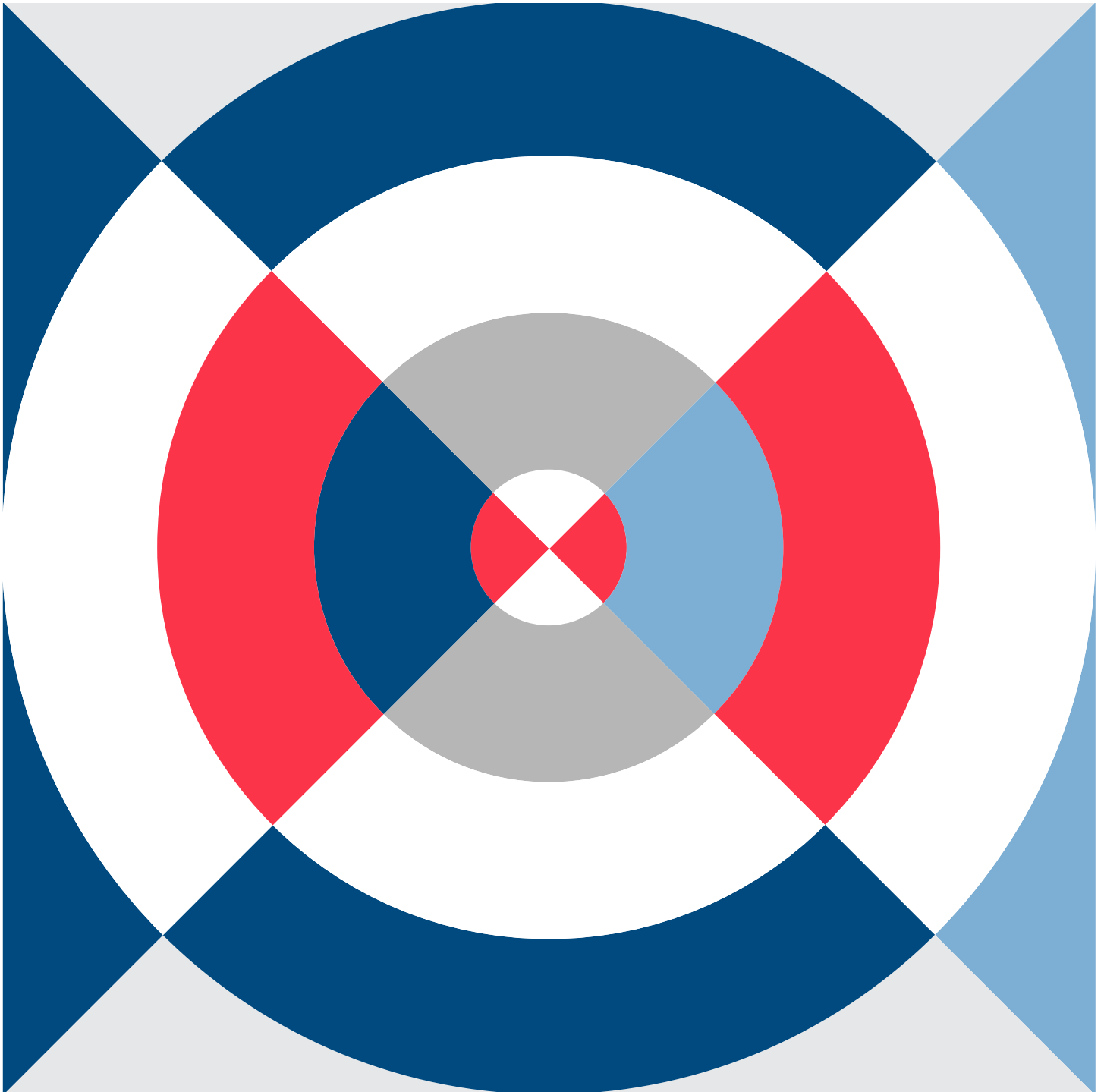


A NATION IN PAIN

FOCUSING ON U.S. OPIOID TRENDS
for TREATMENT OF SHORT-TERM AND LONGER-TERM PAIN



AN EXPRESS SCRIPTS REPORT | DECEMBER 2014



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REPORT SUMMARY

Exactly how are patients in the U.S. using pain medications known as opioids? Can we identify potential ways to improve the safe prescribing of these medications? To gain a deeper understanding of these concerns, Express Scripts conducted an in-depth examination of more than 36 million de-identified pharmacy claims from 6.8 million insured Americans of all ages who filled at least one prescription for an opioid to treat short-term or longer-term pain from 2009 through 2013. Prevalence, utilization and costs were evaluated during the five-year study period, including assessments of trends according to age, gender and geography. The research also looked at users prescribed opioids in combination with other medications.

The analysis looked at both short-term use and longer-term use of opiate pain medicines; however, the majority of this report focuses on longer-term opioid use given the clinical complexities, and the risks of drug dependence and addiction commonly associated with longer-term opioid treatment. For the purposes of this research, short-term users were defined as patients who were prescribed an opiate pain medication for a total supply of 30 days or less within a one-year period. Longer-term users were defined as those prescribed an opiate pain medication for more than a 30-day supply in a one-year period.

The analysis assessed the amount of medication used by patients by examining three metrics: number of prescriptions filled, days' supply (the number of days of medication per prescription), and the morphine equivalent dose (MED).

KEY FINDINGS OF THE RESEARCH INCLUDE:

- **Fewer Patients, Increasing Number of Prescriptions:** The number of Americans filling prescriptions for opioids declined 9.2% between 2009 and 2013, but both the number of prescriptions filled and the number of days of medication per prescription rose approximately 8.4%. **Page 6**
- **Short-Term Use of Prescription Opiates Declined:** The number of longer-term opioid users remained fairly constant over the five years studied; the number of short-term users declined 11.1% between 2009 and 2013. **Page 7**
- **Patients Likely to Use Prescription Opiates Long-Term:** Nearly one-half of patients who took opiate painkillers for more than 30 days in the first year of use continued to use them for three years or longer. Almost 50% of those patients were taking only short-acting opioids, putting them at higher risk of addiction. **Page 8**
- **Younger Adults Use More Opioid Medications:** The elderly have the highest prevalence of opioid use, but younger adults (age 20-44) filled more opioid prescriptions and had the greatest increase in the number of days of medication prescribed, per prescription, of any age group over the five year period. **Page 10**
- **Opioid Use More Prevalent Among Women:** 30% more women than men took prescription opiates in 2013; however, men are more likely to fill more prescriptions and take higher doses of these medications. **Page 13**
- **Pain Prescriptions Most Prevalent in Southeastern Small Cities:** The greatest concentration of opioid use is found in small cities in the Southeastern region of the U.S., with the vast majority of these cities located in four states: Kentucky, Alabama, Georgia and Arkansas. **Page 15**
- **Most Long-Term Opioid Users Take Dangerous Drug Combinations:** Nearly 60% of patients using opioids were taking a combination of drugs that are dangerous and potentially fatal; among these mixtures, almost one in three patients were prescribed anti-anxiety drugs known as benzodiazepines along with an opioid – the most common cause of overdose deaths involving multiple drugs. **Page 17**

BACKGROUND

Opiate pain medications, also known as opioids, are one of the most controversial classes of prescription therapy. These medicines are most effective in providing relief to patients suffering from severe pain; however, their extremely addictive properties pose a serious risk to patients, and make them prone to misuse and abuse.

Opioids, such as codeine, morphine, OxyContin® (oxycodone HCl), and Vicodin® (hydrocodone bitartate and acetaminophen), work by blocking pain signals to the brain. Unlike non-narcotic pain treatments (ibuprofen, acetaminophen, aspirin, naproxen), most opiates do not have a maximum clinically safe dosage limit. Over time, the body can build up a tolerance to the medication, so patients often require an escalation in the dose or strength of the medicine in order to effectively treat chronic pain and achieve the same level of pain relief. However, high doses of these drugs increase side effects and complications, as well as raise the risk of addiction and overdose.

Physicians often prescribe opioids when non-narcotic medication is ineffective, or in conjunction with other painkillers. The most common conditions treated with opioid pain medications include cancer, back pain, osteoarthritis and neuropathic pain¹.

Opioids are derived from opium, which is taken from the poppy plant and has been used for pain relief since as early as 4000 B.C. The pure active ingredient, named morphine, was first isolated in 1805. In 1874, scientists working with the molecule added two acetyl groups and unexpectedly invented heroin, which was originally marketed as a cough suppressant before the discovery of its addictive properties². The Food and Drug Administration (FDA) and the Drug Enforcement Agency (DEA) closely regulate current opiate pain medications and classify them as controlled substances.

Prescription rates for opioids increased dramatically in the past two decades after the government and medical organizations pushed for greater progress in pain control and set new guidelines expanding the use of opioids³. While America claims less than 5% of the world's population, it consumes roughly 80% of the world's opioid supply⁴. In fact, according to IMS Health, Vicodin and non-branded hydrocodone combination painkillers are the most commonly prescribed drugs in the country⁵.

America claims
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More than 5%
of U.S. adults
use opiate pain
medications
nonmedically.

Opioid abuse is an epidemic in the U.S., with more than 5% of the adult population using opiate pain medications nonmedically⁶. Thousands die every year from an opiate pain medication overdose – more than cocaine and heroin combined⁷. The FDA and DEA continue to monitor opioids for abuse potential, and along with dozens of states, have made significant efforts to curb overprescribing of these drugs. Many manufacturers have remade some of the commonly prescribed opioids into abuse-deterrent formulations. Yet, despite the major risks associated with their use, opioids remain the most effective and widely prescribed pain medications available.

KEY TERMS

The following terms are used throughout this report:

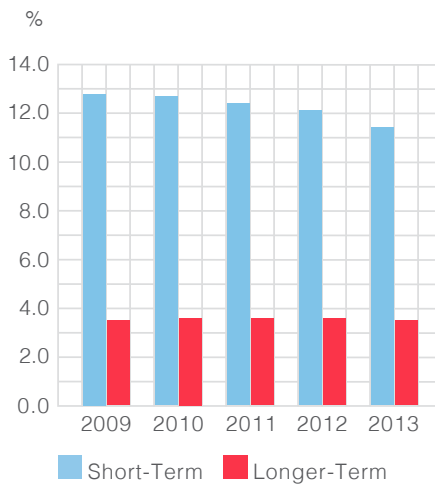
- **Short-acting opioids** work quickly, offering near-immediate pain relief for a short duration of time. Doctors commonly prescribe short-acting opioids (such as hydrocodone) for short-term or intermittent pain relief, or for breakthrough pain, which is pain that “breaks through” the ceiling of pain relief offered by other pain management strategies, such as long-acting opioids.
- **Long-acting opioids** are for patients who need around-the-clock pain relief. Doctors commonly prescribe long-acting opioids (such as fentanyl) for chronic pain, such as that experienced by cancer or fibromyalgia patients.

UTILIZATION TRENDS

Between 2009 and 2013, there was a 9.2% decline in the prevalence of people filling prescriptions for opioids, yet both the number of prescriptions filled per patient and the number of days of medication per prescription increased by approximately 8.4%.

PREVALENCE OF SHORT-TERM AND LONGER-TERM OPIATE PAIN MEDICATION UTILIZATION

2009-2013



Fewer Americans are using opiate pain medications, yet the number of Rx and days of medications per Rx increased 8.4%.

The research also shows distinct trends among patients who are prescribed opioids to treat a short-term condition, such as post-operative or post-injury pain, compared with those who are taking these medications on a longer-term basis, which was defined in the study as someone taking an opioid for more than 30 days during the course of a year.

Short-term opioid users far outnumber longer-term opioid users. Approximately 15% of the population filled at least one opioid prescription in any given year during the past five years; only about one in five of those patients continued to use opiate pain medications beyond 30 days. When we apply our data to the 2013 US Census⁸, we estimate that more than 9.4 million insured Americans were longer-term users of opioids.

The decline in patients on opiate painkillers occurred mainly among those with prescriptions to treat short-term pain, dropping 11.1% from 2009 to 2013. Conversely, the number of patients with longer-term opioid use remained steady over that timeframe.



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UTILIZATION TRENDS

The dramatic rise in opioid abuse and addiction has led to a variety of regulatory, government and law enforcement actions that impact the use of opioids, with the number of people using opioids for short-term treatment declining over the past five years. Contributing to the decline is the number of more commonly prescribed opioids, such as hydrocodone, now classified as Schedule II opioids by the FDA, which subjects them to stricter prescribing practices. Additionally, law enforcement has significantly reduced the operations of “pill mills,” where patients and others could easily procure illegitimate opioid prescriptions.

While the efforts to curb inappropriate opioid use are important in the fight against drug addiction, they can pose a problem for patients suffering from severe, chronic pain who truly need continued access to these medications. The challenge is finding the right balance between abuse prevention and availability of these medications for patients in real pain.

The remainder of this report will focus specifically on longer-term use of opioids since there are greater clinical and societal concerns associated with longer-term use of these drugs.

About half of longer-term opioid users are taking them for three years or more.

CHRONIC OPIOID USE

The Express Scripts analysis reveals that nearly half (46.9%) of new opioid users who take these medications for more than 30 days in the first year continue using them for three years or longer. Signaling a particularly alarming trend, nearly 50% of these patients are only taking short-acting opioids — which can make them more prone to addiction — rather than long-acting formulations, which are designed for extended pain relief^{9,10}. On average, the patients who chronically used these medications filled 56 short-acting opioid prescriptions over three years — nearly 19 prescriptions each year.

Based on a lack of evidence that longer-term use of opioids is effective, the American Academy of Neurology (AAN) recently released a policy statement suggesting that the risks associated with opioids likely outweigh their benefits in treating chronic pain conditions such as headache, fibromyalgia and lower back pain.



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50% of opioid users take only short-acting treatments, putting them at higher risk for addiction.

CHRONIC OPIOID USE

Use of long-acting opioids, such as sustained-release morphine, may be more appropriate for patients with longer-term pain management needs. According to the data, however, it seems more patients are managing longer-term pain with short-acting opioids, and this trend is cause for some concern. The quick spikes and sharp drops in opioid blood levels caused by short-acting medications increase the risk of side effects and complications, make pain control more challenging, as well as raise the potential for both physical and psychological dependence. The goal for most pain treatment regimens is to gradually reduce and discontinue a patient's use of these medications because extended use can lead to increased tolerance requiring higher doses that can result in dependence and addiction. This goal is difficult to achieve if a patient only uses short-acting opioids. While some patients may respond better to short-acting opioids, the risk profile of these drugs should be considered when prescribing them for chronic pain.

Primary care physicians are the leading source of opioid prescriptions.

PRESCRIBING TRENDS

The most commonly prescribed opioids among longer-term users throughout the five-year study period were hydrocodone, oxycodone, tramadol, codeine, Oxycontin® (oxycodone) and fentanyl. However, from 2009 to 2013, the prevalence of use of codeine, Oxycontin and fentanyl declined significantly, down about 14.0% for all three drugs, while increasing for oxycodone (up 7.3%) and tramadol (up 32.5%). Despite fewer patients taking certain drugs, the number of prescriptions filled and the number of days of medication per prescription remained the same, or in some cases increased. Patients using fentanyl and OxyContin had prescriptions with the highest average number of days of medication.

Primary care physicians (family medicine doctors, general practitioners and internists) were the leading source of prescriptions, writing 48.6% of opioid scripts. Only 3.3% of prescriptions came from pain specialists, although they tended to prescribe higher amounts of medication per prescription.

A separate Express Scripts study¹¹ found that 40.0% of opioid prescriptions filled by members with employer-sponsored drug coverage between 2011 and 2012 were written by only 5.0% of prescribers. The analysis also identified prescribers who wrote higher rates of opioid prescriptions than their peers. It found that high prescribers wrote an average of 4.6 prescriptions per opioid-using patient, 3.5 times more than the 1.3 prescriptions per patient written on average by their peer group. Nearly 20.0% of high prescribers were prescribing opioids only for a single patient. There were more primary care physicians in the high opioid prescriber group than any other specialty, even after accounting for the large volume of family and internal medicine doctors.

Younger adults
20-44 years old
fill the most
opiate pain
prescriptions.

AGE TRENDS IN OPIOID USE

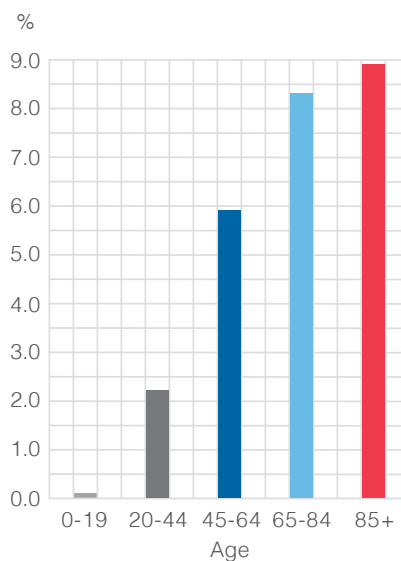
Prevalence of longer-term opioid use increases with age and is highest among those aged 65 and older, with 8.9% of that population taking opiate pain medications in 2013. However, younger adults (ages 20-44) who use opiate pain medications filled more opioid prescriptions per person than any other age group – averaging 10.2 prescriptions in 2013. Younger adults also showed the greatest increase in the number of days of medication per prescription, rising nearly 10% between 2009 and 2013.

The research also examined the amount of opioids used when combining both the strength and quantity of the prescription by calculating the morphine equivalent dose (MED). Studies have shown that an MED of more than 120 milligrams per day of an opioid can expose patients to a greater risk of adverse events and, when used longer-term, can indicate potential drug abuse¹². While the majority of patients using opioids did not exceed that threshold, middle-age Americans (ages 45-64) were more likely to have a MED exceeding this threshold.

In terms of sheer numbers, middle-age Americans are the heaviest users of these drugs given the size of the population and the quantity of medicine they consume.

PREVALENCE OF LONGER-TERM OPIATE PAIN MEDICATION UTILIZATION

BY AGE 2013

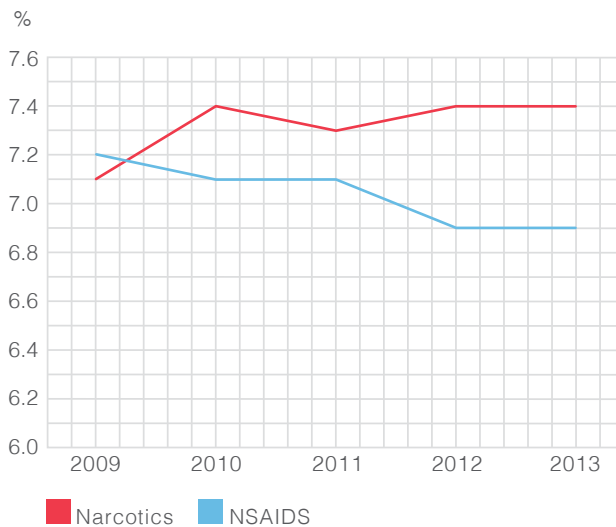


OPIOID USE IN SENIORS

Older Americans who were taking only opioids for pain treatment had a significant increase in prevalence of use, up 4.5% from 2009 to 2013. During that same timeframe, the number of seniors (65+) using only NSAIDs (nonsteroidal anti-inflammatory drugs), and not opioids, declined by 5.1%. This shift away from NSAIDs to opioids occurred after a change in clinical guidelines in 2009 stating that narcotic painkillers are a safer choice for the treatment of chronic pain in the elderly given the adverse events associated with NSAIDs including gastrointestinal bleeds, kidney problems, and cardiovascular risks¹³.

Because of the large numbers of elderly Americans who use opiate pain medication, the highest proportion of patients who are taking these drugs are covered by Medicare Part D – twice the rate found in the commercially insured population and three times the rate of those covered by Medicaid.

PREVALENCE OF LONGER-TERM OPIOID USE VERSUS LONGER-TERM NSAID USE IN SENIORS AGE 65+





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OPIOID USE IN SENIORS

With age comes pain. Chronic and degenerative health problems become more prevalent as we get older, resulting in higher concentrations of the elderly using pain treatments. Until recently, NSAIDs had been the treatment of choice for a variety of conditions, but evidence showing that these medications are not safe to use in the elderly resulted in changes to treatment guidelines.

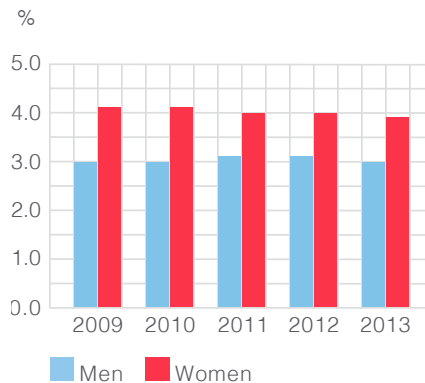
This research confirms that clinicians are following the revised guidelines. However, considering the risks associated with opioid use, these older patients require proper management and monitoring, and should be prescribed the lowest dose possible to effectively treat their pain. Because of their sedating properties, seniors taking opioids are at a greater risk of falls and are twice as likely as patients on nonopioid pain medications to experience a hip fracture, especially when first starting treatment¹⁴. Additionally, seniors are at greater risk of serious drug interactions because they often use a number of different medications at one time, some of which may be dangerous when mixed with opioids.

GENDER TRENDS IN OPIOID USE

Longer-term opioid use is far more prevalent among women than men. Approximately 30% more women than men took opiate pain medication in 2013. Older women have the highest rates of use, with approximately one in 10 on an opioid treatment.

PREVALENCE OF LONGER-TERM PAIN MEDICATION UTILIZATION

BY GENDER 2009-2013



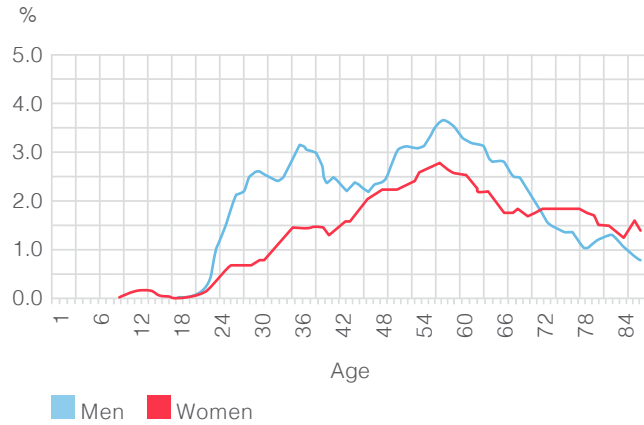
30% more women than men take opioids, but men consume higher amounts.

Even though women use more opioids, men use a greater amount of the medication. In each of the five years, men filled slightly more prescriptions than women (6.9 vs 6.7 on average) and were more likely to use very high doses of these drugs; middle-age men, particularly those in their mid-50's, are the patients most likely to fall into this category. Compared to women ages 20-44, twice as many men of the same age took morphine equivalent doses that exceeded 120 milligrams per day for more than half the time they used these medications in 2013. Use of high doses of opioids potentially places patients at risk for serious adverse reactions and abuse¹⁵. This trend, however, reverses in the elderly — with more women than men taking extremely high doses of opiates.

The quantity of opioids contained in each prescription increased for both women and men over the study period, rising 6.5% in five years.

PATIENTS WITH MED ≥120 MG MORE THAN 50% OF THE TIME

BY GENDER 2013



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GENDER TRENDS IN OPIOID USE

The trend of more women using opioids may reflect their greater propensity to seek medical treatment, which could result in more opportunities to receive prescription medication. Women also have a greater prevalence of painful chronic conditions as they age, such as arthritis, osteoporosis, fibromyalgia and autoimmune diseases that cause joint pain¹⁶.

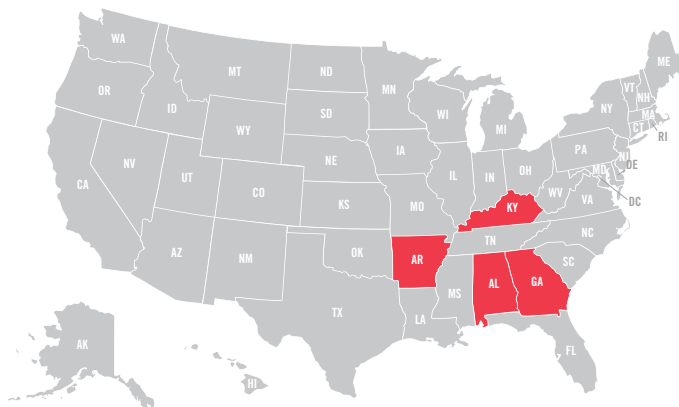
GEOGRAPHIC TRENDS IN OPIOID USE

Looking at longer-term use of narcotic pain medications across the United States, the highest prevalence of use occurs in small cities in the U.S., particularly in the southeast region of the country.

Of the 25 cities with the highest prevalence of longer-term opioid use, 24 have populations fewer than 100,000. The Express Scripts research also found that cities with the largest proportion of their residents using opiate painkillers were clustered in just four states in the southeast: Kentucky, Alabama, Georgia and Arkansas. These four states claim 41 of the 50 cities with the highest prevalence of opioid use nationwide. The average prevalence rate of opioid use for these four states was 7.6% as compared to 3.9% nationally. Among small cities with a population of less than 28,000, the top five with the highest prevalence rates in the nation had between 12.3% and 18% of their population using opioids on a longer-term basis in 2013, compared to an average 5.1% for small cities overall.

Residents ages 45-64 make up the highest proportion of users in these high prevalence cities. In contrast to the high prevalence of use found in small cities, the most populated American cities have opioid rates below the national average. While these large urban centers have a lower percentage of people taking opioids, they have a higher proportion of users taking very high doses of the drug.

STATES WITH THE HIGHEST AVERAGE PREVALENCE OF OPIOID USE





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GEOGRAPHIC TRENDS

The Express Scripts data adds to our understanding of the geographic utilization patterns of opiate pain medications. It also raises concerns about the alarming number of people who are being prescribed these medications within specific areas of the country.

Higher opioid usage rates in less populated southern cities could be the result of a variety of factors. Although small population size allows for a greater likelihood of high prevalence mathematically, one probable contributor is the prevalence of chronic and debilitating diseases that impact the southern region of the country¹⁷. There are especially high rates of obesity and diabetes in these states¹⁸, conditions that often have associated pain that may require opioid treatment¹⁹.

Access to clinical care is another variable. Those living in less populated, more rural areas often have less access to clinicians, particularly specialists. Opioids may be prescribed more frequently when there are limited care alternatives available.

Interestingly, we see that in larger metropolitan areas where access to specialists is greater, patients are often prescribed higher quantities of these medications.

Although there is no indication that patients in these locations use prescription opioids inappropriately, given the high risk of addiction associated with these medications, it is important that these patients receive monitoring and prescribed medications only at doses and for durations as clinically indicated.

CONCURRENT TREATMENTS

In 2013, a majority of patients (58.5%) using opiate pain medications were taking a combination of prescription drugs that carry potentially serious safety risks. Of those taking these multi-drug combinations, 62.3% were women.

Multiple Drug Combinations

Among patients using opioids on a longer-term basis, 29.2% had concurrent prescriptions (prescribed in the same month) for benzodiazepines which include anti-anxiety medications such as Xanax® (alprazolam) and Ativan® (lorazepam); 28.3% had been prescribed muscle relaxants; and 8.0% of patients were taking all three types of medications during the same time period.

Opioids, muscle relaxants and benzodiazepines all have sedating effects and can slow down the respiratory system. Taking these medications together could increase these reactions exponentially. While there are clinical circumstances when the combination of those drugs may be appropriate, these medication mixtures can have serious health consequences if not used with extreme caution. In fact, the combination of benzodiazepines and opioids is the most common cause of overdose deaths involving multiple drugs²¹.

Multiple Opioid Prescriptions

In addition to medication combinations involving different classes of drugs, many patients were also taking multiple short-acting opioids at the same time. The analysis found that 27.5% of longer-term opioid users were taking two or more short-acting opioids concurrently, a practice that may put a patient at risk for drug dependence and addiction.

Multiple Prescribers & Pharmacies

Of the patients who were taking these potentially dangerous combinations of medications, two-thirds (66.6%) were prescribed the drugs by two or more physicians, and 39.8% filled the prescriptions at two or more pharmacies.

Nearly 60%
of opiate pain
medication
users were
taking a risky
combination
of Rx drugs.

Using multiple prescribers and/or multiple pharmacies significantly raises the risk of being hospitalized for opioid-related injuries²² and can be an indicator of aberrant behaviors such as doctor-shopping and opioid abuse.



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CONCURRENT TREATMENTS

Treating patients with chronic pain is a complex practice, particularly because there are often a number of different comorbidities to consider and address. While there could be rare instances when opioids and benzodiazepines or muscle relaxants may be appropriate to prescribe together, seeing these potentially dangerous mixtures used so commonly by such a high percentage of patients is of great concern.

Also concerning is the fact that in a majority of cases where we see potentially hazardous combinations of drugs, there are multiple physicians prescribing these medications and multiple pharmacies filling the prescriptions, indicating that they may not be aware of all the medications the patient is using. Coordination of care is always important but is especially so when it comes to treating patients on opioid therapy.

While not a panacea for the challenges doctors face when treating patients in pain, there are data systems that help. There are insurer-based programs that can alert physicians of potential drug duplications and interactions. There are also state-run prescription monitoring programs that can be very effective in helping physicians identify instances when patients are being put at risk or where there are signs of abuse. In a subset of this analysis, we looked at concurrent use of potentially dangerous medications in patients whose benefit plan was enrolled in the Express Scripts Fraud, Waste and Abuse program in 2013 compared to concurrent use in patients whose benefit plan was not enrolled. The rate of concurrent use among those enrolled in the program was 7.6% less than that observed in the nonenrolled group. When you consider the lengths patients will go to support their addiction, including seeking unnecessary medical treatment

23% fewer
patients using
home delivery
were taking
a potentially
dangerous
combination
of medications.

solely to obtain a prescription pain medication, that 7.6% difference can represent significant waste reduction and cost savings for payers²².

There is also evidence that the use of the Express Scripts Pharmacy for home delivery can reduce these concurrent medication risks. The additional sub-analysis suggested that, when compared to those who filled their prescriptions at a retail pharmacy, 23% fewer patients using home delivery were taking a potentially dangerous combination of medications, and 15% fewer patients were prescribed medications by multiple prescribers. While the use of home delivery is limited even among patients who are taking opioids on a longer-term basis, these also may be the patients most likely to have additional medications prescribed over time, which can result in these dangerous mixtures.

OMISSIONS OF NEEDED TREATMENTS

Best practices when treating patients taking narcotic pain medications call for the use of remedies to prevent constipation, a frequent and sometimes debilitating side effect of prescription opioid use. In addition, patients taking opiates commonly experience nausea as a side effect of the drug, and may need anti-nausea medications to combat this adverse effect, or might benefit from re-evaluation of the opiate dose or choice of therapy²⁴.

The analysis found that these concurrent treatments are rarely prescribed. Only about 9% of longer-term opioid patients fill a prescription for a stool softener and approximately 12% fill prescriptions for anti-nausea medication.

While there are over-the-counter (OTC) remedies that can be used in place of prescription medications, it is unlikely that such a large number of patients are utilizing those OTC options.



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OMISSIONS OF NEEDED TREATMENTS

Constipation is a very common side-effect of opioid use and is especially problematic for patients taking these medications on a longer-term basis. It can be extremely painful and debilitating, and if not treated, can put patients at risk of other serious conditions including cancer²⁵. Unfortunately, our research shows that the prescribing of stool softeners in conjunction with opioids, while a clinically recommended practice, is rarely done. The hope is that physicians are recommending OTC treatments to their patients but research shows that this also may not be happening as often as it should. A study by Express Scripts subsidiary UBC found that fewer than two-thirds of patients being treated with opioids for chronic non-cancer pain reported that their healthcare practitioner asked them if they were experiencing constipation²⁶. It's important that patients be made aware of this side effect, and if their practitioner does not address it, they should take proactive measures on their own by speaking to their physician or pharmacist.

Nonmedical
use of opiate
painkillers
costs the U.S.
\$53.4 billion
yearly.

OPIOID MISUSE AND ABUSE

Opioids have a valuable role in pain treatment but these medications also expose users to a high risk of overdose and addiction. Opiate pain medication abuse has become a significant public health problem in the U.S. Since 1999, there has been a four-fold increase in deaths from unintended opioid overdoses. The nonmedical use of opiate painkillers costs the country \$53.4 billion yearly, including \$42 billion in lost productivity²⁷; and opioid abusers have healthcare costs that are nearly nine times higher than nonabusers²⁸. Prescription opioids are also a known gateway drug for heroin, with one study showing that as many as 80% of heroin users first took prescription opioids before they started on heroin²⁹.

In response to the growing crisis of opioid addiction and overdose deaths, there has been a concerted effort to better control access to these drugs at both the federal and state level that has shown significant success; from 2010 to 2011, prescription drug abuse declined in 10 states and did not increase in any state after years of trending upward³⁰.



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PRESCRIPTION DRUG MONITORING PROGRAMS

Forty-nine of the 50 States (Missouri being the lone exception) now have prescription drug monitoring programs (PDMPs) that include electronic databases of all prescriptions filled for controlled substances. These systems, however, vary dramatically from state to state, and only 16 states require prescribers to use PDMPs when writing prescriptions³¹. When utilized, PDMPs can be highly effective in identifying and reducing cases of opioid misuse and abuse, as well as physicians who overprescribe them. Tennessee saw a 47% drop in the number of people considered inappropriately “high utilizers” of opiate painkillers after implementing a law in 2013 requiring doctors consult PDMPs before prescribing opioids to a new patient³².

The state of Florida, which had been the epicenter of prescription drug abuse³³, has also seen significant improvements after instituting a variety of strategies including a PDMP and an aggressive effort to close down “pill mills.” In 2011, the number of deaths in Florida related to oxycodone declined by more 50%³⁴.

In contrast, Missouri, the only state in America without a PDMP, may be drawing drug-seekers from other states looking for easy access to opioids and other controlled medications. A separate Express Scripts analysis found that residents from seven neighboring states filled opiate prescriptions in Missouri as much as four times more often than residents in Missouri filled opioid prescriptions out of state.

The bottom line is this: PDMPs can be a highly effective tool in curbing abuse, but they are only effective when states consistently apply the necessary resources and enforcement to ensure their success. States also need to collaborate with payers and benefit providers, who can provide additional data and resources to identify cases of abuse, including those who travel across state lines to obtain medications.

Working together, we can more efficiently and effectively identify abuse, and most importantly, help these patients obtain the necessary treatment to fight their addiction.

**PATIENT REVIEW AND RESTRICTION PROGRAMS:
A CASE STUDY**

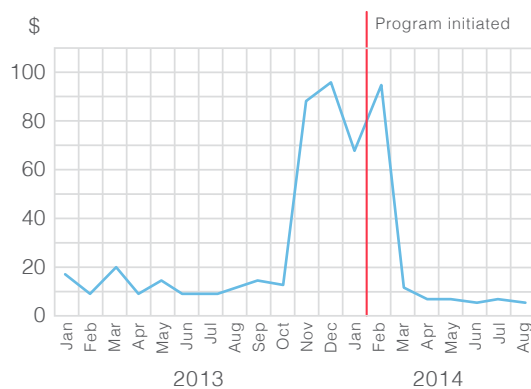
People looking to abuse controlled substances often attempt to obtain prescriptions from multiple prescribers and to fill prescriptions at multiple pharmacies to avoid suspicion and make it more difficult to track their behavior. As such, Patient Review and Restriction (PRR), or pharmacy lock-in, programs are an effective tactic employed by Express Scripts, state Medicaid plans, and other payers to reduce opioid abuse by restricting certain patients to one pharmacy and in some cases, to one prescriber.

A recent example of the impact of the Express Scripts PRR involves a patient identified through the Express Scripts Fraud, Waste and Abuse program. Before the PRR program was initiated, this patient had 38 claims for opiate pain medications between January 2013 and January 2014. After the PRR program was implemented restricting the patient to the use of one pharmacy for filling prescriptions for controlled substances, the number of prescriptions from February through August of 2014 dropped to 13, and spending on those medications went from a high of \$92.82 per month pre-restriction, to a low of \$2.93 per month post-restriction.

Like prescription drug monitoring programs, PRR programs work best when benefit plans implement programs that leverage data and professional expertise to analyze patient behavior, swiftly identify patterns of potential misuse, and then work quickly to implement the restrictions on pharmacy and prescriber.

IMPACT OF EXPRESS SCRIPTS PATIENT REVIEW AND RESTRICTION PROGRAMS

ON OPIOID RX CLAIMS AND SPEND





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OPIOID MISUSE AND ABUSE

The priority when treating patients in pain is to relieve their suffering while at the same time monitoring for signs of dependence. Physicians want and need to trust their patients, but unfortunately also need to proceed with a dose of caution to keep our patients safe and protect our practices.

I once had a patient admitted to my hospice practice for a terminal illness who was taking very high doses of both short-acting and long-acting opioids and benzodiazepines, as well as a large supply of other extremely dangerous mixtures of medications. Despite his terminal illness, these were red flags my staff and I needed to investigate. We began to gather information and additional medical records from his other providers and pharmacies he'd been using. After a very thorough investigation, we uncovered that there was no medical documentation of terminal disease for this patient. Sadly, he had fabricated a terminal illness and admitted himself into hospice care as a means to shop for these medications.

Data is vitally important to accurately identify cases of abuse. It is also key to intervention. By catching potential misuse early on, those who have an addiction to these medications can get the help they need to successfully fight their addiction before it becomes fatal.

APPENDIX

TOP OPIOIDS BY U.S. MARKET SHARE IN 2013

DRUG	MARKET SHARE
VICODIN®/HYDROCODONE WITH ACETAMINOPHEN	46.1%
ULTRAM®/ TRAMADOL	14.7%
PERCOCET®/OXYCODONE WITH ACETAMINOPHEN	13.6%
OXYCONTIN®/OXYCODONE	8.3%
TYLENOL® WITH CODEINE/ CODEINE WITH ACETAMINOPHEN	3.8%

OPIOID MEDICATION SPEND

Spending for opioids rose 3.9% from 2012 to 2013, which represented a lower increase than what was seen for both diabetes medications and anti-infectives, but higher than what was seen for other commonly used traditional drugs such as those used to treat high blood pressure and high blood cholesterol. The recent increase in per member per year (PMPY) spend for opioids is being driven in part by the development of branded, tamper-resistant opioid formulations.

DRUG CATEGORIES	INCREASE IN DRUG SPEND (2013)
DIABETES	14.0%
INFECTIONS	6.2%
ATTENTION DISORDERS	4.0%
SEIZURES	4.0%
OPIOIDS	3.9%
MENTAL/NEURO DISORDERS	-3.0%
ULCER DISEASE	-3.2%
HIGH BLOOD PRESSURE / HEART DISEASE	-8.7%
DEPRESSION	-9.1%
ASTHMA	-14.1%
HIGH BLOOD CHOLESTEROL	-14.4%

OPIOID DRUG DEVELOPMENT TIMELINE

- 4000: Ancient Greeks, Romans and Sumerians use opium for medical B.C. treatment and recreation
- 1527: Laudanum, an alcoholic solution of opium, was first compounded to treat a variety of maladies
- 1803: Opium's pure active ingredient, named morphine, first isolated by German chemist
- 1827: Commercial manufacturing of morphine begins in Germany
- 1830: Codeine first isolated in France to replace raw opium for medical purposes
- 1874: Chemists accidentally invent heroin while searching for less addictive form of morphine
- 1898: Heroin introduced as a cough suppressant by German drug company Bayer
- 1905: The United States bans opium (importation is outlawed in 1909)
- 1916: Oxycodone, the first synthetic opioid, is invented in Germany
- 1920: Hydrocodone first synthesized in Germany
- 1924: Nonmedical use of opioids banned in the United States
- 1959: Fentanyl first synthesized in Belgium
- 1970: The Federal Controlled Substance Act classifies heroin as a schedule I drug
- 1976: U.S. Food and Drug Administration (FDA) approves Percocet®
- 1977: Tramadol is first synthesized in Germany
- 1984: FDA approves Vicodin®
- 1990: FDA approves fentanyl
- 1995: FDA approves OxyContin and tramadol
- 1997: Expert panels encourage doctors to prescribe more pain medication in the Journal of the American Medical Association (JAMA)
- 2000: The U.S. Congress declares the 10-year period beginning January 1, 2001, as the "Decade of Pain Control and Research"
- 2002: Federal funding first offered to states for Prescription Drug Monitoring Programs (PDMPs)
- 2010: Tamper-resistant oxycodone first introduced
- 2011: Centers for Disease Control and Prevention (CDC) calls prescription painkiller abuse an epidemic
- 2013: FDA approves first single-entity, nontamper-resistant opioid painkiller Zohydro™ ER
- 2014: FDA approves abuse-deterrent hydrocodone, Hysingla™ ER

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ABOUT EXPRESS SCRIPTS

Express Scripts manages more than a billion prescriptions each year for tens of millions of patients. On behalf of our clients – employers, health plans, unions and government health programs – we make the use of prescription drugs safer and more affordable. Express Scripts uniquely combines three capabilities – behavioral sciences, clinical specialization and actionable data – to create Health Decision ScienceSM, our innovative approach to help individuals make the best drug choices, pharmacy choices and health choices. Better decisions mean healthier outcomes.

Headquartered in St. Louis, Express Scripts provides integrated pharmacy benefit management services, including network-pharmacy claims processing, home delivery, specialty benefit management, benefit-design consultation, drug-utilization review, formulary management, and medical and drug data analysis services. The company also distributes a full range of biopharmaceutical products and provides extensive cost-management and patient-care services.

Visit Lab.Express-Scripts.com or follow [@ExpressScripts](https://twitter.com/ExpressScripts) on Twitter for more information.

ABOUT THE EXPRESS SCRIPTS LAB

Founded in 2010, The Express Scripts Lab was built to foster collaboration, accelerate learning and enhance care. In 2014, we expanded the facility in size, scope and function, by bringing the experts behind Health Decision Science together under one roof. The expanded Lab is a reflection of our passion for patient care and our alignment with the needs of our clients.

Located on our St. Louis campus, the Lab is where our experts collaborate to solve pivotal healthcare challenges, drive out waste and improve outcomes. Here, the combined strengths of behavioral sciences, clinical specialization and actionable data generate meaningful innovation and develop the best new ways to improve health decision-making. These insights and innovations are then translated into new solutions and deployed throughout our company. The Express Scripts Lab is at the front line of healthcare innovation focused on one goal: better decisions for healthier outcomes.

