

Secular trends in opioid prescribing in the USA

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Abstract: Opioid abuse and misuse in the USA is a public health crisis. The use of prescription opioid analgesics increased substantially from 2002 through 2010, then plateaued and began to decrease in 2011. This study examined prescriptions of branded and generic immediate- and extended-release opioid analgesics from 1992 to 2016. This was juxtaposed against state and federal policies designed to decrease overutilization and abuse, as well as the launch of new opioid products, including opioids with abuse-deterrent properties (OADPs). The data indicate that these health policies, including the utilization and reimbursement of OADPs, have coincided with decreased opioid utilization. The hypothesis that OADPs will paradoxically increase opioid prescribing is not supported.

Keywords: OADP, prescription, utilization trends, legislation, opioids

Introduction

Abuse and misuse of opioid analgesics is a public health crisis in the USA.¹ Over 10 million people aged 12 years and older used opioid analgesics nonmedically in 2014, with almost 2 million meeting diagnostic criteria for opioid use disorder.² Overdose fatalities involving opioid analgesics have increased steadily over the last 15 years.¹

As a result of these trends, numerous policies have been implemented to curb abuse, misuse, and diversion of prescription opioids, and to improve medical practice around opioid use (Table 1).

There has been a concerted effort to decrease the desirability of prescription opioids to abusers by deterring easy physical manipulation and extraction of their active ingredients. In 2015, the US Food and Drug Administration (FDA) finalized a process for approving opioids with abuse-deterrent properties (OADPs).³ To date, seven opioids have met stringent FDA criteria to carry labeling claims that the product is “expected to result in a meaningful reduction” in its abuse.⁴ All OADPs approved to date have been extended-release opioids.

Concerns have been raised that policy efforts to contain and reverse opioid abuse and related deaths may have unintended consequences. For example, some insurers have indicated that abuse-deterrent opioids may give physicians a false sense of security and lead to an increase in opioid prescribing.⁵ Insurers also have concerns that legislative policies mandating coverage of OADPs will shift the market from generic to branded opioid medications, at significant incremental cost to plans and patients.

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The goal of this study is to examine prescribing trends for opioid analgesics against the backdrop of public policies aimed at reducing opioid overutilization and abuse, as well as the introduction and increased use of OADPs.

Method: prescription opioid analgesic market review

This analysis examined US opioid prescriptions from January 1, 1992, to August 31, 2016, in IMS Health National Prescription Audit. This database is the industry standard source for dispensed prescriptions from retail pharmacies in all 50 states. The data set includes 86% of prescriptions captured from a sample of 46,500 pharmacies, stratified by geographic location of retail, mail service, and long-term care. It then uses a proprietary algorithm to project a nationally representative sample. The analysis included all oral, transdermal, immediate-release, extended-release, single-entity, and combination opioid products. Prescription

trends were examined to evaluate changes in opioid market composition—potential effects of new market entrants and policy implementations.

Results

The total number of dispensed opioid analgesic prescriptions grew steadily from 1992 until 2010 (Figure 1, Table S1). In August 2010, a new formulation of OxyContin® (oxycodone hydrochloride) extended-release tablets was introduced. In April 2013, it became the first opioid analgesic to receive labeled description of abuse-deterrent properties, and the New Drug Application (NDA) for the original formulation was withdrawn. Subsequent new opioid launches included three additional extended-release formulations with FDA-approved abuse-deterrent properties: Hysingla® ER (hydrocodone extended-release tablets), Embeda® (morphine sulfate and naltrexone hydrochloride extended-release capsules), and Xtampza® ER (oxycodone extended-release capsules).⁶

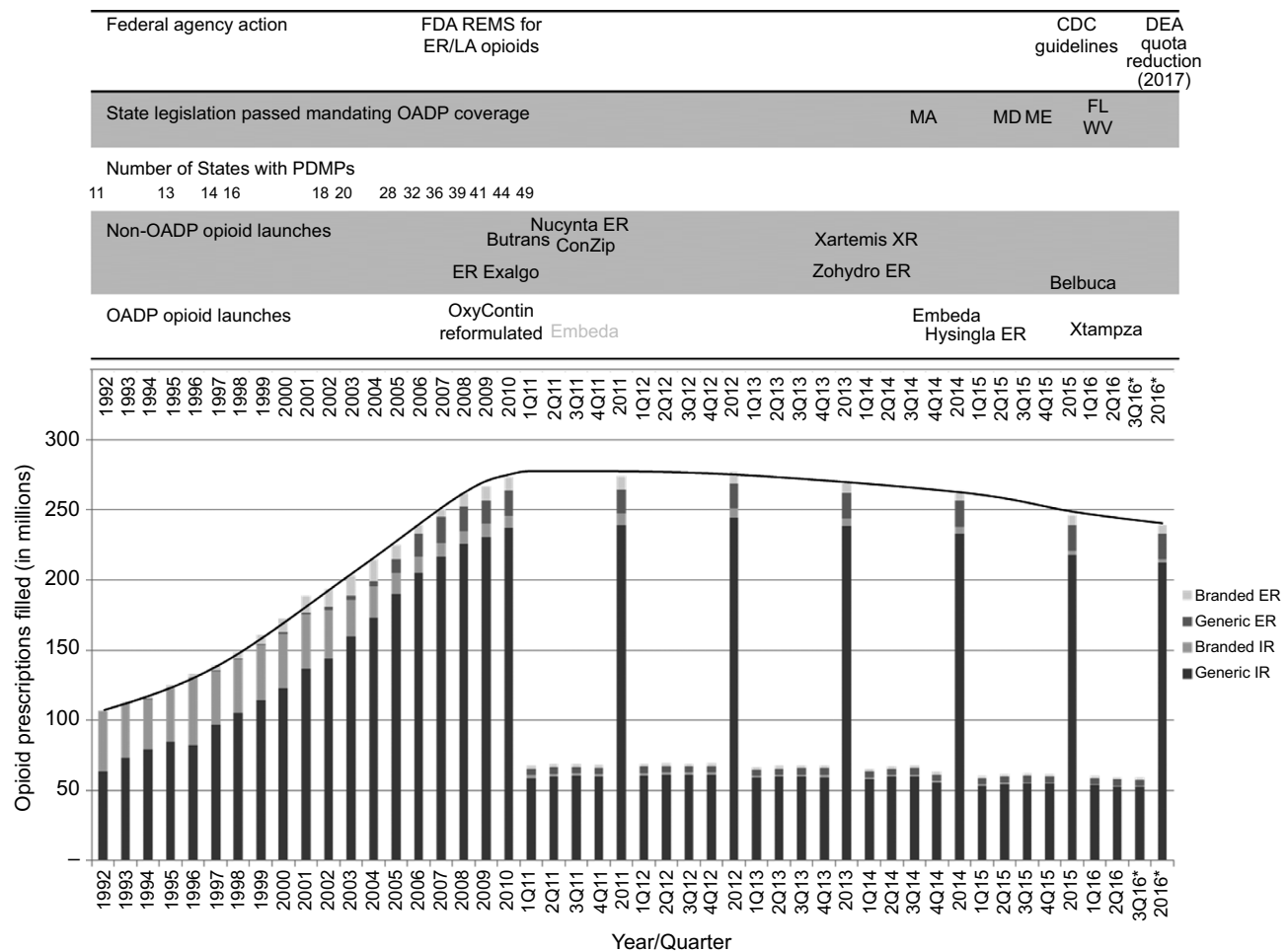


Figure 1 Opioid prescriptions dispensed by year with opioid launches, coverage legislation, PDMP adoption and major federal agency actions.

Note: *Estimated. Data reported quarterly from first quarter 2011.

Abbreviations: CDC, Centers for Disease Control and Prevention; DEA, Drug Enforcement Administration; ER, extended release; ER/LA, extended-release and long-acting; FDA, US Food and Drug Administration; FL, Florida; IR, immediate release; MA, Massachusetts; MD, Maryland; ME, Maine; OADP, opioids with abuse-deterrent properties; PDMPs, prescription drug monitoring programs; REM, risk evaluation and mitigation strategy; WV, West Virginia; XR, Extended-Release.

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During the timeframe that these new OADPs were introduced into the marketplace, an increasing number of policies aimed at reducing opioid overutilization and abuse also came into effect (Table 1 and Figure 1). These included state legislation defining Pain Clinics and Pain Physicians; FDA Risk Evaluation and Mitigation Strategy (REMS) for the Extended-Release, and Long-Acting (ER/LA) Opioid Analgesics; opioid-related prescribing guidelines including those released by the Centers for Disease Control and Prevention; Prescription Drug Monitoring Programs (PDMP); and most recently, state legislation mandating insurance coverage of OADPs.

Together, these forces initiated a market contraction in 2011 that is continuing through 2016.

- The total number of dispensed opioid prescriptions declined by 2.2% in 2014, 6.8% in 2015, and are projected to decrease by 2.9% by year-end 2016.
- Prescriptions dispensed for branded opioid analgesics are a decreasing proportion of the opioid market constituting a 4.8% prescription share in 2014, 4.1% share in 2015, and a projected 3.7% share in 2016.
- Since 2010, the number of dosing units per extended-release opioid prescription dispensed has decreased 20%, from 67 to 54.

Table 1 Selected initiatives at the state and federal levels¹⁴⁻¹⁸

Level	Initiatives
State	<ul style="list-style-type: none"> Prescription Drug Monitoring Programs (PDMPs) Prescribing Guidelines, some with morphine milligram equivalent (MME) dose limits Pain Management CME Requirements State Pain Clinic/Pain Physician Requirements ("Pill Mill" Laws) "Good Samaritan" Laws – immunity to summon medical assistance for overdose Increased availability of naloxone for overdose reversal
Federal	<ul style="list-style-type: none"> Office of National Drug Control Policy – 2011 National Drug Control Strategy Supplement FDA Risk Evaluation and Mitigation Strategies (ER/LA opioids, TIRF) CMS Overutilization Monitoring System for opioids CDC Guideline for primary care providers on Prescribing Opioids for Chronic Pain FDA Opioid Action Plan NIH Pathways to Prevention National Pain Strategy US Surgeon General – Turn-the-tide initiative DEA reduction in opioid controlled substances quotas (to be implemented in 2017)

Abbreviations: CDC, Centers for Disease Control and Prevention; CME, continuing medical information; CMS, Centers for Medicare & Medicaid Services; DEA, Drug Enforcement Administration; ER/LA, extended-release and long-acting; FDA, US Food and Drug Administration; MME, morphine milligram equivalent; NIH, National Institutes of Health; PDMPs, prescription drug monitoring programs; TIRF, Transmucosal Immediate Release Fentanyl.

- Since 2010, the total number of kilograms of opioid prescriptions dispensed in the USA has decreased 16%, from 271,000 to 227,000 kg.
- Since 2010, prescriptions dispensed for extended-release opioids of >90 morphine milligram equivalents (MME) in the USA have decreased 34%, from 5.3 million to 3.5 million.

In addition, without a formal determination by Drug Enforcement Administration (DEA) of aggregate and company active pharmaceutical ingredients (API) quotas, there can be no sudden market expansion of opioids or OADPs.⁷ Recent DEA action, affecting morphine, hydromorphone, oxycodone, hydrocodone, and fentanyl, will reinforce the current reduction in utilization and preclude expansion of the US prescription opioid analgesic market.⁷

Conclusion

The US prescription opioid analgesic market has been consistently contracting since 2011 and continues to shrink in response to changes in public policy and medical practice, notwithstanding the increasing availability of products designed to deter abuse. Fewer patients are being prescribed opioids, the amounts prescribed are less, the daily doses are less, and there is a national emphasis on non-opioid treatment alternatives. These data are consistent with other research on the effectiveness of public policy and the introduction of OADPs.^{4,8-12}

While these data are encouraging, there are other factors that continue to fuel the opioid epidemic in the USA. There has been an increase in the availability of cheap and pure heroin, and an influx of non-pharmaceutical, illicitly-manufactured fentanyl.¹³ While the increase in opioid deaths observed from 2002 to 2011 was largely driven by the misuse and abuse of prescription opioids, data from 2012 to 2014 indicate that deaths involving prescription opioids appear to have stabilized, while deaths involving heroin and illicit fentanyl were driving increases in opioid-involved mortality.¹ While policies and actions intended to curb prescription opioid abuse are having the desired effect, continued action will be necessary to address the broader problem as the opioid crisis evolves.

In conclusion, public health policies and actions have resulted in decreased utilization of prescription opioids. Neither the launch of OADPs nor policies mandating their coverage has grown the opioid market: both branded and generic medications, immediate-release and extended-release, are decreasing. Taken together, these findings indicate that public health policies and the introduction of OADPs are having the intended effect of reducing the inappropriate utilization of opioids, resulting in a contraction in the overall

opioid market, without evidence of paradoxical increases in opioid prescribing, nor increases in market share for branded extended-release opioids.

Disclosure

EJP is a consultant. DR, JGE, JDH, and TJM are employees of Purdue Pharma L.P. The authors report no other conflicts of interest in this work.

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Supplementary material

Table S1 Trends of opioid prescription data by year

TRx (MM)	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007
Generic IR	63.3	73.4	79.1	84.8	82.3	96.7	105.4	114.5	122.8	136.6	144.1	159.6	173.1	189.8	205.0	216.7
Branded IR	42.9	38.3	36.1	38.4	48.3	38.3	38.2	38.9	38.7	38.7	34.6	26.3	22.4	15.1	11.4	9.4
Generic ER	0.1	0.1	0.2	0.3	0.3	0.4	0.5	0.8	1.2	1.6	2.3	2.8	3.6	10.2	16.5	19.0
Branded ER	1.0	1.3	1.5	1.9	2.5	3.4	4.7	6.6	9.7	11.8	12.9	14.7	15.5	10.2	6.1	5.7
All Opioids	107.26	113.12	116.95	125.38	133.38	138.90	148.93	160.90	172.46	188.62	193.89	203.33	214.57	225.27	238.96	250.78
TRx (MM)	2008	2009	2010	1Q11	2Q11	3Q11	4Q11	2011	1Q12	2Q12	3Q12	4Q12	2012	1Q13	2Q13	3Q13
Generic IR	226.0	230.9	237.4	58.8	59.7	60.4	59.9	238.8	60.8	61.1	61.0	61.4	244.3	59.3	59.8	60.0
Branded IR	8.7	9.2	8.5	2.2	2.2	2.0	1.9	8.4	1.8	1.8	1.7	1.4	6.7	0.9	1.3	1.3
Generic ER	17.7	16.6	17.9	4.3	4.4	4.3	4.4	17.4	4.4	4.5	4.5	4.5	17.9	4.4	4.5	4.6
Branded ER	9.5	10.3	9.4	2.4	2.4	2.4	2.4	9.5	2.1	2.1	2.1	2.1	8.4	2.0	2.0	2.0
All Opioids	261.95	266.99	273.29					274.14					277.29			
TRx (MM)	4Q13	2013	1Q14	2Q14	3Q14	4Q14	2014	1Q15	2Q15	3Q15	4Q15	2015	1Q16	2Q16	3Q16*	2016*
Generic IR	59.6	238.7	57.8	59.6	59.9	55.6	232.9	53.3	54.7	55.1	54.8	217.9	53.6	52.7	52.7	212.2
Branded IR	1.7	5.2	1.4	1.4	1.3	1.1	5.2	1.0	0.9	0.7	0.7	3.2	0.7	0.6	0.6	2.6
Generic ER	4.6	18.1	4.5	4.6	4.7	4.7	18.3	4.5	4.6	4.6	4.6	18.2	4.5	4.5	4.5	17.9
Branded ER	2.0	8.0	1.9	1.9	1.9	1.9	7.6	1.7	1.7	1.7	1.7	6.9	1.6	1.5	1.5	6.2
All Opioids		270.06					264.07					246.22				238.98

Note: *Estimated.

Abbreviations: ER, extended release; IR, immediate release; TRx, total prescriptions; MM, million.

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