

Health Policy Opinion


Opioids In Chronic Noncancer Pain: Have We Reached A Boiling Point Yet?

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“The boiling point is the point at which people might do or say something to take definite or extreme action, because of extreme public health issues, frustration, and/or disagreement.”

As we say goodbye to 2013, 2014 brings in the global epidemic of opioid use, inappropriate use, and abuse with related fatalities, which along with the global epidemic of chronic pain with its related disability continue to be major issues for the public, officials, and physician community (1-11). After much controversy with pendulums swinging in different directions over the last 3 decades, it appears that we have reached the boiling point, with disagreements and colliding opinions finally resulting in definitive action with the publication of a policy position paper from the American College of Physicians (ACP) in December 2013 which in our opinion further validates as it is largely in keeping with the philosophy and policies that the American Society of Interventional Pain Physicians (ASIPP) initiated in 2000 (6,10). Starting in 2014, the Medicare participating provider program also encourages providers to actively participate in state prescription drug monitoring programs (12).

However, the global epidemic of opioid use with related fatalities is not a new problem and not limited to a single country, culture, race, or socioeconomic status (4,7-11,13,14). Inappropriate use, overuse, abuse, and rarely underuse is a universal problem (15-21). In fact, a 2011 report of the International Narcotics Control Board (INCB) reported that abuse of prescription drugs was growing rapidly around the world with more people abusing legal narcotics than heroin, cocaine, and ecstasy combined (22). Thus, prescription drug abuse, while most prevalent in the US is also a problem in many countries around the world including Canada, Australia, Europe, Southern Africa, and South Asia with tens of millions of people giving up control of their lives in favor of addiction (7,17-22). The increasing reports of prescription overdose deaths highly popularized in the United States (5), with the over 30 thousand drug overdose deaths exceeding motor vehicle injuries and 2.5 million emergency department visits, this has become a public health problem. Ironically, emergency department visits related to prescription drug abuse now exceed the number of visits related to illicit drug use (7). The same pattern also has been observed in other countries with increasing high overall prescription opioid consumption levels, nonmedical prescription opioid

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use, and harms in Canada, Australia, Denmark, Germany, and other European countries (14-24).

How Did We Get Here?

Opioid prescriptions for chronic noncancer pain skyrocketed in the late 1990s. With data from 1990 to 1996, researchers assessing the trends in medical use and abuse of opioid analgesics (25) concluded that the trend of increasing medical use of opioid analgesics to treat pain did not appear to contribute to increases in health consequences of opioid analgesic abuse. However, their second publication (26), with data from 1997 to 2002, changed the conclusion to the increase in the medical use of opioids was a general indicator of progress in providing pain relief with a caveat that increases in abuse of opioids was a growing public health problem and should be addressed by identifying the causes and sources of diversion, without interfering with legitimate medical practice and patient care. Recent assessment of current data from 2004 to 2011 (8) has shown that opioid use strongly correlates with prescription opioid fatalities. Thus, there is a close relationship between increasing opioid use and increasing inappropriate use and abuse.

In the 1990s opioid prescriptions for chronic noncancer pain skyrocketed. The lifting of the restrictions on opioid prescribing by state medical boards was the primary driver (27). Ironically, these guidelines, prepared to curtail controlled substance abuse, in fact, provided a groundswell of support for opioid prescribing and actually appeared to condone an increase in opioid prescribing (1,4,14,27-29). Thus, these guidelines seem to have had the effect of absolving prescribers from responsibility for their actions and promoted more prescriptions under the guise of appropriate medical treatment (8). Further, these guidelines stated, "no disciplinary action will be taken against a practitioner based solely on the quantity and/or frequency of opioids prescribed" (27). Unfortunately, the revised version of guidance from Federation of State Medical Boards (30) continued to provide inappropriate information in reference to the cost of chronic pain, undertreatment, and other issues based on inadequate or biased evidence synthesis (29-32). Other factors leading to runaway opioid prescriptions were the standards for both inpatient and outpatient pain management, implemented in 2000 by the Joint Commission on Accreditation of Healthcare Organizations, with pain as the fifth vital sign (33) and the concept of a patient's right to pain relief resulting in the validation of a physician's

need to increase their opioid prescribing (4,14,29,34). The legislations of right to pain relief were without understanding of the consequences of inappropriate opioid use in chronic noncancer pain, overuse, and inappropriate use. During the same period many physicians and a number of organizations also called for increasing opioid treatment for patients with chronic noncancer pain (4,14,29,34). The pharmaceutical industry took advantage of physicians and unleashed their marketing machine, promoting all types of opioids for all types of pain, ignoring safety and inappropriate use. However, the majority of the positions taken by organizations and physicians, though well meaning on occasion, were based on misinformation and unsound science for the justification of increased opioid prescribing with an omen that opioid prescribing was safe and effective so long as the opioids were prescribed by a physician (4,14,29,34-37).

As of today, there is no strong scientific evidence that opioids are effective for chronic noncancer pain (4,28,29,37-52). The entire opioid explosion across various nations was based on a single nonrandomized study by Portenoy and Foley (53), involving 38 patients using various types of opioids. In fact, in an interview with Catan and Perez (54), Portenoy described opioid use as his life's work. However, they also stated that Portenoy appears to be having second thoughts. Portenoy has been described as a prominent New York pain-care specialist driving a movement to help people with chronic pain 2 decades ago. He campaigned to rehabilitate a group of pain killers derived from the opium poppy that were long shunned by physicians because of their addictiveness. Catan and Perez wrote that Portenoy's message was widely successful, leading to the country's deadliest drug epidemic. They further said that Portenoy and other pain doctors who promoted the drugs say they erred by overstating the drugs' benefits and glossing over the risks. Considering the present standards, Portenoy felt that his teachings reflected misinformation. Portenoy not only preached the effectiveness, but also the extremely low or absent addiction in 1% of the patients. Portenoy also admitted that he gave enumerable lectures in the late 1980s and 1990s about addiction that were not true. He admitted that if he had an inkling of what he knows now, he wouldn't have spoken in the way that he did. It was clearly the wrong thing to do. Ballantyne, with credentials from Harvard and Washington University and publications in the *New England Journal of Medicine* and other prestigious journals on opioids in chronic pain (55-58), also

agreed with proponents of broad opioid use, but now believes they should be used more selectively. Portenoy and Foley's publication essentially opened the door to much broader prescribing of drugs for more common complaints including sprains, strains, headaches, acute and chronic back pain, and all other ailments. In essence, Portenoy, described as the "king of pain," called opioids a "gift from nature" that were being forsaken because of "opiophobia" among doctors, and his mission was to destigmatize these drugs.

OPIOID TOLL

With the publication of the manuscript by Portenoy and Foley (53) describing 38 cases in an observational study, drug companies took notice (54). In 1996, Purdue Pharma released OxyContin, a form of oxycodone in a patented, time-released form, with numerous others following suit. The marketing exploded, and physicians who were not willing to prescribe opioids were considered as opiophobic and those trying to impose controls with legislation such as NASPER, sponsored by American Society of Interventional Pain Physicians (ASIPP) (10), were described by some as "careless, naïve, and unsympathetic". In fact, NASPER was opposed by multiple organizations and only a few organizations provided lackluster support. In 2012, sales of opioids totaled more than \$9 billion a year (59).

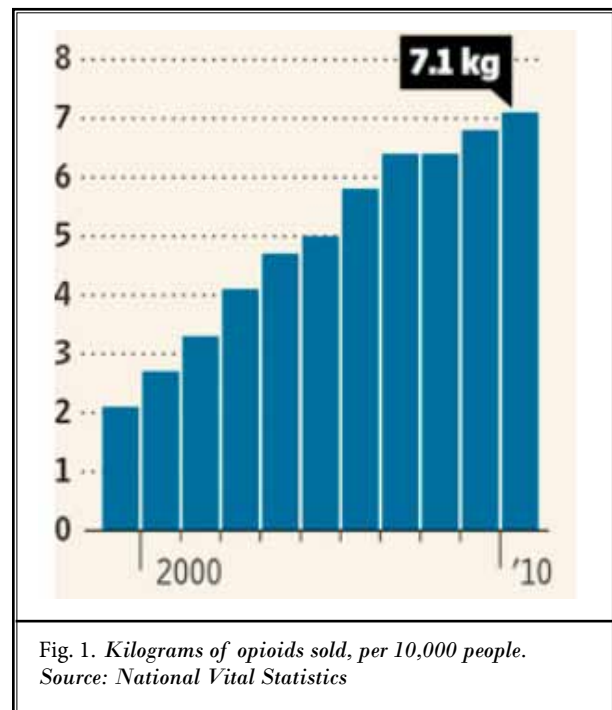
OPIOID SALES ON THE RISE

Ironically, in 2007, Purdue Pharma and 3 executives pleaded guilty to "misbranding" OxyContin as less addictive and less subject to abuse than other pain medicines and paid \$635 million in fines (54). Further, in the late 1990s, organizations such as the American Pain Foundation, of which Portenoy was a director, urged "hackling" what they called an epidemic of untreated pain. Further, the American Pain Society (APS), of which Portenoy was president, campaigned to make pain what it called the "fifth vital sign" that doctors should monitor along with blood pressure, temperature, respiratory, and heart rate (54). Portenoy was also instrumental in the 1996 consensus statement by the American Academy of Pain Medicine (AAPM) and APS promoting opioids with statements that there was very little risk of addiction or overdose among pain patients (60). This was followed by 1998 Federation of State Medical Boards policy recommendations essentially reassuring physicians that they wouldn't face regulatory action for prescribing even large amounts of narcotics, as long as it was in the course of medical treatment (27).

Further, some groups stated that the undertreatment of pain should be punishable. Much of this information is being looked at by the Senate Finance Committee (61,62). It also led to extinction of the American Pain Foundation (APF) (63). Even though the federation is under investigation, they have released their next set of guidelines which are often followed by medical boards of licensure (30).

Opioid sales in the USA increased 7-fold from 1997 to 2010 from morphine equivalence of 96 mg per person to 710 mg per person (Fig. 1). Described simply, enough opioids are sold so that 15 mg of hydrocodone can be administered everyday to every American adult for 47 consecutive days. In addition, in the 10 year period from 1997 to 2007, methadone sales jumped 1,293%, oxycodone sales jumped 866%, and hydrocodone sales jumped 280% in the United States (14).

The consequences of excessive opioid use continue to be staggering. In a February 19, 2013, publication from the Centers for Disease Control and Prevention (CDC), a continuing trend of opioid deaths, which began more than a decade ago, was confirmed with 16,651 dying of overdoses involving prescription opioids compared to 430 such deaths in 1999, an increase of 313% (Fig. 2) (64). Further, opioid analgesics caused more overdose deaths in 2007 than heroin and cocaine



combined (Fig. 3) (27,65-67). At the same time, suicide caused by drugs increased with 8,400 overdose deaths in the United States by 2007 that were either suicide or the intent could not be ascertained. Approximately 3,000 of those deaths involved opioids (68). A Government Accountability Office (GAO) of the United States report also concluded that key measures of prescription pain reliever abuse and misuse increased from 2000 to 2009 (66).

The economic burden of opioid related fatalities has been well described with costs exceeding over \$20 billion in 2009 in the United States alone (3). Strassels (69), estimating the consequence of opioid misuse, abuse, and diversion from biomedical literature, estimated the cost of \$8.6 million, including workplace, health care, and criminal justice expenditures in 2001. A study prepared for the Office of National Drug Control

Policy (ONDCP) reported that the cost of drug abuse in the US in 2002 was estimated to be US \$180.8 billion (70).

Despite the startling evidence, the opioid crisis continues to accelerate as does chronic pain's prevalence, health care costs, and adverse consequences from opioids. The CDC have reported the percentage of patients with prescription drug overdoses by risk-group in the United States (65). This report showed that approximately 80% were prescribed low doses (less than 100 mg of morphine equivalent dose per day) by a single practitioner. These account for an estimated 20% of all prescription overdoses as shown in Fig. 4. This may appear like a small percent; however, by any scientific means, this is mounting evidence against and incrimination of opioids. Even worse is among the remaining 20% of the patients, 10% were prescribed high doses

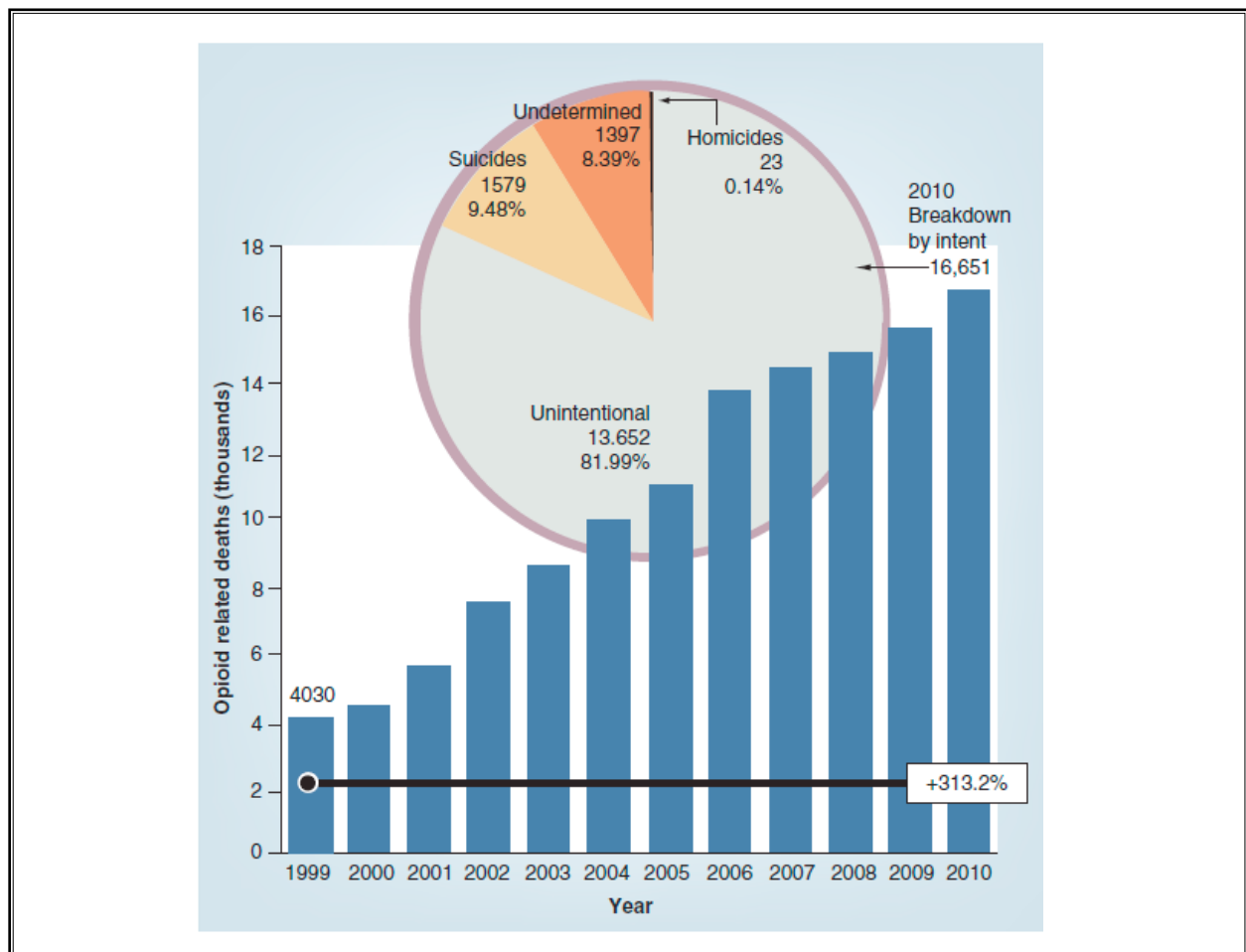
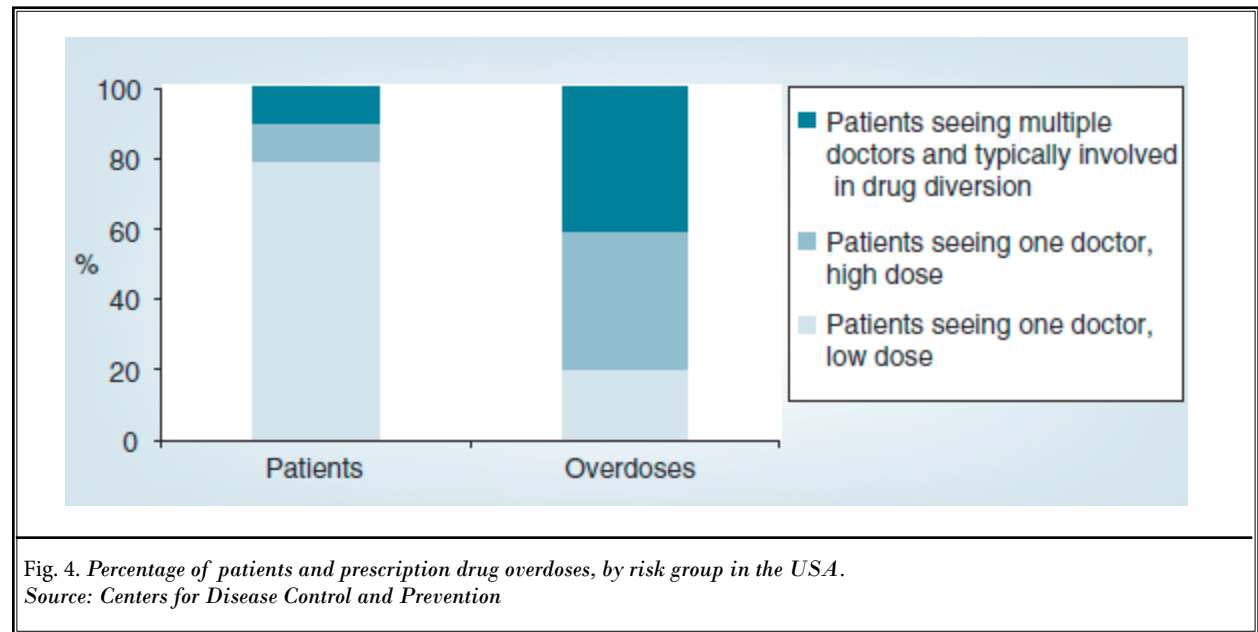
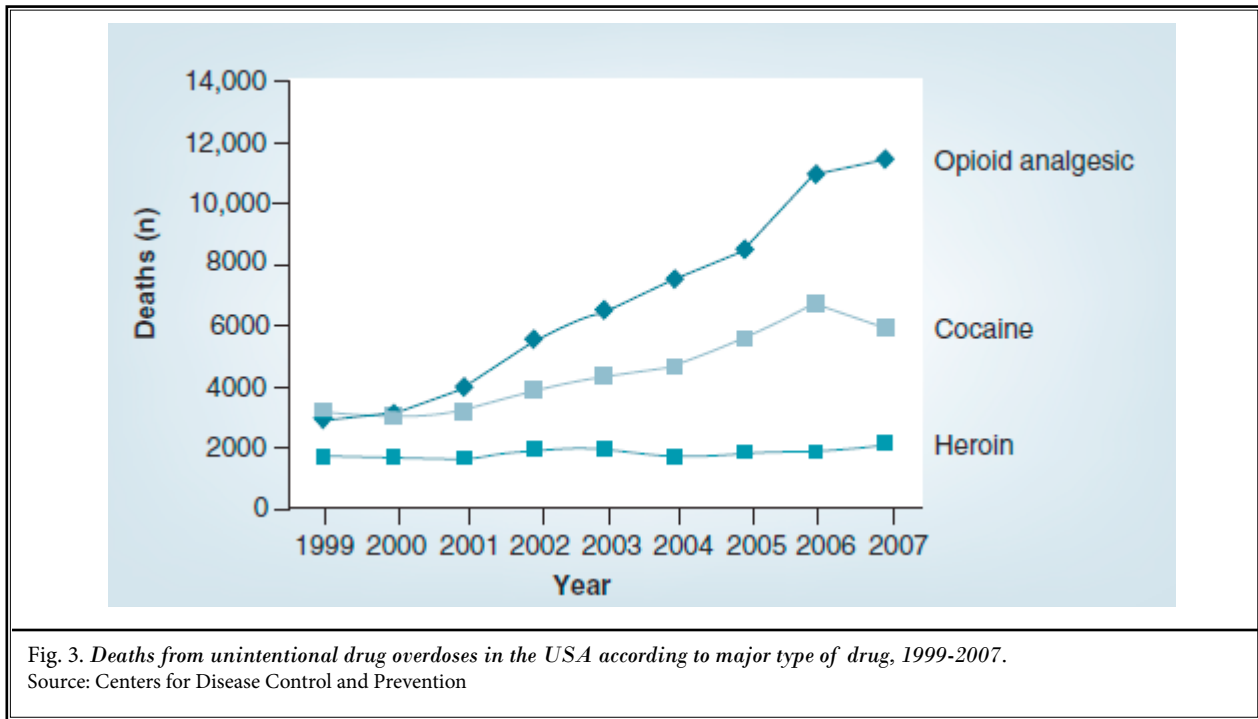


Fig. 2. Opioid-related deaths, 1999-2010 in all categories. Source: Centers for Disease Control and Prevention



of opioids by single prescribers (more than 100 mg morphine equivalent dose per day) (71,72), and the remaining 10% of patients were seeing multiple providers and typically were involved in drug diversion, ac-

counting for 40% of overdoses in each category (73). It is interesting to note that among persons who died of overdoses, a significant proportion did not have a prescription in their records for the opioid that killed

them. In West Virginia, Utah, and Ohio, 25% to 66% of those who died of pharmaceutical overdoses used opioids originally prescribed to someone else (68,73,74).

WHO IS RESPONSIBLE FOR CHANGING TIDES?

In the early 2000s, while multiple organizations were continuing to promote opioid use, which was translated to indiscriminate use, the idea of prescription drug monitoring programs was born (10). There were only 3 programs throughout the nation with access to physicians for monitoring their patients, including Kentucky and 2 other states. A national prescription monitoring program was envisioned by ASIPP called NASPER. This legislation passed the House of Representatives on 2 occasions; however, it never passed the Senate. Despite continuous advocacy by ASIPP, multiple forces, including many organizations, opposed this concept and resisted it. Subsequently, a compromise was reached. NASPER took shape in a different format of state monitoring programs having the ability to connect with contiguous states as a compromise. NASPER has continued to face opposition since becoming law in 2005, signed by President George W. Bush (75). During these years, organizations have continued to promote opioid use even recommending opioids to be off label for chronic noncancer pain beyond 120 days of therapy (34,76).

With the inappropriate use of opioids and resulting fatalities, the focus has shifted to a public health problem rather than undertreatment of pain, resulting in multiple investigations looking at improprieties in preparing guidelines and conflicts of interest for those who have promoted opioids. This has led to stricter regulations from multiple states with various legislation (77), which has been allegedly claimed to reduce patient access and increase physician work by supporters of widespread opioid therapy.

HAVE WE REACHED THE BOILING POINT YET?

We believe that we finally have reached the boiling point with the Drug Enforcement Agency (DEA), Centers for Disease Control and Prevention (CDC), Food and Drugs Administration (FDA), and multiple organizations sharpening the focus to curtail inappropriate use of opioids without affecting access. Consequently, hydrocodone has been recommended to change to Schedule II from Schedule III (78). Further, reformulations, evidence-based indications, dose reduction strategies and extensive monitoring have

been established. There also has been increased focus on educational aspects (79-90). Above all, recognition has come to the most prevalent prescribers with issuance of a policy position paper from ACP on December 10, 2013 (6). This policy position from ACP eliminates the major myth that controlled substance abuse originates and is maintained by pain management physicians. It has been shown that 90% of patients presenting to pain management settings already receive opioids on a long-term basis, sometimes in very high doses (1,4,91). Deyo et al (35) showed that approximately 61% of patients with low back pain in primary care settings were on a course of opioids and that of these, 19% were long-term users. Multiple surveys have illustrated that the majority of prescriptions are from primary specialists, followed by surgical specialties, rather than pain physicians (4,92-95). Thus, 42% of immediate release opioids and 44% of long-acting opioids were prescribed by a primary care physician, whereas specialties identified as pain management, including anesthesiology and physical medicine and rehabilitation, contributed 6% of immediate release opioids and 23% of long-acting opioids in 2009. Further, independent nurse practitioners and physician assistants also contributed to 7.5% of the short-acting immediate release opioids and 10% of long-acting opioid prescriptions.

With continued intense focus by administration, congress, and various agencies, it is well understood that we have reached the boiling point. Now the appropriate control of the inappropriate use of opioids is essential to tackle the massive public health problem. Physicians for Responsible Opioid Prescribing (PROP) has recommended severe restrictions on usage of controlled substances in chronic noncancer pain (34,76). ASIPP has published guidelines with a 10-step process with recommendation for prescriptions only when medically indicated in low doses for limited periods (4). However, a recent analysis of the guidelines (96) continued to rate APS/AAPM guidelines as the most ideal. The authors of this article consider the methodology of that analysis dubious. APS/AAPM guidelines, heavily funded by industry, conclude that even though the evidence is limited, an expert panel concluded that opioid therapy can be an effective therapy for carefully selected and monitored patients with chronic noncancer pain (97-99). The Canadian Guidelines, which were also rated as high in the systematic review (100), opined that opioids showed only small to moderate benefits for nociceptive and neuropathic pain in improving function and relief-

ing pain.

The ACP policy statement, a turning point in controlling inappropriate use of opioids, supports a comprehensive national policy on prescription drug abuse containing education, monitoring, and proper disposal and enforcement elements. This is exemplified by Medicare recommendations (12), multiple insurers, and multiple organizations managing Medicaid patients that also have joined forces to control the inappropriate use of opioids. From the authors perspective, it would be helpful if the American Academy of Family Physicians (AAFP) would endorse ACP policy or issue their own policy to curtail the inappropriate use of opioids with strict assessment and monitoring protocols. Starting 2014, the Medicare participating provider program also encourages providers to actively participate in state prescription drug monitoring programs.

Thus, we feel vindicated after over 13 years of intense advocacy for curbing the inappropriate use of opioids while maintaining access when medically needed, most important groups of physicians are involved in this policy with recommendations for a national prescription drug monitoring program or NASPER program. Finally, for 2014 and beyond, there is hope of controlling the inappropriate use of controlled substances.

In summary, it appears that we have reached a boiling point on the public health issue of opioids in chronic noncancer pain. We have to wait for another decade to find out the effectiveness of these changes.

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Conflict of Interest

Dr. Benyamin is a consultant and lecturer for Boston Scientific and Kimberly Clark.

Dr. Falco is a consultant for St. Jude Medical Inc. and Joimax Inc.

Dr. Helm is a clinical investigator with Epimed and receives research support from Cephalon/Teva, Astra-Zeneca, and Purdue Pharma, LP. He has attended an advisory group meeting for Activas.

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