The association between longitudinal trends in receipt of buprenorphine for opioid use disorder and buprenorphine-waivered providers in the United States

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Abstract

Aims, Design and Setting: We sought to describe longitudinal trends in buprenorphine receipt and buprenorphine-waivered providers in the United States from 2003 to 2021 and measure whether the relationship between the two differed after capacity-building strategies were enacted nationally in 2017. This was a retrospective study of two separate cohorts covering the years 2003–21, testing whether the association between two trends in these cohorts changed comparing 2003 to 2016 and from 2017 to 2021, among buprenorphine providers in the United States, regardless of treatment setting. Patients receiving dispensed buprenorphine at retail pharmacies.

Participants: All providers who have obtained a waiver to prescribe buprenorphine in the United States, and an estimate of the annual number of patients who had buprenorphine for opioid use disorder (OUD) dispensed to them at a retail pharmacy.

Measurements: We synthesized and summarized data from multiple sources to assess the cumulative number of buprenorphine-waivered providers over time. We used national-level prescription data from IQVIA to estimate annual buprenorphine receipt for OUD.

Findings: From 2003 to 2021, the number of buprenorphine-waivered providers in the United States increased from fewer than 5000 in the first 2 years of Food and Drug Administration (FDA) approval to more than 114 000 in 2021, while patients receiving buprenorphine products for OUD increased from approximately 19 000 to more than 1.4 million. The strength of association between waivered providers and patients is significantly different before and after 2017 ($P < 0.001$). From 2003 to 2016, for each additional provider, there was an average increase of 32.1 [95% confidence interval (CI) = 28.7–35.6] patients, but an increase of only 4.6 (95% CI= 3.5–5.7) patients for each additional provider, beginning in 2017.

Conclusions: In the United States, the relationship between the rates of growth in buprenorphine providers and patients became weaker after 2017. While efforts to increase buprenorphine-waivered providers were successful, there was less success in translating that into significant increases in buprenorphine receipt.

KEYWORDS
Buprenorphine capacity, buprenorphine receipt, buprenorphine-waivered providers, longitudinal trends, medications for opioid use disorder, opioid use disorder

INTRODUCTION

Buprenorphine is a medication to treat opioid use disorder (OUD) that reduces the frequency of opioid use and the risk of opioid overdose [1]. There is concern that not enough people with OUD are benefiting from buprenorphine and other medications for OUD (MOUD). In 2019, the proportion of people with OUD receiving MOUD could have been as low as 13.4% [2], although the gap in care for people with OUD is challenging to enumerate due to the unreliability of OUD prevalence data [3].

There have been many efforts to increase buprenorphine receipt, most notably strategies to increase the pool of buprenorphine-waivered providers. Until recently, to prescribe buprenorphine, physicians, physician assistants, nurse practitioners, clinical nurse specialists, certified registered nurse anesthetists and certified nurse–midwives needed to obtain a so-called 'X-waiver' from the Drug Enforcement Administration (DEA) first. This was a multi-step process, burdensome enough to preclude providers from prescribing buprenorphine entirely [4]. As part of the Consolidated Appropriations Act of 2023 (also known as the Omnibus bill), the federal government eliminated the X-waiver, allowing any prescriber with a general DEA license to offer buprenorphine [5].

Before eliminating the X-waiver, there were several policy changes intended to increase buprenorphine-waivered providers. In particular, the Comprehensive Addiction and Recovery Act (CARA), passed in 2016, included provisions for nurse practitioners and physician assistants to prescribe buprenorphine [6], which led to an 11% increase (beyond additional physicians) in waivered providers a year later [7]. Additionally, resources from the State Opioid/Targeted Response (STR/SOR) funds, first released in mid-2017, have been devoted to training and incentives to obtain a waiver [8], although estimates of how many additional waivered providers this has yielded have not been made available. Other factors, such as increased awareness of the opioid overdose crisis or state-level initiatives, have probably also contributed to more providers obtaining their X-waiver in the last few years. Several recent papers have documented the recent growth in buprenorphine-waivered providers [9–11], most notably from 2017 to 2018 [11], indicating that the myriad policies have probably had some positive effect on waiver obtainment.

Logically, if the underlying theory of change is correct (that more buprenorphine-waivered providers will increase buprenorphine receipt beyond the increases in receipt already occurring), then we would expect to see growth in buprenorphine receipt in recent years increase after the rapid growth in providers, which began in approximately 2017 [11]. Indeed, buprenorphine receipt for OUD rose over the last decade, whether measured per capita [12] or as raw totals [2]. However, whether the rise in buprenorphine providers is associated with a similarly large rise in buprenorphine receipt has not been established.

This report has two main contributions. First, we provide estimates of two critical time-series, both from 2003 to 2021, that are necessary to understand recent national trends in buprenorphine capacity and receipt estimate: (1) the number of patients receiving buprenorphine for OUD, using IQVIA Total Patient Tracker (TPT)® data, and (2) buprenorphine-waivered providers. Secondly, we test whether the relationship between the number of providers and patients has changed over time, using 2017 as the inflection point due to two significant federal initiatives starting at approximately that time (CARA expanding eligible practitioners and STR/SOR increasing federal funding support).

METHODS

Data

We collected and synthesized longitudinal data for buprenorphine providers and patients in the United States. We analyzed peer-reviewed publications, governmental reports, the US DEA Diversion Control Division database [13] and the website of the Substance Abuse and Mental Health Services Administration (SAMHSA) [14] to estimate the cumulative number of buprenorphine-waivered providers annually since 2003, the first full year that buprenorphine was authorized by the US Food and Drug Administration (FDA). All sources reported the total number of waivered providers, not just those who were listed on SAMHSA's treatment locator or who were actively practising (see Supporting information, Table S1).

We used IQVIA TPT® data to estimate the annual number of patients dispensed a buprenorphine product intended to be prescribed for OUD from 2003 to 2021. Specifically, we included patients who received buprenorphine products with the Uniform System of Classification (USC) code associated with drug dependence (78340), which excludes buprenorphine products approved to treat pain (categorized as USC 022XX). The USC is an accepted classification system developed by IQVIA for pharmaceutical products [15]. Included products were Bunavail®, buprenorphine/naloxone, buprenorphine, Probuphine®, Sublocade®, Suboxone® and Zubsolv®.

IQVIA TPT® reflects projected estimates of the annual number of unique patients dispensed buprenorphine for OUD in the United States, although IQVIA's coverage of retail pharmacies has increased from 74% in 2006 to 93% in 2021 among a sample of 48 700 retail pharmacies. IQVIA projects its estimates from this coverage to the known universe of retail pharmacies (see Supporting information, Table S2).

We followed Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for observational studies.

Statistical analysis

We first visualized the trends in the numbers of waivered providers and patients over time. We then tested the implicit hypothesis behind the capacity-building strategies that, compared to earlier years, increases in providers beginning in 2017 would be associated with a change in magnitude in the increase in patients. To do so, we

assessed whether the strength of the association between waivered providers and patients was stable over time, indicated by the stability of linear model parameters, using a Chow test [16]. The Chow test examines whether the coefficients in two different regression models are equal for split data sets, and is typically used with time-series data to determine if there is a breakpoint in the data. A significant test result indicates that the pattern in the data is significantly different before and after that breakpoint. We split the data at 2017, the first year in which CARA 2016 and STR/SOR funds, two significant policy changes aiming to increase waivered providers, would have shown an effect. We fitted separate linear regression models to each part of the split data set (2003–16 versus 2017–21) and used the Chow test to assess whether the strength of the association between waivered providers and patients was equal between these two time-periods.

We used a significance level of 0.05 in all tests, and all reported *P*-values are two-sided. Data were analyzed using R version 4.2.1 [17]. The analysis codes are available at: https://github.com/tseyanglim/BupTrends. The analysis was not pre-registered, and the results should be considered exploratory.

RESULTS

Figure 1 shows the longitudinal data for buprenorphine-waivered providers and patients receiving buprenorphine.

From 2003 to 2021, the total number of buprenorphine-waivered providers increased from fewer than 5000 in the first 2 years of FDA approval to more than 114 000 in 2021, while patients receiving buprenorphine products for OUD increased from approximately 19 000 to more than 1.4 million (Figure 1).

The Chow test indicated that the strength of association between waivered providers and patients is significantly different before and after 2017 ($P < 0.001$). From 2003 to 2016, for each additional provider there was an average increase of 32.1 [95% confidence interval (CI) = 28.7–35.6] patients, but an increase of only 4.6 (95% CI = 3.5–5.7) patients for each additional provider from 2017 to 2021. Thus, the relationship between the rates of growth in providers and patients has become weaker in later years.

DISCUSSION

This is the first study, to our knowledge, that reports longitudinal data for buprenorphine-waivered providers and patients receiving buprenorphine for their OUD over 19 years, and investigates the association between the two trends. Several federal initiatives, especially in 2016 and 2017, tripled the number of providers by the end of 2021, but patients continued to increase approximately linearly. Providers added starting in 2017 were associated with only 14% as many additional patients per provider compared to providers added before 2017 (32.1 versus 4.6). This is consistent with recent findings that many buprenorphine-waivered providers treat few patients, if any, with 5% of prescribers writing 50% of prescriptions from 2017 to 18 [18]. The median patient case-load was 1.5 (mean = 13.8) [18], whereas providers can legally prescribe to up to 30 patients in their first year.

The rapid increase in buprenorphine-waivered providers might have supported the continually linear increase in patients receiving buprenorphine, whereas in a counterfactual world, without the rapid increase in providers, we might have seen patient receipt plateau or even decline. However, if the goal is to increase patients more rapidly, perhaps even on par with the tripling of providers observed, then much more is needed.

There are two main categories of people facing much steeper barriers than the (now removed) X-waiver: providers and patients. Providers are not currently able to treat anywhere near the 30 or more they are legally allowed to treat. While the X-waiver has been eliminated by Congress as part of the Consolidated Appropriations Act of 2023, the Legislation imposes additional training requirements for prescriber registrants, requiring not less than 8 hours of training on the treatment and management of OUD patients [5]. Notwithstanding those requirements, while removal of the X-waiver means more providers are theoretically able to prescribe buprenorphine, as demonstrated in this study, translating those extra providers into the critical outcome of more patients actually receiving much-needed OUD treatment cannot be taken for granted [19].

More must be done to support providers who wish to reach more patients and to reduce stigma among those who are reluctant to
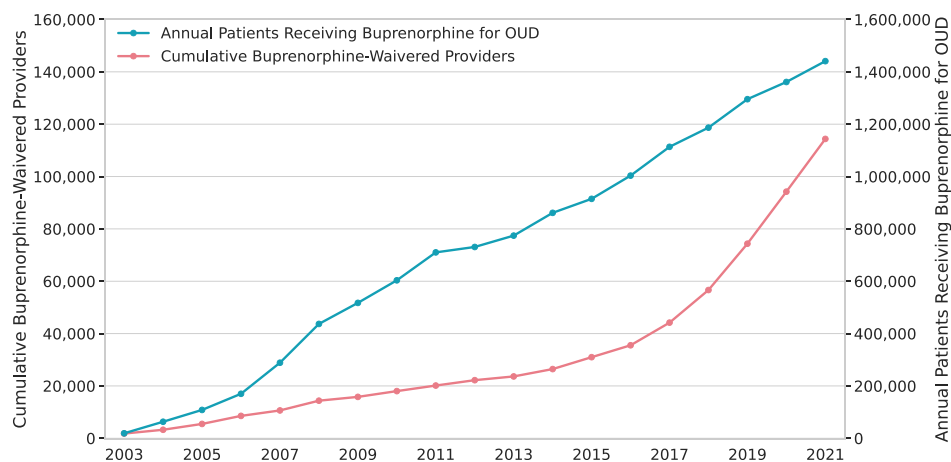
FIGURE 1 Cumulative number of buprenorphine-waivered providers and the annual number of patients dispensed buprenorphine products for opioid use disorder (OUD); United States, 2003–21.

prescribe [10, 20–22]. This could include peer support in prescribing, especially in the early stages [22], and developing strategies that depend upon the intensiveness of providers' existing prescribing practices (e.g. 'super-prescribers' versus 'dabblers') [23]. Such work is highly intensive, often requiring one-on-one time in an already over-worked population, but it could help with overcoming logistical barriers that arise any time providers change their practice scope. Such intensive support could also help to address barriers such as insufficient time [20].

However, patients also face formidable barriers to treatment, including stigma, lack of knowledge, unaffordability and clinic practices that make it challenging to access and stay in care [24, 25]. Even providers who are willing to treat many more people might find these patient-level barriers nearly impossible to overcome without additional support and structural change. Structural change such as reducing burdensome intake processes could incentivize low-barrier care [26], making it easier for patients to access treatment. Research on effective destigmatization and education efforts targeting both patients and providers is sorely needed.

This analysis has limitations. IQVIA's coverage has increased in recent years, so the variation around the true number of patients (which is unknown) might be larger in the earlier years due to less information. However, IQVIA projects to national estimates when estimating total receipt. Moreover, the Treatment Episode Data Set–Admissions in 2017–19 indicate that episodes with planned medication-assisted opioid therapy (which includes but is not limited to buprenorphine) averaged 8.4% growth from 2016 to 2019 [27], similar to the growth in IQVIA's data set and much lower than the growth in providers. Finally, we did not account for all possible factors leading to the rapid increase in waivered providers beginning in 2017, as our intent was not a comprehensive analysis of all factors leading to an increase in waivered providers, but rather to identify whether the relationship between growth in patients and providers had changed as a result.

Increasing patient engagement in buprenorphine treatment more rapidly will require additional efforts beyond increasing providers. Such efforts could include supporting existing providers to reach new patients and addressing the multiple patient-level barriers.

AUTHOR CONTRIBUTIONS

Erin J. Stringfellow: Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); writing—original draft (equal); writing—review and editing (equal). **Tse Yang Lim:** Conceptualization (equal); investigation (equal); methodology (equal); software (equal); writing—review and editing (equal). **Huiru Dong:** Formal analysis (equal); investigation (equal); methodology (equal); software (equal); validation (equal); writing—review and editing (equal). **Ziyuan Zhang:** Data curation (equal); software (equal); validation (equal); visualization (equal). **Mohammad S. Jalali:** Conceptualization (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); supervision (equal); writing—review and editing (equal).

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DECLARATION OF INTERESTS

None.

DATA AVAILABILITY STATEMENT

Data and analysis codes are available in the supplementary document and online repository.

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SUPPORTING INFORMATION

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