

Challenges of Chronic Pain Management: Public Health Consequences and Considered Responses

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This article reviews the public health consequences of current approaches to chronic pain management, particularly those related to prescription of opioid analgesics and other controlled medications. This article also reviews factors contributing to these negative trends and discusses potential strategies for reversing them.

Prescribing rates for opioid medications have risen dramatically over the past 15 years, doubling or even quadrupling depending on the particular analgesic. The total amount of opioids prescribed in the United States measured in morphine-equivalent doses (MEDs) increased more than 600% between 1997 and 2007 [1], and more than 200 million opioid prescriptions are now written every year. With the increased availability of opioids, diversion of these medications to nonmedical use has also increased. In 2010 more than 12 million individuals in the United States were estimated to have used opioid analgesics nonmedically during the previous year, and approximately 1.8 million people had abused or had been dependent on these drugs [2]. As a consequence of this trend, health care providers in clinical practice are more commonly observing medical and traumatic complications of opioid use. Between 2004 and 2010, the number of emergency department visits for hydrocodone misuse or abuse more than doubled, and the number of visits related to oxycodone tripled [3].

Accidental overdose deaths underscore the seriousness of this problem. Nationally, the rate of unintentional deaths due to prescription drug overdoses has nearly tripled over the past 10 years [1]. In 2010 approximately 16,000 overdose deaths were attributed to prescription opioids, while only 2,000 were related to heroin [2]. While opioids are the primary cause for concern, other controlled medications also have potentially serious overdose risks. In 2010 there were almost 400,000 emergency department visits and approximately 6,000 overdose deaths involving benzodiazepines [2]. Nationally, deaths due to drug poisoning are now the primary cause of accidental deaths, exceeding traffic fatalities [2, 4]. The North Carolina Office of the Chief Medical Examiner reports that deaths due to overdoses of controlled medications—primarily opioid analgesics—have more than doubled over the past 10 years in North Carolina, with almost 900 such deaths reported in 2011 (William Bronson, written communication).

These numbers provide only a broad outline of the more obvious public health consequences of opioid misuse. Mean annual direct health care costs are nearly 8.7 times higher for individuals who abuse these medications than for those who do not [5]. Along with these economic effects on individuals, there are also incalculable emotional consequences for families and communities. Prescription medications, primarily opioid analgesics and benzodiazepines, have surpassed marijuana to become the new gateway drugs—the first illicit drugs used by teenagers [6]—which hints at their broad impact and foreshadows the continuation of this societal and clinical problem for many years to come.

An Evolving Standard of Care

Each year, a large majority of the global supply of opioid analgesics is consumed in the United States, including more than 80% of the global opioid supply and 99% of the global supply of hydrocodone [7]. This imbalance reflects socio-cultural and economic factors as well as clinical standards. Therapeutic decisions, including the decision to prescribe opioids, are based not only on the clinician's knowledge base but also on patient preference, availability of nonmedical treatment modalities, complexities and biases in third-party reimbursement, aggressive pharmaceutical marketing, and medicolegal concerns. These and other factors have tended to skew the standard of care in the United States toward an overreliance on opioids for long-term management of chronic pain.

Viewed in a historical context, the standard of care for the management of chronic noncancer pain has changed dramatically over the past 20 years. The United States has long had high rates of chronic pain and associated suffering, disability, and impaired quality of life. Approximately 15–20 years ago, physicians were seen as being unresponsive to this pressing clinical need, and they were accused of ignoring pain or treating it inadequately [8]. At that time a concerted effort was made to respond to this unmet need with educational and regulatory initiatives, such as

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Prescription Drug Overdose and Misuse:

Data from Carolinas Poison Center

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Carolinas Poison Center is a telephone resource center that provides confidential triage, information, and management advice to a wide spectrum of callers in North Carolina. As a result of these calls, Carolinas Poison Center has a dataset of self-reported information from the public and medical information from health care providers about the substances involved in poisonings, their clinical effects, and the management of these cases. The calls can relate to anything that causes toxicity—including medications, illicit drugs, chemicals, gases, venoms, and plants.

A widely held perception is that Carolinas Poison Center receives calls mainly from parents of small children who are exposed to toxic substances in the home. Although children younger than 6 years of age do account for just under half of calls related to human exposures, the most complicated poisoning cases involve adults who have been exposed to multiple drugs, and opioids are increasingly involved in these latter cases.

In calendar years 2011 and 2012, Carolinas Poison Center handled 98,115 calls involving humans who were exposed to prescription or nonprescription pharmaceutical substances. The top 5 categories of such agents were analgesics; sedatives, hypnotics, and antipsychotics; cardiovascular drugs; antidepressants; and antihistamines. Prescription pain medications containing opioids, either alone or in combination with acetaminophen or salicylates, accounted for 6,137 of these calls, representing 29.8% of all calls regarding human exposure to analgesic medications. The top 3 opioids implicated in these cases were (in rank order) hydrocodone, oxycodone, and tramadol.

In the majority of the prescription pain medication cases reported to Carolinas Poison Center, the involved individual underwent treatment in a health care facility; naloxone was administered in 22.0% of these cases. Of the cases managed in a health care facility that involved opioids only (without acetaminophen or aspirin), 7.6% had an outcome of death and/or major effects, such as respiratory depression, and/or moderate effects that responded rapidly to therapy, such as hypotension. Only 32.5% of prescription pain medication cases were managed at the site of the caller, outside a health care facility.

The increased use of extended-release products, long-acting substances such as methadone, and partial agonist/antagonists such as buprenorphine can make management of opioid-related poisonings difficult. Even when naloxone is administered, the duration of action of the

opioid is often much longer than that of naloxone, which necessitates longer observation times and possibly additional doses or continuous infusions of naloxone. Health care providers must also monitor for nonopioid effects of these agents. Carolinas Poison Center staff members assist health care providers with management recommendations and monitoring advice.

In addition to providing services to the general public, health care providers, law enforcement professionals, schools, and other agencies, Carolinas Poison Center also engages in research and awareness campaigns to help prevent poisoning injuries. For example, Carolinas Poison Center is currently working with the Injury Prevention Research Center at the University of North Carolina at Chapel Hill to study the effectiveness of a care coordination program to prevent prescription drug overdoses. This randomized controlled trial will evaluate the efficacy of a care coordination plan for patients who have made numerous visits to 13 emergency departments for treatment of chronic, subjective pain that is not associated with cancer or sickle-cell disease. This study is being conducted in conjunction with the Centers for Disease Control and Prevention.

Finally, Carolinas Poison Center is also conducting a campaign aimed at reducing the misuse and abuse of prescription medications by teenagers. This campaign, which debuted in April 2013, was created with the assistance of teen focus groups. It primarily targets middle school students, who are deemed to be most open to awareness outreach, but it will also be used in high schools. NCMJ

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the “pain as the fifth vital sign” campaign. In addition, the Model Policy for the Use of Controlled Substances for the Treatment of Pain was developed by the Federation of State Medical Boards in an attempt to alleviate physicians’ concerns about regulatory oversight [8].

Clinical practice subsequently shifted to include more

widespread use of opioid analgesics. Previously opioids had typically been used only for acute, time-limited pain. Successful use of opioids for chronic cancer-related pain led to increasing use of these drugs to treat chronic noncancer pain as well. Although well intended, this expansion in the use of opioids was made without adequate attention to

potential risks and despite the paucity of clinical research supporting such a change [9].

There is now a need for a more balanced, evidence-based standard of care for management of chronic pain—one that assures access to needed treatment while minimizing the potential for overuse and abuse of medications. This effort will require paying attention to 2 parallel, overlapping imperatives. First, there is a need for training in effective, multidimensional pain management strategies with a more proscribed role for opioids, particularly high-dose opioids. Second, new standards of care will need to define and apply safer prescribing practices through adequate risk stratification, appropriate treatment planning, and conscientious monitoring.

Training Needs

US medical schools report devoting an average of only 9 hours of curricular time to pain, and a majority of primary care physicians report that they do not feel confident about managing chronic pain [10]. There is thus a clear need for more education on topics such as how to differentiate categories of pain (such as nociceptive, inflammatory, and neuropathic pain), how to identify which treatment modalities are likely to be effective for these types of pain, and how to determine when pain is likely to be responsive to opioids. Currently, most clinical protocols list opioids as indicated for moderate to severe pain, and they state that these drugs are to be used only after other modalities have proven inadequate [11]. Yet primary care clinicians and specialists at times use opioids as first-line treatment for a broad range of chronic pain syndromes.

Dosing is another important area in which training is needed. Specific topics that should be addressed include safe and effective dose initiation and titration; when and how to use different opioids, including short-acting and long-acting formulations; how to establish when an adequate dose has been reached; and when and how to stop prescribing opioids. Achieving the optimal dose for each patient is particularly important because there is an escalation in risk with increasing dosages of opioids. In a study of opioid overdoses among patients with chronic noncancer pain [12], the hazard ratio for serious overdose events was 1.0 at a daily MED up to 20 mg, 3.11 at a daily MED of 50–99 mg, and 11.18 at a daily MED of 100 mg or greater. Clinicians also need to know what constitutes an adequate trial of opioid therapy. When faced with complaints of inadequate pain management or requests for higher doses, the clinician may decide—rather than increasing the dose—to discontinue opioid therapy, rotate among opioids, or use these drugs with greater attention to other pharmacologic or behavioral interventions.

More broadly, a recent Institute of Medicine report, *Relieving Pain in America* [13], reinforced the importance of framing chronic pain as a unique chronic disease state with complex neurophysiological, emotional, and social components—all of which make its management quite distinct

from that of acute pain. The “suffering” aspects of chronic pain require a different level of attention and intervention than that available through medications alone. Traumatic experiences, depression, changes in self-image, disruptions in employment and other social roles, stresses on family caregivers, and a host of other subtle aspects of chronic pain clearly point to the need for a biopsychosocial treatment model. Cognitive behavioral therapies and the development of coping skills have demonstrated effectiveness in pain management, and patients’ motivation and engagement are important in establishing realistic goals for the management of their pain. A collaborative model of care is thus critically important to a successful outcome [13].

Implementing a Safer and More Balanced Approach to Prescribing

Many of the current proposals for adapting prescribing practices to minimize the potential for misuse and addiction are not really new. Rather, they reapply guidelines for conscientious medical practice to this particular clinical area [8, 14]. The emphasis is now on the need to apply these guidelines universally and to routinely use newer tools such as the North Carolina Controlled Substances Reporting System (NCCSRS) as part of ongoing risk assessment and monitoring [15]. Applying these strategies to all patients, regardless of age or other demographic characteristics, is crucial, as overdoses are not just occurring among young, naïve street addicts. One review [4] found that overdose rates in 2008 were actually highest among those 45–54 years of age, while those 15–24 years of age had some of the lowest reported overdose rates (25 deaths per 100,000 and 5 deaths per 100,000, respectively). Some guidelines also recommend wider use of abuse-resistant formulations of pain medications. Whether such formulations will have a significant impact on misuse and abuse is not yet clear; while they may indeed provide some added safety, they are no substitute for conscientious clinical care.

Most of the evolving protocols for safer prescribing share certain features, even if specific applications or tools vary [11, 16]. One important feature of these protocols is risk stratification. Specifically, deciding whether or how to use opioids should be dictated by risk assessment that is based not only on the patient’s self-report but also on information obtained from prior clinicians or medical records, from the NCCSRS, and from the results of preliminary drug screening.

Treatment agreements are another common feature of prescribing protocols. These are written, signed agreements that educate the patient about risks, set realistic collaborative goals, and define the parameters for safe use that must be maintained in order for patients to have continued access to their medication [11, 17].

Ongoing monitoring is also commonly imposed. Treatment effectiveness should be determined by improvement in functionality and adequate pain management, not by pain eradication [18]. Safety is gauged through the absence

Prescription Drug Diversion: A Law Enforcement Perspective

Donnie R. Varnell

The Diversion and Environmental Crimes Unit (DECU) of the North Carolina State Bureau of Investigation (SBI) is the only statewide law enforcement group that is dedicated to investigating all criminal violations involving prescription drugs and controlled substances, including the diversion of these substances. (Readers can learn more about the North Carolina SBI at <http://www.ncdoj.gov/SBI.aspx>.) This role gives DECU a unique perspective on the growing epidemic of prescription drug diversion, which affects not only the criminal justice system but also health care professionals and citizens.

For many years, hydrocodone was the most commonly diverted drug, and it continues to be one of the most popular medications among individuals who commit these violations. Over the past 2 years, however, oxycodone (in a 30-mg dose) has far surpassed all other prescription narcotics as the drug of choice among drug seekers and those who abuse prescription drugs. DECU has also witnessed a disturbing increase in the number of young people in the high school and college populations who buy, sell, and trade amphetamine/dextroamphetamine (a stimulant that is indicated for the treatment of attention deficit hyperactivity disorder). Finally, benzodiazepines such as alprazolam are frequently diverted by a wide range of individuals.

From 2004 to 2009, DECU saw a 400% increase in the total number of investigations of diversion; additionally, from 2010 to 2012, the number of investigations that involved health care professionals increased 35%. DECU's resources were nearly overwhelmed by the number of organized drug rings that used forged computer-generated prescriptions to obtain large amounts of controlled substances, and these drugs then quickly found their way onto the streets and into the hands of citizens. These highly profitable criminal groups, which operate in multiple jurisdictions, no longer need to "doctor shop" to obtain these powerful and addictive drugs; they only need to steal a prescriber's Drug Enforcement Administration (DEA) number and use it to produce fraudulent prescriptions. These groups normally consist of 10-30 members and fraudulently obtain more than 4,000 dosage units per week; this amount is easily worth more than \$120,000 when sold on the street.

The consequences of diversion and subsequent investigations are often severe and can extend far beyond the individual who has committed the violation. A person who is found guilty of diverting a Schedule II drug will often be charged with and convicted of trafficking opium-based substances, and he or she may face several years of mandatory prison time. In addition to criminal penalties, having vast amounts of powerful and potentially deadly narcotics available for sale on the streets poses consider-

able dangers. DECU is now dealing with a 300% jump in the number of overdose deaths that are being investigated as homicides and manslaughter cases. Furthermore, my colleagues and I recently gave a presentation at a local high school that is suspending or charging 3 students per week due to violations involving the possession of prescription drugs at school.

DECU has often stated that arrests alone are not the solution to this problem. We know that we must use a multidisciplinary partnership to combat these trends. We are therefore working closely with regulatory groups such as the North Carolina Medical Board, the North Carolina Board of Nursing, and the North Carolina Board of Pharmacy in an effort to curtail this growing problem. DECU has given awareness training to more than 4,000 individuals over the past year and will continue to provide this service in the future.

We also advise citizens to take full advantage of medicine take-back programs, such as Operation Medicine Drop, in order to remove unused medications from their homes. Most young people who use prescription controlled substances obtain these drugs in their own home or in the home of a friend. Over the past 3 years, DECU, the DEA, and Safe Kids North Carolina have collected and destroyed more than 20 million dosage units of medication. In addition, we strongly suggest that health care professionals check their own prescription profiles in the North Carolina Controlled Substances Reporting System (NCCSRS). We have had several physicians check the NCCSRS and learn that someone had fraudulently written hundreds of controlled substance prescriptions using their DEA number.

Diversion of prescription drugs is undoubtedly the fastest growing and most severe drug problem in America today. Only by working together will we be able to combat these trends and better protect the citizens of North Carolina. **NCMJ**

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of impairment or aberrant behaviors, use of recurrent drug screening, and review of NCCSRS data.

Most protocols also call for adapting the treatment plan when necessary. Inadequate pain relief calls for reevaluation of multimodal treatment options and for active engagement with the patient, rather than simply an increase in dosage. Referrals for evaluation or additional treatment may also be indicated, particularly if higher doses are to be considered.

In addition, most safe-prescribing protocols recommend intervening when the patient's behaviors appear to be risky or aberrant. Further assessment is often required to determine what type of intervention is needed, after which clinicians may choose to increase their frequency of contact with the patient, discontinue refills, refer the patient for mental health or substance abuse evaluation, or discontinue the use of controlled substances.

Implementation of these recommendations will depend on how they are adapted to various primary care, specialty, or emergency settings. Methodologies must be time-efficient, take advantage of electronic medical records and other information system technologies, make use of personnel in team-based models, and link patients with available mental health and substance abuse services in the community.

Clinical Conundrums: Functional Addiction and Functional Dependency

One looming challenge is how to deal with the large number of individuals who are currently dependent on prescribed opioids, many of whom have been taking these drugs for long periods of time, sometimes at high dosages. This is generally a poorly delineated group: Some patients may still have severe pain that requires opioids at some dose. Others may be continuing opioid therapy primarily to avoid rebound pain or withdrawal. Many may be using opioids not to treat physical pain but to ameliorate emotional or situational distress, which is called "chemical coping." Finally, since many patients have not been monitored adequately for functionality, impairment, or aberrant behaviors, some patients may be "functional addicts"—people who are addicted but have not yet been identified as such—while other patients who show no evidence of impairment or aberrant behaviors could be referred to as "functionally dependent" rather than addicted. Patients in different categories will clearly require very different clinical approaches.

One obvious approach would be to try to decrease opioid doses to safer levels while attempting or reattempting a more multidimensional treatment approach. However, successfully transitioning these patients from opioid therapy to an alternative therapy—or even significantly lowering the dosage they are receiving—will likely be challenging. Long-term maintenance therapy with opioids induces a complex set of neuroadaptations, often making the opioid necessary for the individual to feel normal or at ease; thus it is difficult to decrease the patient's dosage or to discontinue therapy. Studies have shown that attempts to discontinue metha-

done after long-term maintenance therapy for opioid addiction have generally been unsuccessful. Even after prolonged periods of stability, up to 80% of these individuals return to opioid use after stopping methadone therapy [19]. Patients who are taking methadone for opioid addiction could be said to represent a very different clinical and demographic cohort than most other patients with chronic pain. However, studies of buprenorphine for the treatment of opioid dependence, which have been conducted in cohorts that overlap significantly with the population of chronic pain patients, show the same high tendency for relapse after discontinuation of buprenorphine therapy, even when the drug is tapered over a period of several months [20].

If chemical coping is involved, then decreasing or discontinuing opioid use is likely to be especially difficult, making the utilization of mental health services essential. Distress management and alternative coping skills are necessary for those who have become emotionally as well as physically dependent on opioids. Likewise, access to addiction services is critically important for patients who are at high risk for aberrant use, such as those with current or prior substance abuse problems or those who have demonstrated an inability to use opioids safely. In particular, access to buprenorphine or to a combination of buprenorphine and naloxone will likely improve addiction-related treatment outcomes, provide some analgesia if needed, and reduce addiction-related mortality [21]. In France, widespread use of medication-assisted therapy, primarily buprenorphine treatment, was found to be associated with an 80% decrease in overdose deaths from heroin or cocaine [22].

Ongoing Initiatives

Many medical practitioners, health care systems, regulatory boards, and medical societies are showing a great deal of initiative in responding to this public health challenge. The Federation of State Medical Boards is currently revising its guidelines for chronic pain management to balance access to care with safeguards to avoid misuse. Specialty societies and other organizations are also developing educational resources related to safe opioid prescribing. The American Academy of Family Practice and the American Society of Addiction Medicine have both been awarded grants to support the nationwide availability of free training regarding risk mitigation strategies, and physicians who attend this training can earn Continuing Medical Education credit. In North Carolina, the Governor's Institute on Substance Abuse has taken a lead role in making similar training available within the state. [Editor's note: For more information on the work of the Governor's Institute on Substance Abuse, please see the sidebar by Finch and McEwen on pages 233-234.]

An example of an innovative health systems approach to chronic pain management is the Chronic Pain Initiative of Community Care of North Carolina (CCNC). [Editor's note: Lancaster and colleagues discuss this initiative in more detail on pages 237-241.] Building on the successful com-

munitywide approach taken by Project Lazarus [23], CCNC is using its patient-centered medical homes and systems of care pathways to implement many of the recommendations outlined above. Using clinical training provided through the Governor's Institute, CCNC is working in collaboration with local pain, mental health, and substance abuse practitioners to change the standard of care for chronic pain management among its several thousand prescribers across the state.

Implementing more training in medical schools and residency programs will be essential for long-term change. Chronic pain management will continue to be a major clinical need, as a large cohort of patients are already dependent on these medications. Primary care specialists must continue to provide the majority of chronic pain management, but they will need the help of a broad range of specialists. There are not enough pain management or addiction medicine specialists to meet this need, so clinicians in all areas of medicine need to be informed and involved if the pendulum of care is to be pushed toward the common goal of available, effective, and safe management of chronic pain. **NCMJ**

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