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ORIGINAL ARTICLE

Changes in transmucosal buprenorphine utilization for opioid use disorder treatment during the COVID-19 pandemic in Kentucky

Feitong Lei MPH[1] | Michelle R. Lofwall MD[2,3] | Patricia R. Freeman PhD[3,4] | Emily Slade PhD[1] | Rachel Vickers-Smith PhD[5] | Svetla Slavova PhD[1,6]

[1]Department of Biostatistics, College of Public Health, University of Kentucky, Lexington, Kentucky, USA

[2]Department of Behavioral Science and Psychiatry, University of Kentucky, Lexington, Kentucky, USA

[3]Center on Drug and Alcohol Research, University of Kentucky, Lexington, Kentucky, USA

[4]Department of Pharmacy Practice and Science, University of Kentucky, Lexington, Kentucky, USA

[5]Department of Epidemiology, College of Public Health, University of Kentucky, Lexington, Kentucky, USA

[6]Kentucky Injury Prevention and Research Center, University of Kentucky, Lexington, Kentucky, USA

Correspondence
Svetla Slavova, Department of Biostatistics, College of Public Health, University of Kentucky, Healthy Kentucky Research Building RB2, Office 261, 760 Press Ave, Lexington, KY 40536, USA.
Email: ssslav2@uky.edu

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Abstract

Purpose: With surging opioid-involved overdoses, maintaining access to opioid use disorder (OUD) treatment is critical during the COVID-19 pandemic. We examined changes in transmucosal buprenorphine prescribing for OUD treatment in Kentucky after the national COVID-19 emergency declaration, with a focus on rural-urban differences.

Methods: Using 2019-2020 prescription monitoring data, we performed segmented regression analysis for an interrupted time series design to evaluate changes in weekly rates (per 100,000 residents) of dispensed prescriptions, unique individuals with dispensed prescriptions, and average days' supply for dispensed prescriptions of transmucosal buprenorphine.

Findings: The weekly rates of dispensed prescriptions and unique individuals with dispensed prescriptions were higher for rural residents than urban residents. After the national COVID-19 emergency declaration, rural and urban residents experienced similar immediate drops in the rate of dispensed prescriptions (rural −33.4; urban −24.3) and unique patients with dispensed prescriptions (rural −25.0; urban −17.1), followed by similar sustained increases. Both measures surpassed the prepandemic levels in mid-June 2020. Patients residing in urban areas received averagely longer prescriptions at baseline (urban: 11.0 days; rural: 10.5 days). The average weekly days' supply increased in the week after the national emergency declaration, but the estimated increase was higher ($P = .004$) for urban (0.8 days) versus rural (0.5 days) residents.

Conclusions: Transmucosal buprenorphine utilization increased during the COVID-19 pandemic after experiencing interruption during the initial weeks of the pandemic. Future studies should evaluate the contribution of the relaxed telemedicine buprenorphine prescribing regulations during the COVID-19 national emergency on initiation and maintenance of buprenorphine treatment.

KEYWORDS
buprenorphine, COVID-19 pandemic, interrupted time series, opioid use disorder, rural-urban difference

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INTRODUCTION

Opioid-involved overdoses have surged during the coronavirus disease 2019 (COVID-19) pandemic.[1–4] This is often due to untreated opioid use disorder (OUD), despite the fact that there are effective medication treatments for OUD that decrease mortality.[5–8] To help prevent opioid-related mortality, it is critical to provide low-barrier and continuous access to medication treatment for opioid use disorder (MOUD). Buprenorphine is one of the 3 medications approved by the US Food and Drug Administration (FDA) to treat OUD and has been shown to significantly reduce all-cause and opioid-related mortality.[5–8] Although the utilization of buprenorphine treatment, primarily the transmucosal (TM) formulations, has increased since its FDA approval in 2002, there remain substantial barriers to availability and access, with majority of persons with OUD never receiving MOUD.[6,9]

On March 13, 2020, the COVID-19 outbreak was declared a national emergency in the United States, with most states enacting stay-at-home orders and recommendations for postponement of elective medical procedures.[10–12] To prevent disruptions in treatment for OUD, the US Drug Enforcement Administration (DEA), Substance Abuse and Mental Health Services Administration (SAMHSA), and other federal agencies adopted policies to provide flexibility in the prescribing of buprenorphine, a Schedule III medication.[13,14] On March 16, 2020, the secretary of Health and Human Services partnered with the DEA to temporarily suspend the in-person visit required by the Ryan Haight Act for initiation of all Schedule II-V controlled substances,[13,15] thereby allowing buprenorphine to be initiated via telemedicine using audio and video technology. To promote even more flexibility in buprenorphine access, particularly for new patients, on March 31, 2020, the DEA authorized qualified practitioners to initiate buprenorphine after conducting an initial evaluation via telephone (no video requirement).[14]

Prior to the COVID-19 pandemic, there were notable disparities in buprenorphine treatment availability between people living in urban and rural areas.[16–21] Of the 36% of US counties that have a high need for OUD treatment, 61% are in rural areas.[16] However, a 2021 study reported that about one third of all rural US counties and more than half of small and remote rural counties did not have buprenorphine waivered providers.[18] The utilization of telemedicine during the pandemic may diminish the existing rural-urban disparities;[22] however, there were concerns that the expansion of telemedicine use could actually increase disparities for rural populations who may have more limited access to digital technology compared to urban populations.[23] Fortunately, policies issued during the COVID-19 pandemic that authorized buprenorphine treatment initiation via telephone provided an opportunity to improve access to treatment in rural areas.[14,24]

Previous studies have investigated state- or national-level trends in the use of buprenorphine before and after the implementation of the COVID-related prescribing policies,[25–31] using mostly commercial insurance data that do not include patients with Medicaid or uninsured patients.[25,27–29] These patients reportedly represent more than half of American adults with OUD.[32] Further, while there are well-documented rural-urban differences in the trends of buprenorphine treatment for OUD prior to the COVID-19 pandemic, this topic has not been well-studied during the pandemic. Investigating the rural-urban difference is critical for understanding how COVID-19-related buprenorphine initiation policies may have impacted OUD treatment inequities, and for informing discussions around policy sustainability.

The primary goals of this study were to examine the possible disruptions in TM buprenorphine prescribing for OUD treatment related to the COVID-19 national emergency and to examine rural-urban differences in changes of prescribing trends from prior to during the pandemic in Kentucky. Kentucky has been particularly affected by the opioid crisis. Eastern Kentucky was among the first geographic areas targeted for promotion of OxyContin® (Semi-synthetic opioid drug) in the 1990s, which was an integral piece of the national opioid crisis.[33] Kentucky has historically ranked among the top 5 states with the highest age-adjusted drug overdose mortality.[34,35] In 2020, the provisional Kentucky drug overdose death rate indicated a 45% increase from 2019, with significant increases across all demographic groups.[36]

Using statewide prescription drug monitoring program data, which includes dispensed prescriptions from all payor sources, we evaluated statewide and urban/rural trends of TM buprenorphine prescribing for OUD in Kentucky from 2019 to 2020 to estimate if there were any abrupt changes associated with the COVID-19-related national emergency declaration, as well as to compare the rural-urban differences in changes of prescribing trends.

METHODS

Data sources

Data were extracted from the Kentucky All Schedule Prescription Electronic Reporting (KASPER) program from January 1, 2019, to December 31, 2020.[37] KASPER includes information on all dispensed controlled substances (Schedule II-V) from pharmacies and other dispensers in Kentucky regardless of payor source. Prescription-level records for dispensed TM buprenorphine products approved by the FDA for the treatment of OUD were identified via National Drug Codes linked with Medi-Span Generic Products Identifiers.[38] Every individual who received a TM buprenorphine prescription was categorized as a resident from an urban or rural area, based on their resident address ZIP code as submitted by the dispenser to KASPER, using the 2010 Rural-Urban Commuting Area (RUCA) codes.[39] RUCA codes are a classification to categorize the rurality status and commuting relationships to other areas for all census tracts, based on population density, level of urbanization, and commuting. Prescriptions for individuals residing outside of Kentucky were excluded.

Measures

We considered 3 weekly outcome measures for TM buprenorphine prescribing: (1) number of dispensed prescriptions, (2) number of unique individuals with dispensed prescriptions, and (3) average days' supply for dispensed prescriptions. To compare rural versus urban area trends, we analyzed the first 2 outcomes as rates (per 100,000 residents); rates were not needed to compare rural-urban trends for the third outcome.

Weeks were defined with Monday being the first day of the week. The first week of 2019 (from January 1, 2019, to January 6, 2019) and the last week of 2020 (from December 28, 2020, to December 31, 2020) contained less than 7 days. To ensure consistency when calculating the weekly outcome measures, the observations for these 2 incomplete weeks were excluded. There were 103 weeks in the final study period, from January 7, 2019, to December 27, 2020.

In line with previous studies,[40,41] residency status was classified as urban (RUCA codes 1-5) or rural (RUCA codes 6-10). There were 1,476 (0.067%) prescriptions for Kentucky residents that failed to be classified as rural-urban based on the listed ZIP code, either due to data entry error or failure of linkage. These records were excluded from rural-urban analyses. When calculating the number of unique individuals with dispensed prescriptions stratified by rural-urban residency, if an individual had prescriptions with different ZIP codes within a period, we used data from the most recent prescription reported to KASPER to identify rural-urban classification. Using the earliest prescription within a period, recalculated number of unique individuals with dispensed prescriptions stratified by rural-urban residency was used in a sensitivity analysis, aiming to explore if any inconsistencies in the reported patient address would change the results and the interpretation of the study findings.

Statistical analysis

An interrupted time series (ITS) design was implemented because the COVID-19 national emergency declaration and related circumstances were considered a possible interruption to the existing trends of buprenorphine prescribing for OUD treatment.[42–44] The week after the national emergency declaration, that is, the week of March 16, 2020, was considered the "index week," which is the first week of the COVID-19 national emergency period in the United States. In this study, the period before the index week was called the "prepandemic period," and the period starting from the index week was called the "pandemic period." A segmented regression with an autoregressive error model was used to assess changes in the trends for each study outcome from the prepandemic to the pandemic period.[44] We performed single ITS analyses to estimate the changes in the statewide buprenorphine prescribing and performed comparative ITS analyses to explore rural-urban differences.[45]

Upon initial inspection of the outcome measures, we observed notable drops in the weekly number of prescriptions and number of unique individuals being prescribed TM buprenorphine during the weeks of Thanksgiving and Christmas, as well as notable increases in the average days' supply for the prescriptions dispensed during the weeks preceding the 2 holidays. This phenomenon reflects the normal dynamic of patient care around these holidays. To isolate the effect of these holiday weeks on the associations of interest, an indicator variable for each of these 2 holidays was included in the regression models. When modeling the number of dispensed prescriptions or the number of unique individuals with a dispensed prescription, the 2 indicators had a value of 1 for the weeks of Thanksgiving and Christmas, respectively, and a value of 0 otherwise. When modeling the average days' supply for the prescriptions dispensed, the 2 indicators had a value of 1 for the week before Thanksgiving and the week before Christmas, respectively, and a value of 0 otherwise. The following models were used in the study:

1) Single ITS analysis:

$$Y_t = \beta_0 + \beta_1 * Week + \beta_2 * Emergency + \beta_3 * Week\_after\_Emergency + \beta_4 * Thanksgving + \beta_5 * Christmas + e_t$$

2) Comparative ITS analysis:

$$\begin{aligned} Y_t = \beta_0 &+ \beta_1 * Week + \beta_2 * Emergency + \beta_3 * Week\_after\_Emergency \\ &+ \beta_4 * Thanksgving + \beta_5 * Christmas + \beta_6 * Rural + \beta_7 * Rural * Week \\ &+ \beta_8 * Rural * Emergency + \beta_9 * Rural * Week\_after\_Emergency + e_t \end{aligned}$$

In both models, Y_t is the outcome measure in week *t; Week* is the week number, taking values from 0 (for the week of January 7, 2019) to 102 (for the week of December 21, 2020); *Emergency* is an indicator variable representing whether the COVID-19 outbreak had been declared a national emergency (ie, 0 before the index week; 1 otherwise); *Week_after_Emergency* is a numerical variable indicating the time in weeks after the declaration (0 before the index week; takes value from 1 [for the index week] to 41 [last week of the study period]); *Thanksgiving* and *Christmas* are binary variables indicating the holiday weeks. In the comparative ITS model, *Rural* is equal to 0 for residents in urban areas and 1 for residents in rural areas. The residents in urban areas were treated as the reference group in the comparative ITS analysis. *Rural* Week*, *Rural*Emergency*, and *Rural* Week_after_Emergency* are interaction terms among previously described variables. The error term, e_t, represents the random variability, which is not explained by the model at week *t*. The error term consists of 2 parts: a normally distributed random error and an error term at time *t*, which could be correlated to errors at time points before time *t*.[42]

Our primary interest is the effect of the COVID-19 national emergency on the established trend of each study outcome measure. This effect could be described as (1) an abrupt effect (also called *level change*β_2) and (2) a sustained effect (called *trend change*β_3). The estimated value of $\beta_2$is interpreted as an immediate effect of the COVID-19 national emergency on the level of an outcome measure. The estimated value of β_3 represents the difference between the slope of the

TABLE 1 Summary statistics for weekly outcome measures for transmucosal buprenorphine prescribing for treatment of opioid use disorder from the prepandemic period (January 7, 2019-March 15, 2020) to the COVID-19 pandemic period (March 16, 2020-December 27, 2020) in Kentucky overall and stratified by rural-urban status

	Prepandemic period	Pandemic period
Weekly outcome measures	**Mean (SD)**	**Mean (SD)**
Number of dispensed prescriptions		
State	20,830.5 (1,065.8)	21,895.1 (1,237.8)
Urban areas	12,098.3 (595.8)	12,694.0 (692.8)
Rural areas	8,719.5 (487.1)	9,187.5 (545.2)
Number of dispensed prescriptions per 100,000 residents		
State	467.5 (23.9)	491.4 (27.8)
Urban areas	344.3 (17.0)	361.3 (19.7)
Rural areas	929.5 (51.9)	979.4 (58.1)
Number of unique individuals with dispensed prescriptions		
State	18,908.1 (988.2)	20,513.5 (1,103.9)
Urban areas	10,907.5 (572.4)	11,897.8 (629.1)
Rural areas	7,988.5 (433.7)	8,599.7 (482.4)
Number of unique individuals with dispensed prescriptions per 100,000 residents		
State	424.4 (22.2)	460.4 (24.8)
Urban areas	310.4 (16.3)	338.6 (17.9)
Rural areas	851.6 (46.2)	916.7 (51.4)
Average days' supply for dispensed prescriptions		
State	11.2 (0.4)	12.3 (0.3)
Urban areas	11.6 (0.4)	12.9 (0.3)
Rural areas	10.7 (0.3)	11.4 (0.3)

Abbreviation: SD, standard deviation.

regression line for the pandemic period and the slope of the regression line for the prepandemic period.

All analyses were conducted with SAS® Enterprise Guide version 8.3 (SAS Institute Inc., Cary, NC), using the AUTOREG procedure to implement regression models with autocorrelated errors.[46] The Durbin-Watson statistic was utilized to check for serial autocorrelations of the residuals. Diagnostic plots generated by the AUTOREG procedure were used to check model assumptions and fit. Statistical significance was set a priori as 2-sided P values <.05. Parameter estimates and 95% confidence intervals (CIs) are reported. This study was approved by the University of Kentucky Institutional Review Board.

RESULTS

From January 7, 2019, to December 27, 2020, a total of 2,189,296 eligible prescription-level records of TM buprenorphine products for OUD were extracted. Overall, the means for all weekly outcome measures increased from the prepandemic period to the pandemic period (Table 1). Statewide, there was a 5% increase in the average weekly number of dispensed prescriptions (from 20,831 to 21,895; Table 1), an 8% increase in the average weekly number of unique patients (from 18,908 to 20,514; Table 1), and a 10% increase in the mean days' supply for dispensed prescriptions averaged across weeks (from 11.2 to 12.3; Table 1). When stratified by rural-urban residency, the increases in corresponding outcome measures were similar to those observed statewide (Table 1). During the study period, the weekly rates (per 100,000 residents) of dispensed prescriptions and unique individuals with dispensed prescriptions were approximately 2.5 times higher for rural residents than urban residents. For example, during the pandemic period, the average weekly rate of unique individuals with dispensed prescriptions was 916.7 in rural versus 338.6 in urban areas (Table 1). Patients in urban areas received dispensed prescriptions with a longer days' supply than patients in rural areas (Table 1).

Weekly number of dispensed buprenorphine prescriptions

The weekly number of dispensed buprenorphine prescriptions decreased immediately after the COVID-19 emergency declaration,

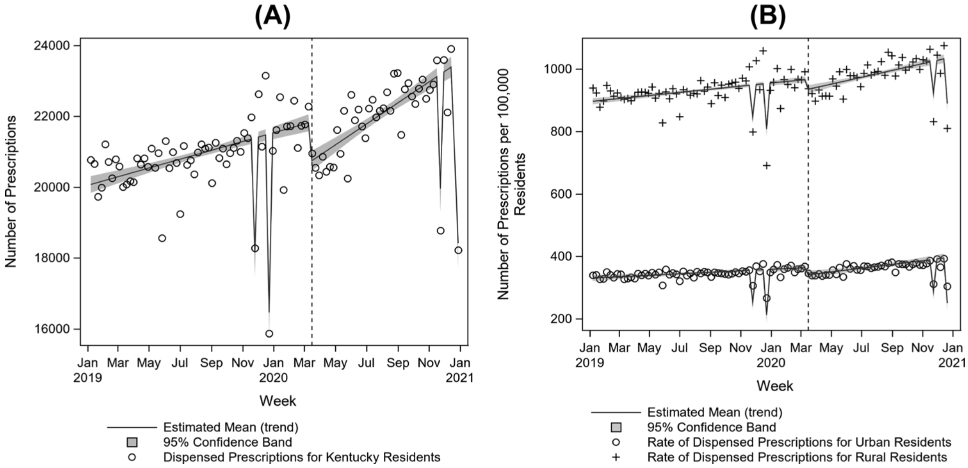

FIGURE 1 (A) Weekly number of dispensed transmucosal buprenorphine prescriptions for the treatment of opioid use disorder (OUD) for Kentucky residents, January 7, 2019-December 27, 2021. (B) Weekly rate (per 100,000 residents) of dispensed transmucosal buprenorphine prescriptions for the treatment of OUD, by rural/urban residency status of the patient, January 7, 2019-December 27, 2021. The dotted vertical lines represent the week of March 16, 2020, the first week after COVID-19 was declared a national emergency on March 13, 2020

but after a few weeks, this measure rebounded and even exceeded the prepandemic levels statewide (Figure 1A), as well as for urban and rural residents (Figure 1B). Fewer prescriptions were dispensed during the weeks of Thanksgiving and Christmas, which reflects the normal dynamic of patient care during this time of the year (Figure 1 and Table S1).

During the first week of the prepandemic period (the week of January 7, 2019), an estimated 20,078 TM buprenorphine prescriptions were dispensed in Kentucky. Compared with the prepandemic level (the estimated number of prescriptions in the last week of the prepandemic period; the week of March 9, 2020), the level of dispensed prescriptions dropped significantly by 1,133.9 prescriptions (CI: −1,521.5 to −746.2) in the week after the COVID-19 emergency declaration (Table 2). We estimated a significant weekly increase (prepandemic slope) of 28.5 prescriptions (P<.001) in the prepandemic period. The estimated slope for the weekly number of dispensed TM buprenorphine prescriptions during the pandemic was significantly higher than the prepandemic slope by an additional 39.3 prescriptions per week (CI: 24.1-54.4). Figure 1A shows that by early June 2020, the weekly number of dispensed TM buprenorphine prescriptions returned to, and subsequently passed, the prepandemic level.

The segmented regression analysis for the comparative ITS showed immediate decreases in prescription rates, for patients in both urban and rural areas, in the week after the emergency declaration (level changes: rural −33.4, CI: [−51.5 to −15.4]; urban −24.3, CI: [−42.5 to −6.1]; Table 3 and Table S1). The slopes of the weekly dispensed prescription rates for patients in both urban and rural areas during the pandemic period were significantly higher than those before the pandemic (urban trend change: estimated increase of 0.8 prescriptions per 100,000 residents per week [P = .014]; rural trend change: estimated increase of 1.3 prescriptions per 100,000 residents per week [P<.001]). The rural and urban trend changes were comparable (P = .253).

Weekly number of unique individuals with dispensed prescriptions

As shown in Figure 2A and B, there were declines in the weekly number of unique individuals with dispensed TM buprenorphine prescriptions during the first few weeks after the emergency declaration, but afterward, the growth during the pandemic was steeper than before the pandemic, overall and stratified by rural-urban residency. Results obtained from the sensitivity analysis, using the address from the first prescription in a study week to classify patients' residency as rural or urban, were similar to those based on the last prescription in the study week.

There was a drop (level change: −750.3; CI: −1,122.8 to −377.9) in the number of unique individuals with dispensed TM buprenorphine prescriptions in the week after the emergency declaration (Table 2). However, the estimated average weekly increase in unique individuals in treatment during the pandemic was 30.7 patients per week higher than that before the pandemic (P<.001). The estimated slope during the pandemic period was 65.3 (prepandemic slope 34.6 + trend change 30.7; Table 2) additional unique patients every week. Based on the segmented regression model, we estimated that 20,106 unique individuals received TM buprenorphine prescriptions in the week of June 1, 2020, thus exceeding for first time the estimated prepandemic level (n = 20,073).

Results from the comparative ITS analyses showed significant immediate drops in the rate of unique individuals with dispensed TM buprenorphine prescriptions in the week after the COVID-19 emergency declaration (level change urban: −17.1 [CI: −32.9 to −1.4]; rural: −25.0 [CI: −40.7 to −9.4]) (Table 3, Table S1, and Figure 2B). For patients in both urban and rural areas, the changes in the average weekly rates during the pandemic period were both significantly higher than those before the pandemic (trend change urban: 0.6, P = .032; rural: 1.2,

TABLE 2 Parameter estimates for segmented regression analysis of weekly transmucosal buprenorphine prescribing for opioid use disorder in Kentucky from the prepandemic period (January 7, 2019-March 15, 2020) to the COVID-19 pandemic period (March 16, 2020-December 27, 2020)

	Number of dispensed prescriptions per week		Number of unique individuals with dispensed prescriptions per week		Average days' supply per dispensed prescription per week	
Parameter estimates	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value	Estimate (95% CI)	*P*-value
Prepandemic intercept[a]	20,077.7 (19,845.8, 20,309.7)	<.001	17,960.2 (17,747.4, 18,172.9)	<.001	10.8 (10.7, 10.9)	<.001
Prepandemic slope[b]	28.5 (21.5, 35.5)	<.001	34.6 (28.5, 40.8)	<.001	0.01 (0.01, 0.02)	<.001
Level change after the COVID-19 National Emergency Declaration[c]	−1,133.9 (−1,521.5, −746.2)	<.001	−750.3 (−1,122.8, −377.9)	<.001	0.6 (0.5, 0.8)	<.001
Trend change[d]	39.3 (24.1, 54.4)	<.001	30.7 (17.1, 44.2)	<.001	−0.01 (−0.02, 0.00)	.013
Thanksgiving holiday	−3,228.7 (−3,911.7, −2,545.6)	<.001	−2,868.4 (−3,520.9, −2,215.8)	<.001	0.6 (0.4, 0.9)	<.001
Christmas holiday	−5,036.1 (−5,750.9, −4,321.4)	<.001	−4,254.6 (−4,932.7, −3,576.6)	<.001	1.2 (0.9, 1.5)	<.001

Note: The COVID-19 National Emergency Declaration was issued on March 13, 2020. The week after the national emergency declaration (the week of March 16, 2020) defines the prepandemic and pandemic periods in our segmented regression analysis.
Abbreviation: CI, confidence interval.
[a]Outcome measure at baseline (the week of January 7, 2019).
[b]Average weekly change in the outcome measure before the COVID-19 pandemic.
[c]Immediate change in the level of the outcome measure from the prior segment.
[d]Change in the slope of the outcome measure during the pandemic period compared to the slope before the pandemic. The slope of the regression line during the pandemic period can be calculated as the prepandemic slope + the trend change.

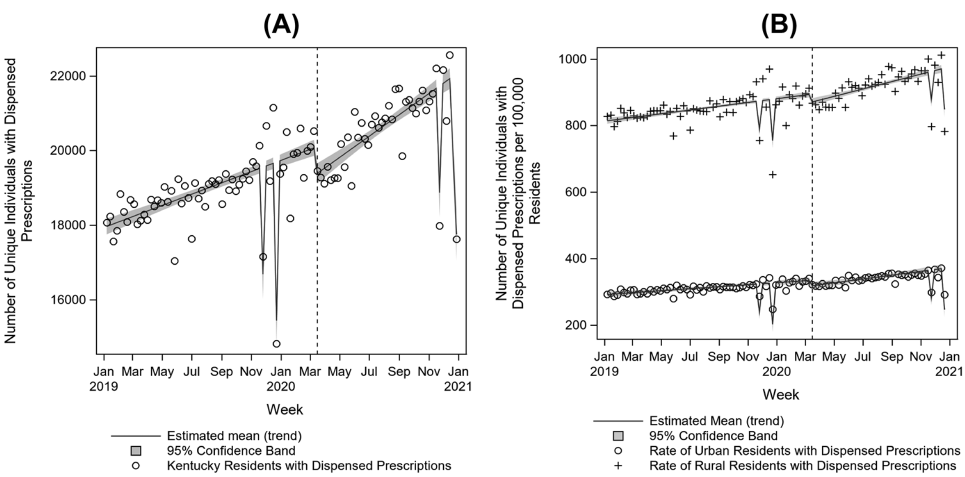

FIGURE 2 (A) Weekly number of unique Kentucky residents with dispensed transmucosal buprenorphine prescriptions for treatment of opioid use disorder (OUD), January 7, 2019-December 27, 2021. (B) Weekly rate of unique Kentucky residents with dispensed transmucosal buprenorphine prescriptions for treatment of OUD (per 100,000 residents), by rural/urban resident status, January 7, 2019-December 27, 2021. The dotted vertical lines represent the week of March 16, 2020, the first week after COVID-19 was declared a national emergency on March 13, 2020

P<.001; Table 3). There were no significant rural-urban differences in level changes (*P* = .449) or the trend changes (*P* = .121; Table 3).

Weekly average of the days' supply of dispensed prescriptions

The weekly average of the days' supply of dispensed TM buprenorphine prescriptions steadily increased before the pandemic. After the emergency declaration, there was a substantial increase in average days' supply for dispensed prescriptions, and then, the measure somewhat leveled off during the pandemic (Figure 3A). Before the weeks of Thanksgiving and Christmas, there was a substantial increase in average days' supply for dispensed prescriptions (Figure 3A and Table S1).

In the week immediately after the COVID-19 emergency declaration, there was a significant increase in the estimated average days' supply for dispensed prescriptions in Kentucky (level change of

TABLE 3 Parameter estimates for segmented regression analysis for comparative interrupted time-series of weekly transmucosal buprenorphine prescribing for treatment of opioid use disorder for urban and rural Kentucky residents, from the prepandemic period (January 7, 2019-March 15, 2020) to the COVID-19 pandemic period (March 16, 2020-December 27, 2020)[a]

	Urban		Rural		Difference[b]	
Parameter estimates	Estimate	*P*-value	Estimate	*P*-value	Estimate	*P*-value
Weekly rate of dispensed prescriptions (per 100,000 residents)						
Prepandemic intercept[c,d]	330.8		897.1		566.3	<.001[e]
Prepandemic slope[f]	0.5	<.001[e]	1.1	<.001[e]	0.6	.003[e]
Level change after the COVID-19 National Emergency Declaration[g]	−24.3	.009[e]	−33.4	<.001[e]	−9.1	.451
Trend change[h]	0.8	.014[e]	1.3	<.001[e]	0.5	.253
Weekly rate of unique individuals with dispensed prescription (per 100,000 residents)						
Prepandemic intercept[c,d]	292.2		814.2		522	<.001[e]
Prepandemic slope[f]	0.7	<.001[e]	1.3	<.001[e]	0.6	.001[e]
Level change after the COVID-19 National Emergency Declaration[g]	−17.1	.033[e]	−25.0	.002[e]	−7.9	.449
Trend change[h]	0.6	.032[e]	1.2	<.001[e]	0.6	.121
Weekly average of the days' supply for dispensed prescriptions						
Prepandemic intercept[c,d]	11.0		10.5		−0.5	<.001[e]
Prepandemic slope[f]	0.02	<.001[e]	0.01	.042[e]	−0.01	<.001[e]
Level change after the COVID-19 National Emergency Declaration[g]	0.8	<.001[e]	0.5	<.001[e]	−0.3	.004[e]
Trend change[h]	−0.010	.048[e]	−0.001	.823	0.010	.007[e]

Note: The COVID-19 National Emergency Declaration was issued on March 13, 2020, defining the prepandemic and pandemic periods in our segmented regression analysis.

[a]Estimates for indicator of holidays and confidence intervals for estimates not shown; complete model output is available in Table S1.

[b]Difference = the difference between the rural and urban estimates.

[c]*P*-value is not reported for the intercept estimates for rural and urban.

[d]Outcome measure at the baseline (the week of January 7, 2019).

[e]*P*<.05.

[f]Average weekly change in the outcome measure before the COVID-19 pandemic.

[g]Immediate change in the level of the outcome measure right after the national emergency declaration compared to the prior segment.

[h]Change in the slope of the outcome measure during the pandemic period compared to the slope before the pandemic. The slope of the regression line during the pandemic period can be calculated as the prepandemic slope + the trend change.

0.6 days per prescription; *P*<.001; Table 2 and Figure 3A). The estimated average days' supply for a dispensed prescription increased to 12.2 days in the index week. The estimated slope for the average days' supply measure during the pandemic period was practically 0 (constant rate).

During the first week of the prepandemic period (the week of January 7, 2019), the estimated average days' supply for dispensed TM buprenorphine prescriptions for patients in urban areas was 11.0 days, which was 0.5 days longer than for patients in rural areas. From the comparative ITS segmented regression analysis, the estimated immediate change in the average days' supply in the week after the COVID-19 emergency declaration was an increase of 0.5 days for patients in rural areas, significantly lower than the increase of 0.8 days for patients in urban areas (difference of –0.3 days; *P* = .004; Table 3). There was a significant difference in the slopes of 2 segmented regression lines for the urban days' supply measure (trend change: –0.01, *P* = .048), but no significant trend changes for the rural days' supply measure (–0.001, *P* = .823) (Table 3).

DISCUSSION

The primary goal of this study was to examine the changes in the trends of TM buprenorphine prescribing for OUD treatment in Kentucky during the COVID-19 pandemic and evaluate the difference in the changes for patients residing in urban and rural areas. Generally, the weekly rates of dispensed prescriptions and unique individuals with dispensed prescriptions were higher for rural residents than urban residents; patients in urban areas received dispensed prescriptions with longer days' supply than patients in rural areas. Results from the ITS analyses revealed immediate declines in the number of dispensed TM buprenorphine prescriptions and the number of unique individuals with dispensed TM buprenorphine prescriptions in the initial weeks of the COVID-19 pandemic. However, the TM buprenorphine utilization measures rebounded and eventually surpassed prepandemic levels by early June 2020. In the first weeks after the national emergency declaration in Kentucky, prescribers appeared to remedy the challenges in access to health care services by increasing the average days'

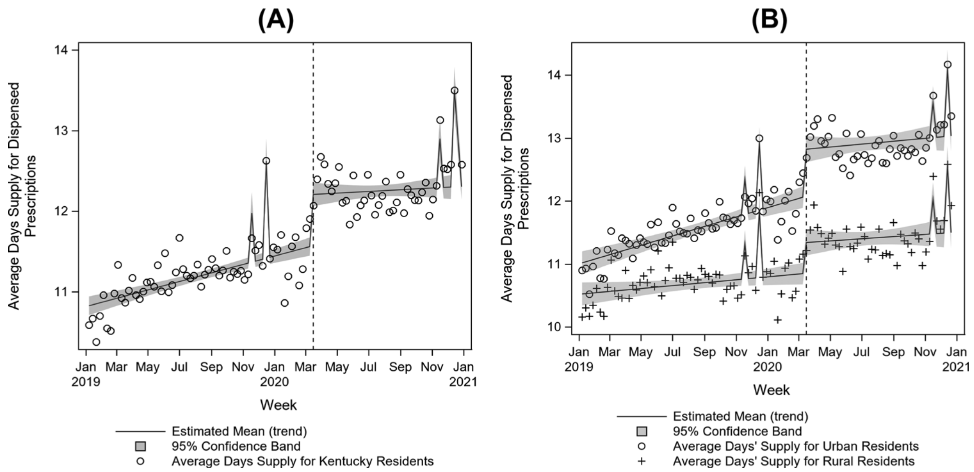

FIGURE 3 (A) Weekly average days' supply for dispensed transmucosal buprenorphine prescriptions for Kentucky residents, January 7, 2019-December 27, 2021. (B) Weekly average days' supply for dispensed transmucosal buprenorphine prescriptions, by patient's rural/urban Kentucky residency status, January 7, 2019-December 27, 2021. The dotted vertical lines represent the week of March 16, 2020, the first week after COVID-19 was declared a national emergency on March 13, 2020

supply of their prescriptions. From the prepandemic period to the pandemic period, no significant differences in the changes of levels and slopes of rates of dispensed prescriptions and of unique individuals with dispensed prescriptions were found between patients from rural and urban areas.

The overall increase in TM buprenorphine prescribing observed during the pandemic is encouraging and suggests that the steps taken by the DEA and SAMHSA, which provided flexibility in buprenorphine prescribing via expanded use of telemedicine and telephonic visits, may have supported access to TM buprenorphine treatment during the COVID-19 pandemic in Kentucky, both for urban and rural residents. Initially, there was a concern that rural populations could be disadvantaged due to limited broadband and digital health information access compared to urban populations.[23] However, the later DEA guidance for initiating buprenorphine treatment for OUD via telephone was issued to address this concern alongside the Centers for Medicare and Medicaid Services issuing a waiver allowing for temporary reimbursement of in-home telehealth visits.[14,47] Further research using health claims data is needed to evaluate how modality of visits (ie, in person, telemedicine audio + video, or audio only) is associated with the observed weekly changes in TM buprenorphine prescribing in Kentucky overall and by rural-urban residency status.

We identified immediate drops in both the number of dispensed TM buprenorphine prescriptions and the number of unique individuals with dispensed TM buprenorphine prescriptions after the COVID-19 emergency declaration, aligning with a previously published study conducted in Pennsylvania.[31] However, unlike the Pennsylvania report, we found that in Kentucky, the average growth rates for these 2 measures during the pandemic were significantly higher than the growth during the prepandemic period. After the initial immediate drop, both measures kept increasing, which is consistent with other studies that found that buprenorphine utilization continued to increase during the COVID-19 pandemic.[26–28] While the exact causes of the reductions in TM buprenorphine prescribing observed during the initial weeks of the COVID-19 pandemic cannot be determined from this study, they are likely multifactorial. Stay-at-home orders and fear of exposure to the SARS-CoV-2 virus may account for patients' delay or avoidance of medical care.[48] The implementation of protective measures and social distancing in hospitals resulted in marked reductions in the capacity of medical institutions to treat many chronic conditions like OUD.[49] Additionally, many providers were moved to other departments to prepare for the surge of COVID-19 patients, and many nonessential medical visits were canceled or discouraged.[12] Meanwhile, pharmacies and pharmacy professionals were facing multiple challenges to support patients during the COVID-19 pandemic.[50] Actions like reducing store hours or temporary closures were adopted in some pharmacies to ensure safely dispensed prescriptions and pharmacists' reasonable workloads,[51] which may also have affected the availability of and access to buprenorphine. Similar declines were seen in other care-seeking behaviors during the pandemic, such as emergency department visits,[52,53] chronic disease management,[54] and cancer care.[55]

Consistent with previous studies,[26,31] our findings suggest that Kentucky prescribers attempted to remedy these access challenges by increasing the average days' supply per prescription during the initial weeks of the COVID-19 pandemic. However, while statistically significant, these increases were relatively modest clinically. Extending TM buprenorphine days' supply for OUD is one strategy proposed to maintain treatment during the ongoing pandemic.[56,57] The results showed that while prescribers adopted this strategy in the early stages of the pandemic after buprenorphine prescribing rebounded in June 2020, the average days' supply per dispensed prescription remained stable and no longer increased. This may suggest that the prescribers returned to prepandemic treatment practice despite the ongoing pandemic. It is not well-understood whether KY's buprenorphine providers were aware that the state's medical board regulations for buprenorphine that stipulate the duration of prescriptions were suspended during the declared state of emergency. A lack of knowledge around this change may explain why the duration of prescriptions was not substantially lengthened.

The changes in TM buprenorphine prescribing observed during the pandemic were not significantly different between residents from urban and rural areas, with 1 exception: though the average days' supply for dispensed prescriptions increased from the prepandemic to pandemic period for patients from rural areas and for patients from urban areas, increases in this measure for patients from rural areas were lower than those from urban areas. This study expands on existing studies,[25–28,30,31] suggesting that patients' access to TM buprenorphine treatment during the COVID-19 pandemic was successfully maintained for both residents from urban and rural areas. Furthermore, there was sustained growth in OUD treatment among both urban and rural residents. One possible explanation could be the effectiveness of telehealth for initiation of patients on TM buprenorphine.[24,58,59] Expanded availability using telehealth may have increased access to buprenorphine treatment during the pandemic, especially for patients from rural areas, who historically have suffered from buprenorphine prescriber shortages.[18,58,60,61] The weekly rates of dispensed TM buprenorphine prescriptions and unique individuals with dispensed prescriptions for patients in rural areas were more than 2.5 times that of patients in urban areas in Kentucky. These results align with the history of the opioid crisis in Kentucky, whereby prescription opioids became widely available in rural areas in the 1990s.[33,62] The findings are also consistent with studies conducted in other states/populations reporting a higher prevalence of OUD in rural versus urban areas.[63–65] Differences in socioeconomic factors, health behaviors, and access to health care services contribute to these differences. Patients in urban areas had on average dispensed prescriptions with 1 day longer days' supply compared to patients in rural areas. It is difficult to conclude if this is a clinically meaningful difference. The differences in days' supply for rural versus urban residents could be related to difference in prescribing practices or concerns about medication diversion.

This study has limitations. First, it was limited to Kentucky residents with dispensed TM buprenorphine prescriptions from Kentucky pharmacies and other dispensers; thus, the generalizability of our findings to other states remains unknown. However, results from studies in other states support some of our findings, such as immediate declines in dispensed buprenorphine prescriptions after the emergency declaration[31] and growth in buprenorphine prescribing during the pandemic.[27,28] Second, the date of the national emergency declaration of COVID-19 was very close to the dates of the federal policies easing restrictions on buprenorphine treatment initiation and continuation; thus, we were unable to disentangle the specific impacts of the COVID-19-related closures and the federal policies on the changes in TM buprenorphine prescribing soon after the emergency declaration. However, the subsequent sustained increase in the number of buprenorphine prescriptions and unique individuals in treatment may imply that the positive impact of the policies outweighed the negative impact of the pandemic on access to buprenorphine treatment. Third, we did not analyze changes in the number of new patients versus existing patients. However, increased weekly numbers of unique individuals with dispensed TM buprenorphine prescriptions may indicate that practices successfully maintained existing patients and admitted new patients during the pandemic. While the weekly increase in the number of unique individuals receiving TM buprenorphine treatment during the pandemic is higher than the weekly increase before the pandemic, the overall impact on addressing the statewide need for treatment capacity is relatively modest. A limitation of the paper is that we did not explore if different classifications for rurality would provide alternative results and conclusions.

Our results reveal that TM buprenorphine utilization increased during the pandemic despite experiencing interruption during the initial weeks of the COVID-19 pandemic. Federal agencies, such as DEA and SAMHSA, quickly recognized the concerns for declined MOUD treatment and issued timely policies to lift some restrictions on MOUD initiation and prescribing in March 2020. Future studies are needed to examine treatment retention for individuals initiated on TM buprenorphine via telemedicine. Those studies, in addition to the findings herein, would provide important information for policymakers and public health officials to make data-driven decisions on expanding treatment for OUD in response to surging overdose deaths.

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DISCLOSURE

Dr. Lofwall has served as a scientific consultant for Titan Pharmaceuticals in the last year. The other authors have no conflicts of interest.

ORCID

Feitong Lei MPH https://orcid.org/0000-0002-1757-4858

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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