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THE AMERICAN OPIOID EPIDEMIC: POPULATION HEALTH IMPLICATIONS AND POTENTIAL SOLUTIONS. REPORT FROM THE NATIONAL STAKEHOLDER PANEL

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Population Health Management Supplement Policy

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The American Opioid Epidemic: Population Health Implications and Potential Solutions. Report from the National Stakeholder Panel

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Editorial

The Unintended Consequences of an Opioid-Centric Approach to Pain Management

David B. Nash, MD, MBA

Today, without doubt, the United States is in the throes of a prescription drug crisis. In particular, national statistics show that widespread opioid misuse, abuse, addiction, and associated deaths have devastated the lives of countless Americans, irrespective of sex, age, race, or socioeconomic status. The societal costs associated with this opioid epidemic are staggering in terms of billions of dollars in health care expenses and millions of lives lost—46 lives every day—because of deadly overdose.¹

Responding to the magnitude of this opioid epidemic, local, state, and national legislators have mobilized task forces and implemented policy changes in an attempt to prevent further escalation and reverse the trajectory. The resulting initiatives—mandates for abuse-deterrent formulations, more stringent prescription monitoring programs, widespread availability of naloxone to reverse the effects of overdose, and greater emphasis on addiction recovery and rehabilitation services—have been crucial for combatting the crisis. However, these approaches fail to address the underlying issue (ie, they assume a continuing influx of opioids into our communities, working *reactively* to make these drugs more difficult to abuse, to “scam” from the health care system, to become dependent upon, and to die from). Getting to the crux of the problem will require a *proactive* approach that minimizes the introduction of opioids into general circulation by reducing or eliminating avoidable exposure. This presents a formidable challenge because it entails a reappraisal of well-entrenched prescribing practices.

Curtailing the use of opioids in the treatment of chronic pain may prove difficult; however, there is compelling evidence that the routine use of these drugs could be decreased exponentially in the acute postsurgical setting where an opioid-centric analgesic approach is no longer necessary, appropriate, or safe. Each year, roughly 53 million inpatient and 57 million outpatient surgical procedures are performed in the United States²; among those receiving opioids, a staggering 1 in 15 will become a long-term user.³ Although there is little doubt that opioids are effective in alleviating pain, efficacy often comes at a price. As detailed later in this report, the side effects of opioids delay recovery and diminish patient quality of life at best; at worst, they result in dependency and death.

In early 2015, a multidisciplinary group of clinicians convened at the Jefferson College of Population Health in an effort to raise awareness of the often overlooked connection between routine opioid prescribing practices—particularly in the inpatient setting—and the overall societal burden, and to discuss proactive approaches to reduce patients' exposure to opioids for acute pain.

To me, this topic could not have been more relevant to population health—and the potential upstream solution could not be more practical.

Introduction

Atypical and insidious, the American opioid epidemic is a frightening reality. Its origins can be traced to rural Appalachia where for years abject poverty, chronic pain, and depression have driven large numbers of residents to drugs for solace.⁴ The term “drug epidemic” conjures up the image of someone—usually a young person—seeking euphoria or escape from distress by means of illegally produced and/or sold compounds. In contrast, the opioid epidemic is fueled by legitimately prescribed medications. It is estimated that 2.1 million Americans

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suffered from disorders related to opioid pain relievers in 2012⁵ and the number of unintentional overdose deaths from prescription pain relievers has more than quadrupled since 1999.⁶ By 2002, opioid analgesic poisoning was listed as a cause of death more frequently than “street drugs” such as heroin and cocaine.⁷

In June of 2014, a White House Summit was convened to address the pervasive and devastating impacts of opioid abuse on public health and safety in the United States. Among other grave findings, it was noted that US health care providers wrote 259 million prescriptions for analgesics in 2012, a sufficient quantity to supply every American adult with a bottle of pills.⁸

The downstream effects of US physicians’ tendency to overprescribe opioids—often with the best of intentions—are numerous, ranging from patients’ incomplete understanding of the potential for dependence and side effects of these drugs to misuse, abuse, diversion, and addiction. National statistics are alarming:

- Between 1999 and 2010, twice as many lives were lost as a result of an opioid overdose than the lives that were lost during the Vietnam War.⁹
- More than 75% of people who misuse prescription analgesics use medication prescribed to someone else; this is inclusive of individuals of all ages¹⁰—even teenagers, who reported in a 2009 survey that prescription drugs were easier for them to obtain than beer.¹¹
- Diversion of opioids negatively impacts health care economics, costing insurers up to \$72.5 billion per year.¹²

Given the preceding, it is not surprising that the US Centers for Disease Control and Prevention (CDC) has characterized the rampant misuse and abuse of prescription opioids as an “epidemic that continues to worsen” and that has a “devastating impact on public health and safety.”^{13,14}

These realizations, coupled with the urgent need for solutions, were compelling reasons to convene a meeting of leaders in relevant fields. On February 6, 2015, a multi-stakeholder panel comprising clinical experts in behavioral health, orthopedic surgery, and anesthesiology, and leaders in health economics, veterans’ affairs, pharmacotherapy, and health policy was convened by the Jefferson College of Population Health in Philadelphia, Pennsylvania, with sponsorship by Pacira Pharmaceuticals, Inc., to (1) review the evidence pertaining to the issues underlying the American opioid epidemic; (2) compare and contrast the clinical, health economic, and societal implications of unimodal versus multimodal pain management; and (3) explore alternative approaches to postsurgical pain that lessen adverse events, reduce hospital length of stay, and decrease the need for opioids.

The expert panel was organized around a series of high-level presentations and related discussions that drew on the combined expertise of the panelists. The following summary report synthesizes the proceedings of the meeting and represents the collective contributions of the expert panelists (Table 1).

The Evolution of Opioid Use in the United States

Pain—and the desire to relieve it—is a fact of human existence. It is natural for people to seek relief from pain associated with illness and trauma and, for centuries, performing treatments and prescribing medicines to allay pain has been a core competency for the healing professions. The

insidious road to the present opioid epidemic has been paved with good intentions.

In nineteenth century America, virtually unregulated opiates and cocaine were prescribed and sold as remedies for maladies that ranged from toothaches to diarrhea; in fact, Bayer made its first fortunes in the late 1890s when it marketed aspirin and heroin as cough and cold remedies for adults and children.¹⁵

The Harrison Narcotics Tax Act (1914) began to regulate the importation, manufacture, and distribution of opium and cocaine, and, because addiction was not recognized as a disease, doctors who prescribed maintenance supplies of these agents to their addicted patients risked loss of their licenses and/or incarceration.¹⁶ The criminalization of addiction ultimately led to the undertreatment of legitimate pain. There followed years of advocacy for the humane treatment of pain by professional organizations and many articles were published on the efficacy and safety of opioids, culminating in the adoption of the intractable pain statutes by a number of states in 1997.¹⁷

With the preceding as background, it is easy to understand how the current opioid-focused model evolved. The unidimensional, unimodal approach to intractable pain for end-of-life and cancer populations was gradually generalized to populations with noncancer pain, and pain management became synonymous with opioids. This set the stage for the so-called opioid epidemic that now confronts the nation.

Today, opioids enter the community at an alarming rate. For example, a 2013 update of a workers’ compensation prescription drug study revealed that narcotics account for 25% of all paid prescription costs and that almost half (45%) of narcotics costs are for drugs with oxycodone HCl as an active ingredient.¹⁸ In fact, the brand name Oxycontin accounted for 25.5% of all prescribed narcotics and ranked first on the top 20 drug list for service year 2011 based on the total claims paid. Other top 20 agents included hydrocodone-acetaminophen (#5), oxycodone HCl-acetaminophen (#13), oxycodone-HCl (#15), and Percocet (#20).

The impact of the opioid epidemic on US veterans cannot be overstated. Among US veterans of Iraq and Afghanistan, mental health diagnoses, especially post-traumatic stress disorder, have been associated with an increased risk of receiving opioids for pain, high-risk opioid use, and adverse clinical outcomes.¹⁹ A study of Veterans Health Administration patients (2001–2009) provided evidence of a population-level association between trends in opioid prescribing and deaths from opioid overdose.²⁰

Unintended Consequences of Postsurgical Pain Management

An unfortunate confluence of events may have acted as a catalyst for our society’s overreliance on prescription analgesics, particularly in the postsurgical setting where opioid use is ubiquitous despite alternate modalities.

Given their potency, opioids have long played a role in alleviating pain and, since the invention of the hypodermic needle in the 1950s, opioids have been a mainstay in postsurgical pain management. In designating pain as the “5th vital sign” and advocating for an evaluation of a patient’s pain at every clinical assessment,²¹ the American Pain Society was perhaps the first unwitting protagonist in opioid-centric prescribing practices. By 2000, the Joint Commission had

TABLE 1. EXPERT PANEL

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adopted pain-as-the-5th-vital-sign as a standard²² and President Clinton had declared 2000–2010 as the Decade of Pain Control and Research.²³ These initiatives sought to ensure that patients received the best care to manage their pain without sufficient understanding of the risks and drawbacks. As a result, opioids were prescribed with increasing frequency without adequate evaluation regarding appropriate use.

A 2003 survey of patients' experience with postsurgical pain revealed that 82% of patients experienced pain after surgery, and that the majority of patients characterized their pain as moderate or severe. Despite the national emphasis on pain management, these results surpassed those of the initial (1993) survey in which 77% of patients reported postsurgical pain.²⁴

A deeper look into the downstream effects of inadequately managed postsurgical pain revealed an association with increased complications, resource utilization, and health care costs related to longer hospital stays, higher rates of readmission,²⁵ and potential for progression from acute to chronic pain.²⁶

Opioids continued to be used almost exclusively for postsurgical pain mitigation until their unwanted, and potentially life-threatening side effects began to negatively impact patient care and hinder the recovery process. Recognizing the need to optimize postsurgical analgesia, investigators turned to identifying alternate opioid delivery mechanisms rather than alternative drugs. For example:

- The patient-controlled analgesia (PCA) pump was developed, enabling patients to self-administer a powerful opioid analgesic at will.
- Adjunctive medications were developed to alleviate inevitable opioid-related side effects, allowing dose

escalation and maintenance of higher overall doses in patients who otherwise would not have tolerated such dosages.

- Oral opioid formulations provide the greatest ease with respect to self-administration and extended-release formulations now offer around-the-clock opioid exposure.

The newer oral opioid formulations are prescribed for a majority of postsurgical patients upon discharge from the hospital or surgery center, often without education regarding side effects or addiction risks. Recent restrictions on clinicians' ability to prescribe additional opioids via telephone have led to unnecessarily large initial prescriptions written "just in case." The unused pills can be abused by others; in fact, two thirds of individuals abusing opioids are taking someone else's prescription medication surplus.²⁷

In retrospect, our well-intentioned efforts to ensure total pain control have exposed patients to increasing numbers of potent opioid formulations at higher doses and in higher quantities. Because this was done under the misassumption that opioids prescribed for acute pain held little risk for abuse, misuse, or addiction, prescriptions were given without appropriate patient education related to risks and warning signs. Health care providers and policy makers can play a pivotal role by reevaluating the current opioid-centric approach to managing pain for postsurgical patients.

Pivotal role of postsurgical prescribing practices

Traditional postsurgical opioid prescribing practices create a ready conduit for controlled prescription drugs to enter

the community. With increasingly complex surgery being performed during a single-day hospital stay, more patients are being sent home with prescribed opioids for ongoing management of acute pain.²⁸ The result is a potentially large pool of unused drug available for later use by the patient or others in the community.²⁸ In a study by Rodgers et al, 245 of the 250 patients surveyed following outpatient upper extremity surgery were prescribed an opioid for postoperative analgesia. Although patients were most commonly prescribed 30 tablets, patients used a mean of 10 pills and reported 19 as unused—a total of 4639 leftover tablets for the cohort.²⁹

Children who engage in competitive sports are at particularly high risk of opioid misuse. Adolescents vying for sports scholarships routinely sustain injuries that require painful surgeries and equally uncomfortable rehabilitation. Because they want to return to sports competition as soon as possible, many use opioids prophylactically. A longitudinal examination of medical use and misuse of opioid medication among adolescent sports participants (1540 adolescents participating in 3 waves of data collection between the 2009–2010 and 2011–2012 school years with 82% of the baseline sample completing all 3 waves) comparing those who were involved in organized sports with those who were not revealed that participants were:

- Twice as likely to be prescribed an opioid medication.
- At 10 times greater risk for medical misuse of an opioid by taking too much.
- At 4 times greater risk for medical misuse of an opioid to get high.³⁰

Retrospective and prospective studies show that opioid prescriptions following surgery can lead to long-term use and may become a substantial source for misuse and diversion. Although opioid alternatives exist, most surgeons and anesthesiologists are unaware of their value in terms of risk minimization and optimal pain management. There is ample evidence (ie, 62 randomized controlled trials in a recent meta-analysis³¹) that, although opioids are more effective than placebo for nociceptive and neuropathic pain on a short-term basis, long-term use puts certain populations at greater risk for opioid abuse and overdose (eg, acute postoperative population, cancer population, military veterans, chronic noncancer population).³²

Similarly, Singh and colleagues conducted a longitudinal study of predictors of pain and use of pain medications following primary total hip arthroplasty (THA). They measured pain medication use, sex, age, body mass index (BMI), depression, and anxiety at 2 and 5 years following surgery and found that BMI and female sex were significant predictors of continued analgesic use at both intervals.³³ Depression was associated with higher nonsteroidal anti-inflammatory drug (NSAID) use and anxiety was associated with higher opioid use. In a study of opioid consumption following outpatient upper extremity surgery,²⁹ Rodgers et al concluded that excess opioid analgesics are often prescribed after elective upper extremity surgery and that these could potentially become a source for diversion.

Prospective longitudinal studies of patients undergoing different types of surgery have revealed strong associations between opioid use for postoperative pain and a range of adverse drug events. In a pilot cohort study of the deter-

minants of longitudinal opioid use after surgery, Carroll and colleagues concluded that preoperative factors, including legitimate use of prescribed opioids, depression, and self-perceived risk of addiction, independently predicted more prolonged use of opioids postoperatively.³⁴

Even as increasingly complex surgical procedures are being performed, the length of the associated hospital stay continues to decrease and prescription opioids to be self-administered at home is now routine practice. Macintyre and colleagues catalog a wide range of risks including acute adverse drug effects (eg, opioid-induced breathing impairment), unconsumed opioids available for later use by the patient or others in the community, and problems with nonmedical use.²⁸

Population health and societal implications. Defining, measuring, diagnosing, and addressing opioid dependence and opioid addiction in the population is highly complex and exceptionally difficult at best. However, mitigation can begin in the acute pain phase where opportunities exist to (1) assess the risk of abuse in patients receiving opioid therapy for acute and chronic pain and (2) develop population-based prevention strategies.

The 2011 Institute of Medicine report on pain set forth 4 principles:

1. Effective pain management is a “moral imperative.”
2. Pain should be considered a disease with a distinct pathology.
3. There is a need for interdisciplinary treatment approaches.
4. There is a serious problem with diversion and abuse of opioid drugs.³⁵

Since that time, government and health care professional organizations have taken appropriate action. Because opioid-related adverse drug reactions are a leading cause of preventable harm in the hospital setting, the Joint Commission revised its pain management standard³⁶ and issued a Sentinel Event Alert on the safe use of opioids.³⁷ Organizations such as the American Society of Anesthesiologists have recommended weighing the risks and benefits of systemic opioids and multimodal pain management. The CDC and other agencies have begun to offer financial support for opioid reducing or sparing initiatives and, recognizing that prescription opioid-related deaths are one of the nation's leading preventable public health problems, the Department of Health and Human Services Office of Disease Prevention and Health Promotion developed a National Action Plan for Adverse Drug Event Prevention.³⁸ Some states have begun to respond to the crisis as well. Effective solutions must target providers, payers, businesses, communities, and families as well as patients.

The Case for Multimodal Pain Management for Surgical Patients

Optimizing health outcomes

Because pain is multifactorial (ie, nociceptive, visceral, neuropathic, inflammatory, muscle spasm), treatment should target all relevant components—and no single drug can adequately accomplish this. The emerging opioid profile, especially in terms of its associated side effects (eg, T-cell

suppression, central sleep apnea, opioid tolerance, abuse/misuse/diversion), is further impetus to examine and reconsider traditional approaches to pain management.

Emerging profile of opioids: pros and cons. There are 2 reasons that opioids became the overwhelming drug of choice for surgical patients: (1) they are potent analgesics and (2) they can be titrated within a wide range. To a great extent, they remain the preferred drug despite their common side effects of gastrointestinal issues, respiratory depression/obstructive sleep apnea, sedation, confusion, mental status changes, intracranial pressure, and hemodynamic concerns. The emerging opioid side effect profile raises serious new concerns: potential T-cell suppression that increases the risk for infection and tumor growth; central sleep apnea; hormonal suppression; opioid tolerance; opioid-induced hyperalgesia; tumor angiogenesis; and abuse, misuse, and diversion.³⁹

Every opioid has a ceiling effect. Rather than increasing a patient's dosage reactively, a clinician should approach its usage as a trial (ie, if there is no benefit, do not use the drug). An informed consent before administering opioids would be useful for patient education and serve as an aid to shared decision making.

Planning for perioperative pain. Although surgery is known to cause pain, there is usually very little advance planning for its management. There are certain periods during pain therapy when pain is unrelieved.⁴⁰ This may occur for a number of reasons. A Premier database study revealed that 98% of Americans continue to receive opioids for postoperative pain management.⁴¹ These patients may delay treatment because of the drug's unpleasant side effects (eg, nausea, vomiting) or fear of dependence. Gaps in pain relief also may occur during the transition between therapies and as a result of technological issues (eg, epidural, intravenous [IV] PCA, continuous peripheral nerve blocks.)

To paraphrase Chantler,⁴² medicine used to be simple, ineffective, and relatively safe...now it is complex, effective, and potentially dangerous. IV PCA is a complex process—and, as complexity increases, the likelihood for error multiplies and the cost of care rises (eg, delivery to a single patient requires up to 6 people and 132 steps). From 2005–2009, there were 56,000 reported adverse events related to infusion pumps and 87 pump recalls were instituted.⁴³ An estimated 407 errors occur per 10,000 IV PCA patients per year.⁴⁴ Moreover, 80% of IV PCA errors are related to human factors (eg, programming errors, pump failures, syringe and IV line problems, family administration by proxy, patient tampering, inadequate staff training).⁴⁵

The American Society of Anesthesiologists 2012 Guidelines for Perioperative Pain Management strongly recommend a multimodal approach to pain management.⁴⁶ The physician-led perioperative surgical home model addresses clinical coordination before, during, after, and beyond an acute episode of care. It can be adapted to a specific facility, tailored by procedure, and—importantly—adjusted to an individual patient's characteristics. The perioperative surgical home also connects with a patient's primary care physician. Evidence of the benefits of multimodal therapy following surgery (eg, reduction in opioid and related side effects, fewer analgesic “gaps,” chronic pain reduction, improved patient satisfaction) is growing.

The growing emphasis on pain management and patient satisfaction is beginning to affect a hospital's accreditation status and reimbursement. In its revisions to the pain management standard (effective January 1, 2015), The Joint Commission states that pain treatment strategies—including nonpharmacologic and pharmacologic approaches—should be patient-centered and should consider the risks (dependency, addiction, and abuse) as well as the benefits associated with available options.³⁶

The Joint Commission now requires an institutional pain performance improvement plan as part of its hospital accreditation process.⁴⁷ Local, regional, and/or national patient satisfaction data are now being reported via the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS survey)⁴⁸ and, under the Affordable Care Act (ACA), the Centers for Medicare & Medicaid Services has begun to incorporate HCAHPS scores in their formula for calculating reimbursement.⁴⁸ Although patient satisfaction is a widely used metric, the relationship between resource utilization, expenditures, and outcome are ill defined. In fact, higher patient satisfaction has been associated with greater inpatient use, higher health care and prescription drug use and expenditures, and increased mortality.⁴⁹ Clearly, giving patients what they want, or think they need, is not always in their best interest.

Minimizing risk of postsurgical overuse and misuse of opioids. What works to decrease opioid use? Evidence regarding preemptive multimodal approaches is growing. For instance:

- Perioperative lidocaine for complex spine surgery significantly reduced pain intensity and slightly lowered the complication rate.⁵⁰
- Perioperative pregabalin for total knee arthroplasty reduced incidence of chronic neuropathic pain with less opioid consumption and improved range of motion in the first 30 days of rehabilitation,⁵¹ and improved pain and functionality outcomes 3 months after lumbar discectomy.⁵²
- Perioperative pregabalin for lumbar spinal fusion significantly reduced opioid consumption and the use of additional pain resources for 48 hours after surgery.⁵³

With multiple delivery routes available, acetaminophen is generally safe and has minimal side effects (although contraindicated in patients with severe hepatic impairment). A study of intravenous acetaminophen for pain relief after hip and knee surgery demonstrated a 33% decrease in morphine consumption over the first 24-hour postoperative period compared with placebo. Nausea and vomiting were reduced and patient satisfaction rose.

Selective and nonselective NSAIDs are widely used in orthopedic surgery with safety and efficacy. Although their potential effects on bone healing are inconclusive in humans, they do not appear to have a negative effect on osteointegration or soft tissue healing. Importantly, they do have a positive impact on dynamic pain.⁵⁴

For opioid-tolerant patients with new acute pain, ketamine has proven effective in reducing opioid requirements and improving pain control—perhaps a new role for this drug in the multimodal armamentaria of postoperative analgesia.^{55–57}

Formulated from naturally occurring lipids, liposomes are sustained-release, targeted drug delivery systems that improve

efficacy and tolerability by increasing the drug circulation time. The range of current applications of this technology is broad—chemotherapy, local anesthesia (eg, epidural), and delivery by means of intrathecal, infiltration, and inhalation administration.⁵⁸

Drugs developed and launched in the new health care environment must be patient-centered. In the acute pain space, where patients now ask for drugs by name, there is unprecedented risk of overprescribing, overuse, and misuse—particularly of opioid drugs. EXPAREL® (bupivacaine liposome injectable suspension) is an opioid alternative with equivalent pain control that reduces the need for postsurgical opioids and devices.

The injectable drug delivery system used for EXPAREL was first conceived and introduced more than a decade ago as a means for administering an opioid analgesic directly into the cerebrospinal fluid, thereby achieving effective pain relief at substantially smaller doses than oral or parenteral routes.⁵⁹ This innovative delivery system is similar to a pomegranate in design (Fig. 1). An outer membrane encapsulates discrete chambers within a lipid matrix, each filled with an aqueous solution of drug, thus managing the rate of dissolution over an extended period of time. When EXPAREL is used for postsurgical pain management, this innovative drug delivery technique has proven very effective in minimizing opioid use following surgery (eg, by 50% in orthopedic procedures.)^{60–63}

Optimizing economic outcomes by managing pain differently

An individual's willingness to pay for something shows the dollar value he or she attaches to it; for a population, value is determined by a collective willingness to pay for a certain thing.⁶⁴ With respect to US health care, this implies a pressing need for more—and better—information on what works and what it costs.

The ACA's 3-pronged approach of expanded health insurance, payment and care delivery reforms (fee for service to bundled payment), and better information (health information technology, data systems, comparative effectiveness research) calls for research that goes beyond clinical trials and

incorporates real-world and retrospective data. Value must be addressed as an evidence issue (ie, it must be measured over time rather than merely asserted). Payment and delivery reforms will have wide-ranging impacts (eg, the Patient-Centered Outcomes Research Institute will focus on pain from a patient perspective such as out-of-pocket costs). Also, the Agency for Healthcare Research and Quality may prove to be a home and repository for research into value. Emphasis must be on the patient when defining outcomes.

Contrary to conventional wisdom that prevention saves money, a comprehensively referenced article in the *New England Journal of Medicine* suggests that generalizations about the cost-saving potential of prevention are overstated. Many studies have concluded that although prevention is a good *value* over the long term, it does not always save money—cost-effectiveness depends on the type and cost of the intervention and the target population. More and better analyses are needed to understand costs and benefits such that these can be considered as “evidence.”

From an economic standpoint, pain management is complex because the costs of an intervention spill over into other systems including:

- Hospital costs such as medication, equipment, placement, non-opioid adverse event, readmission, length of stay, hospital personnel, productivity, opioid-related adverse events.
- Judicial system costs incurred as a result of controlled prescription drug diversion and abuse.
- A replication study of opioid abuse in a commercially insured population showed that the prevalence of diagnosed abusers increased from 15.8/10,000 subjects in 2009 to 26.6/10,000 subjects in 2012. The diagnosed abusers incurred excess annual health care costs of \$11,386 per patient.⁶⁵

Recent evidence of the prevalence of opioid-related adverse events has strong implications for health policy. Retrospective analyses of 320,000 surgeries (Premier hospital data) revealed that the 12.2% of patients who experienced opioid-related adverse drug events (ORADEs) had higher costs (\$22,000 vs. \$17,000) and longer hospital stays (7.6 vs. 4.2 days).⁶⁶ Another retrospective administrative claims analysis (37,031 surgical patients who underwent a common procedure in a 26-hospital system) revealed even more striking findings. Among all surgical patients, 98.6% received opioids and 13.6% of these experienced an ORADE. Patients with an ORADE had a 55% longer hospital stay, 47% higher costs of care, a 36% increase in risk for 30-day readmission, and a 3.4 times greater risk of inpatient mortality than the patients who did not experience an ORADE.⁴¹ Policy response was creation of the National Action Plan for Adverse Drug Event Prevention.

Higher doses of opioids are associated with higher incidence of postoperative ileus, a well-documented consequence and complication of gastrointestinal, pelvic, and some non-abdominal surgeries. Use of opioids in patients who develop ileus is associated with prolonged hospitalization, greater costs, and increased readmissions (Fig. 2).⁶⁷

In 2007, the US societal costs of prescription opioid abuse were estimated at \$55.7 billion.⁶⁸ Diversion of controlled prescription drugs costs payers up to \$72.5 billion per year.¹² Based on the concepts discussed earlier, the added costs

FIG. 1. DepoFoam® technology used to deliver bupivacaine (EXPAREL®). A color version of this figure is available in the online supplement at www.liebertpub.com/pop.

FIG. 2. Opioid abuse results in high health care costs. Costs are in 2003 dollars. The differences between all mean annual costs of opioid abusers and nonabusers are statistically significantly different at the 1% level ($P < 0.01$) except for “Other Costs,” for which the “Other Place of Service” component is significantly different at the 5% level ($P < 0.05$). †“Other Costs” include “Other Place of Service” and “Emergency Room” costs.

attributable to misuse and abuse of opioid prescriptions originating in the acute care setting are considerable. With steadily increasing numbers of surgical procedures being performed, even small increments in the percentage of chronic opioid users will create an unsustainable societal burden.

Expert Panel Insights

There was general consensus that the opioid epidemic is an urgent population health issue and an appropriate target for robust health policy initiatives. Some health systems and medical centers are leading the way and addressing the issue by providing financial support for in-house physicians and pain management nurses. The experts concurred that, beyond deploying clinical treatment teams, effective pain management systems must focus on defining standards, building curricula, and educating the community. Currently, the US military is seeking guidance on disposal of drugs; a government decision affecting the Veterans Administration likely would lead to similar decisions in the private sector.

Clinician panelists concurred that acute pain management is ascendant as a clinical specialty—and that subspecialty status will confer the political power to use analgesics more appropriately. A drug that can be administered intraoperatively enables the clinician to manage a surgical patient's postoperative pain and reduces the need for opioids following discharge from the hospital.

Physician and patient perception is important. It is not uncommon for patients to pressure their physicians to prescribe opioids. It takes mere seconds for a primary care physician to write a prescription for an opiate; it takes 30 minutes to explain why he/she is unwilling to do so. The

challenge lies in reeducating and changing clinicians' and patients' perceptions. A comprehensive pain management strategy should be adopted for every patient and alternatives to opioids should always be considered as an initial option, reserving opioids as a potential “rescue” drug if other modalities are not effective. Patients should always receive adequate pain management without unnecessary exposure to the acute and long-term risks associated with opioids.

A wide variety of effective alternatives to opioids for pain management are available and patients need to be educated on what strategies are most appropriate for their procedure.

Conclusion

There is compelling evidence that an American opioid epidemic exists and that measures should be taken to reduce the population's exposure to these drugs. The emerging opioid side effect profile (eg, respiratory depression, sleep apnea, potential T-cell suppression) raises serious concerns. Opioid dependence, misuse, and abuse—often originating with postsurgical discharge prescriptions—have substantial clinical and economic repercussions. Mitigation must begin before an opioid is prescribed for acute or chronic pain.

There is evidence that adverse drug events, misuse, abuse, and diversion of opioids stems from traditional perioperative pain management and postsurgical prescribing patterns. Effective alternatives to opioid drugs should be considered in order to optimize postsurgery pain management and minimize health risks. Pain is multimodal and it must be approached by clinicians and patients as such.

Tackling the postsurgical opioid issue will require a 3-pronged approach that effectively targets (1) prevention of

adverse drug events, (2) promotion of multimodal care, and (3) reduction of misuse, abuse, and diversion.

Author Disclosure Statement

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