Pediatric Opioid Prescribing: A Call for Calm

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As a pediatric substance use disorder specialist, it would seem that I should be the last person to call for calm in the middle of an ongoing national opioid problem. However, calmness and a critical view of available data are needed, especially when considering how clinical and policy decisions may affect our young patients. Legislation, prescribing guidelines, and other sweeping recommendations need to be based on relevant, high-quality data.

Regarding the US opioid problem, the primary direct impact is among adult populations, in which there had been clear evidence of opioid overprescribing for chronic nonmalignant pain, and in which the bulk of opioid use disorder (OUD) diagnoses and overdoses occur. In response, many states now require prescription monitoring databases and some states mandate prescribing limits.

In youth, opioids are prescribed less often, with the very young more likely to accidentally ingest an adult's medication and teenagers now more often experiencing overdose involving heroin or synthetic opioids.[1] Prescriptions for adults have certainly been a source for youth opioid nonmedical use (defined here as use of medication that is not prescribed to the individual or use of one's own medication in a way other than prescribed) initiation,[2] and reductions in adult prescriptions have likely contributed to declines in pediatric opioid-related morbidity. Opioid nonmedical use in youth can be a precursor to, but does not usually result in, OUD, and heroin use is increasing as the initial opioid used by those who go on to develop OUD.[3] There are several studies linking pediatric opioid prescribing to risk of future OUD development, but evidence supporting a causal relationship between pediatric opioid prescribing for pain and subsequent OUD development is lacking.

In 2016, to a large extent on the basis of expert consensus, the Centers for Disease Control and Prevention issued opioid-prescribing guidelines for chronic pain in adults.[4] These guidelines are of unknown relevance to children,[5] for whom chronic prescribing is rare compared with adults. In contrast to those examining adult rates, studies examining pediatric opioid prescribing rates have yielded mixed results, from modest to no increases from pre-to post onset of the US opioid crisis that began around the late 1990s.[6,7] Increases in opioid-related pediatric adverse events did occur during this same period,[1,8] but these have yet to be uniquely tied to prescriptions for youth.

With this as background, the study by Chua et al[9] in this issue of *Pediatrics* sheds more recent light on pediatric-specific opioid prescribing. The authors accessed a national pharmacy database that captured >4 million opioid prescriptions dispensed for youth ages 0 to 21 years during 2019. The authors

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focused on several high-risk prescribing behaviors, with "high risk" being defined by the Centers for Disease Control and Prevention prescribing guidelines for adults and some selected pediatric studies.[9] Their efforts in applying meaningful analyses to a complex issue and data set are commendable. Here, I highlight a few important concerns.

Chua et al[9] found that just under one-half of the dispensed prescriptions were associated with at least 1 high-risk prescribing behavior, including >40% exceeding a 3-day supply in opioid-naïve patients. Although a 3-day course of treatment may often be adequate for acute pain in youth, depending on the indication, a longer duration may be both appropriate and necessary. Examples of evolving guidelines for pediatric opioid prescribing focus on anticipating the duration of moderate-to-severe pain and a plan to reassess, rather than a strict number of days.[10] Duration of prescription could reflect high-risk prescribing, but reducing that measure to strict day limits may overemphasize risk, is not established to be pediatric-relevant, and could fuel further legislative and other restrictions on pediatric prescribing that delay or otherwise interfere with effective pediatric pain treatment.

Consistent with other studies, Chua et al[9] found that dentists and surgeons accounted for almost two-thirds of opioid prescriptions. Those disciplines have responded with their own initiatives[11] and initial specialty-specific pediatric opioid guidelines.[12,13] Because they are evolving, such guidelines are not without debate,[14] but they are a great start. A recent survey of pediatric surgeons by Hunsberger et al[15] suggests that the overwhelming majority recommended nonopioid analgesics as a mainstay of pharmacologic therapy, and, when opioids were prescribed, they were predominantly for hydrocodone-acetaminophen products, with other opioids, including codeine, being used far less often. Although respondents endorsed prescribing supplies of ≤7 days at least 90% of the time, there was limited consensus around opioid dosing, reflecting procedure-specific, institutional, and regional practices. In this context, it is unclear how results by Chua et al[9] reflect on surgical practices: Do the 2019 results indicate improvement, worsening, or no change? Do they indicate additional interventions are in fact needed and, if so, how do they inform the type of intervention that is appropriate? This cross-sectional study of 2019 does not tell us the answers to these questions. This is less a criticism of Chua et al[9] and more an overall critique of our approaches so far to measurements and data interpretation of opioid-prescribing practices for children. Collectively, both studies emphasize the need for ongoing interdisciplinary collaboration in the complex determination of pediatric opioid best practices, determination of consistent pediatric and procedure-relevant outcomes measures, and relevant interventions for high-risk prescribing practices.

Another challenge to both pediatric relevance and risk determination is age groupings. Long-standing databases[16] and studies, including Chua et al,[9] use age brackets that contain overlapping developmental periods. Between these periods are distinct prescribing patterns and different risk behaviors. Overlapping these groups can overlook age group differences and make it difficult to make comparisons between studies and across time, including detecting improvements. To illustrate, Chua et al[9] break the data into 2 age groups: 0 to 11 years and 12 to 21 years. This dichotomization overlaps the 0 to 4 years group, which tends to have more overdoses involving adult's medications,[1] with the lower risk 5 to 9 years bracket. Chua et al[9] also overlap the lower risk group of those aged 10 to 14 years with the group of those aged 15 to 19 years, the latter of which exhibits the peak of opioid overdoses in those aged <18 years.[1] With inconsistent age groupings, how can we relate the prescription findings of Chua et al[9] to, for example, toxicity data during a similar period of measure? We need to advocate for consistency and the collection and inclusion of meaningful age grouping moving forward.

This commentary made clear for the surgical context why diagnostic information is critical in understanding dosing variability. Another example is the finding of Chua et al[9] that just below 5% of the individuals aged 12 to 21 years were coprescribed a benzodiazepine with an opioid. That combination may be high risk but may also be appropriate. For example, a patient receives a short-term opioid prescription for acute pain and a benzodiazepine for as-needed use in a seizure indication or for preprocedure anxiolysis. Coingestion is high risk, but only using dispensed prescriptions as the proxy measure may inflate that risk.

Finally, Chua et al[9] point out that data on patient income, race, ethnicity, and prescription indication were not included in their study. In pediatrics, there are increasing efforts to elevate clinician awareness of the history of race as a social construct and its detrimental impact on child well-being.[17] These efforts notwithstanding, there are robust data to indicate that clinicians often perceive white individuals to be more pain sensitive than Black individuals[18] and are more likely to order opioids

for white children for the same painful indications.[19,20] The lack of racial and ethnicity information, combined with lack of clinical indication in the Chua et al[9] study, leaves us unable to determine the presence of disparities, if any. To enhance future efforts at detecting and combating racial and ethnic disparities in opioid prescribing, we need to have consistent inclusion of racial and ethnic information.

In summary, Chua et al[9] make an important contribution to the literature regarding pediatric opioid prescribing. Strengths include the use of a large national database that captured the bulk of outpatient prescriptions and attempts at operationalizing and detecting high-risk prescribing. However, caution should be exercised in interpreting these findings because of the points raised above. Moving forward, interdisciplinary collaboration should continue to develop consensus on pediatric opioid prescribing best practices and defining outcomes and age groups in ways that allow the impact of interventions to be detected.

ABBREVIATION

OUD: opioid use disorder

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