The National Opioid Epidemic and the Risk of Outpatient Opioids in Children

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It is impossible to watch broadcast news or read a newspaper without encountering a story of the “opioid epidemic,” an unfortunate phrase used by the Centers for Disease Control and Prevention (CDC)1 from whom “epidemic” carries an emotive connotation. The national interest in the opioid epidemic began when the New England Journal of Medicine,2 followed by other sources,3–7 documented increasing opioid-related deaths in the United States. With media attention (Fig 1) the topic became politicized, later followed by regulations, statutes, and litigation against the pharmaceutical industry in an attempt to solve the “crisis,” while punishing pharmaceutical manufacturers for causing this epidemic.

Media attention produced many experts, pundits, and politicians who offer simplistic blameworthy origins for the problem (eg, overprescription of opioids, deceptive marketing of opioids, The Joint Commission, and/or an inability of Americans to endure discomfort), as well as simplistic solutions (eg, draconian restriction of prescribing, mandatory use of prescription drug monitoring programs, nonopioid alternatives to opioids, acupuncture, meditation, and/or yoga).

Against this background, Chung et al8 have contributed a publication in this journal, “Outpatient Opioid Prescriptions for Children and Opioid-Related Adverse Events.” In this editorial, we will comment on their findings and put them into what we believe is the proper context. But before we do, there are 2 caveats:

First is that the authors of this editorial are not champions of opioid use, per se. We know that opioids are associated with many untoward side effects and are potentially lethal. But we believe there is a reason why opioids have been used to treat pain since the Sumerians 5000 years ago: no other analgesics equal in potency and effect have been discovered or developed to reduce suffering. We are staunch advocates for the need to provide adequate treatment of pain and suffering after surgeries, burns, physical trauma, and medical illnesses such as sickle cell crisis, cancer, and pancreatitis, to name but a few.

Second is that data used in our national debate about opioids are not accurate. CDC reports “opioid-related deaths,” which are deaths that occur with opioids in the blood, without any other attribution for the cause of death. Although many of these deaths are indeed the result of opioid toxicity, many are the result of suicide, fatal illness in which opioids were used to alleviate suffering, and still more, indeed most, are the result of multiple drug ingestion. For example, when a patient dies at home with alcohol, benzodiazepines, and opioids found on toxicology examination, death will be coded as “opioid-related” by the CDC,9 although the death may have been caused by other substances (the average number of drugs identified in postmortem toxicology is 610). And it is for this reason that CDC officials recently admitted that in the past few years their statistics likely overestimated the prevalence of prescription opioid deaths by 100%.11 In other words, the opioid epidemic
is better called the “polypharmacy overdose epidemic,” and furthermore the annual number of “opioid related” deaths pales in comparison with other public health hazards and causes of deaths in America such as tobacco-related deaths, alcoholic hepatic disease, and even hospital-acquired infections.12–14

Additionally, many in speaking and writing of the opioid epidemic conflate the annual statistics of all drug deaths (~60,000–70,000), all opioid deaths (~30,000–40,000, including both illicit opioids and prescription opioids), and prescription opioid deaths (~15,000), further exaggerating the magnitude of the problem in the public mind. The present problem is therefore much more one of deaths from illicit drugs than from prescription opioids and more about deaths from illicit use of prescriptions than from medical use of prescription opioids. In other words, we have an epidemic of substance use disorder (SUD) that is embedded in a complicated matrix of despair and hopelessness across the United States and correlates closely with socioeconomic factors such as unemployment, poor education, availability of illicit street and diverted prescription opioids,15,16 genetic predisposition to SUD,17,18 and psychiatric morbidity.19 Thus, there is scant evidence to support the existence of an epidemic of deaths due to the appropriate use of prescribed opioids.

Nevertheless, there is much we need to learn about the epidemiology of opioid prescription, use, misuse, and effects in children in the United States. To contribute to this knowledge, Chung et al8 examined Medicaid records of >1 million children and adolescents in Tennessee between 2 and 17 years of age who had no complicating severe medical illness and who were prescribed opioids as outpatients. They then identified those who had an “opioid-related adverse event,” defined as an emergency department visit, hospitalization, or death after an opioid prescription. To confirm the relationship of the opioid prescription to the adverse event, medical records were then obtained on a subset of ~875 cases, which were reviewed by 2 study investigators for confirmation of opioid etiology. Their conclusion is alarming: “One of every 2611 study opioid prescriptions was followed
by an opioid-related emergency department visit, hospitalization, or death.”

But, as in many retrospective studies, there are inherent factors that can lead to false conclusions: investigator bias (given that the investigators have previously published drug toxicity papers) and population bias (having used indigent patients from a rural state, many or most of whom would likely use emergency departments as a primary source of care and thus meet criteria for an opioid-adverse event by merely presenting to an emergency department despite having only a minor opioid side effect).

The data included in this study also coded symptoms of opioid toxicity that are vague or typically not associated with opioid toxicity as opioid adverse events, such as “neuropsychiatric” symptoms (found in 27.5% of opioid toxicity cases). Twenty-three percent of cases of opioid toxicity were caused by unintentional overdose, opioid abuse, or self-harm despite the premise that this was a study of the complications of “appropriate therapeutic use,” suggesting that these cases might have been better off being excluded from the study analysis.

Grouping of “adverse events” also leaves us unable to compare the frequency of common and self-limited side effects (pruritus, nausea, vomiting, constipation) with what are severe or life-threatening events (respiratory depression, hypotension, and/or central nervous system depression). In addition, we are not informed which prescribed opioids were associated with which symptoms of toxicity or of any detail of the few fatalities they reference. Which opioids resulted in fatalities? Were these intentional overdoses, unintentional overdoses, fatalities associated with mixing opioids with other medications and/or alcohol, or the result of SUD? Or, were they tragic outcomes of appropriate use of an analgesic? This is really the question here. Clearly, these data are vital and, in our view, if they were available to the investigators, they should and could have been included.

Nevertheless, we compliment the authors on the magnitude of work required to study such a database and note there are facts that we may derive from their work that are important.

First is that the largest group of opioid prescribers to this Medicaid population were dentists, not physicians. These findings parallel data from a study revealing that in the 15- to 24-year age group, dentists are by far the highest prescribers of opioids.20 This finding suggests the most fruitful avenue for provider education, for example that nonsteroidal anti-inflammatory drugs are usually sufficient for most dental procedures21–23.

The second is that the list of opioids prescribed to outpatients without significant complicating medical conditions included codeine, which is the subject of a black box Food and Drug Administration warning and recommendation not to prescribe. The list also included long-acting opioids (methadone, transdermal fentanyl [Duragesic], sustained-release morphine [MS-Contin] and controlled-release oxycodone [OxyContin]), which have no place in the management of acute pain in opioid naïve pediatric patients.

Although it is reassuring that only 3 deaths were identified among the 1.4 million opioid prescriptions in this 5-year period, the commonality of opioid prescribing in children mandates that objective data about the use, abuse, and risks of opioids in children be collected. Mining large databases, as was done by Chung et al,8 and using comprehensive data from large health maintenance organizations prospectively to highlight the socioeconomic and geographic diversity of various pediatric populations using opioids will allow safer treatment of children in the future.

In conclusion, it is not possible to use the data reported by Chung et al8 to support or refute the prevalence or the severity of opioid adverse effects or the epidemic as it affects children and adolescents. Similarly, the data as presented cannot be considered causal for associating opioid prescribing with severe morbidity, more hospital emergency department visits, and even death for reasons highlighted in this commentary.

If the concern is that opioid prescriptions to children lead to SUD, other work reveals that first exposure to nonmedical use of opioids in adolescents occurs most often from access to family members’ or friends’ prescriptions, not their own.24 In a comprehensive article, Miech et al25 concluded that “In the very lowest risk stratum … legitimate use of prescription opioids before high school completion does not predict opioid misuse after high school.”

Pediatric practitioners must use their best judgment when using opioids with solid indications and should always make good use of nonopioid alternatives. But providing appropriate opioid prescriptions for moderately to severely painful conditions should not be curtailed on the basis of the data reported by Chung et al.8 Too often, consideration of the need to prevent and treat pain can be lost in the national discussion.

**ABBREVIATIONS**

CDC: Centers for Disease Control and Prevention

SUD: substance use disorder
and receives honoraria for lecturing on pain and analgesia. Dr Walco has provided consultation for Pfizer Pharmaceuticals, Collegium Pharmaceuticals, Endo Pharmaceuticals, and Inspirion Pharmaceuticals and receives honoraria for lecturing on pain and analgesia.

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