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Potentially Inappropriate Medication Combination with Opioids among Older Dental Patients: A Retrospective Review of Insurance Claims Data

Jifang Zhou^{1,2,*}, Gregory S. Calip^{1,3,*}, Susan Rowan⁴, Jessina C. McGregor⁵, Rosanne I. Perez⁶, Charlesnika T. Evans^{7,8}, Walid F. Gellad^{9,10}, Katie J. Suda^{9,10}

¹University of Illinois at Chicago, College of Pharmacy, Chicago, IL

²School of International Pharmaceutical Business, China Pharmaceutical University, Nanjing, Jiangsu, China

³Flatiron Health, New York, NY

⁴University of Illinois at Chicago, College of Dentistry, Chicago, IL

⁵Oregon State University, College of Pharmacy, Corvallis, OR

⁶University of Illinois at Chicago, College of Medicine, Chicago, IL

⁷Northwestern University Feinberg School of Medicine, Chicago, IL

⁸Center of Innovation for Complex Chronic Healthcare, Hines VA Hospital, Hines, IL

⁹University of Pittsburgh, Department of Medicine, Pittsburgh, PA

¹⁰Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, PA

Abstract

Introduction—Opioid prescribing by dentists for older patients receiving medications with potential contraindications and the subsequent impact on acute care outcomes is not well described.

Objectives—Our objective was to evaluate the use of potentially inappropriate medication combinations (PIMC) involving opioids prescribed by dentists according to the Beers criteria and risks of 30-day emergency room (ER) visits and all-cause hospitalization among commercially insured dental patients ages 65 years and older.

Methods—We conducted a retrospective cohort study of 40,800 older dental patient visits where opioids were prescribed between 2011 and 2015 using the Truven Health MarketScan® databases.

Corresponding author: Dr. Gregory S. Calip, University of Illinois at Chicago, Center for Pharmacoepidemiology and Pharmaco-economic Research; 833 South Wood Street MC 871, Chicago, Illinois 60612; gcalip@uic.edu; **Phone:** 312-355-5318

Twitter handle: @gregcalip.

*Authors contributed equally

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Data collection from dental, medical, and pharmacy claims included information on the concurrent use of PIMCs and outcomes of all-cause acute care utilization over the 30-day period after dental encounters.

Results—For the overall cohort, the median age was 69 years, and 45% were female. The prevalence of PIMCs per Beers Criteria was 10.4%. A total of 947 all-cause acute care events were observed in the 30 days post-dental visit. Patients with PIMCs involving opioids prescribed by dentists according to the Beers criteria had higher rates of acute care use (3.3% vs. 2.2%, $p<0.001$), which were associated with an increased risk of all-cause acute care utilization (adjusted RR 1.23; 95% CI 1.02–1.48). A dose-response relationship was seen with increasing oral morphine equivalents prescribed and increased acute care utilization ($P<0.001$).

Conclusion—A significant proportion of older patients receiving opioids at dental visits use psychotropic medications that in combination should be avoided according to the American Geriatric Society Beers criteria.

Keywords

Potentially inappropriate medications; Beers criteria; dentistry; opioids; geriatrics

INTRODUCTION

The United States is experiencing a devastating public health crisis that causes over 33,000 deaths annually related to opiate analgesics.^{1, 2} Opioid use is common among older patients given the increasing prevalence of medical conditions associated with acute and/or chronic pain, including opioids prescribed in dental settings.^{3–7} Rates of polypharmacy are high among older patients⁸, often a result of necessary medication management of multiple comorbidities.⁹ However, this is problematic due to increased risk for medication-associated adverse effects and drug-drug interactions.¹⁰

The American Geriatrics Society Beers criteria provide guidance to limit potentially inappropriate medication combination (PIMC) use in older adults.¹¹ Among their recommendations is the identification of central nervous system (CNS)-active medications in the following classes to be high risk: antipsychotics; benzodiazepines, nonbenzodiazepine receptor agonist hypnotics (NBRAs), tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and opioids.¹² CNS polypharmacy (use of 3 or more of these drugs) is associated with higher risk of falls¹³, fracture^{13, 14} and cognitive decline.¹⁵ In addition, it is strongly recommended to avoid overlapping use of benzodiazepines, gabapentin, and pregabalin with opioids. Co-prescribing of opioids and benzodiazepines is associated with greater risk of opioid overdose deaths.¹⁶

Evidence about the adverse consequences of CNS polypharmacy in combination with acute opioid treatment in outpatient dental settings is limited. Recently, the American Dental Association issued a clinical reference manual and statement on restricting opioid prescriptions by dentists.¹⁷ Awareness of the Beers Criteria along with supporting comprehensive medication reconciliation among older patients in community dental settings may be an important step in curbing the poor outcomes associated with the opioid

epidemic. Our objective was to determine the prevalence of PIMCs in combination with opioids prescribed by dentists among older dental patients and its impact on subsequent hospitalizations and emergency room (ER) visits.

METHODS

Study design and data source

We conducted a population-based retrospective cohort study of patients ages 65 years and older who received dental services between 2011 and 2015 using the Truven Health MarketScan Commercial Claims/Encounters, Medicare Supplemental, Coordination of Benefits Research Databases. These databases contain claims from inpatient, outpatient, and pharmacy encounters from commercially-insured patients in the U.S. Within this national sample, a convenience sample of 8 million patients with enrollment in health plans covering dental, pharmacy, and medical benefits was included in the present study.

This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline and was determined to be exempt from requiring informed consent by the University of Illinois at Chicago Institutional Review Board.

Study population

We identified over 1.4 million dental visits among older patients who concurrently had a new prescription for an opioid-containing analgesic medication on the same date. All individuals who contributed eligible dental visits to the analytical cohort were required to have at least 12 months of continuous enrollment in their health plan including medical and prescription drug benefits prior to their dental visit, as well as at least 30 days after their dental services date. We used Dental Procedures and Nomenclature (CDT) codes to identify and classify dental visits in accordance with a standardized coding structure established by the American Dental Association (ADA). All opioids originating from outpatient settings were identified using National Drug Codes (NDCs) from pharmacy dispensing records. We further ascertained medical conditions using International Classification of Diseases (ICD) codes; ICD-9 codes before 10/1/2015 were converted to ICD-10 codes based on the guidance from the Centers for Disease Control and Prevention.¹⁸

Our cohort included patients ages 65 years and older receiving opioid prescriptions on the same day as their dental visit, but excluded those with the following: (i) any hospice stay in the past 12 months; (ii) a prior medical provider encounter occurring within the prior 7 days; (iii) evidence indicating history of medical conditions involving chronic pain using a validated algorithm¹⁹(e.g., inflammatory spondylopathy, psychogenic pain) or diagnoses for oral pain; (iv) history of sickle cell disease;(v) history of cancer and/or (vi) recent treatment with chemotherapeutic agents within the 30 days prior to the dental visit. We excluded opioids in forms other than tablet and capsules and dispensing records of opioids with missing quantity or strength.

Potentially inappropriate medication combination (PIMC) and CNS polypharmacy

We defined PIMCs involving dental opioids prescription according to the Beers Criteria using the date of dental visits involving an opioid prescription as the index date (Supplemental Figure 1). The list of psychotropic medications included in this study is summarized in Supplemental Table 1. A time-varying approach was used to identify episodes of PIMC use based on days' supply starting from the dispensing date in outpatient settings. Use of PIMC and polypharmacy was assessed on a daily basis over the duration of days' supply for dental visit-related opioid prescriptions. At least one day of overlap was required with benzodiazepines, gabapentin, pregabalin, and/or at least two CNS-active medications to define PIMC exposure according to the Beers criteria.

Outcome measures

All-cause and opioid-related ER visits over the 30-day period following dental encounters were defined based on procedure codes, revenue codes, and place-of-service codes. Hospital admissions were identified according to discharge summaries, and ICD-9-CM codes were used to identify opioid-related outcomes. We defined opioid-related ER visits and hospital admissions based on diagnosis codes indicating opioid poisoning or opioid-related clinically significant adverse events. ICD-9 diagnosis code for poisoning by opiates and related narcotics (9650x); alteration of consciousness (7800x); malaise, fatigue, or lethargy (7807x); respiratory failure (51881, 51882); or constipation (5640x) were identified from discharge summaries and claims from ER settings.²⁰ An ER encounter was identified by procedure and revenue center codes. The rates of all-cause ER encounters and hospitalization, as well as any encounter related to clinically significant opioid events were compared between patients receiving PIMC according to Beers criteria and those that did not.

Covariates

Demographic and clinical characteristics of the study cohort were ascertained over the 1-year baseline period prior to the eligible dental visit associated with opioid prescriptions. Age groups were categorized into 65 to 74 years, 75 to 84 years, and 85 years and older. Region was classified as South, West, East, and Midwest consistent with the U.S. Census Bureau. We determined the burden of comorbidities by ICD-9 codes during the 12-month pre-index period and calculated the Charlson Comorbidity Index.^{21, 22} Pre-index mental health disorders were assessed using diagnosis codes and categorized into mood disorders, psychosis, and behavioral disorders.²³ To account for baseline healthcare utilization patterns, we examined ER visits and hospitalizations occurring in the 90 days prior to the dental visit-related opioid prescription. We calculated oral morphine equivalent (OME) by converting opioids to oral morphine doses as a metric based on established conversion factors to evaluate possible dose-response relationships between increasing OME and risks of acute care events.²⁴ The potency of different opioid therapies was assessed using OME throughout the whole treatment duration (at the prescription level). Pain intensity associated with the dental visits was defined using established criteria and evaluated and categorized separately using CPT and HCPCS codes.^{25, 26}

Statistical analyses

We calculated the proportion of dental visits involving opioid prescriptions considered to be PIMC per Beers Criteria. We compared the medians of continuous variables and categorical variables using the Wilcoxon rank-sum test and the chi-square test, respectively. Multivariable generalized estimating equations (GEE) were used to model the association between patient and visit characteristics with dental opioid co-prescribing that was potentially inappropriate, calculating adjusted odds ratios (OR) and robust 95% confidence intervals (CI). Because the unit of observation in our data is a dental visit with an opioid prescription dispensed on the same day, some patients contributed multiple observations over the study period. We therefore adjusted our standard errors for clustering at the patient level.²⁷ A first-order autoregressive matrix was incorporated into all GEE models to account for correlation of multiple visits. Similarly, we examined the association between PIMC and acute care utilization using modified Poisson regression models with robust standard errors, calculating adjusted rate ratios (RR) and 95% confidence intervals, after adjusting for relevant covariates specified *a priori*.

To assess the potential dose-dependent relationship on both opioid and CNS medication, we assessed the treatment effect of one additional day of overlap as well as number of CNS medications being co-administered after the dental visit. We also conducted stratified analyses restricting to patients with pre-existing mental health disorders.

SAS 9.4 (SAS Institute, Inc, Cary, NC) was used for all analyses. A priori hypothesis tests were performed with a two-tailed α level of 0.05.

RESULTS

A total of 40,800 eligible dental visits during which opioids were prescribed was included in our analytical sample. A flow diagram describing the application of our inclusion and exclusion criteria is shown in Supplemental Figure 1. Among these eligible dental encounters, 45% were female patients, and the median age at the dental visit was 69 years [interquartile range 66–75]. (Table 1) The majority of dental visits included diagnostic codes for oral and maxillofacial surgery (60%) and/or diagnostic procedures (45%).

Results on PIMC per Beers and opioids prescribed by dentists

Using the Beers criteria, 4,239 (10%) dental visits with same day opioid prescriptions also had PIMC prescribed. Among these dental visits, 6.4% of dental opioids were administered with two or more CNS-active drugs; and 5.7% and 2.1% involved co-prescribing of benzodiazepines and gabapentin/pregabalin, respectively. Patients with PIMC use were older (72.6 vs. 71.5 years, $P<0.001$), more likely to be female (57.2% vs. 43.6%, $P<0.001$), and were more likely to have a higher Charlson Comorbidity Index (score of 5+, 46.8% vs 35.8%; $p<0.001$).

Patient and clinical characteristics associated with PIMCs

In the multivariable logistic GEE model (Table 3) of patients receiving opioids at their dental visits, PIMC prescribing was more likely for women (OR 1.68; 95% CI 1.57–1.80), and

for patients aged 75–84 years (compared to 65–74 years) (OR 1.15, 95% CI 1.05–1.26). PIMC prescribing was also more prevalent among patients with pre-existing mental health conditions including mood disorders (OR 3.14, 95% CI 2.79–3.52) and psychoses (OR, 4.02; 95CI 3.46–4.68). A history of ER visits and hospitalizations over the prior 90 days was not associated with PIMC use.

Results on all-cause and opioid-related acute care uses.

Over the period following dental visits, all-cause acute care use was higher among dental patients receiving opioids and PIMC compared to patients without PIMC (7-day period, 0.8% vs. 0.6% $P=0.037$; 30-day period, 3.3% vs. 2.2% $P<0.001$, respectively). (Table 2) In the unadjusted analysis, we observed a trend toward greater opioid-related ER visits and hospitalizations over the 30-day period (0.4% vs. 0.2% $P=0.069$), but these increased rates were not statistically significant.

Association between exposure and 30-day acute care utilization

The multivariable modified Poisson regression model was adjusted for patient demographic and clinical factors, as well as history of acute care utilization in the past 90 days from the dental visits associated with opioid dispensing by dentists (Table 4). Dental visits with opioids and PIMC prescribing were associated with a 23% increase (95% CI 2%–48%, $P=0.032$) in 30-day all-cause ER visits and hospitalizations as compared to visits with opioids only. After controlling for age, sex, comorbidities, 90-day ER and hospitalization history, specific opioid agent, and pre-existing mental health conditions, we found that increasing OME were positively associated with increased all-cause ER visit and hospitalization risks ($P=0.027$) in patients receiving PIMCs.

Sub-analysis

We further assessed the effect of opioid prescribing and PIMC use and found that having two or more psychotropic medications irrespective of medication class was associated with an increased risk of all-cause acute care utilization compared to no psychotropic medications (RR 1.33 95% CI 1.02–1.72) (Supplemental Table 2). Additionally, duration for overlapping use of opioids and PIMC for more than 3 days were associated with a 47% increased risk (95% CI 11–95%) of 30-day all-cause acute care use after dental visits (Supplemental Table 3).

We assessed subjects exposed to CNS-active drugs on the day before the dental visit based on their pharmacy dispensing records and found that 8,737 (21.4%) of all eligible visits had concomitant use of a CNS-active drug one day before the dental encounter. The proportion of pre-existing CNS-active drug exposure one day before dental visits was significantly higher in the PIMC group than dental visits without PIMCs involving opioids from dental encounters (93.0% vs. 13.1%, $P<0.001$). (Table 1)

DISCUSSION

In this large retrospective study of dental visits for older patients where opioids were prescribed, we found that one in ten dental visits involved co-prescribing of opioids

and CNS-active drugs that were potentially inappropriate according to Beers criteria. Patients receiving these medications experienced an increased risk of all-cause ER visits and hospitalization in the 30-day period following dental visits. In the updated Beers Criteria, listed drug-drug interactions involving opioids were expanded, reflecting evidence of substantial harms. Consequently, the population-level prevalence of PIMC is expected to rise with successive guideline updates.

Our study identified a high proportion of older patients with pre-existing mental health conditions requiring medical treatment. Use of psychotropic medications has increased among older adults in the U.S.; elderly CNS polypharmacy more than doubled between 2004–2006 and 2011–2013.²⁸ A systematic review found that patient-level prevalence of potentially inappropriate medication use ranged between 14% and 23.5% in the elderly as defined by the Beers criteria.²⁹ In another study of 400 elderly ER patients, an opioid with concomitant Beers Criteria medication was found in 29% of the subjects.³⁰ Patients receiving opioids and benzodiazepines increased by 8% and 31%, respectively, from 2002 to 2014; concomitant use of both classes of drugs increased from 6.8% to 9.6%.³¹ Together, these studies signal a need for increased vigilance to identify possible overlap of these medications subsequent to dental visits and procedures.

Evidence on the impact of PIMC on mortality and quality of life is inconsistent, although inappropriate medications are associated with increased risk of hospitalization in community-dwelling elderly.³² CNS drug-drug interactions with opioids, even when prescribed for a short period of time, deserve clinical attention by pharmacists and other practitioners able to perform comprehensive medication reconciliation.³³ The greater prevalence of CNS-active medication use increases the likelihood that incidental co-prescribing of CNS-active drugs will occur with opioids prescribed for acute pain management, including in dental settings. Our findings affirm the Beers update in 2019 that indicate that even a short days' supply or opportunity for drug-drug interaction carries significantly increased risk for acute care utilization. Drug-drug interactions involving cytochrome P450 enzymes are common among older individuals with chronic comorbid conditions.³⁴ Pharmacodynamic interactions between benzodiazepines and other CNS-active depressants, PIMCs of interest for their interaction with acute opioid prescribing, have synergistic effects on CNS depression, causing confusion, and contributing to risk of falls.³⁵ In addition, non-pharmacologic strategies for pain management should be considered such as patient education, counseling and other behavioral interventions.

Greater accessibility of comprehensive electronic health records to oral health practitioners may be the key to comprehensive capturing of medication history. The ability of dentists to obtain an adequate medication history for older patients through self-report is limited and may be a contributing factor to the risk of adverse co-prescribing of opioids. A number of studies have investigated trends in opioid prescribing by dentists. One study using data from the South Carolina prescription drug-monitoring program found that oral health professionals prescribed a disproportional percentage of immediate-release opioids in South Carolina.⁶ Prescription drug monitoring programs (PDMP) have been shown to reduce prescribing of opioids by dentists³², although options for acute pain relief among older patients may be limited. Alternatives to opioid analgesics such as nonsteroidal anti-

inflammatory drugs may not always be possible given their contraindication with other disease states or concurrent medications. Pharmacists have an opportunity to serve as moderators for hazardous co-prescribing, understanding that dispensing even short courses or as-needed opioid analgesic treatments carry these adverse consequences.

Strengths and limitations of this study

Our study has a number of strengths. This is the first study evaluating opioid and CNS-active PIMC co-prescribing among older patients receiving dental services, with population-based, nationally representative data. Second, we adopted conservative measures to minimize misclassification of opioid prescriptions from non-dental settings. We further restricted our analytical cohort to dental visits with opioids dispensed on the same date as the dental procedure to enhance the specificity of the opioid-related dental visits. Moreover, we excluded patients with chronic diseases or cancer requiring frequent opiate analgesics from the beginning. In this way, we minimized the likelihood of observing opioids attributed to health care visits outside of dental settings.

These results should be interpreted in light of the study's limitations. First, our analyses are based on a sample of commercially insured patients with both medical and dental coverage. Many subjects in our databases were covered by Medicare Advantage plans. As a result, these findings may not be representative of patients with public plans such as Medicare and Medicaid and those who are uninsured. Second, we relied on patients who used emergency room or inpatient services to account for adverse effects associated with PIMC with dental opioids. This approach could underestimate the true risks of overdoses because at least a proportion of adverse events occurred outside of ER/hospital care settings, or patients did not seek immediate medical attention. It is also possible that events such as falls, cognitive decline, or fractures are under-represented in a claims dataset. Third, our use of pharmacy dispensing data to define medication exposure assumes that patients take the medications immediately, consistently and as directed. Last, a limitation of nonrandomized medication use such as ours is the potential for confounding by indication, whereby the risk of our outcome of interest (i.e., ER visits and hospitalization) is greater among patients with medical conditions (e.g., mental health disorders) that predispose them to use of our exposure (i.e., CNS-active PIMCs). We addressed this potential confounding through: (i) covariate adjustment for history of recent ER visits and hospitalizations prior to the dental visit; and (ii) stratification of mental health conditions in fully adjusted multivariable models. Still, confounding by unmeasured covariates and residual confounding by indication cannot be fully ruled out.

CONCLUSIONS

These findings have important implications and deserve clinical attention. Dentists' limited access to and resources for comprehensive medication reconciliation may be increasing the risks of adverse events when prescribing opiate analgesics. Dentists should be familiar with the Beers criteria cautioning against prescribing of opioids in older patients taking multiple psychotropic medications, such as benzodiazepines and gabapentin. Also, when prescription opioids are indicated, a short-term prescription at the lowest effective dose should be

prescribed, as we observed a dose-response relationship with duration of overlapping co-prescribing and number of CNS-active drugs. Other health care practitioners with a comprehensive history of patients' medication use, such as pharmacists, are positioned to support dentists' prescribing of opioid and non-opioid analgesics.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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REFERENCES

1. Dart RC, Surratt HL, Cicero TJ, et al. Trends in opioid analgesic abuse and mortality in the United States. *The New England journal of medicine* 2015;3:241–8.
2. O'Donnell JK, Gladden RM, Seth P. Trends in Deaths Involving Heroin and Synthetic Opioids Excluding Methadone, and Law Enforcement Drug Product Reports, by Census Region - United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017;34:897–903.
3. Suda KJ, Durkin MJ, Calip GS, et al. Comparison of Opioid Prescribing by Dentists in the United States and England, 2016. *JAMA Netw Open* 2019;5:e194303.
4. Farag A, York J, Finkelman M, Desai B. Prescription of potentially inappropriate medications in geriatric patients: data from a single dental institution. *Oral Surg Oral Med Oral Pathol Oral Radiol* 2019;1:e6–e12.
5. Gupta N, Vujicic M, Blatz A. Opioid prescribing practices from 2010 through 2015 among dentists in the United States: What do claims data tell us? *Journal of the American Dental Association* (1939) 2018;4:237–45.e6.
6. McCauley JL, Hyer JM, Ramakrishnan VR, et al. Dental opioid prescribing and multiple opioid prescriptions among dental patients: Administrative data from the South Carolina prescription drug monitoring program. *Journal of the American Dental Association* (1939) 2016;7:537–44.
7. Suda KJ, Zhou J, Rowan SA, et al. Overprescribing of Opioids to Adults by Dentists in the U.S., 2011–2015. *American journal of preventive medicine* 2020;4:473–86.
8. Qato DM, Wilder J, Schumm LP, Gillet V, Alexander GC. Changes in Prescription and Over-the-Counter Medication and Dietary Supplement Use Among Older Adults in the United States, 2005 vs 2011. *JAMA Intern Med* 2016;4:473–82.
9. Wise J. Polypharmacy: a necessary evil. *BMJ* 2013;f7033. [PubMed: 24286985]
10. Herxheimer A, McGettigan P. Problems of polypharmacy. *BMJ* 2013;f7500. [PubMed: 24366533]
11. Panel AGSBCUE, Fick DM, Semla TP, et al. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society* 2019;4:674–94.

12. Griebbling TL. Re: American Geriatrics Society 2019 Updated AGS Beers Criteria(R) for Potentially Inappropriate Medication Use in Older Adults. The Journal of urology2019;101097ju0000000000000409.
13. Hanlon JT, Boudreau RM, Roumani YF, et al. Number and dosage of central nervous system medications on recurrent falls in community elders: the Health, Aging and Body Composition study. The journals of gerontology Series A, Biological sciences and medical sciences2009;4:492–8.
14. Boudreau RM, Hanlon JT, Roumani YF, et al. Central nervous system medication use and incident mobility limitation in community elders: the Health, Aging, and Body Composition study. Pharmacoepidemiol Drug Saf2009;10:916–22.
15. Wright RM, Roumani YF, Boudreau R, et al. Effect of central nervous system medication use on decline in cognition in community-dwelling older adults: Findings from the Health, Aging and Body Composition Study. Journal of the American Geriatrics Society2009;2:243–50.
16. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. BMJ (Clinical research ed)2015;h2698.
17. Association AD. American Dental Association Statement on Opioids, February 27, 2018. Available from <https://www.ada.org/en/press-room/news-releases/2018-archives/february/american-dental-association-statement-on-opioids>. Accessed 2 June 2020.
18. CDC. International Classification of Diseases, (ICD-10-CM/PCS) Transition, November, 62015. Available from https://www.cdc.gov/nchs/icd/icd10cm_pcs_resources.htm. Accessed 13 November, 2019.
19. Tian TY, Zlateva I, Anderson DR. Using electronic health records data to identify patients with chronic pain in a primary care setting. Journal of the American Medical Informatics Association : JAMIA2013;e2:e275–80.
20. Hartung DM, Middleton L, Haxby DG, Koder M, Ketchum KL, Chou R. Rates of adverse events of long-acting opioids in a state Medicaid program. Annals of Pharmacotherapy2007;6:921–28.
21. Cost H, Project U. Agency for Healthcare Research and Quality. Clinical Classifications Software for ICD-9-CM. 2011. “Generic”
22. Brown J, Hutchison LC, Li C, Painter JT, Martin BC. Comparison of inappropriate prescribing criteria for the elderly–Beers 2003, Beers 2012, and STOPP Criteria–in a large administrative claims database.
23. Organization WH. The ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: World Health Organization, 1992.
24. Nielsen S, Degenhardt L, Hoban B, Gisev N. A synthesis of oral morphine equivalents (OME) for opioid utilisation studies. Pharmacoepidemiol Drug Saf2016;6:733–7.
25. Hersh EV, Kane WT, O’Neil MG, et al. Prescribing recommendations for the treatment of acute pain in dentistry. Compendium of continuing education in dentistry (Jamesburg, NJ : 1995)2011;3:22, 24–30; quiz 31–2.
26. Suda KJ, Calip GS, Zhou J, et al. Assessment of the Appropriateness of Antibiotic Prescriptions for Infection Prophylaxis Before Dental Procedures, 2011 to 2015. JAMA Netw Open2019;5:e193909.
27. Bertrand M, Duflo E, Mullainathan S. How much should we trust differences-in-differences estimates? The Quarterly journal of economics2004;1:249–75.
28. Maust DT, Gerlach LB, Gibson A, Kales HC, Blow FC, Olsson M. Trends in Central Nervous System-Active Polypharmacy Among Older Adults Seen in Outpatient Care in the United States. JAMA Intern Med2017;4:583–85.
29. Aparasu RR, Mort JR. Inappropriate Prescribing for the Elderly: Beers Criteria-Based Review. Annals of Pharmacotherapy2000;3:338–46.
30. Harrison L, O’Connor E, Jie C, Benzoni T, Renner CH, McCracken R. Potentially inappropriate medication prescribing in the elderly: Is the Beers Criteria relevant in the Emergency Department today? The American Journal of Emergency Medicine2019.

31. Hwang CS, Kang EM, Kornegay CJ, Staffa JA, Jones CM, McAninch JK. Trends in the Concomitant Prescribing of Opioids and Benzodiazepines, 2002–2014. *American journal of preventive medicine* 2016;2:151–60.
32. Jano E, Aparasu RR. Healthcare Outcomes Associated with Beers' Criteria: A Systematic Review. *Annals of Pharmacotherapy* 2007;3:438–48.
33. Sherry TB, Sabety A, Maestas N. Documented pain diagnoses in adults prescribed opioids: Results from the National Ambulatory Medical Care Survey, 2006–2015. *Annals of internal medicine* 2018.
34. Pergolizzi J, Raffa R. Common opioid-drug interactions: what clinicians need to know. *Pract Pain Manage* 2017;1–3.
35. Pérez-Mañá C, Papaseit E, Fonseca F, Farré A, Torrens M, Farré M. Drug Interactions With New Synthetic Opioids. *Front Pharmacol* 2018;1145–45. [PubMed: 30364252]

Table 1.

Descriptive characteristics of dental patient visits with concurrent opioid prescriptions by co-occurrence of potentially inappropriate medication combination (PIMC) per the Beers criteria*

	Total N= 40,800		PIMC N= 4,239		No-PIMC N= 36,561		P
	n	(%)	n	(%)	n	(%)	
Age, years							
<i>Mean (SD)</i>	71.58	6.64	72.6	7.13	71.46	6.57	<.001
<i>Median (interquartile range)</i>	69	66–75	70	67–78	69	66–75	<.001
<i>65–74</i>	29672	72.7	2796	66.0	26876	73.5	
<i>75–84</i>	8649	21.2	1102	26.0	7547	20.6	<.001
<i>85+</i>	2479	6.1	341	8.0	2138	5.8	
Female sex	18350	45.0	2425	57.2	15925	43.6	<.001
U.S. Census Bureau Region							
<i>Northeast</i>	5606	13.7	485	11.4	5121	14.0	
<i>Midwest</i>	14381	35.2	1395	32.9	12986	35.5	
<i>South</i>	17118	42.0	2017	47.6	15101	41.3	<.001
<i>West</i>	3683	9.0	340	8.0	3343	9.1	
<i>Unknown</i>	12	0.0	2	0.0	10	0.0	
Dental procedure classification							
<i>Diagnostic</i>	18450	45.2	1945	45.9	16505	45.1	0.360
<i>Preventive</i>	1132	2.8	188	4.4	944	2.6	<.001
<i>Restorative</i>	3293	8.1	408	9.6	2885	7.9	<.001
<i>Oral and maxillofacial surgery</i>	24460	60.0	2477	58.4	21983	60.1	0.033
<i>Periodontics</i>	3395	8.3	285	6.7	3110	8.5	<.001
<i>Adjunctive general services</i>	3314	8.1	392	9.2	2922	8.0	0.005
<i>Endodontics</i>	4920	12.1	471	11.1	4449	12.2	0.045
<i>Implant services</i>	2779	6.8	252	5.9	2527	6.9	0.018
<i>Prosthodontics</i>	2345	5.7	285	6.7	2060	5.6	0.004
<i>Orthodontics</i>	6	0.0	2	0.0	4	0.0	0.066
<i>Maxillofacial prosthetics</i>	27	0.1	5	0.1	22	0.1	0.166
<i>Category not available</i>	89	0.2	9	0.2	80	0.2	0.932
Pain intensity of dental procedures**							
<i>Severe</i>	7505	18.4	880	20.8	6625	18.1	
<i>Moderate</i>	12091	29.6	1307	30.8	10784	29.5	
<i>Mild</i>	14594	35.8	1456	34.3	13138	35.9	<.001
<i>Inconclusive</i>	6610	16.2	596	14.1	6014	16.4	
Charlson Comorbidity Index							
<i>3</i>	14870	36.4	1163	27.4	13707	37.5	
<i>4</i>	10847	26.6	1094	25.8	9753	26.7	<.001
<i>5+</i>	15083	37.0	1982	46.8	13101	35.8	
Dental OME in mg							

	Total N= 40,800		PIMC N= 4,239		No-PIMC N= 36,561		P
	n	(%)	n	(%)	n	(%)	
Mean (SD)	106.03	6.28	114.77	85.6	105.01	5.95	<.001
Median (IQR)	90	75–120	100	75–120	90	75–120	<.001
Opioid prescribed							
Codeine	7501	18.4	674	15.9	6827	18.7	<.001
Dihydrocodeine	3	0.0	1	0.0	2	0.0	0.193
Hydrocodone	29259	71.7	3066	72.3	26193	71.6	0.348
Hydromorphone	11	0.0	2	0.0	9	0.0	0.397
Meperidine	141	0.3	18	0.4	123	0.3	0.354
Morphine	2	0.0	1	0.0	1	0.0	0.066
Oxycodone	2179	5.3	256	6.0	1923	5.3	0.033
Tapentadol	4	0.0	0	0.0	4	0.0	0.496
Tramadol	1776	4.4	234	5.5	1542	4.2	<.001
OME above 120 mg							
Yes	9192	22.5	1046	24.7	8146	22.3	0.000
No	31608	77.5	3193	75.3	28415	77.7	
Days' supply over 3 days							
Yes	19763	48.4	2121	50.0	17642	48.3	0.028
No	21037	51.6	2118	50.0	18919	51.7	
History of mental health conditions							
Mood disorders	2293	5.6	752	17.7	1541	4.2	<.001
Psychoses	1342	3.3	575	13.6	767	2.1	<.001
Behavior disorders	1212	3.0	213	5.0	999	2.7	<.001
CNS-active drug exposure a day before dental visits	8737	21.4	3944	93.0	4793	13.1	<.001
History of ER visits***	1255	3.1	181	4.3	1074	2.9	<.001
History of admission***	482	1.2	80	1.9	402	1.1	<.001

Abbreviations: PIMC, potentially inappropriate medication combination; SD, Standard deviation; BEERS, Beers Criteria for Potentially Inappropriate Medication Use in Older Adults; OME, oral morphine equivalent; CNS, central nervous system; ER, emergency room.

Boldface indicates statistical significance accounting for up to 50 multiple comparisons and maintaining the family-wise type I error rate of 0.05.

* American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019;67(4):674–694. doi:10.1111/jgs.15767

** Pain intensity of dental procedures was defined according to Hersh, et al.1 CPT and HCPCS codes were not categorized by Hersh, et al and were categorized separately.

*** History of acute care utilization including hospital admission and emergency room visits were assessed in the 3 months prior to dental visit

Table 2.

Cumulative incidence of all-cause and opioid-related ER visits and hospital admissions at 7 and 30 days post-dental visit

	Total N= 40,800		PIMC N= 4,239		No PIMC N= 36,561		P-values
	n	(%)	n	(%)	n	(%)	
All-cause ER in 7 days	204	0.5	25	0.6	179	0.5	0.381
All-cause ER in 30 days	763	1.9	106	2.5	657	1.8	0.001
All-cause admission in 7 days	74	0.2	14	0.3	60	0.2	0.016
All-cause admission in 30 days	316	0.8	52	1.2	264	0.7	<.001
All-cause ER or admission in 7 days	250	0.6	36	0.8	214	0.6	0.037
All-cause ER or admission in 30 days	947	2.3	141	3.3	806	2.2	<.001
Opioid-related ER in 7 days	12	0.0	0	0.0	12	0.0	0.238
Opioid-related ER in 30 days	50	0.1	5	0.1	45	0.1	0.928
Opioid-related admission in 7 days	12	0.0	2	0.0	10	0.0	0.476
Opioid-related admission in 30 days	47	0.1	11	0.3	36	0.1	0.003
Opioid-related ER or admission in 7 days	24	0.1	2	0.0	22	0.1	0.741
Opioid-related ER or admission in 30 days	93	0.2	15	0.4	78	0.2	0.069

Abbreviations: PIMC, potentially inappropriate medication combination; ER, emergency room.

Table 3.

Characteristics associated with co-occurrence of potentially inappropriate medications with opioids per the Beers Criteria

	Adjusted OR	95%CI		P-values
Female sex	1.68	1.57	1.80	<.001
Age group				
65–74 (<i>ref</i>)				
75–84	1.15	1.05	1.26	0.003
85+	1.02	0.88	1.18	0.797
Charlson Comorbidity Index				
3				
4	1.20	1.09	1.32	<.001
5+	1.39	1.26	1.54	<.001
Claims-based frailty index				
<i>Frail</i>	1.08	0.71	1.64	0.718
<i>Pre-frail</i>	1.59	1.45	1.74	<.001
<i>Robust</i>				
History of mental health conditions				
<i>Mood disorders</i>	3.14	2.79	3.52	<.001
<i>Psychoses</i>	4.02	3.46	4.68	<.001
<i>Behavior disorders</i>	1.17	0.98	1.39	0.084
History of ER visits**	1.03	0.86	1.24	0.722
History of admission**	1.00	0.75	1.32	0.989
<i>Hydrocodone (ref)</i>				
<i>Oxycodone</i>	1.07	0.92	1.24	0.365
<i>Codeine</i>	0.81	0.74	0.88	<.001
<i>Others</i>	1.03	0.89	1.19	0.719
Dental procedure classification				
<i>Preventive</i>	1.30	1.08	1.56	0.005
<i>Restorative</i>	1.12	0.99	1.26	0.063
<i>Oral and maxillofacial surgery</i>	0.83	0.78	0.90	<.001
<i>Periodontics</i>	0.88	0.78	1.00	0.046
<i>Adjunctive general services</i>	1.19	1.06	1.33	0.004
<i>Endodontics</i>	0.84	0.75	0.93	0.002
<i>Implant services</i>	0.89	0.78	1.02	0.087
<i>Prosthodontics</i>	1.17	1.02	1.34	0.027
<i>Orthodontics</i>	4.18	0.85	20.43	0.078
Every 10 mg OME increase	1.02	1.01	1.02	<.001

Abbreviations: OR, odds ratio; CI, confidence interval; PIM, potentially inappropriate medication; ER, emergency room; OME, oral morphine equivalent.

* Adjusted OR using Proc GenMod – Modified logistic regression model This method leads to the robust error variance estimation and produces 95% CIs with the correct coverage, using AR(1) correlation structure

^{**} History of acute care utilization including hospital admission and emergency room visits were assessed in the 3 months prior to dental visit

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Table 4:

GEE model output on all-cause 30-day acute care utilization post-index by Beers criteria compliance

Characteristics*	Adjusted RR**	95%CI		P-values
Any PIM combination (ref: no PIM)	1.23	1.02	1.48	0.032
Female sex	1.01	0.89	1.15	0.881
Age group				
65–74 (ref)				
75–84	1.19	1.02	1.40	0.031
85+	1.57	1.26	1.95	<.001
Charlson Comorbidity Index				
3 (ref)				
4	1.17	0.96	1.42	0.113
5+	1.76	1.47	2.10	<.001
History of mental health conditions				
Mood disorders	1.13	0.88	1.46	0.335
Psychoses	1.65	1.26	2.15	<.001
Behavior disorders	0.93	0.64	1.35	0.698
History of ER visits**	1.64	1.22	2.20	0.001
History of admission**	1.51	1.00	2.28	0.052
Hydrocodone (ref)				
Oxycodone	0.94	0.70	1.27	0.687
Codeine	1.05	0.89	1.23	0.554
Others	1.28	0.99	1.66	0.059
Every 10 mg OME increase	1.01	1.00	1.02	0.027

Abbreviations: GEE: generalized estimating equations; RR, relative risk; CI, confidence interval; PIM, potentially inappropriate medication; ER, emergency room; OME, oral morphine equivalent.

* Due to low event per category in dental procedure variable, we did not include the dental procedures into the model to avoid sparse data bias and its resulting considerable upward bias.

** Adjusted RR using Proc GenMod – Modified Poisson regression model Poisson regression without robust error variances may result in a conservative CI (i.e., wider CI). A “modified Poisson” method has been proposed to estimate the RR using a robust error variance (Zou 2004). This method leads to the robust error variance estimation and produces 95% CIs with the correct coverage.

Using AR(1) correlation structure