). This study was therefore undertaken to ascertain the association between three facility types, MM, LP, and RO, and urinalyses of the patients treated there.

Data Analysis

The SPSS-V.24 statistical software program was applied to conduct analyses (SPSS, IBM Corporation, Armonk, NY, USA). Descriptive statistics were generated. Group mean differences for continuous outcomes were examined using an analysis of variance and Tukey HSD post hoc test where appropriate. Group differences for categorical outcomes were assessed by the χ^2 statistic.

Analyses Conducted

Patients from each of the three facility types who were prescribed buprenorphine during the calendar year 2015 were studied. Those patients who had buprenorphine prescribed during that calendar year and a second buprenorphine prescription prior to July 1, 2017 (N = 13 281) were subjects for analysis. The period between the first and second prescription for those patients with two buprenorphine prescriptions during the above period was designated as a buprenorphine episode (BE), and results of their urinalyses at the time of the second buprenorphine prescription were analyzed for secondary opioids. This was done in order to ascertain the relationship between a BE and secondary opioid use. Secondary opioids, as the term is applied here, are ones other than the prescribed buprenorphine that were detected on the urinalyses; they reflect ingestion of opioids other than the prescribed buprenorphine at the time that the second prescribed buprenorphine of the BE was detected in the urine. Analysis was also done on the interval between the first and second prescription for buprenorphine of the BE. Urinalyses of patients who had only one buprenorphine prescription in the facilities between January 1, 2015 and July 1, 2017 (N = 7248) were not studied.

Analysis of Secondary Opioid Use

For patients who had a BE (ie, a second buprenorphine prescribed before July 1, 2017), the urine drug tests at the time of the second buprenorphine prescription were studied. They were analyzed for the presence of any other opioids, namely codeine, fentanyl, heroin metabolite, hydrocodone, hydromorphone, methadone, methadone metabolite, morphine, norbuprenorphine, norcodeine, norfentanyl, norhydrocodone, noroxycodone, norpropoxyphene, o-desmethyltramadol,

TABLE 1. Comparison of urine drug test rates positive for other opioids stratified by any urine drug test prior to the buprenorphine episode

	None		≥1			
	N	% (+)	*N*	% (+)	χ^2	Cohen's *h*
Medication management only	1587	68	1116	64	4.916*	0.08
Limited psychosocial	394	45	351	42	1.158	0.06
Recovery oriented	1782	42	1063	32	77.756***	0.21
Total	4101	53	2574	44	107.531***	0.18

Cohen's *h* is interpreted as follows: small effect = 0.20 to 0.49; medium effect = 0.50 to 0.79; and large effect = 0.80 or greater.
*$P < .05$, ***$P < .001$.

oxycodone, oxymorphone, or tramadol (nobuprenorphine was not included here as a secondary opioid).

Urine testing was performed at the diagnostic laboratory by quantitative immuno-assay and confirmatory analysis by liquid chromatography dual mass spectroscopy (LCMSMS). It was not done at the point of contact. A patient who had other opioids detected in the second buprenorphine prescription was designated as opioid-positive. These other opioids may have been prescribed by a different physician or may represent illicitly obtained opioids. If no other opioids were detected in the urine at the time of the second buprenorphine, the patient was designated as opioid-negative.

Further analyses were done on the patients with a BE (ie, had a second buprenorphine prescription). The mean period of time from their first urine drug test conducted at the facility to their first buprenorphine prescription in 2015 was calculated, serving as a proxy for duration of prior contact with the facility. These findings may clarify whether there is a benefit relative to the likelihood of abstinence from secondary opioids for patients with engagement in any one of the three facility types. This was done to ascertain whether negative urines during the BE were more likely if a patient had prior treatment at the respective facility (ie, MM, LP, or RO).

The patients were then divided into three groups by facility type, MM, LP, and RO. The portion of urine drug tests positive for opioids at the time of their second buprenorphine prescription was calculated for patients in the three respective facility types. For each facility type, a calculation was then made comparing the portion of urine drug tests positive for opioids at the time of the second buprenorphine prescription, comparing those patients who had no previous urine drug tests reported to those who had prior urine drug tests done (an estimation of new vs established patients). This served as a proxy for estimating the relative impact of prior experience at the respective facilities on changes in opioid positivity. The duration of patients' activity at the facility was estimated as the period between the first urine drug test they ever had at the facility up to the first buprenorphine prescription of their BE. This served as a proxy for how long they had been active in their respective facility.

RESULTS

As indicated in Figure 1, there were 20 993 patients who had buprenorphine prescribed in the calendar year 2015. The mean duration of time from their first urine drug tests at the facility to the buprenorphine prescribed of their BE was 7.36 (SD, 16.26) months, indicating a proxy for the average length of contact with the facility prior to the 2015 buprenorphine prescription; this indicated that many patients were not new to the clinic at the time of their BE. The mean time between the first and second buprenorphines of the BEs was 1.47 (SD, 2.97) months.

Patients who had a second buprenorphine prescription prior to July 1, 2017, were 4088 (68%) of MM patients, 1706 (67%) of LP patients, and 7487 (65%) of RO patients, indicating that the three program types had similar portions of patients studied who had a BE. The mean portion of urine drug tests negative for other opioids where the second buprenorphine was prescribed was calculated. Altogether, 34% (N = 1345) of the samples were negative for MM

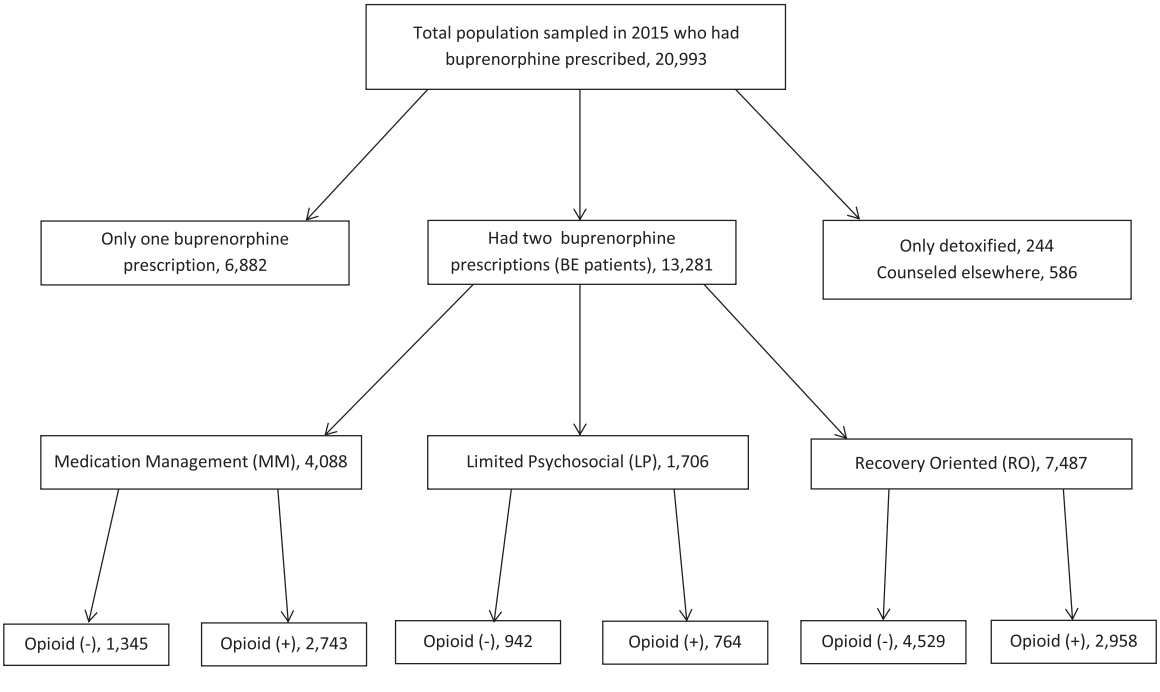

FIGURE 1. Patients who had a urine toxicology positive for buprenorphine. BE = buprenorphine episode.

TABLE 2. Patients studied who had a buprenorphine positive urinalysis in 2015

Characteristics	Medication management (MM)[a]	Limited psychosocial (LP)[b]	Recovery oriented (RO)[c]	χ^2/F	*P* value	Cohen's *hld*		
						MM vs LP	LP vs RO	MM vs RO
New at first buprenorphine screen								
With buprenorphine episode	1738 (42.5%)	829 (48.6%)	3281 (43.8%)	18.35	<.001	−0.12	0.1	−0.03
Without buprenorphine episode	698 (36.2%)	319 (37.5%)	1035 (25.2%)	102.5	<.001	−0.03	0.27	0.24

[a] $\chi^2 = 21.8$; $P < .001$; Cohen's $h = 0.13$.
[b] $\chi^2 = 28.32$; $P < .001$; Cohen's $h = 0.22$.
[c] $\chi^2 = 391.89$; $P < .001$; Cohen's $h = 0.39$.

facilities, 56% (N = 961) for LP facilities, and 62% (N = 4642) for RO facilities ($X^2 = 849.55$, $P < .001$). A post hoc analysis revealed that there was a significant difference between LP and RO, $X^2(1) = 18.77$, $P < .001$, indicating that RO programs had the highest portion of patients who had urine drug tests free of opiates at the time of the second toxicology of the BE.

As indicated in Table 1, a comparison was made between patients who had no previous urine drug test at the facility at the time of the first buprenorphine prescription to those who previously had a urinalysis performed. During that time, some patients may have had buprenorphine prescribed before their BE was initiated in 2015, while others may not have had buprenorphine prescribed prior to that period. The facilities for which there was a difference in secondary opioid use between those patients with prior urine drug tests and those with none were the RO facilities (42%-32%, a 24% difference) compared with MM (68%-64%, a 6% difference) and LP (45%-42%, a 7% difference). The decrease in urinalyses positive for secondary opioids during the interval from the period before the BE to the first buprenorphine of the BE period itself was measured. Patients in RO facilities showed a greater decrease than the MM and LP facility types in secondary opioids during this interval. This suggests that RO patients may improve more than the MM and LP patients from their first appearance at the facilities. Table 2 gives a comparison for MM, LP, and RO of patients with and without a BE for their recency of arrival at the respective facilities. It includes statistical comparisons both across and (within the footnotes) within the three facilities. The former facilities typically include increased counseling involvement with an orientation toward a 12-step-based recovery.

DISCUSSION

The relative adherence by patients to pharmacotherapeutic regimens is an issue of concern broadly in medical practice.[6] One report published by the World Health Organization provided an estimate that adherence rates in developed countries to pharmacotherapies overall averaged only about 50%.[7] Causes for poor adherence may include patient-related factors, such as lack of motivation, inadequate involvement in the treatment decision-making process,[8] and, in the case of opioid treatment, it may be even more compromised. Doctor-patient communication can be compromised by denial of illness.[9]

The marked increase in opioid-related deaths in recent years has led to an appreciation of the need for medication-assisted treatment (MAT).[10] When buprenorphine was approved for the treatment of opioid use disorders in 2000, it was stipulated that practitioners should have the capacity to refer patients for appropriate counseling.[11] Federal guidelines posited that patients should have "reasonable access" to counselors to receive counseling services.[11] More specifically, This points to the presumed importance of the availability of attendant

counseling to stabilize the recovery of opioid-dependent patients. This also relates to avoiding misuse of secondary opioids during ongoing buprenorphine treatment.

The outcome of buprenorphine treatment can vary depending on factors apparently independent of counseling services. In one report, the outcome of short-term buprenorphine treatment (16 weeks) with MM alone yielded a better outcome for patients with prescription opioid misuse if they had no history of concomitant heroin use than if they had used heroin as well.[12] A difference is also observed when different buprenorphine preparations were compared; adding of naloxone to buprenorphine resulted in less likelihood of patients injecting or diverting the buprenorphine.[13] Additionally, patients given buprenorphine implants were found to have less frequent secondary opioid use.[14]

There may be limitations in the degree to which added counseling can yield an increment of improvement. Feillin et al[15] reported that over a period of 6 months of treatment, once weekly buprenorphine dispensing along with manualized medical management was found to be as effective as more frequent dispensing or extended weekly counseling. Furthermore, inferences based on unobserved home induction onto buprenorphine have been found to be problematic, as randomization of patients either to other treatments, the intensity of psychosocial services or patient characteristics were not preformed.[16] Weiss et al[17] found that adding counseling to medical management in a 12-week maintenance period did not improve on the outcome of MM alone, but better outcomes were found for those patients who did attend added counseling. A lack of benefit was found with the addition of either cognitive-behavioral therapy or contingency management in a 16-week medically managed maintenance regimen.[18]

On the contrary, there are studies that reflect on the incremental benefit of added counseling in certain circumstances. In relation to opioid detoxification, a Cochrane review[19] revealed that when psychosocial treatments were offered in addition to pharmacologic intervention, clinical outcome was improved. For longer periods of maintenance, there are some studies showing benefits in a particular format for counseling. One retrospective study found better retention when patients who were veterans were counseled in a group format rather than individually.[20] Additionally, when heroin addicts attended drug counseling in addition to MM, they did better than those who received MM and did not attend the sessions.[21] One analysis of cost in care-integrated health systems by Lynch et al[22] revealed that the addition of counseling to buprenorphine treatment reduced the use of medical visits and emergency services. Furthermore, improved access to counseling along with buprenorphine maintenance has been found to be useful in some settings, such as primary care.[2] In one study of private practice, 58% of buprenorphine patients reported receiving adjunctive counseling and 75% of the patients were judged to have a positive outcome.[23] Controlled studies on the issue of counseling are limited in conclusive outcome. Such studies, however, do not specify the randomization or type of counseling provided. Carroll and Weiss[24] undertook a review of randomized controlled studies on the relative efficacy of concomitant behavioral interventions, and recommended that physicians consider a stepped care model in which patients can be initiated with relatively non-intensive treatment, with the option of increasing counseling intensity as clinically needed.

Another issue is that medically assisted treatment may not be fully accessible across clinical settings. One recent survey of administrators in privately funded substance abuse treatment organizations revealed that MAT for opioid dependence had been adopted only in 34% of drug treatment programs.[1] This is particularly relevant, since counseling services as part of MAT might become more difficult to sustain relative to the number of patients that practitioners maintain on buprenorphine at any given time, given the fact that the ceiling on buprenorphine patients in treatment by a given physician had been raised from 100 to 275. An increase in patient loads may limit the time for arranging relevant counseling. Additionally, nurse practitioners and physician assistants can now prescribe buprenorphine as well, thereby adding to the volume of patients prescribed for.

The analysis of pharmacy claims, but not patient records, by Daubresse et al[5] drew on organized, individual-level, all player pharmacy claims to identify incident users of buprenorphine who filled an opioid prescription during a buprenorphine treatment episode. This was done to ascertain the portion of patients who filled an opioid prescription both during (43%) and after (67%) the treatment episode. (No distinction was made as to the clinical settings where prescriptions were given.) There is, however, utility in quantifying the degree of inappropriate use of opioids, including illicit opioids, concomitant with buprenorphine use, relative to the character of community-based treatment settings. This can be useful clinically, in understanding the relative role of different levels in adjunctive counseling support for medically assisted treatment.

We are reporting on urine drug test results restricted to samples collected when the clinician had prescribed buprenorphine. Urine drug tests for all opioids can lend some clarity to the ecology of buprenorphine use in community settings. There is a literature on misuse of buprenorphine internationally, particularly when it is not combined with naloxone (to prevent self-injection).[25,26] In the United States, use of buprenorphine to get "high" was reported in one study by 30% to 35% of patients applying for opioid treatment.[27] In another study, 46% of physicians certified for prescribing buprenorphine were aware of it being sold on the street.[28]

The patients studied here are in some measure of active treatment, and the buprenorphine was prescribed by treating physicians. Additionally, involvement in treatment is likely for many of the patients. The mean interval between the two

buprenorphine urinalyses of the BE was 1.47 months, although the SD of 2.97 suggests considerable variability in frequency of the buprenorphine dosing for different community-based patients. The BEs studied were not typically ones that were for patients new to the facilities; since considerable time had passed since the very first urine drug test recorded for many of them at the respective facilities, a mean of 7.36 months. Furthermore, the fact that the patients had agreed to provide urine samples, suggests a measure of engagement. Nonetheless, it is of note, that in all three facility types, about one-third of patients did not have a second prescription for buprenorphine during the 18-month period studied, suggesting that for a significant portion of facility patients there was a lack of active, ongoing buprenorphine management, and benefit from the medication among them may be limited. The majority of patients had a significant difference across facility types as to whether urine samples were negative for other opioids, with the RO facilities showing the largest portion negative for other opioids, with the RO facilities showing the largest portion negative and the MM and LP facilities the smallest.

Table 2 shows the relative portion of patients who were new to the facilities for MM, LP, and RO. A smaller portion of RO patients without a BE was likely to be new to the facility. It is possible that RO facilities treated patients with buprenorphine sooner after arriving at the facility, that is, when they were relatively newer to the clinic. The data reported in this table also underline the significance of the sizeable number of patients who are prescribed one dose of buprenorphine without receiving a second dose within 18 months. Findings such as these also illustrate the multiplicity of variables that reflect on the difficulty of drawing inferences from community-based data. Nonetheless, the large numbers of persons being prescribed buprenorphine in the community is important. This is because it reflects the actuality of the medication's impact on the effectiveness of treatment in the diversity of treatment facilities that are currently addressing the high prevalence (colloquially, epidemic) of opioid use disorder.

There was, however, less opioid positivity among patients with previous records of urine drug tests in the facilities (ie, had previous evidence of enrollment in the facility) than ones who had no previous urine drug tests (ie, no evidence of previous enrollment in the facility). There was no difference between the longer-term and newer enrollees for the MM and LP patients (3% and 7%, respectively), but a sizable difference for the RO patients (23%). This suggests that the RO patients may receive greater benefit over time. It would therefore appear that the patients in facilities that offered the more active counseling, including those with a 12-step orientation, may be more likely to see a decline in the use of opioids after buprenorphine dosing. In an early study by Gossop et al[29] the frequency of 12-step attendance was associated with an enhanced outcome following inpatient opioid treatment. This is compatible with the findings of Weiss et al[30] in their cohort of patients dependent on prescribed opioids in a long-term follow-up, where mutual-help group attendance was independently associated with opioid abstinence.

Limitations

Community-based data may vary considerably from findings in well-controlled studies,[31] but the role of a medication like buprenorphine in the community may be particularly difficult to ascertain. We have attempted here to characterize the role of buprenorphine in a sample of 573 such treatment settings by employing data on urine drug tests conducted there. While useful in approximating the role of buprenorphine among patients being treated, this methodology is subject to certain limitations.

We have characterized facilities based on a description of the counseling applied. Certain data were not available, in particular, doses of buprenorphine prescribed. These may vary considerably across facilities and would bear on outcome. This would require further research in characterizing this important variable. The indications for referral to the facilities, the nature of patients' opioid use, and the socioeconomic status of patients as well were not evaluated. Other issues are important, as well, such as patient demographics, secondary psychiatric and general medical diagnoses, patients' possible attendance at other clinical settings, and misuse of other drugs.

Another limitation is the way a "buprenorphine episode" is characterized. Neither the continuity of treatment nor the possibility of an intervening period of inpatient care between the buprenorphine prescriptions were ascertained. Additionally, our data do not address the overall duration of treatment with buprenorphine, as there is a wide variability in retention rates across different studies,[32] and insurance benefits can also impact on retention.[33] Future studies on community-based treatment should, therefore, best include an analysis of physician reporting and patient demographics, as has been done for general pharmacotherapies.[34] The indications for referral to the facilities, socioeconomic status of patients, and recovery-oriented services patients actually accessed, were not evaluated. Important, as well, is an understanding of which modalities of psychosocial treatment are most effective, and at what "dose" these should be applied. We only characterized facilities' format, rather than classifying treatment by specifics of modalities applied.

Although the recovery-oriented facilities' urine drug tests suggest a treatment outcome more positive than the ones in the MM and limited psychosocial settings, any of the above factors may be biasing any conclusive inferences regarding an apparent benefit from the enhanced availability of a 12-step orientation and the multiple modalities applied in the RO settings. It may also be that the volume of counseling is a determining factor in outcome. The RO facilities typically include a 12-step orientation, but the relative role of this approach, as opposed to more time invested in counseling was not evaluated. To date, studies of large samples of

community-based patients on opioid medication assisted treatment typically do not have access to all such patient information. This is either because of a lack of systematic recording of this clinical information in facility records, or the unreliability of facilities' data collection. This problem pertains to other studies on treatment outcome with large databases of community-based buprenorphine prescribing, for example, studies published on pharmacy records,[5] criminal justice,[35] changes in the choice of formulary preparation,[36] and veteran samples.[37] The importance of further access to such information points to the need for systematic and retrievable record-keeping to facilitate further research on treatment outcome in community-based populations.

We acknowledge these limitations but present our findings here in order to introduce issues that are pertinent to community-based treatment of opioid use disorder. Facilities like those studied here represent the majority of settings that provide buprenorphine for opioid use disorder, conducted without the controls and formal protocols applied in published structured studies. Similarly, the study by Daubresse et al[5] presents prescription data without reference to specific modalities applied. Limitations described here therefore point to other areas that need to be further evaluated for community treatment of this major public health problem.

CONCLUSION

In this study sample, it is notable that many patients (a third of those studied here) did not get a second prescription of buprenorphine from the facility at all during a follow-up period of at least 18 months, reflecting a significant deficit in the utility of the medication for long-term care in those settings. This reflects the difficulty in collecting data from all patients in this study design. However, when a second prescription is given, it appears that regimens of buprenorphine-based medication-assisted treatment with extensive counseling oriented to addiction recovery and a 12-step orientation may be associated with a more positive outcome. Nonetheless, a variety of clinical confounds bear on this observation, and these need to be studied further.

In any case, it is clear that the outcome of buprenorphine treatment can vary considerably across different clinical settings, and can vary as well, depending on the particular clinical modalities applied. This suggests that it would be valuable for research to be conducted on clinical outcome relative to the counseling practices in community-based opioid treatment facilities, not only treatment effectiveness observed in well-controlled settings. From a broader health perspective, this is also important in terms of determining the actual outcome of the buprenorphine based treatment in the population overall.

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Declaration of Interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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