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Opioid and non-opioid analgesics prescription patterns by dentists in the United States

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DISSERTATION

OPIOID AND NON-OPIOID ANALGESICS PRESCRIPTION PATTERNS BY DENTISTS IN THE UNITED STATES

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DEDICATION

To my parents,

To my sisters,

To my mentors and teachers,

Without whom none of my success would be possible

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Last but not least, I would like to dedicate this work to my parents, for their love and support throughout my life.

Opioid and Non-Opioid Analgesics Prescription Patterns by Dentists in The United States

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Boston University, Henry M. Goldman School of Dental Medicine, 2020

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Abstract

In the United States, prescription opioids have been a major problem that contributed to the opioid crisis in the country. As dentists prescribe analgesics routinely for dental pain management, further investigation into opioid and non-opioid prescription patterns by dentists on a national level is needed. This research project aimed to examine 1) the trends in opioid and non-opioid analgesic prescriptions by dentists in the US,2) to examine the racial-ethnic disparities in receiving an opioid and non-opioid prescription from a dental professional, 3) the effect of federal Rescheduling of hydrocodone combination on opioid prescription patterns by dentists in a school setting. Data on analgesic prescriptions by dentists were obtained using medical panel survey MEPS (1996- 2015), and Boston University Henry M. Goldman School of Dental Medicine clinical repository (2010 -2019). On average about 31,206 individuals of all ages were interviewed for MEPS each year. The trend in analgesics prescription was reported weighted numbers and proportions of total and dental analgesics prescriptions were reported. Kendall tau correlation test was used to examine trends in the rate of opioid prescriptions per 100 persons over survey years. Racial differences were examined using MEPS data (2002-2015) on dental analgesic

prescriptions, dental care utilization, patients' race, and other demographic information. The outcome was analgesic prescription received. The main independent variable was the patients' race/ethnicity. Covariates included in the analysis were gender, age, marital status, income, geographical region, and survey year. Using BUSDM data (2010-2019) we examined 12,807 patients who received an opioid prescription from a dentist. The primary outcome variables were opioid prescriptions and opioid morphine milligram equivalent (MME). The primary predictor used is the date of opioid prescription (Time before and after the intervention). To assess the effect of hydrocodone medication reclassification on the outcome variables we used an interrupted time series (ITS) analysis with a segmented regression model. Our results showed a decrease in the proportion of dental opioids out of total opioids from 9.76% in 1996 to 4.5% in 2015. Kendall tau correlation indicated an increase in prescribing rate over the years in total opioids but not in dental opioids. Racial differences were found in opioid prescriptions by dentists with whites having a lower risk of receiving an opioid analgesic compared to other racial minorities. The effect of federal rescheduling of hydrocodone combination on opioid prescription patterns by dentists showed specifically a reduction in non-hydrocodone opioids prescribing rate by morphine milligram equivalent (MME). In conclusion dentists' contribution to the increase in prescription opioids in the United States seem to be limited compared to other health care professionals. Nevertheless, racial differences were found in whites when compared to other racial minorities. Efforts to curb the use of opioids should be encouraged even more so with evidence supporting the effectiveness of non-opioids analgesics in control of dental pain.

STATEMENT

I would like to declare that this work is original. I was responsible for the literature review search, writing, analysis and interpretation under the guidance of the committee members.

We know of no conflicts of interest associated with this work, and there has been no significant financial support for this work that could have influenced its outcome. As Corresponding Author, I confirm that the work has been read and approved for submission by all the named committee members.

We hope you find our manuscript suitable for publication and look forward to hearing from you in due course.

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INTRODUCTION AND LITERATURE REVIEW

INTRODUCTION

Pain is a complex experience that consists of a specific sensation, and the reactions evoked by that sensation. The International Association for the Study of Pain defines it as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[1,2] The ability to feel pain varies from one individual to another. Having pain sensation can be caused by intense or damaging stimuli. It is the body's way of letting us know that something is wrong.[3] Oral pain usually occurs due to odontogenic source, which refers to pain that started from the teeth or their supporting structures, the gingivae, alveolar bone, or periodontal membrane.[4]

In dentistry, management of acute pain usually starts by providing dental treatment such as restorative and endodontic treatment.[5,6] In certain situations, pain persists postoperatively, and the dentist needs to prescribe medications to help the patient deal with the pain until it subsides.[5,7] Post-operative pain management poses many challenges to dentists, whether it's deciding the best treatment to use, improving quality of recovery, or identifying patients at risk for poor pain management or uncontrolled pain.[6,8] Medications prescribed usually include analgesics that work by either interrupting the ascending nociceptive impulses or depress their interpretation within the central nervous system (CNS).[9]

Analgesics used in dentistry are classified into opioids, non-opioids, and a combination of the two. This classification is based on their mechanism of action. Non-opioid analgesics

include acetaminophen (APAP) and non-steroidal anti-inflammatory drugs (NSAIDs) e.g., ibuprofen. The analgesic effect of non-opioids is attributed to their ability to inhibit cyclooxygenase (COX), which is required for the synthesis of various families of prostaglandins.[10] Opioid analgesics have a different mechanism of action. They produce an analgesic effect by acting as agonists at opioid receptors (e.g., mu (m, μ), kappa (k, κ), delta (d, δ)) at supraspinal, spinal, and peripheral sites.[11]

Opioid Analgesics:

Opioids are mainly used for their analgesic effects. This group of medications bind to specific receptors present in the central nervous system(CNS) and as well as in the peripheral tissue to produce analgesia. The main receptor responsible for the opioid mechanism of action are the m, K, and d receptors. All opioids work on m receptors, while their work on K and d receptors varies. M receptors, when activated, lead to supraspinal analgesia and other adverse effects such as respiratory depression, sedation, and euphoria. K receptors usually work on spinal analgesia and produce similar adverse effects. d receptors' adverse effects are slightly different and include dysphoria and psychomimetic effects.[11,12]

All types of opioid analgesics undergo metabolization through phase I and phase II enzymes. These enzymes, due to genetic variations, affect opioid deposition, absorption, metabolism, and excretion differently among individuals. In turn, this influences the analgesic response from one person to another using the same medication. Opioids' potency (affinity to the μ-opioid receptor) depends on the metabolite produced during its metabolism in the liver. [13,14]

Opioid analgesics codeine, hydrocodone, and tramadol are classified as prodrugs. When metabolized in the liver, by enzyme CYP2D6, they produce the more potent metabolite morphine, hydromorphone, and o-desmethyltramadol, respectively. Only a small percent of codeine and hydrocodone are converted to these potent metabolites, while the rest form an inactive norcodeine and norhydrocodone. On the other hand, tramadol gets mainly metabolized to o-desmethyltramadol. [13,15]

Other opioids such as morphine, hydromorphone, oxycodone, oxymorphone, fentanyl, and methadone have a higher affinity to m receptors. Morphine and hydromorphone have a low oral bioavailability; they go directly through phase II enzymes to metabolize by UGT2B7 into inactive 3-glucuronide metabolites with a small amount being converted to the active 6-glucuronide metabolites. Oxycodone and methadone are synthetic opioids that have relatively high bioavailability. Oxycodone is metabolized into inactive noroxycodone, with a small amount of active oxymorphone by CYP2D6, while methadone is metabolized into inactive metabolites by CYP2B6.[9]

Non- Opioid analgesics:

Unlike opioids, non-opioid analgesics are not mediated by opioid receptors. Their mechanism of action is usually mediated by cyclooxygenase (COX) inhibition. COX is important for the synthesis of prostaglandin PGD2, PGE2, PGF2α, PGI2, and thromboxane A2. Thus, when inhibited by non-opioid analgesics, it causes a reduction in PGE2 and prostacyclin synthesis, giving the desired analgesic effect. Other additional effects may accompany analgesia, depending on the type of COX enzymes inhibited.COX-1 is present in the gastrointestinal lining and usually involved in its protection. On the other hand,

COX-2 is predominately present at sites of inflammation, and its inhibition induces the analgesic, anti-inflammatory, and antipyretic effects. [10]

Non-steroidal anti-inflammatory drugs (NSAIDs) constitute the majority of over the counter (OTC) non-opioid analgesics. They vary in the degree of COX-1 and COX-2 inhibition. Ibuprofen, naproxen, and indomethacin have a higher potency in COX-1 inhibition. While other NSAIDs are more selective COX-2 inhibitors (e.g., Meloxicam, diclofenac, celecoxib, and rofecoxib). Some NSAIDs can affect the physiologic functions in the gastrointestinal, cardiovascular, and renal systems, depending on their COX inhibition. COX-1 inhibition has been associated with decreased platelet aggregation and gastrointestinal toxicity. COX-2 produces (PGI2) that promotes vasodilation and inhibition of platelet aggregation; its inhibition can increase cardiovascular events risk.[16]

Acetaminophen (APAP) is another commonly used analgesic; it has a strong analgesic and antipyretic effects but a weak anti-inflammatory action.[17]As a non-opioid analgesic, its mechanism of action involves COX-2 inhibition. For pain management, acetaminophen can be used alone or as a combination with other opioid analgesics.[17,18] Acetaminophen has shown to be a very safe medication with minimal side effects; thus, it is usually chosen as the first-line choice for pain management.[18]

In the United States, prescription opioids have been a major problem that have contributed to the opioid crisis in the country. In 2014, there were 47,055 drug overdose-related deaths, 28,647 of them involved an opioid.[19] Since 2000, the opioid-related overdose deaths increased about three times, from 3 per 100,000 persons in 2000 to 9 per 100,000 in 2014. [20] This increase in opioid-related overdose deaths coincided with a

tremendous increase in prescription opioids.[21] In 2015, about half of all opioid-related overdose deaths involved a prescription opioid, therefore overprescribing of opioid analgesics was responsible for 15,000 deaths that year.[19]

Dentists have been identified as one of the leading professionals who prescribe opioids, hence contributing to the problem. A study examining opioid prescribing rates in 2009 found that opioids are mainly prescribed by family medicine physicians, as they were responsible for 28.8% of the prescriptions written, followed by internal medicine physicians (14.6%) and dentists (8%). [22] During the same year, it was estimated that more than 118.4 million outpatient opioid prescriptions were dispensed, making dentists responsible for 9.472 million of outpatient opioid prescriptions in 2009.[23]. As the epidemic of abuse largely involves prescription opioid products, it is possible that opioids from dentists may be ingested in the context of nonmedical use or abuse.[24]

The aim of this dissertation is to examine the role of dentistry in the opioid epidemic and understand the factors associated with dentists' prescribing practices, using cross-sectional and nationally representative data. This dissertation includes three studies. The first paper will examine the trends in opioid and non-opioid analgesic prescriptions by dentists in the US using data from the Medical Expenditure Panel Survey (MEPS). The second paper, also using MEPS data, will examine racial-ethnic disparities in receiving an opioid prescription from a dental professional. Lastly, the third paper will investigate the effect of federal rescheduling of hydrocodone combination on opioid prescription patterns by dentists in a school setting using the Boston University Henry M. Goldman School of Dental Medicine clinical data repository.

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JOURNAL ARTICLE ONE

Trends in Opioid and Non-Opioid Analgesic Prescriptions by Dental Professionals in The United States (1996-2015)

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ABSTRACT

OBECTIVE: The goal of our study is to investigate the patterns of opioid analgesic prescriptions by dental professionals in the United States and to determine their contribution to the recent increase in the use of prescription opioids. **METHODS:** Data on analgesic prescriptions and expenditure by dentist were obtained from medical panel expenditure survey (1996-2015). On average about 31,206 individuals of all ages were interviewed for MEPS each year. The trend in analgesics prescription was reported weighted numbers and proportions of total and dental analgesics prescriptions were reported. Annual rates of total and dental opioid perceptions were computed. Kendall tau correlation test was used to examine trends in rate of opioid prescription per 100 persons over survey years. **RESULTS:** The proportion of dental opioids out of total opioids decreased from 9.76% in 1996 to 4.5% in 2015. Kendall tau correlation showed a strong positive correlation between total opioids prescribing rate per 100 persons and years of survey ($r=0.91$, $p<0.0001$). Thus, indicating an increase in prescribing rate over the years. On the other hand, we did not find a similar trend when examining opioids prescribed by dentists ($r=-0.06$, $p=0.72$). **CONCLUSION:** Dentists contribution to the increase in prescription opioids in the United States seem to be limited compared to other health care professionals. Nevertheless, efforts to curb the use of opioids should be encouraged even more so with evidence supporting the effectiveness of non-opioids analgesics in control of dental pain.

Keywords: opioids, analgesic prescriptions, dental.

INTRODUCTION

Opioids abuse and misuse is a major contributor to increased drug overdose deaths in the United States.[1] Although new reports from the Center of Disease Control and Prevention (CDC) indicate some reduction in opioids related deaths in recent years, the numbers are still high with 69.5% of drug overdose deaths involving an opioid in 2018.[2] The risk from using opioid analgesics is attributed to its mechanism of action. They affect the central nervous system and produce side effects including nausea, vomiting, sedation and the most serious effect respiratory depression.[3] Prolonged use of opioids may cause tolerance, physical dependence and addiction, thus leading to increased chance of severe respiratory depression and death.[4,5]

Past increases in opioid overdose deaths in the United States have been associated with prescription opioids.[6] This association was clear in 2018, as new data showed a 2% reduction in death rates related to opioid analgesics from the previous year. This decrease was led by reduction in prescription opioids related deaths.[2]Prescription opioid analgesics include oxycodone, methadone, hydrocodone, and others.[7] Results from the 2018 National Survey on Drug Use and Health highlighted the sources of opioid misuse, identifying friends and relatives as the main source. Approximately 38.6% of those abusing opioids in 2018 obtained it for free from a friend or a family member; 9.5% bought it from a friend or a family member; and 3.2% took it without asking. Furthermore, 34.7% obtained the opioid through a prescription or stolen from a health care provider. A much lower percentage reported getting it from a drug dealer.[8] When friends and family of a known

opioid abuser were asked about their source of prescription opioids, the vast majority (86.6%) reported obtaining it from a health care provider. [8,9]

Dentists play a role in the prescription of opioid analgesics.[10] A study published in JAMA examining health care providers' contribution to the increase in opioid prescriptions found that in 2009, primary care physicians accounted for 28.8% of the opioid prescriptions followed by internal medicine physicians (14.6%) and dentists, who accounted for 8% of the opioid prescriptions.[11] Dentists often prescribe opioid analgesics for management of post-operative pain following dental treatment.[12] These prescriptions are mostly given as pills with immediate release formulations (IR).[13] Following outpatient surgical tooth extraction, more than half of opioids prescribed can be left unused by patients, lending them to abuse and misuse by patients or their relatives. [14]

Current literature on opioids prescription patterns by dentists is limited.[11,15-17] Despite the national recognition of the role prescription opioids play in the opioid abuse epidemic, there is little evidence examining the role of and trends in dentists' prescriptions of opioids nationally over past years.

The objective of our study is to investigate the patterns of opioid analgesic prescriptions by dental professionals in the United States. In this study we aim to answer the following questions:

What are the national trends of opioid analgesic prescriptions by dental professionals from the year 1996 to 2015?

How much of the increase in prescription opioids analgesics is contributed by dentists from the year 1996 to 2015?

MATERIALS AND METHODS

Data Source

Data from 1996 - 2015 Medical Expenditure Panel Survey (MEPS) were used. MEPS is a set of large scale surveys of families and individuals along with their health care providers across the United States. The survey collects data on health care services use in the country, how frequently they are used, the cost of these services, and how they are paid for.

The Household Component (HC) of the survey provides data from individual households and their members, which is supplemented by data from their medical providers. These data are collected through interviews, which include detailed questions regarding the following: demographic characteristics, health conditions, health status, use of medical services, access to care, satisfaction with care, health insurance coverage, income, and employment.

Other components of the survey include Insurance (IC) and medical provider components (MPC). Insurance is a separate survey of employers that provides data on employer-based health insurance. Medical Provider Component (MPC) covers hospitals, physicians, dentists, home health care providers, and pharmacies identified by HC participants. Its purpose is to supplement and/or replace information received from the HC participants. This information is later incorporated into the HC data files. In this study only HC will be used along with its supplemental information provided by MPC. HC data files used: Dental Visits, Prescribed Medicines, Condition-Event link.

Study Population

Every year, a range of 21,571 to 33,893 individuals, of all ages, were interviewed for HC. Of those interviewed, approximately an average of (41.4%) reported having dental visits every year.

Sampling Method

MEPS household component participants selected from communities across the United States, taken from a nationally representative subsample of households that participated in the prior year's National Health Interview Survey(NHIS). These NHIS surveys are sampled using stratified multi-stage design. The first stage is forming the Primary Sampling Units (PSUs) which each consist of one or more county. Within each PSU, density strata were made with knowledge about distribution of racial /ethnic groups within a single or groups of blocks. In every density stratum, clusters of households were formed and a sample of these clusters was selected for use over several years of the survey. Households were selected from these clusters for each calendar year of the NHIS. Households of Hispanic and Black population were oversampled at rates of approximately 2 and 1.5 times, respectively, the rate of other households.

Data Collection

Interviews are conducted using computer-assisted personal interviewing (CAPI). This data collection instrument consists of sections that are composed of a series of computer

screens containing questions, interviewing instructions, and skip pattern directions, as well as computer programming notes embedded along with each data item.

Variables of Interest

The primary outcome variables of our study are opioid prescriptions. Information on medications prescribed were captured in the HC of the survey, for every medical or dental event reported, using these questions: During this visit, were any medicines prescribed for you/PERSON? Please include only prescriptions which were filled. Please tell me the names of the prescriptions from this visit that were filled. This information is later confirmed or edited using medical providers, dental providers and pharmacies who provided care to MEPS Household participants.

In this study, opioids prescribed were defined using Multum Lexicon classification as any narcotic analgesics prescribed alone or in combination with other analgesics.Variables used: Medication name (RXNAME) and Multum Lexicon opioids classification (TC1=57, TC1S1=58, TC1S1_1=60, 191). These variables were provided in the prescribed medications data file.

Annual expenditure variables were calculated using the sum of 12 sources of payment, and re-categorized into 4:(private insurance, public insurance, out of pocket, others). Dental visits were used to identify analgesics prescribed by dentists. This information was captured in the HC of the survey using the following questions about medical and dental events: Where did you/PERSON receive the care?

Statistical Analysis

All analyses were conducted using SAS Software version 9.4 (SAS Institute Inc., Cary, NC, USA). Survey procedures were used to account for MEPS complex, multistage sampling design. Sampling weights were applied to account for unequal selection probabilities. Descriptive data were presented including weighted numbers and proportions of total and dental opioid prescriptions. Annual rates of total opioid perceptions and annual rates of opioid prescriptions by dentist were computed. Kendall tau correlation test was used to examine trends in rate of opioid prescription per 100 persons based on the pattern on concordance and discordance.

RESULTS

An average of 31,206 individuals of all ages were interviewed for MEPS household component each year. These samples represent all noninstitutionalized civilians residing in the United States each year. (Table 1) During the study period (1996-2015), an average of 42.6% of the U.S population reported having at least one dental visit every year. (Table 1) From 1996 to 2015, on average, dentists in the US prescribed almost 6 million opioid analgesic prescription for management of dental pain every year. (Table 2) The number of opioid prescriptions by dentists seems to be steadily increasing with 6,405,143 prescriptions in 1996 and 6,859,011 prescriptions in 2015. (Figure 1) The total opioid prescriptions provided by all health care professionals each year also seems to be increasing significantly over the past 20 years. In 2015, about 147 million opioid prescriptions were

made compared to 65 million in 1996. (Figure 2) Dentists don't appear to be contributing to this increase over the years. The proportion of dental opioids out of total opioids decreased from 9.76% in 1996 to 4.5% in 2015. (Figure 3)

Total expenditures on opioid prescriptions increased from $1.3 billion in 1996 to $10.3 billion in 2015. A less prominent increase in expenditure was seen in dental opioids with $93 million in 1996 to $332 million in 2015. (Figure 4) The source of payment for these dentists' prescribed opioids seems to be changing over the years, with less out of pocket payments and more paid by private and public insurance. (Figure 5)

Looking at opioid prescriptions as a rate per 100 persons, our results indicate a rate of 24.1prescription per 100 persons were given by health professionals in 1996. On the other hand, dentists were responsible for 2.32 prescription per 100 persons in the same year. In 2015, the rate was 45.70 prescription per 100 persons given by any health professional, and dentist were responsible for 2.06 prescription per 100 persons that year. (Figure 6)

Kendall tau correlation showed a strong positive correlation between opioids dispensed rate per 100 persons and years of survey. ($r=0.91$, $p<0.0001$), indicating an increase in prescribing rate over the years. On the other hand, we did not find a similar trend when examining opioids prescribed by dentists ($r=-0.06$, $p=0.72$). (Table 3)

DISCUSSION

The results of our study show that prescription opioids increased tremendously in number between 1996 to 2015. Although dentists are one of the health professionals that prescribe opioids for pain management, their role in the increase seems to be small

compared to other health professionals. The rate of opioid prescribing by dentists remained steady, approximately 2 per 100 persons throughout the study period, and the proportion of dental opioids out of total opioids decreased steadily from 1996 to 2015.

The current literature on overall opioid prescriptions in the United States showed similar results. The CDC found an increase in total opioid prescriptions since 1999, but also suggested a plateau in opioids prescribing rate per 100 persons in 2010-2012, followed by a reduction in 2015. [18] Although our results don't show a plateau, a slight reduction was seen in 2011, followed by a reduction in 2015. Despite the reduction in 2015, the number of prescribed opioids remains substantially high.

Dental related prescription opioids showed a steady increase from 1996 to 2015. These results seem to be in accordance with another study that looked into MEPS dental opioid prescriptions. [17] On the other hand, our analysis also investigated the rate of prescribing per 100 persons which takes into account the increase in population over the years. The results of Kendall tau correlation test showed very little correlated increase in rate over increase in years, indicating that dentists are not a major contributor to the increase of prescription opioids. These results could be attributed to the nature of dental pain. Dentist tend to prescribe opioid analgesics following a definite diagnosis, or following a dental procedure that usually warrant an opioid prescription. Therefore, unnecessary prescribing of opioid analgesics is limited.

The results of our study also show that the amount of opioid prescriptions written by dentists out of total prescriptions have decreased from 9.66% in 1996 to 4.51% in 2015. Volkow et. al reported that dentists were responsible for 8% of total prescriptions in 2009.

Our results found that dentists were only responsible for 4.99% in 2009. This overestimation could be attributed to the total opioids prescription collected in their data which they mentioned only represented 39% of estimated opioid prescriptions dispensed in the US in 2009. [11]

Gupta and colleagues investigated claims data of privately insured patients in the United States, and reported an increase in prescribing rate of opioids by dentists from 2010 to 2015. We believe this increase can be explained by the increase in expenditure in private and public insurance, as our results indicate reduction in out of pocket payments and increase in public and private insurance coverage.[19]

Despite the limited contribution by dentists to the increase in opioid prescriptions, opioid naïve patients can get their first exposure through a dental professional thus resulting in a subsequent higher rate of opioid use and abuse.[20] Efforts to reduce the prescription of opioids by dentists should be encouraged, as new recommendations support the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for dental pain management.[21] Furthermore, the use of NSAIDs combined with acetaminophen at proper time intervals can be as effective as opioids in controlling dental pain. [22] Following these recommendations along with the use of prescription drug monitoring programs will aid in controlling any unnecessary opioid prescriptions.

The findings of our study should be considered with limitations. Data collection of prescription medicine purchases are only confirmed and linked to dental professionals if it is reported by the participants. Therefore, although prescriptions are verified by the pharmacy they are considered self-reported data. Our study used self-reported dental

services use and medications prescribed, which can potentially be underreported by the participants. Nevertheless, the use of MEPS data provides a nationally representative estimates of opioids prescriptions by dentists in the United States.

CONCULSION

Dentists' contribution to the increase in prescription opioids in the United States seems to be limited compared to other health care professionals. Nevertheless, efforts to curb the use of opioids should be encouraged even more so with evidence supporting the effectiveness of non-opioids analgesics in control of dental pain.

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TABLE 1.1 Descriptive Statistics of Total MEPS sample and those receiving dental visits by Years, MEPS 1996-2015.

Year	Sample size	Weighted sample	Reporting Dental Visits	Reporting Dental Visits (weighted N)	Dental Visits (weighted %)
1996	21,571	268,905,490	8,653	115,429,059	42.93
1997	32,636	271,278,585	12,245	113,380,204	41.79
1998	22,953	273,533,690	8,628	115,985,367	42.40
1999	23,565	276,410,767	9,221	119,001,824	43.05
2000	23,839	278,405,516	9,033	115,819,145	41.60
2001	32,122	284,247,327	12,462	121,133,295	42.62
2002	37,418	288,181,763	14,373	125,336,166	43.49
2003	32,681	290,604,436	12,284	127,995,357	44.04
2004	32,737	293,527,003	12,330	128,061,306	43.63
2005	32,320	296,185,002	12,043	128,273,284	43.31
2006	32,577	299,267,035	12,161	129,019,644	43.11
2007	29,370	301,309,149	11,392	131,329,906	43.59
2008	31,262	304,375,942	11,639	128,529,401	42.23
2009	34,920	306,660,588	12,828	129,402,690	42.20
2010	31,228	308,573,976	11,244	127,335,043	41.27
2011	33,622	311,125,758	11,803	127,897,978	41.11
2012	37,182	313,489,853	12,938	129,913,757	41.44
2013	35,068	315,721,982	12,864	133,901,513	42.41
2014	33,162	318,440,423	12,111	135,774,346	42.64
2015	33,893	321,423,251	12,853	137,835,719	42.88

TABLE 1.2 Descriptive Statistics of Total Opioids Prescriptions and Dental Opioid Prescriptions by Years, MEPS 1996-2015.

Year	Total Opioid Prescriptions Sample N	Total Opioid Prescriptions Weighted N	Dental Opioids Prescriptions Sample N	Dental Opioids Prescriptions Weighted N	Dental Opioids Prescriptions Weighted % of Total Opioids
1996	4,852	64,703,857	471	6,247,252	9.66%
1997	7,694	61,607,267	603	5,284,053	8.58%
1998	5,454	59,017,632	408	5,279,154	8.95%
1999	5,240	63,943,532	395	4,774,211	7.47%
2000	5,598	70,046,850	412	4,898,357	6.99%
2001	8,899	82,194,364	608	5,889,269	7.17%
2002	10,765	85,926,833	759	6,208,274	7.23%
2003	9,379	87,198,063	648	6,329,487	7.26%
2004	10,943	102,461,939	721	7,017,788	6.85%
2005	11,108	103,681,064	658	6,494,909	6.26%
2006	12,263	108,932,018	697	6,808,224	6.25%
2007	10,316	107,202,589	552	6,088,302	5.68%
2008	10,585	116,543,667	512	5,413,803	4.65%
2009	12,052	118,411,064	639	5,905,356	4.99%
2010	11,136	127,685,971	514	5,774,282	4.52%
2011	11,658	126,651,899	511	5,309,443	4.19%
2012	14,089	143,912,902	496	4,904,333	3.41%
2013	13,712	142,392,451	686	7,557,580	5.31%
2014	14,663	159,900,806	616	6,831,767	4.27%
2015	14,278	146,885,484	612	6,628,669	4.51%

TABLE 1.3 Correlation Between Years and Opioids Prescribing Rate Per 100 persons in The United States, MEPS 1996–2015.

Year	N	Median	Minimum	Maximum	Correlation Coefficient	P-Value
Total Opioids	20	35.3	21.6	50.2	0.91	<.0001
Dental Opioids	20	2.0	1.6	2.4	-0.06	0.72

FIGURE 1.1 Total Analgesics Prescribing Patterns by Dentists. MEPS 1996-2015.

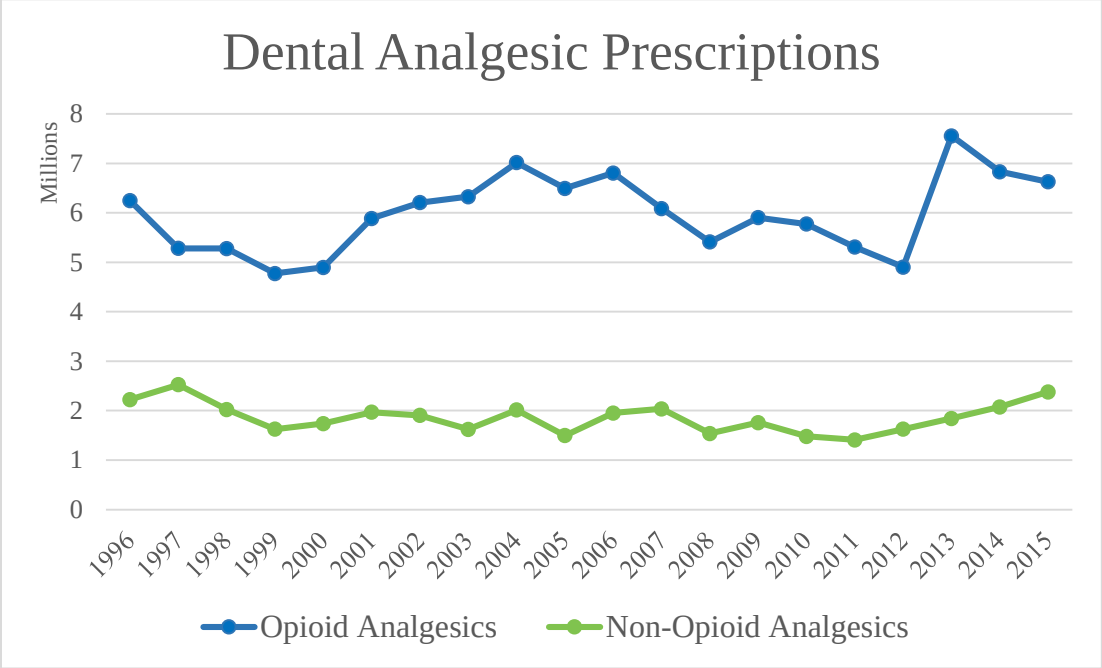


FIGURE 1.2 Total Analgesics Prescribing Patterns by any Healthcare Provider. MEPS 1996-2015.

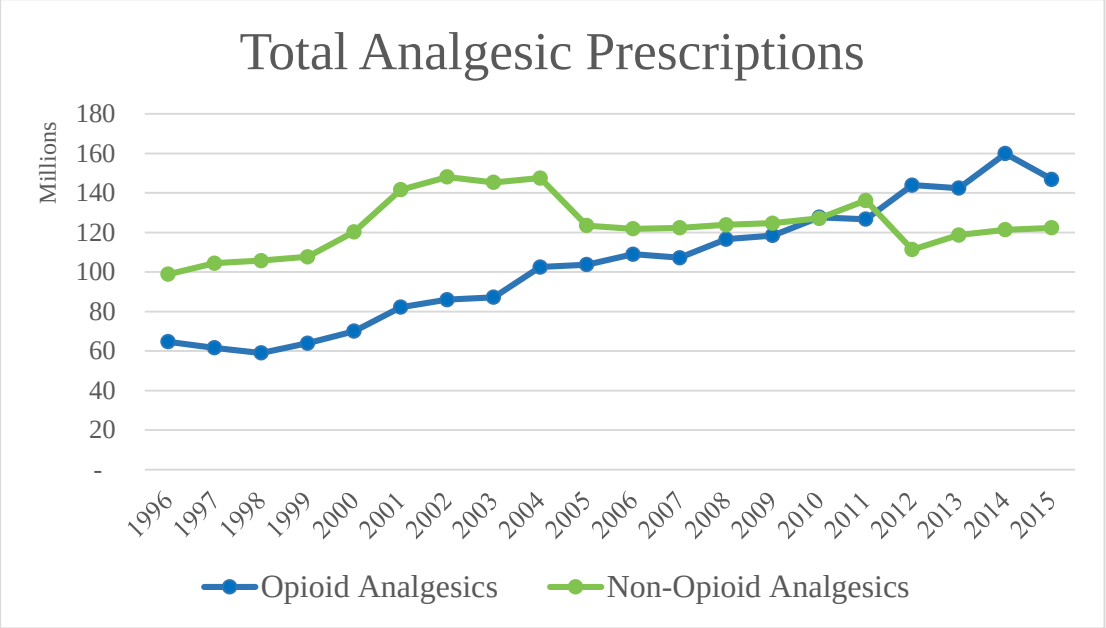


FIGURE 1.3 Proportion of Dental Opioids Out of Total Opioids Prescriptions in The US. MEPS 1996-2015.

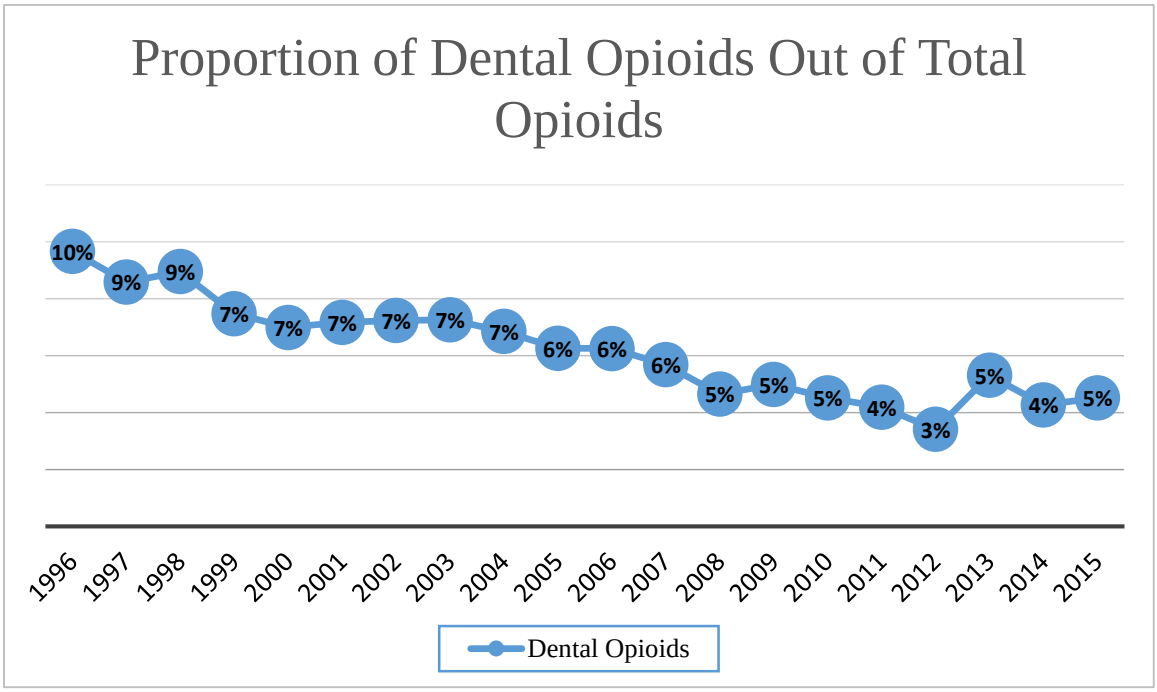


FIGURE 1.4 Total Expenses of Prescribed Opioids in 2015 Dollars, MEPS 1996-2015.

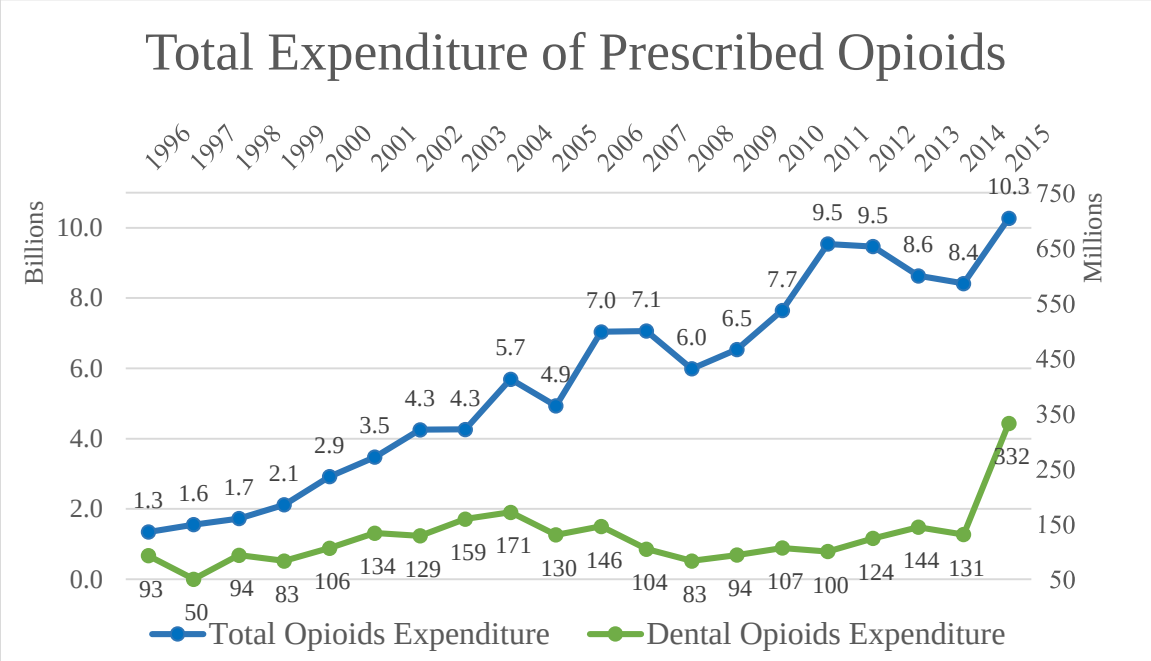


FIGURE 1.5 Proportion of Payment Source for Prescribed Dental Opioids in 2015 Dollars, MEPS 1996-2015.

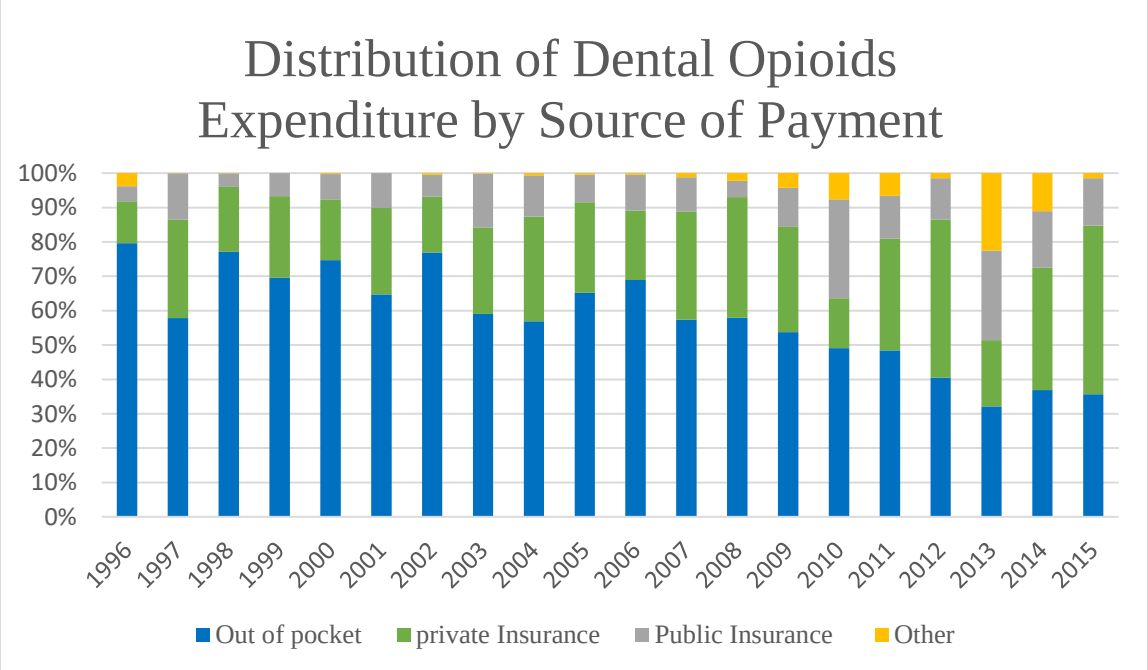
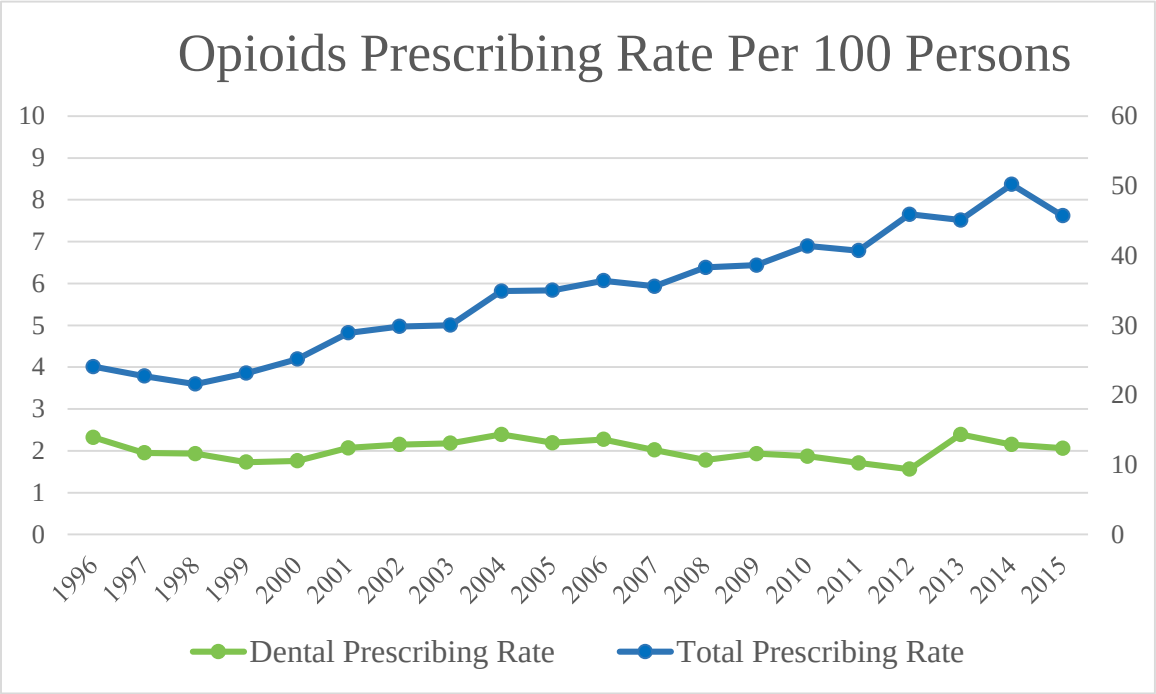


FIGURE 1.6 Change in Rate of Total and Dental Opioid Prescribing in The US, 1996–2015.



JOURNAL ARTICLE TWO

Racial Disparities in Opioid and Non-Opioid Analgesic Prescriptions by Dental Professionals in The United States

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ABSTRACT

OBECTIVE: The purpose of this investigation was to examine the association between race/ethnicity and the risk of receiving an opioid analgesic prescription by dental professionals in the United States. **METHODS:** Data on dental analgesic prescriptions, dental care utilization, patients' race and other demographic information were obtained from the Medical Expenditure Panel Survey (2002–2015) for 11,659 analgesic prescription received by a dentist. The outcome was analgesic prescription received. The main independent variable was patents' race/ethnicity. Covariates included in the analysis were gender, age, marital status, income, geographical region, and survey year. To obtain unbiased point estimates and correct variance estimation, proper sampling weights and statistical survey procedures were used. **RESULTS:** Poisson regression analysis showed that Non-Hispanic Blacks had a lower risk of receiving and opioid analgesic prescription when compared to non- Hispanic Whites (RR=0.86, 95%CI=0.82-0.89). Similarly, Hispanics and Asians showed a lower risk of receiving an opioid analgesic prescription from their dentists when compared to non-Hispanic Whites (RR=0.75,95%CI= 0.71-0.79), (RR=0.79, 95%CI=0.71-0.88). **CONCLUSION:** Racial/ ethnic disparities in opioid analgesic prescriptions by dental professionals exists in the United States. It is unclear whether it is due to overprescribing opioids to non-Hispanic whites or under prescribing to other racial minorities.

Keywords: opioids, analgesic prescriptions, race, dental.

INTRODUCTION

Prescription opioids abuse has been a growing problem in the United States. Over-prescribing of such analgesics by health professionals may unintentionally contributed to this increase in their misuse.[1-4]Due to the national growing concern and efforts to combat this problem, health professionals may relay subconsciously on subjective signs to spot drug-seeking behaviors when prescribing opioid analgesics. [5-8]

Patients' race has shown to be influential in the physicians' perception.[9] Non-Hispanic blacks were found to be perceived more negatively than non-Hispanic whites when it comes to behavioral tendencies.[10] Several published studies examined such differences in opioid prescriptions by emergency department physicians. One of the early studies, examining specifically pain management of long bone fracture in the UCLA emergency department, found that non-Hispanic whites were twice as likely to receive an analgesic compared to Hispanics.[11] Similar patterns were found between non-Hispanic whites and non-Hispanic blacks.[12] A more nationally representative study exploring racial differences found that physicians were less likely to prescribe opioids to non-Hispanic Blacks during emergency visits complaining of a migraine, back pain, and long bone fracture. The differences were more pronounced in migraine, a condition with less objective findings, compared to other complaints.[13]

A more recent study examining trends in emergency department opioid prescriptions from 1993 to 2005 found that even with the increases in opioid prescriptions, racial differences in receiving opioid analgesics persist. [14] When focusing on the management of dental pain, racial disparities in receiving an opioid in the emergency department(ED) were

not seen. Minority groups showed lower odds in receiving an opioid compared to non-Hispanic whites, but this difference was not statistically significant.[15]

Due to increased attention on the role dentists play in the prescription opioid analgesics crisis, dentists may follow the same pattern of prescribing analgesics as the emergency department physicians in an effort to reduce opioids misuse.

The objective of our study is to investigate the racial differences in receiving an opioid analgesic prescription by dental professionals in the United States. In this study, we are aiming to answer the following questions:

Is there a difference in receiving an opioid prescription from dentists in the U.S between different racial groups?

METHODS

Data Source

Data from 2002 - 2015 Medical Expenditure Panel Survey (MEPS) were used. MEPS is a set of large scale surveys of families and individuals along with their health care providers across the United States. It collects data on health care services use in the country, how frequently they are used, the cost of these services, and how they are paid for.

The Household Component (HC) of the survey provides data from individual households and their members, which is supplemented by data from their medical providers. These data are collected through interviews, which includes detailed questions about the following: demographic characteristics, health conditions, health status, use of

medical services, access to care, satisfaction with care, health insurance coverage, income, and employment.

Other components of the survey include Insurance (IC) and medical provider components (MPC). Insurance is a separate survey of employers that provides data on employer-based health insurance. Medical Provider Component (MPC) covers hospitals, physicians, home health care providers, and pharmacies identified by HC participants. Its purpose is to supplement and/or replace information received from the HC participants. This information is later incorporated into the HC data files. In this study only HC will be used along with its supplemental information provided by MPC.

HC data files used: (Full Year Population Characteristics, Dental Visits, Prescribed Medicines, Condition-Event link)

Study Population

Every year, a range of 21,571 to 33,893 individuals, of all ages, were interviewed for HC. Of those interviewed, approximately an average of (41.4%) reported having dental visits every year.

Sampling Method

MEPS household component participants are selected from communities across the United States, taken from a nationally representative subsample of households that participated in the prior year's National Health Interview Survey(NHIS). These NHIS surveys are sampled using stratified multi-stage design. The first stage is forming the Primary Sampling Units (PSUs) which each consist of one or more county. Within each PSU density, strata were made with knowledge about distribution of racial /ethnic groups

within a single or groups of blocks. In every density stratum, clusters of households were formed and a sample of these clusters was selected for use over several years of the survey. Households were selected from these cluster for each calendar year of the NHIS. Households of Hispanic and Black population were oversampled at rates of approximately 2 and 1.5 times, respectively, the rate of other households.

Data Collection

Interviews are conducted using computer-assisted personal interviewing (CAPI). This data collection instrument consists of sections that are composed of a series of computer screens containing questions, interviewing instructions, and skip pattern directions, as well as computer programming notes embedded along with each data item.

Variables of Interest

The primary outcome variables of our study are opioid prescriptions. These variables are provided in the Prescribed medications data file. Information on medication prescribed were captured in the HC of the survey, for every medical or dental event reported, using these questions:

During this visit, were any medicines prescribed for you/PERSON? Please include only prescriptions which were filled.

Please tell me the names of the prescriptions from this visit that were filled.

This information is later confirmed or edited using medical providers, dental providers and pharmacies who provided care to MEPS Household participants.

In this study opioids prescribed were defined using Multum Lexicon classification as any narcotic analgesics prescribed alone or in combination with other analgesics.Variables

used: Medication name (RXNAME), Multum Lexicon opioids classification (TC1=57, TC1S1=58, TC1S1_1=60, 191).

The primary predictor variable is Race/ethnicity. This information was captured in the HC of the survey and it was categorized as: non-Hispanic white, non-Hispanic black, Hispanics, Asian, and others. Earlier years prior to 2002 were excluded due to change in race/ethnicity categories (Prior to 2002 whites and others were collapsed into a single category). Covariates included age, gender, marital status, geographical region, year, and family income.

Age was categorized into: younger than 18,18-24,25-30,31-39,40-49,50-64, 65 and older. Gender was categorized into: male, female. Marital status was categorized into: married, not married. Geographical region was categorized into: Northeast, Midwest, South, and West. Year was categorized into survey years from 2002 to 2015.Family income was determined based on federal poverty line and categorized into adults in families with income less than 125 percent of the Federal poverty line, including those who reported negative income (poor/near poor income); families with income from 125 percent to less than 200 percent of the Federal poverty line (low income); families with income from 200 percent to less than 400 percent of the Federal poverty line (middle income); or families with income greater than or equal to 400 percent of the Federal poverty line (high income).

Statistical Analysis

All analyses were conducted using SAS Software version 9.4 (SAS Institute Inc., Cary, NC, USA). Survey procedures were used to account for MEPS complex, multistage sampling design. Sampling weights were applied to account for unequal selection

probabilities. Descriptive analysis was performed to include all variables. Bivariate analysis was done using Chi-square test. Poisson regression analysis was performed to evaluate the relationship between patients' race and the pattern of opioid and non-opioid analgesics prescription by dentists. The model was adjusted for possible confounders.

RESULTS

Our sample is representative of analgesic prescriptions associated with adults' dental visits in the United States, using data from the MEPS from 2002 through 2015. Among all 172,863 adults who reported having at least one dental visit, a total of 11,659 analgesic prescriptions were associated with these dental visits, and 8,612 of them were for opioid analgesics. The population receiving analgesic prescriptions were mostly comprised of non-Hispanic Whites (50.62 %), females (59.36%), ages above 31 (65.58%), and of middle/high income (55.21%).

Among non-Hispanic Whites that received an analgesic prescription to control dental pain, about 82% received an opioid prescription. On the other hand, for non-Hispanic Blacks, Hispanics, and Asians the proportion receiving an opioid prescription was lower with 70.96 % ,61.07%, and 64.04% respectively. Racial minorities were more likely to receive a non-opioid analgesic with 29.04% of non-Hispanic Blacks, 38.93% of Hispanics and 35.96% Asians reported receiving a non-opioid analgesic. On the other hand, only 17.68 % of non- Hispanic Whites reported receiving similar prescription from the dentist. (Table 1)

Multiple Poisson regression analysis demonstrated an association between a patient's race/ethnicity and the type of analgesic prescribed for pain by their dentist. Non-Hispanic Blacks had about 14% lower risk of receiving and opioid analgesic prescription when compared to non- Hispanic Whites (RR=0.86, 95%CI=0.82-0.89). Similarly, Hispanics and Asians showed a lower risk of receiving an opioid analgesic prescription from their dentists when compared to non-Hispanic Whites (RR=0.75,95%CI= 0.71-0.79), (RR=0.79, 95%CI=0.71-0.88) respectively. (Table 2)

Differences in analgesic prescriptions were also apparent by the geographical location with those in the northeast area of the United States having lower risk of receiving an opioid prescription compared to other regions of the country. Furthermore, those younger than 18 years of age were less likely to receive an opioid analgesic when compared to adults aged 18 and above. (Table 2)

DISCUSSION

In this study of analgesics prescriptions by dental professionals, we examined the association between the patients' race/ethnicity and their risk of receiving an opioid versus a non-opioid prescription. The findings of our study showed that racial minorities (non-Hispanic Blacks, Hispanics, and Asians) were less likely to receive an opioid prescription than non-Hispanic Whites when visiting the dental clinic.

Previous literature in the 1990 and early 2000s showed similar disparities in analgesic prescriptions in the emergency department. In 1993, Todd and colleagues found disparities between Hispanics and non-Hispanic whites in receiving pain medications at the

emergency department for long bone fractures. [16] Similar differences were also found between non-Hispanic blacks and non-Hispanic whites.[12]

More recent literature, also focusing on analgesics prescription in the emergency department, suggested all racial groups were equally likely to receive some form of analgesic when visiting the emergency department for migraine, back pain, or long bone fracture. However, disparities were found in receiving an opioid analgesic. These differences where more evident in patients complaining of migraine and back pain than in those complaining of long bone fracture. [13,17,18] Furthermore, despite the increase in opioid prescriptions over the years, studies found no evidence of narrowing racial/ethnic disparities in opioids prescribing in the emergency department.[14]

The results of our study focused on racial disparities in opioid prescriptions related to dental professionals. To our knowledge no other available study examined this relation. Available studies investigated the use of analgesics for management of non-traumatic dental pain in the emergency department and did not find similar racial/ethnic disparities. [19] Moreover, unlike back pain and abdominal pain, dental pain complains in the emergency department were not associated with racial/ethnic disparities in receiving opioid prescriptions. [15]

The results of our study were unexpected as dental professionals often prescribe opioids following a definitive dental procedure, which should lead to lower racial gap in receiving such analgesics. As more evidence supporting the use of nonsteroidal anti-inflammatory drugs (NSAIDs) for effective post-operative pain management emerges, dentists may lean into prescribing such medications to avoid possible adverse effects.[20] Therefore, it is

unclear whether these differences represent overprescribing of opioids to non-Hispanic Whites or under prescribing to racial minorities.

Although our study found an association between race/ethnicity and the patterns of opioid and non-opioid prescriptions, this finding should be considered in light of some limitations. Dental diagnosis was not provided, thus actual need for opioid prescription could not be measured. Missed non-opioids analgesics prescriptions when patients are asked to take over-the-counter analgesics might result in inaccurate assumptions of prescribing patterns. Furthermore, the study relies on self-reported MEPS household data. These data may have some under reporting by the participants. A strength of the data used is that MEPS oversamples for minority groups and provides the statistical power to examine these groups.

CONCLUSION

In conclusion, racial/ ethnic disparities in opioid and non-opioid analgesics prescriptions by dental professionals exist in the United States. It is unclear whether it is due to overprescribing opioids to non-Hispanic whites or under prescribing to other racial minorities. Identifying the causes of these differences is important to implement the appropriate intervention. Therefore, further studies are needed to understand the fundamental causes of disparities in analgesics prescriptions in the dental office.

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Table 2.1 Descriptive Statistics for Patients Who Reported Receiving an Analgesic Prescription.

		Opioid Analgesics N=8,612; Weighted N=87,208,356		**Non-Opioid Analgesics N=3,047; Weighted N=25,131,851**		
	Sample %	Sample N	Weighted %	Sample N	Weighted %	P-Value
Race						
White	50.62	4870	82.32	1032	17.68	<.0001
Black	23.94	1985	70.96	806	29.04	
Hispanic	19.08	1243	61.07	982	38.93	
Asian	3.33	234	64.04	154	35.96	
Other	3.03	280	79.30	73	20.70	
Gender						
Male	40.64	3491	77.66	1247	22.34	0.97
Female	59.36	5121	77.61	1800	22.39	
Age						
<18	8.86	660	70.47	373	29.53	0.01
18-24	13.17	1158	79.97	378	20.03	
25-30	12.38	1113	79.81	330	20.19	
31-39	16.79	1482	77.99	476	22.01	
40-49	19.14	1659	77.85	573	22.15	
50-64	22.04	1882	77.06	688	22.94	
65+	7.61	658	77.54	229	22.45	
Married						
Yes	40.13	3511	78.85	1168	21.15	0.07
No	59.87	5101	76.70	1879	23.30	
Income						
Poor	22.30	1889	77.63	711	22.37	0.0001
Near poor	6.54	524	74.31	239	25.68	
Low	15.94	1258	71.04	601	28.96	
Middle	28.50	2511	78.87	812	21.13	
High	26.71	2430	79.32	684	20.68	

Region						
Northeast	13.07	1009	70.6722	515	29.3278	<.0001
Midwest	22.84	2017	77.9136	646	22.0864	
South	37.88	3496	81.7934	921	18.2066	
West	26.20	2090	75.1202	965	24.8798	
Year						
2002	8.65	759	76.53	250	23.47	0.37
2003	7.05	648	79.60	174	20.40	
2004	8.07	721	77.78	220	22.22	
2005	7.26	658	81.26	189	18.74	
2006	8.00	697	77.70	236	22.30	
2007	6.34	550	74.90	189	25.10	
2008	5.94	512	77.88	181	22.12	
2009	7.33	637	76.98	218	23.02	
2010	5.72	513	79.59	154	20.41	
2011	5.82	511	79.04	167	20.96	
2012	6.01	496	75.11	205	24.89	
2013	8.15	686	80.39	264	19.61	
2014	7.52	615	76.65	262	23.35	
2015	8.12	609	73.50	338	26.49	

Table 2.2 Crude and Adjusted Risk Ratios of Receiving an Opioid Analgesic relative to a non-opioid analgesic.

		RR	95% CI	
Crude model				
Race	White	**1.00**		
	Black	**0.86**	**0.83**	**0.90**
	Hispanic	**0.74**	**0.70**	**0.79**
	Asian	**0.78**	**0.70**	**0.86**
	Other	0.96	0.90	1.04
Adjusted model*				
Race	White	**1.00**		
	Black	**0.86**	**0.82**	**0.89**
	Hispanic	**0.75**	**0.71**	**0.79**
	Asian	**0.79**	**0.71**	**0.88**
	Other	0.96	0.90	1.03
Gender	Male	1.00		
	Female	1.00	0.97	1.03
Age	<18	**1.00**		
	18-24	**1.13**	**1.06**	**1.20**
	25-30	**1.13**	**1.06**	**1.20**
	31-39	**1.10**	**1.03**	**1.17**
	40-49	**1.09**	**1.03**	**1.16**
	50-64	**1.07**	**1.01**	**1.13**
	65+	1.08	0.99	1.17
Income	High	**1.00**		
	Middle	1.00	0.96	1.04
	Low	**0.93**	**0.88**	**0.98**
	Near poor	0.97	0.91	1.04
	Poor	1.00	0.96	1.04
Region	Northeast	**1.00**		
	Midwest	**1.08**	**1.02**	**1.15**
	South	**1.16**	**1.10**	**1.23**
	West	**1.10**	**1.03**	**1.16**

JOURNAL ARTICLE THREE

The Effect of Federal Rescheduling of Hydrocodone Combination On Opioids Prescription Patterns by Dentists in a Dental School Setting

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ABSTRACT

OBECTIVE: The purpose of this investigation was to examine the potential effect of the DEA policy on opioid prescription protocols in dentistry. **METHODS:** Data from GSDM's clinical repository were used from July 2010 through July 2019. The primary outcome variables were opioid prescriptions and opioid morphine milligram equivalent (MME). The primary predictor used is date of opioid prescription (Time before and after the intervention). To assess the effect of hydrocodone medication reclassification on our outcome variables we used an interrupted time series (ITS) analysis with a segmented regression model. **RESULTS:** Oral surgery department prescribed only 32.5% of opioids following the DEA policy compared to 52.93% prior to its implementation. The ITS analysis showed an immediate reduction only in non-hydrocodone opioids prescribing rate by morphine milligram equivalent (MME) following the DEA policy (25.90 MME, P=0.0007). **CONCLUSION:** The 2014 intervention showed a more pronounce decrease in non-hydrocodone opioids. This may represent the success of other efforts focused on reduction of opioids prescribing by dentist rather than just a consequence of the federal policy.

Keywords: Opioids, hydrocodone, public policy

INTRODUCTION

Overprescribing of opioid analgesics by health professionals resulted in unintentional misuse and abuse of such medications.[1] The increased attention to this problem raised investigations among health care providers to assess the current pain management protocols using opioid-containing analgesics aiming to reduce its use.[2-4] In dentistry, practitioners are advised to limit opioids use to specific cases, assess pain following treatment, and not exceed three days' prescription fill. Furthermore, dentists are encouraged to register with and utilize prescription drug monitoring programs (PDMP) to promote the appropriate use of opioid analgesics for legitimate purposes and reduce its misuse.[5,6]

On a national level, new federal policies were set to manage the increasing opioids prescribing rates. In 2014, the Drug Enforcement Administration (DEA)set a policy to change the schedule of hydrocodone combination opioids from schedule III (drugs with moderate abuse potential) into schedule II (drugs with high abuse potential).[7] The intent was to limit new hydrocodone combination prescriptions and their refills, as it is one of the most commonly abused opioids.[8] A noticeable decline in the overall hydrocodone combination prescriptions (22%) occurred within a year following the 2014 policy.[9,10]However, non-hydrocodone opioid prescriptions increased by 5% within the same period.[10] Most of the opioids prescribed by dentists are combined with non-opioid analgesics (such as acetaminophen).[2,6] As a result, the 2014 policy, is expected to significantly influence the opioid prescribing patterns by dentists.

The primary objective of this study is to explore the potential effect of the DEA policy on opioid prescription protocols in dentistry looking at prescription data from an urban dental school setting.

In this study, we are aiming to answer the following questions:

- What dental procedures are opioids are often prescribed for? Among different dental specialties, who prescribe the most opioids?
- What is the impact of the hydrocodone schedule change (schedule III to II) on opioid prescription Patterns by dentists?

METHODS

Data Source

Data from the Boston University Henry M. Goldman School of Dental Medicine (GSDM) clinical repository were used. The clinical repository data are routinely collected data extracted from GSDM's electronic dental record, Salud, from all dental school patient treatment clinics from July 2010 through July 2019.

Study Population

The dataset contains 223,740 patients that had at least one dental visit in the school. Every month an average of 11,160 dental visits to GSDM clinics were recorded with 1,216,405 total number of visits throughout the nine-year period. Out of these visits, 12,807 received an opioid analgesic prescription for pain management. The total sample included

those who had at least one dental visit and received an opioid analgesic prescription for pain management. The study sample included 12,807 dental visit.

Data Collection

Data were collected routinely at the dental clinics of GSDM using face to face interview and clinical examination.

Variables of Interest

The primary outcome variable is opioid prescriptions and opioid morphine milligram equivalent (MME). MME is the amount of morphine in milligrams equivalent to the strength of the opioid dose prescribed. It was calculated using this formula:

dosage* number of tablets dispensed* morphine Conversion Factor

The primary predictor used is date of opioid prescription (time before and after the intervention). Prescription date is recorded by (month / year).

Other covariates used: Gender, Age, Dental Clinic, Dental Procedure, and type of opioid analgesic.

Gender was categorized into: male, female. Age was categorized into: younger than 18,18-25,26-35,36-45,46-55,56-64, 65 and older. Dental clinics included were categorized into: oral surgery, periodontics, implant, endodontics, advanced general dentistry, screening clinics, pre-doc clinics, emergency clinics, prosthodontics, and others. Dental procedures included were categorized into: non-surgical extraction, surgical extraction, periodontal surgery, implant placement, bone graft and site augmentation, other oral surgery procedures, emergency treatment, endodontic surgery, follow up, non-surgical endodontic procedures, diagnostic procedures, and other procedures. Types of opioid

analgesics prescribed were categorized into: hydrocodone containing opioids (hydrocodone/acetaminophen), and non-hydrocodone containing opioids (codeine/acetaminophen, oxycodone/acetaminophen, oxycodone, oxycodone/ibuprofen, tramadol, meperidine).

Statistical Analysis

All analyses were conducted using SAS Software version 9.4 (SAS Institute Inc., Cary, NC, USA). Descriptive analysis was performed to include all variables. Bivariate analysis was done using Chi-square test. Interrupted time series (ITS) analysis using a segmented regression model with maximum likelihood estimation and assuming an autoregressive correlation structure was performed to assess the effect of the hydrocodone rule change on our outcome variables. ITS models analyze changes in level and trend before and after an intervention. A key assumption of ITS is that baseline observations would have been predictive of outcome trends had the intervention of interest not occurred. Thus, the difference between actual observations and the predicted observation represents the impact of the intervention of interest. Durbin–Watson statistic was used to test for autocorrelation of the error terms in the regression model.

RESULTS

In total, our sample included 12,807 dental visit in which an opioid prescription was given by a dentist at BUSDM. From 2010 to 2019, hydrocodone-containing opioids were the most frequently prescribed (36.19%), followed by codeine/ acetaminophen combination (33.75%) and oxycodone/acetaminophen combination (27.11%). (Table1)

When looking at opioid prescribing patterns by dentists during the study period, oral surgery clinics seem to be responsible for (45.19%) of total opioids prescribed followed by perio-clinics (20.48%), implant clinics (16.19%) and, endodontic clinics (8.5%). Non-surgical and surgical extractions were associated with higher percentage of dental opioids (30.94% and 14.49%) when compared to other dental procedures. Periodontal surgeries and implant placement followed extractions with (12.2% and 11.06%) of total opioids prescribed. (Table1)

These distributions were slightly different between time periods before and after the rescheduling of hydrocodone containing analgesics. Patients after the intervention showed higher percentage of people aged 46 and older when compared to before the intervention. Oral surgery clinics were responsible for 52.93% of the opioid prescriptions before the intervention, this dropped to only 32.50% of total opioids after the intervention. More opioids were associated with periodontics and implant clinics following the intervention. Similarly, there was an increase in the percentage of periodontal surgeries and implant placement surgeries associated with opioid prescription following the intervention when compared to time period before the intervention. (Table1)

The type of opioid analgesics distribution also changed following the rescheduling intervention with a decrease in hydrocodone containing prescriptions (42.67% vs 25.57%) and an increase in codeine containing prescriptions (25.72% vs 46.90%). (Table1)

Interrupted time series analysis indicates a slight initial and monthly decrease in opioid prescription rate per 100 persons following the October 2014 intervention, but the observed

decrease wasn't statistically significant (B2=-.45, P=0.77 / B3=-0.08, P=0.32). (Table2) (Figure1) Similar results were seen after stratifying by the type of opioids, both hydrocodone and non-hydrocodone containing medications showed an initial decrease in prescribing rate per 100 persons, and a monthly decrease in rate following the intervention, but both were not statistically significant. (Table 2) (Figure 3,4)

When examining prescribing rates by morphine milligram equivalent (MME), the results showed a monthly decrease of 27.61 in MME rate per 100 persons in the months following the schedule change (P=0.01). Although an immediate reduction of 201.24 MME rate per 100 persons was also observed following the intervention, this decrease wasn't statistically significant (P=0.45). (Figure2)

After stratifying based on the type of opioids, non-hydrocodone opioids prescribing rate by morphine milligram equivalent (MME) showed a monthly decrease of 25.90 in MME rate per 100 person following the intervention (P=0.0007). (Figure6) Hydrocodone opioids showed a reduction immediately after the intervention and over the months following the intervention but it wasn't statistically significant (P= 0.84, P=0.69). (Figure5)

DISCUSSION

Following the hydrocodone reschedule in October 2014, monthly reduction in all opioids of 27.61 in MME rate per 100 persons was observed in our study. This reduction was mostly attributed to reduction in MME rate per 100 person of non-hydrocodone opioids prescribed by dentists.

In the current literature, several studies investigated the effect of the hydrocodone combination medications schedule change on the total opioid prescriptions, as well as hydrocodone containing opioids.[11-15] A nationally representative data showed a marked reduction in total opioid prescriptions by 11%, and a 26% reduction in hydrocodone containing medications from 2013 to 2015. [16] Similar results were found among Medicaid population. [14]

Jones and colleagues investigated the change in opioid prescriptions following the intervention by types of health care professionals and found almost 21% reduction in opioid prescriptions by oncologists and 38.4% reduction by surgeons. Similarly, dentists showed a 5.7% reduction in prescriptions and 2% reduction in number of tablets dispensed.[10] Although our results showed similar results with reduction in the proportion of hydrocodone opioids by 17% out of total opioids following the intervention, this reduction was not seen in the rate of prescribing per 100 persons.

Rescheduling of hydrocodone medications showed a prominent effect on the hydrocodone opioids refills which accounted for 73.7% of the reduction.[10] This can explain the limited effect of the intervention on dental hydrocodone prescriptions, as dental opioid prescriptions are made following dental procedures and are rarely refilled. [17]

When examining the rate of MME per 100 persons we found a reduction in the slope following the intervention rather than an immediate effect. Furthermore, it was more apparent in non-hydrocodone opioids. This reduction can be explained by the collective efforts implemented to control overall opioids prescriptions (e.g. Use of Prescription Drug Monitoring Program) rather than the rescheduling intervention alone.[6,16]

Our study has several limitations to consider. First, our data are taken from a single institution and the results cannot be generalized to all U.S dentists. Second, the prescriptions are only representative of the dental records and No claims data were used to confirm if the patients filled the prescriptions. The strength of the study can be seen in the use of rates per 100 persons to account for change in the number of people seen in the clinic rather than just the number of the opioid prescriptions. Furthermore, ITS design has the added advantage to control for autocorrelation in the data, as past prescription patterns can affect future prescriptions.

CONCLUSION

The 2014 intervention is associated with a decrease in the rates of opioids MME per 100 persons. This decrease was more pronounced in non-hydrocodone opioids. This may represent the success of other efforts focused on reduction of opioid prescribing by dentists rather than just a consequence of the federal policy. Our study highlights the need for more studies to explore the potential effect of different interventions in changing the prescribing rates of opioid analgesics by dentists.

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Table 3.1 Demographic and Clinical Characteristics of Patients Receiving an Opioid Analgesic Before and After Rescheduling of Hydrocodone.

		No. (%) of Opioid Prescriptions				
	Sample %	Before (N=7954)	Before %	After (N=4853)	After %	P-Value
Gender						
Male	50.39	4056	50.99	2397	49.39	0.079
Female	49.61	3898	49.01	2456	50.61	
Age						
<18	2.47	270	3.39	46	0.95	<.0001
18-25	10.52	936	11.77	411	8.47	
26-35	16.89	1397	17.56	766	15.78	
36-45	16.05	1348	16.95	708	14.59	
46-55	22.55	1732	21.78	1156	23.82	
56-64	18.59	1254	15.77	1127	23.22	
65+	12.93	1017	12.79	639	13.17	
Dental Clinic						
Oral Surgery	45.19	4210	52.93	1577	32.50	<.0001
Periodontics	20.48	1232	15.49	1391	28.66	
Implant	16.19	1008	12.67	1066	21.97	
Endodontics	8.50	774	9.73	315	6.49	
AEGD	3.37	260	3.27	172	3.54	
Screening	2.28	255	3.21	37	0.76	
Pre-Doc	2.12	145	1.82	126	2.60	
Emergency	0.87	9	0.11	102	2.10	
Prosthodontics	0.57	37	0.47	36	0.74	
Others	0.43	24	0.30	31	0.64	
Dental Procedure						
Non-Surgical Extraction	30.94	2552	32.08	1410	29.05	<.0001
Surgical Extraction	14.49	1384	17.40	472	9.73	
Periodontal Surgery	12.20	807	10.15	756	15.58	

Implant Placement	11.06	741	9.32	676	13.93	
Bone Graft and Site Augmentation	7.21	410	5.15	514	10.59	
Other Oral Surgery Procedures	6.68	687	8.64	169	3.48	
Emergency Treatment	4.87	395	4.97	229	4.72	
Endodontic Surgery	4.47	413	5.19	160	3.30	
Follow Up	2.79	126	1.58	231	4.76	
Non-Surgical Endodontic Procedures	2.72	242	3.04	106	2.18	
Diagnostic Procedures	1.54	118	1.48	79	1.63	
Other Procedures	1.02	79	0.99	51	1.05	
Opioid Analgesic Type						
Hydrocodone/Acetaminophen	36.19	3394	42.67	1241	25.57	
Codeine/Acetaminophen	33.75	2046	25.72	2276	46.90	
Oxycodone/acetaminophen	27.11	2442	30.70	1030	21.22	
Oxycodone	2.11	19	0.24	251	5.17	<.0001
Oxycodone/ibuprofen	0.52	41	0.52	26	0.54	
Tramadol	0.23	0	0	29	0.60	
Meperidine	0.09	12	0.15	0	0	

Table 3.2 Interrupted Time Series Analysis of the Association Between Hydrocodone Rescheduling and Dental Opioids Prescription.

VARIABLE	COEFFICIENT (SE)	P-VALUE
Prescription rate per 100 person		
All opioids		
Intercept β_0	3.81 (1.56)	0.02
Baseline trend β_1	0.05 (0.05)	0.33
Level change after rescheduling β_2	-0.45 (1.50)	0.77
Trend change after rescheduling β_3	-0.08 (0.08)	0.32

Hydrocodone prescriptions		
Intercept β_0	1.44 (0.65)	0.03
Baseline trend β_1	-0.01 (0.02)	0.71
Level change after rescheduling β_2	-0.06 (0.54)	0.91
Trend change after rescheduling β_3	-0.01 (0.04)	0.67
Non-hydrocodone prescriptions		
Intercept β_0	1.38 (0.63)	0.03
Baseline trend β_1	0.02 (0.02)	0.25
Level change after rescheduling β_2	-0.55 (0.70)	0.43
Trend change after rescheduling β_3	-0.06 (0.03)	0.09
MME rate per 100 person		
All opioids		
Intercept β_0	792.98 (207.07)	0.0002
Baseline trend β_1	11.65 (7.21)	0.11
Level change after rescheduling β_2	-201.24 (266.25)	0.45
Trend change after rescheduling β_3	-27.61 (10.62)	0.01
Hydrocodone prescriptions		
Intercept β_0	202.41 (93.58)	0.03
Baseline trend β_1	-1.07 (3.03)	0.73
Level change after rescheduling β_2	-15.31 (78.01)	0.84
Trend change after rescheduling β_3	-2.01 (5.00)	0.69
Non-hydrocodone prescriptions		
Intercept β_0	589.51 (145.41)	0.0001
Baseline trend β_1	11.95 (5.13)	0.02
Level change after rescheduling β_2	-104.78 (196.33)	0.59
Trend change after rescheduling β_3	-25.90 (7.38)	0.0007

Figure 2.1 Interrupted Time Series Analysis Showing Opioids Prescribing Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.

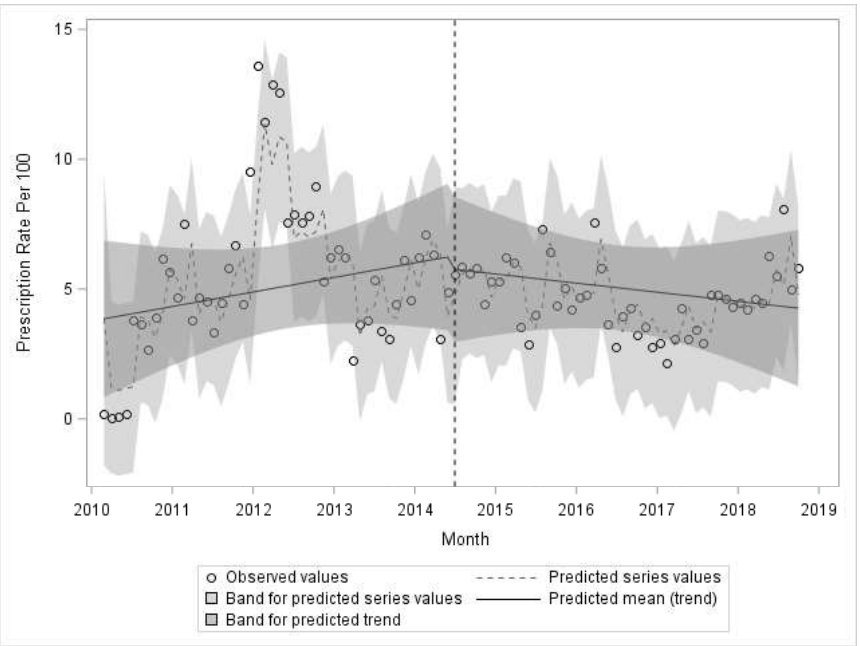


Figure 2.2 Interrupted Time Series Analysis Showing Opioids Morphine Milligram Equivalent (MME) Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.

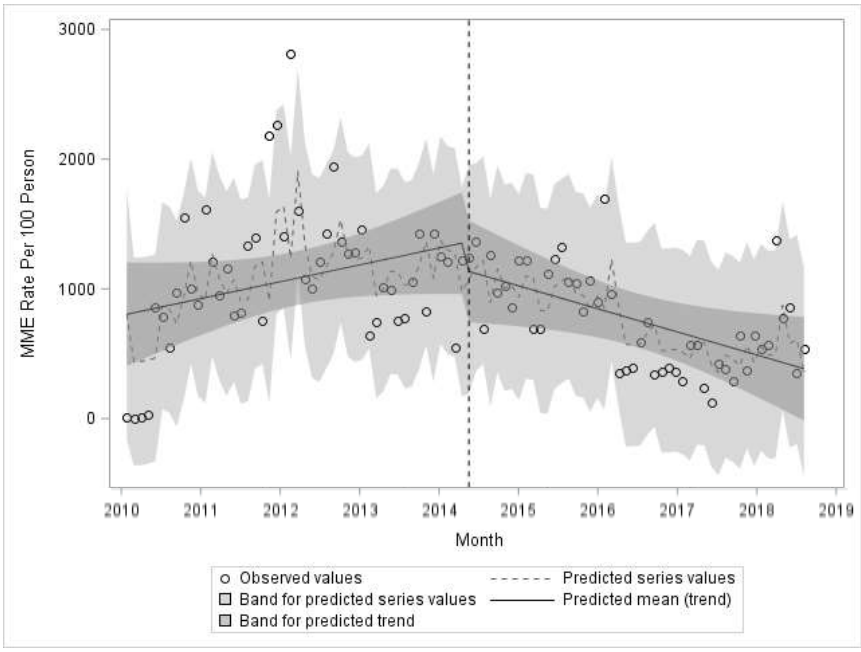


Figure 2.3 Interrupted Time Series Analysis Showing Hydrocodone Opioids Prescribing Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.

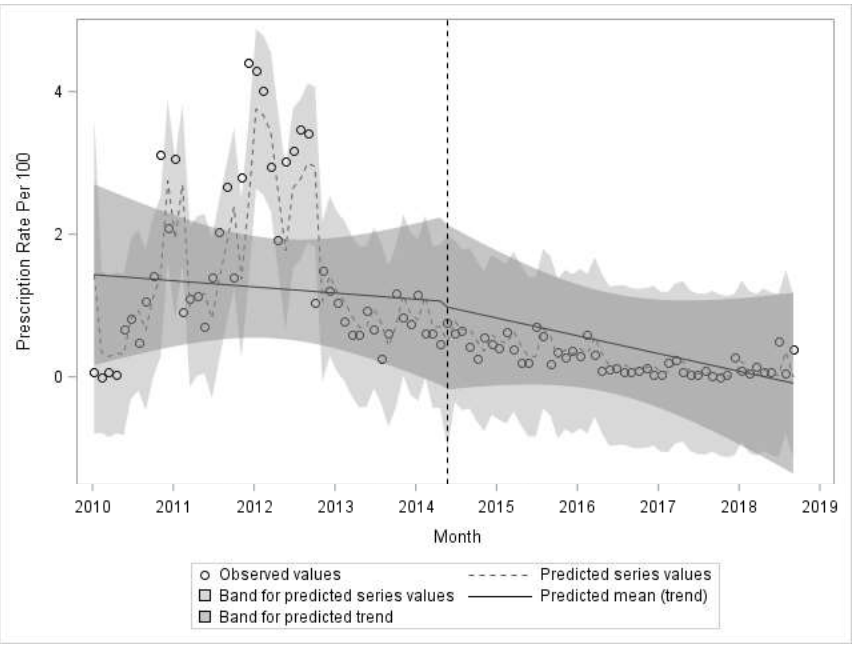


Figure 2.4 Interrupted Time Series Analysis Showing Non-Hydrocodone Opioids Prescribing Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.

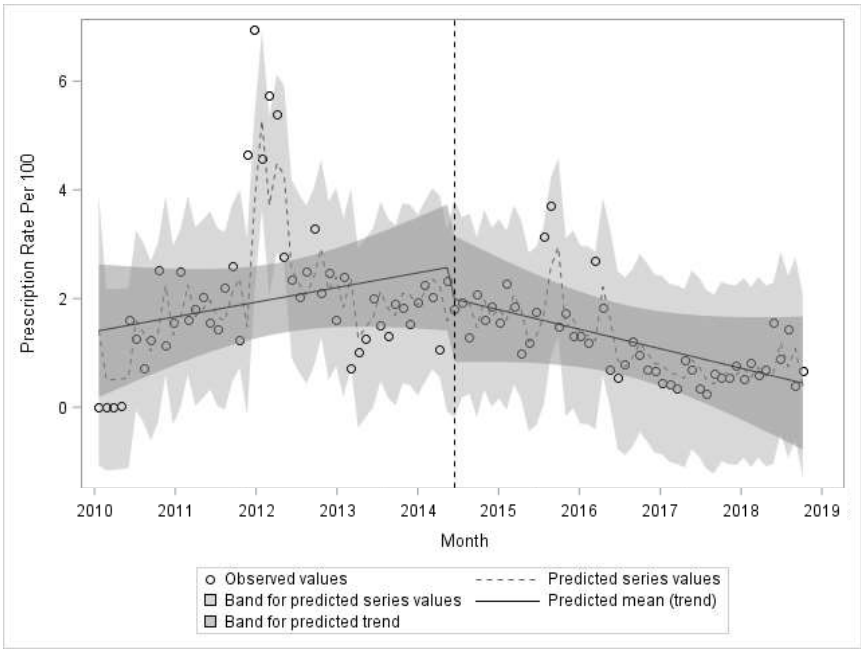


Figure 2.5 Interrupted Time Series Analysis Showing Hydrocodone Opioids Morphine Milligram Equivalent (MME) Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.

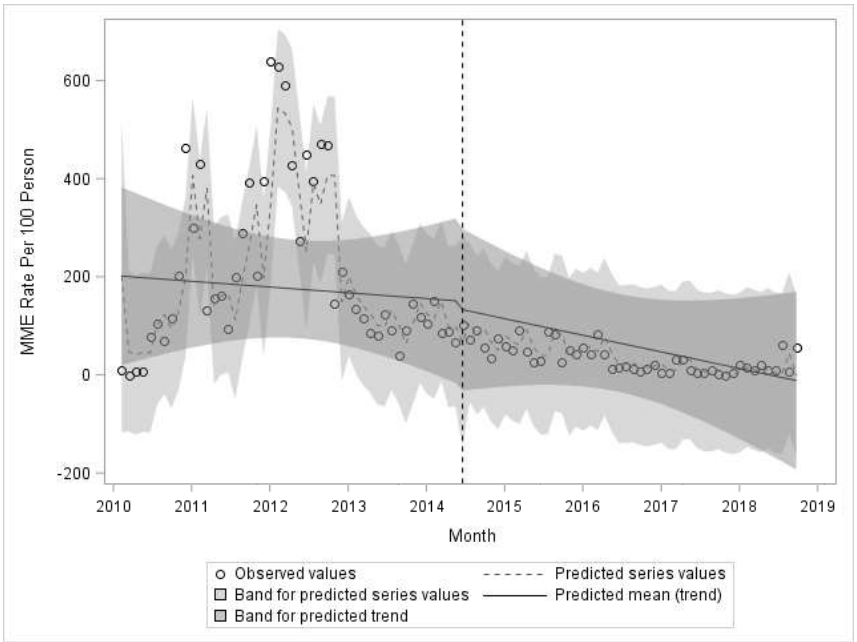
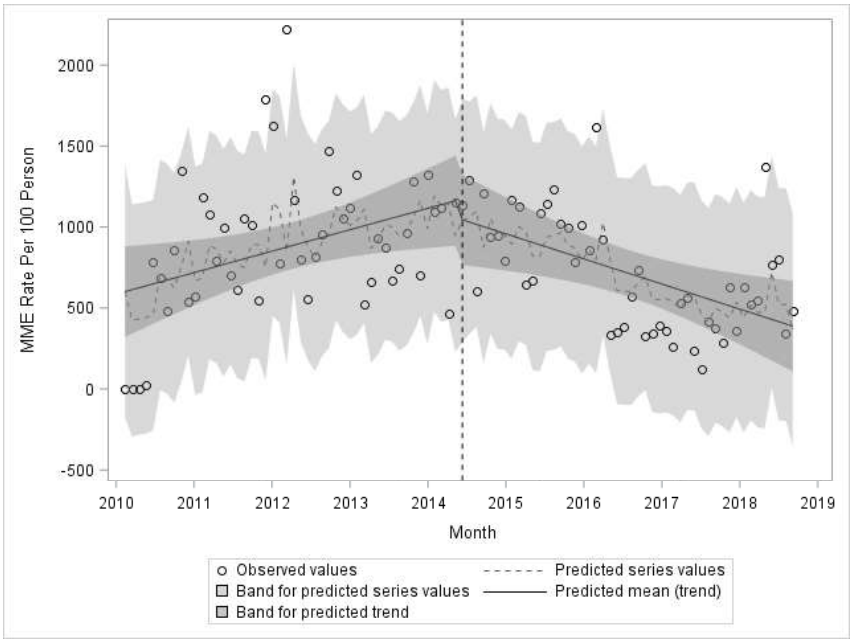


Figure 2.6 Interrupted Time Series Analysis Showing Non-Hydrocodone Opioids Morphine Milligram Equivalent (MME) Rate Per 100 Person Following the Rescheduling of Hydrocodone Medications.



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List of Abbreviated Journal Titles:

Br J Oral Surg…. British Journal of Oral and Maxillofacial Surgery

*Br J Pain….*The Brazilian Journal of Pain

*Br J Pharmacol ….*British Journal of Pharmacology

Clin Infect Dis….Clinical Infectious Diseases

*Clin Toxicol (Phila)….*Clinical toxicology (Philadelphia, Pa.)

Curr Med Res Opin….Current Medical Research and Opinion

*JAMA Intern Med….*Journal of the American Medical Association Internal Medicine

*JAMA Surg….*Journal of the American Medical Association Surgery

*JAMA….*The Journal of the American Medical Association

J Am Geriatr Soc….Journal of the American Geriatrics Society

*J Gen Intern Med….*Journal of General Internal Medicine

*J Manag Care Spec Pharm….*Journal of Managed Care & Specialty Pharmacy

J Opioid Manag…. Journal of Opioid Management

*Med Care….*Journal of Medical Care

*Pharmacoepidemiol Drug Saf….*Pharmacoepidemiology and Drug Safety

Pharmacol Rev…. Pharmacological Reviews

Scand J Pain…. Scandinavian Journal of Pain

*S D Med….*Journal of the South Dakota State Medical Association

*World J Emerg Med….*World Journal of Emergency Medicine

*West J Emerg Med….*Western Journal of Emergency Medicine

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