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High-Risk Opioid Prescribing Trends: Prescription Drug Monitoring Program Data from 2010–2018

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Abstract

OBJECTIVE—Deaths due to opioids have continued to increase in South Carolina, with 816 opioid-involved overdose deaths reported in 2018, a 9% increase from the prior year. The objective of the current study is to examine longitudinal trends (Quarter (Q)1 2010 through Q4 2018) of opioid prescribing volume and high-risk opioid prescribing behaviors in South Carolina (SC) using comprehensive dispensing data available in the South Carolina Prescription Drug Monitoring Program (SC PDMP).

DESIGN—Retrospective analyses of SC PDMP data were performed using general linear models to assess quarterly time trends and change in rate of each outcome Q1 2010 through Q4 2018.

PARTICIPANTS—Opioid analgesic prescription fills from SC state residents between Q1 2010 through Q4 2018.

MAIN OUTCOME MEASURES—High-risk prescribing behaviors included: (1) opioid prescribing rate; (2) percent of patients receiving opioids dispensed ≥ 90 average morphine milligram equivalents daily; (3) percent of opioid prescribed days with overlapping opioid and benzodiazepine prescriptions; (4) rate per 100,000 residents of multiple provider episodes; and (5) percent of patients prescribed extended release opioids who were opioid-naive.

RESULTS—A total of 33,027,461 opioid prescriptions were filled by SC state residents within the time period of Q1 2010 through Q4 2018. A 41% decrease in the quarterly prescribing rate of

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opioids occurred from Q1 2010 to Q4 2018. The decrease in overall opioid prescribing was mirrored by significant decreases in all four high-risk prescribing behaviors.

CONCLUSION—PDMPs may represent the most complete data regarding the dispensing of opioid prescriptions and as such be valuable tools to inform and monitor the supply of licit opioids. Our results indicate that public health policy, legislative action, and multiple clinical interventions aimed at reducing high rates of opioid prescribing across the healthcare ecosystem appear to be succeeding in the state of SC.

Keywords

High-Risk Prescribing Behavior; Opioid Prescribing; Prescription Drug Monitoring Program

INTRODUCTION

The annual economic burden of the opioid epidemic is in excess of $78.5 billion.[1] High rates of opioid prescribing in the late 1990s and early 2000s have been credited with fueling this public health emergency.[2,3] Exposure to opioids through a legitimate prescription is frequently reported by individuals who go on to develop opioid use disorders and those transitioning to heroin use.[4,5] Though provisional data released by the CDC indicate that drug overdose deaths dropped for the first time since 1990,[6] deaths due to opioids have continued to increase in SC, with 816 opioid-involved overdose deaths reported in 2018, a 9% increase from the prior year.[7]

Several factors have been identified as risk factors for prescription opioid overdose. A dose-response relationship between prescribed daily morphine milligram equivalents (MME) and risk for drug overdose has been demonstrated, with doses over 90 – 100 MME/day commonly identified as “high-risk.”[8,9] Second, use of high-dose, extended release/long acting (ER/LA) opioids for opioid naïve patients is associated with overdose risk.[10,11,12] Third, co-prescribing opioids and benzodiazepines increases risk of respiratory depression and overdose, with some evidence suggesting that concomitant use may increase risk of overdose by 4 to 12 times that of low-dose, lone opioid use. [10,13,14] Finally, multiple prescribers in the same time frame may indicate diversion and is associated with overdose. Over the past decade, public health efforts to monitor prescriptions and increase prescriber coordination have been instituted as a method to address high-risk prescribing, doctor shopping, and diversion.[15,16,17,18]

Although numerous individual studies have leveraged administrative claims data to estimate opioid prescribing indicators, many of these studies have been limited by only capturing a segment of opioids prescribed, representing prescriptions from a single healthcare system or single payer such as commercially insured, Medicaid, or Medicare only.[19,20] More complete data is made available annually by the Centers for Disease Control and Prevention, which produces prescribing maps that show the geographic distribution of retail opioid prescriptions dispensed per 100 persons between 2006 and 2016 for each state (and county) within the US.[21] The source for all CDC prescribing data is the QuintilesIMS Transactional Data Warehouse, which is based on a sample of approximately 59,000 retail pharmacies which dispense almost 88% of all retail prescriptions paid for by commercial insurance,

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Medicaid, Medicare, or cash in the US.[21] Perhaps the most complete data regarding the dispensation of opioid prescriptions are the state-operated prescription drug monitoring programs (PDMPs).

This study examines longitudinal trends for SC PDMP indicators defined by the Centers for Disease Control and Prevention (CDC) for their Prescription Drug Overdose Prevention for States surveillance program.[22] For the years 2010 through 2018, we report trends in the SC PDMP reflecting: (1) number and rate of opioid analgesic prescriptions dispensed per 1,000 state residents; (2) percent of patients receiving opioids dispensed an average daily dose ≥ 90 MME; (3) percent of opioid prescribed days with overlapping opioid and benzodiazepine prescriptions; (4) rate per 100,000 residents of multiple provider episodes; and, (5) percent of patients prescribed ER/LA opioids who were opioid-naive.

DATA AND METHODS

DATA

The South Carolina Reporting & Identification Tracking System (SCRIPTS) database is the SC PDMP implemented in 2008 by the Bureau of Drug Control at the SC Department of Health and Environmental Control (DHEC). SCRIPTS aggregates state-mandated information daily from records of Schedule II-IV controlled substances dispensed from any retail or outpatient hospital pharmacy and mail-order controlled substance delivered into the state. The SC PDMP does not include long-term care and assisted living dispensing, SAMHSA designated opioid treatment programs, emergency room dispensing of less than a 48-hour supply, or most veterinarian dispensing. Data reporting for Veteran Administrations began in Q4 2014.

METHODS

This study was deemed exempt from IRB oversight as not human subjects research. The following data were provided to the Medical University of South Carolina through an agreement with the SC DHEC in 2016 to evaluate the SC PDMP data: de-identified unique prescriber number; de-identified unique patient number; age; first three digits of zip code; product National Drug Code (NDC); product name; quantity of drug dispensed; number of days' supply; refill status; date prescription was written; and date filled. An NDC product file was constructed and validated for all drugs dispensed between 2010 and 2018 and reported to SCRIPTS. The product file was based on the product name and NDC from the SCRIPTS datasets. Our analysis file was created by adding the following information to each unique product: generic name, strength per unit, unit of measure, MME conversion factor, opioid (yes/no), benzodiazepine (yes/no), muscle relaxant (yes/no), opioid exclusion (yes/no), opioid classification, long-acting/extended release formulation (yes/no), and DEA Class. Brand and generic NDCs with the same unique product name from SCRIPTS formed a single grouping. To ensure accuracy of the product name and newly added fields, a single NDC from each grouping was chosen to cross-reference the 2013 Redbook File and the 2018 CDC MME Conversion File. Strength per unit, unit of measure, and MME conversion factor for each opioid product were obtained from the CDC MME Conversion file. The

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initial file was constructed for 2010 – 2016 products reported to SCRIPTS, with annual updates performed to incorporate new products reported in 2017 and 2018.

All opioid substances on our product list were included in the analysis, except tramadol and propoxyphene. Tramadol was excluded because it was not consistently reported until reclassification as a class IV-controlled substance in August 2014 and propoxyphene was withdrawn in 2010. From 2010 – 2014, the total number of tramadol prescriptions reported to SCRIPTS was 414,547; the annual numbers reported 2015 – 2018 were 947,414, 964,501, 912,170, and 824,585, respectively. Injectable opioids, cough and cold formulations, and buprenorphine were excluded based on CDC recommendations.[22] Benzodiazepines were included in one indicator.

We measured: (1) rate of opioid analgesic prescriptions dispensed per 1,000 state residents: as number of opioid analgesic prescriptions dispensed per quarter divided by annual census estimate (taken at midyear) for corresponding year; (2) percent of patients receiving opioids dispensed an average daily dose of opioid analgesics ≥ 90 MME: as count of patients dispensed ≥ 90 MME divided by count of patients dispensed an opioid in a given quarter; (3) percent of days with overlapping opioid and benzodiazepine prescriptions: as count of days with an overlap of at least one opioid and one benzodiazepine prescription summed across patients divided by the sum of opioid prescription days across patients in a given quarter; (4) rate per 100,000 residents of multiple provider episodes: as count of individuals with five or more prescribers and five or more pharmacies in a six-month period divided by annual census estimate (taken at midyear) for corresponding year; and (5) percent of patients prescribed ER/LA opioids who were opioid-naive: as count of patients prescribed an ER/LA who had not been prescribed an opioid analgesics in the 60 days prior to their index ER/LA prescription divided by total number of individuals prescribed an ER/LA opioid in a corresponding quarter.

We estimated a general linear model for quarterly time trend (using Proc Autoreg with the Durban-Watson statistic to assess autocorrelation) to determine whether the rate of each outcome changed significantly from Q1 2010 through Q4 2018. Significance was determined at the 0.05 level and SAS v9.4 (SAS Institute, Inc., Cary, NC) was used for analyses.

RESULTS

A total of 33,027,461 opioid prescriptions were filled within the time period. The number of opioid analgesics per 1,000 state residents decreased significantly over the study period (Figure 1), with a 41% drop in quarterly prescribing rate from Q1 2010 to Q4 2018 ($p=0.0001$). Figure 2 shows the percent of opioid prescribed patients receiving an average daily dose of ≥90 MME of opioid analgesics, percent of opioid naïve patients prescribed ER/LA opioids, percent of prescription days with overlapping opioid and benzodiazepine prescriptions, and rate of multiple provider episodes per 100,000 residents. Each indicator decreased significantly over the study period ($p\leq0.005$ for all) by 23%, 31%, 35%, and 92%, respectively.

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DISCUSSION

The current study reports trends in opioid prescribing over the most recent decade (2010 – 2018) derived from a uniquely comprehensive, statewide PDMP database. PDMP data represent perhaps the most complete information on opioid prescriptions. Our findings show that the volume of dispensed opioid prescriptions in SC decreased by more than 41% between 2010 and 2018. This dramatic reduction was accompanied by significant decreases in all four high-risk prescribing indicators: 1) high daily MMEs; 2) co-prescribing opioids and benzodiazepines; 3) number of multiple prescriber episodes; and 4) percent of patients prescribed ER/LA opioids who were opioid-naive.

Across the US and Canada, recent data suggest declining rates for both the number of people prescribed opioids as well as the number of physicians prescribing opioids.[23,24] Consistent with trends observed in the current data, the CDC report of annual data from IQVIA Xponent national administrative claims data indicated that total number of prescriptions peaked nationally in 2012 and has subsequently declined; however, prescribing rates continue to remain high in certain areas of the country and vary widely across different states and counties.[21] SC annual rates of opioid prescribing from IQVIA data indicate a 19.6% decrease from 2010 (98.6) to 2017 (79.3). A larger 41% decrease in quarterly prescribing rate for the same timeframe was found in the comprehensive PDMP data.

Our results are also consistent with findings from several administrative claims databases showing general decreases in high-risk prescribing indicators including: multiple provider episodes, incidence of initial opioid prescriptions among opioid naïve individuals, proportion of persons receiving high (>90 MME) daily doses, number of extended release opioid prescriptions, and co-prescription of benzodiazepines.[25,26,27,28,29] The most notable declines were evinced for multiple provider episodes. Though the current data cannot speak to mechanisms or drivers of this stark decline, findings suggest that PDMPs may be particularly useful in assisting in the identification of “doctor shopping” or diversion. Of note, national data pulled from IQVIA (2006 through 2017) indicate that while trends in high-risk prescribing hold when examined nationally, between 2 to 3-fold variations in these outcomes were observable by state.[28]

PDMPs may be valuable clinical tools for informing and monitoring opioid prescribing and are an important risk mitigation strategy to help reverse the prescription opioid drug epidemic by promoting more conservative prescribing practices. Several multi-pronged efforts to increase PDMP use were undertaken in SC to address high rates of opioid prescribing. These efforts included: (1) Revised Joint Pain Management Guidelines (November 2014 revision incorporated PDMP use as mandatory for safe pain treatment, August 2017 revision aligned with CDC Guidelines); (2) addition of data from major Veterans Administration hospitals to PDMP (December 2014); (3) integration of PDMP data into electronic health records (EHRs) for two initial emergency department sites (September 2015); (4) online PDMP registration for prescribers (November 2015); (5) insurer/payer mandates for PDMP use (spring 2016); (6) SC PreSCriptions – Medication Safety Matters statewide initiative (launched September 2016); (7) legislative mandate for PDMP use prior

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to prescribing Schedule II controlled substance (spring 2017); and (8) Academic Detailing to Primary Care Providers, including hands on PDMP training (launched June 2017).

The current study cannot definitively attribute decreases in overall and high risk prescribing to any specific intervention(s); however, efforts reflected in this state are common across the U.S. For example, as of 2017, 22 states had at least one type of MME Daily Dose policy in place, most commonly in the form of guidelines (14 states), followed by: prior authorizations, rules and regulations, legislative acts, claim denials, and automatic patient reports.[30] The literature regarding impact of specific PDMP-related interventions is mixed. Data (2010–2015) from the state PDMPs of Ohio, Kentucky, and West Virginia were recently compared to control states.[31] Reports show that mandatory PDMP use laws increased prescriber registration and utilization of the PDMP in mandated states compared with non-mandated states. The rate of opioid prescribing, rate of overlapping prescriptions, multiple provider episode rate, and rate of overlapping opioid/benzodiazepine prescriptions decreased in 2 of 3 states evaluated; however, magnitude of these changes varied among mandated states. In contrast, a recent systematic review did not find evidence to support an association between PDMPs (policy and use) and reduced opioid prescribing and dispensing.[32]

The current study has limitations. First, our analysis is limited to a single state and may not be representative of other states; opioid prescribing varies widely across the US[28,33] and patterns of high-volume opioid prescribing vary by drug type and region of the US.[34] Second, while there is inherent public health value in monitoring trends in opioid prescribing we cannot measure the clinical appropriateness of reductions in prescribing. Third, tramadol was excluded from the indicators presented in this study since tramadol prescriptions were not consistently reported in PDMP data until its reclassification in August 2014. The data available 2015 – 2018 indicate that though tramadol prescription rates were high (ranging from 824,585 to 964,501 prescriptions per year), their inclusion in analyses did not substantially alter the prescribing trends reported in this study. Finally, while missing/unusable data is very small it has potential for biasing our results.

Our results indicate that public health policy and legislative action aimed at reducing high rates of opioid prescribing are bearing fruit. However, it is critical that future research examines more granular issues regarding the drivers and impact of reductions in opioid prescribing. For example, recent data suggest that, independent of absolute opioid dose, high dose variability is associated with a significantly increased risk of overdose compared with low dose variability.[35] Future research should examine more nuanced aspects of opioid prescribing practices, including: which prescriber types drive overall reductions in opioid prescriptions; provider-level correlates of reduced prescribing; clinical appropriateness of prescribing reductions; impact of prescribing reductions on patients' access to care; and potential negative impacts on patient care and safety.

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Abbreviations

CDC	Centers for Disease Control and Prevention
DHEC	Department of Health and Environmental Control
EHR	Electronic Health Record
ER/LA	Extended release/long acting
MME	Morphine milligram equivalents
NDC	National Drug Code
PDMP	Prescription Drug Monitoring Program
SAMHSA	Substance Abuse and Mental Health Services Administration
SC	South Carolina
SCRIPTS	South Carolina Reporting & Identification Tracking System

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IMPLICATIONS FOR POLICY & PRACTICE

- Monitoring data is essential for understanding how policy changes affect population health. The SC PDMP system shows an encouraging decline in opioid prescriptions. Over 8 years the opioid prescriptions filled have decreased, and these changes are seen in all areas that are targets of policy, regulatory, and provider interventions aimed at decreasing opioid overdose deaths.
- The data show modest reductions in long-acting and extended release prescriptions, which are steadily decreasing by 0.7% per year, and the rate of high dose prescriptions (≥ 90 MME), which has declined from 8.6% to 6.6%.
- The most dramatic decrease was evidenced by multiple provider “doctor shopping” events, which are now less than $1/10^{th}$ of the rate seen in 2010, and overlapping dispensing of opioids and benzodiazepines, which declined by 35.2% since 2010.
- Now the challenge is to determine appropriate patient management. For example, high-dose prescriptions have fallen by 2 percentage points; is this reflecting better pain management practice or potential under-treatment of severe chronic pain?

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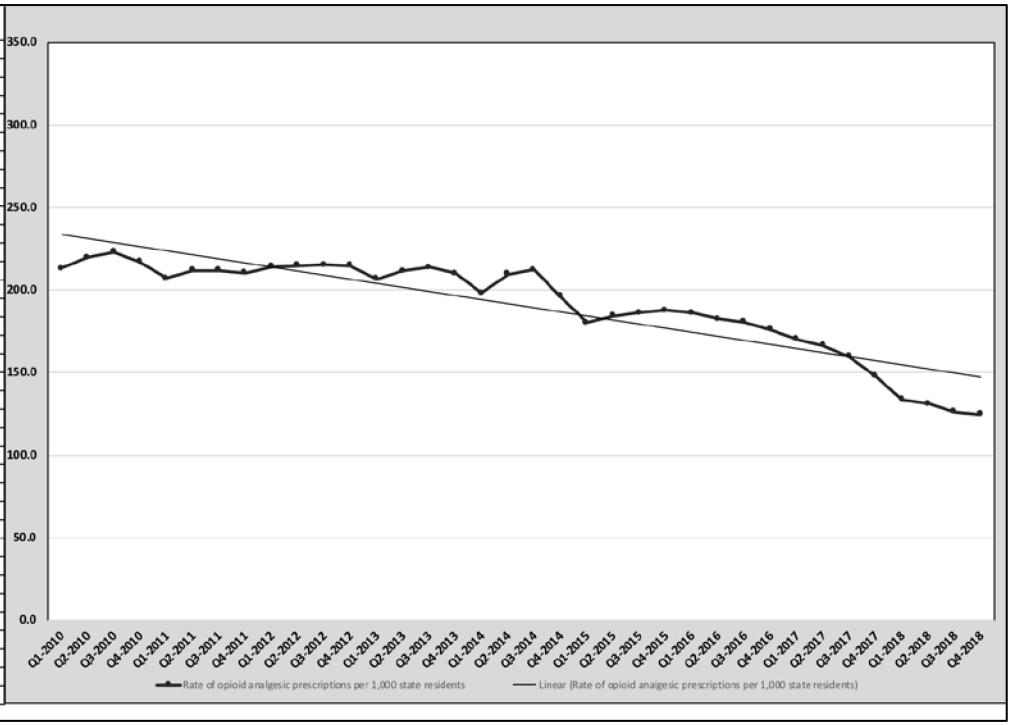
Qtr/Year	Opioids Dispensed	SC Population	Rate
Q1-2010	987,638	4,635,894	213.0
Q2-2010	1,019,026	4,635,894	219.8
Q3-2010	1,034,034	4,635,894	223.0
Q4-2010	1,006,351	4,635,894	217.1
Q1-2011	967,703	4,672,733	207.1
Q2-2011	989,851	4,672,733	211.8
Q3-2011	990,157	4,672,733	211.9
Q4-2011	983,934	4,672,733	210.6
Q1-2012	1,011,121	4,721,341	214.2
Q2-2012	1,015,315	4,721,341	215.0
Q3-2012	1,016,786	4,721,341	215.4
Q4-2012	1,013,948	4,721,341	214.8
Q1-2013	986,337	4,768,498	206.8
Q2-2013	1,009,650	4,768,498	211.7
Q3-2013	1,019,794	4,768,498	213.9
Q4-2013	1,002,622	4,768,498	210.3
Q1-2014	957,174	4,829,160	198.2
Q2-2014	1,012,937	4,829,160	209.8
Q3-2014	1,026,122	4,829,160	212.5
Q4-2014	947,420	4,829,160	196.2
Q1-2015	881,885	4,896,146	180.1
Q2-2015	903,091	4,896,146	184.4
Q3-2015	912,170	4,896,146	186.3
Q4-2015	920,025	4,896,146	187.9
Q1-2016	912,763	4,896,146	186.4
Q2-2016	892,859	4,896,146	182.4
Q3-2016	884,606	4,896,146	180.7
Q4-2016	863,512	4,896,146	176.4
Q1-2017	855659	5,024,369	170.3
Q2-2017	836604	5,024,369	166.5
Q3-2017	802159	5,024,369	159.7
Q4-2017	742485	5,024,369	147.8
Q1-2018	678983	5,084,127	133.5
Q2-2018	666210	5,084,127	131.0
Q3-2018	641649	5,084,127	126.2
Q4-2018	634881	5,084,127	124.9

Data Source: DHEC Received: 05/17/2019



Carolina residents from 2010 – 2018

Figure 1: Rate of opioid analgesic prescriptions dispensed per 1,000 South Carolina residents from 2010 – 2018

Numerator: Schedule II, III, and IV opioid analgesic prescriptions dispensed to South Carolina residents

Denominator: Midyear population for the calendar year under surveillance

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Qtr/Year	% ≥90 MME	% LA/ER Rx for Opioid Naive Pts	% Overlapping Rx Days	Rate of Mltple Prov Episodes
Q1-2010	8.6%		15.9%	49.4
Q2-2010	8.3%	17.9%	16.7%	
Q3-2010	8.4%	20.0%	16.6%	45.9
Q4-2010	8.4%	18.9%	16.6%	
Q1-2011	8.4%	18.6%	15.7%	40.0
Q2-2011	8.1%	18.3%	16.3%	
Q3-2011	8.3%	17.0%	16.4%	39.3
Q4-2011	8.4%	17.8%	16.4%	
Q1-2012	8.4%	18.5%	15.9%	40.4
Q2-2012	8.2%	17.7%	16.7%	
Q3-2012	8.2%	16.9%	16.7%	37.9
Q4-2012	8.4%	16.8%	16.7%	
Q1-2013	8.5%	16.8%	16.1%	35.5
Q2-2013	8.1%	16.5%	16.7%	
Q3-2013	7.8%	16.4%	16.7%	35.0
Q4-2013	8.0%	17.3%	16.6%	
Q1-2014	8.3%	19.6%	16.0%	33.1
Q2-2014	7.7%	15.3%	16.8%	
Q3-2014	7.6%	15.1%	16.8%	35.8
Q4-2014	8.1%	17.1%	16.2%	
Q1-2015	8.4%	17.4%	14.3%	26.4
Q2-2015	7.9%	14.8%	14.8%	
Q3-2015	7.8%	16.0%	14.7%	24.7
Q4-2015	8.3%	18.0%	14.9%	
Q1-2016	8.4%	14.8%	14.7%	20.0
Q2-2016	8.0%	13.1%	15.2%	
Q3-2016	7.9%	13.0%	15.0%	15.0
Q4-2016	8.1%	13.4%	14.8%	
Q1-2017	8.1%	13.3%	13.9%	12.4
Q2-2017	7.7%	12.1%	14.2%	
Q3-2017	7.6%	12.2%	13.8%	8.1
Q4-2017	7.8%	12.1%	13.0%	
Q1-2018	7.9%	15.2%	11.3%	5.3
Q2-2018	7.3%	12.5%	11.5%	
Q3-2018	6.8%	12.8%	10.6%	4.0
Q4-2018	6.6%	12.4%	10.3%	

Data Source: DHEC Received: 05/17/2019

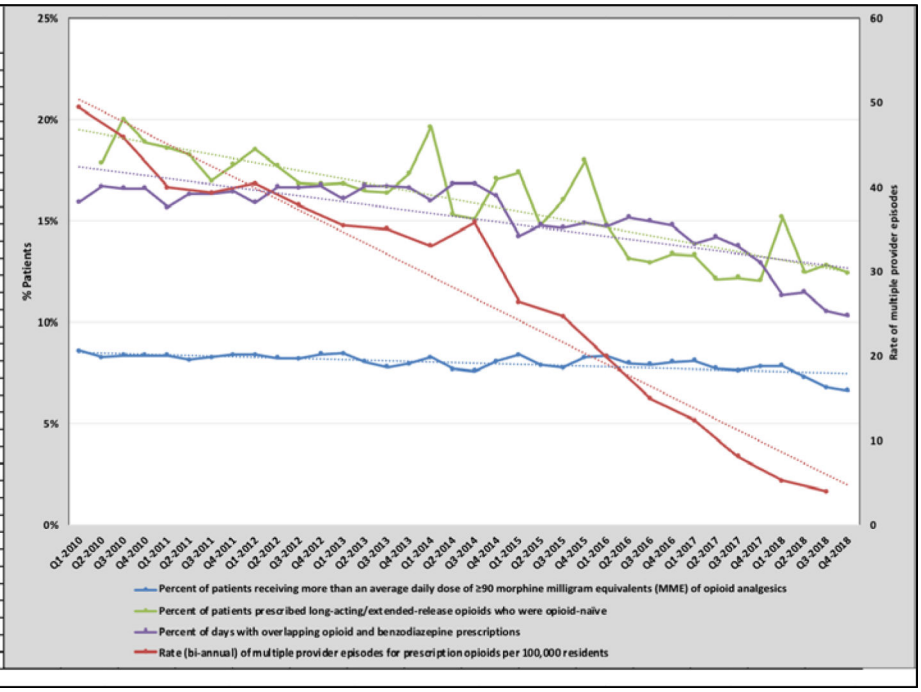

Figure 2:
Opioid high-risk prescribing trends for South Carolina residents from 2010 – 2018