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Taking adolescent prescription opioid use in context: Risk stratification in early mid-life based on medical and non-medical use

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Currently, prescription opioids (POs) are the leading cause of drug overdose deaths in America, and the yearly cost of non-medical PO use in the U.S. is over \$50 billion [3, 7]. Opioid prescribing dramatically increased in the 1990s in response to perceived safety, grave safety concerns regarding alternate analgesics (NSAIDs), and increased marketing to clinicians[5]. Studies have reported rates of addiction between 0.14–0.27% [9]. However, high participant attrition, unclear participant recruitment methods, and concomitant use of adjuvant treatments precludes firm conclusions regarding the risk of addiction in the context of open-label case series, and open-label case series after the completion of short-term RCTs examining chronic opioid therapy for a duration of at least 6 months [9]. At present, PO use is fueling the drug overdose epidemic through ED admissions, addiction, diversion, and death.

The iatrogenic pathway to opioid misuse and addiction should not be overlooked. Currently, the rates of addiction following legitimate PO exposure may be as high as 10% [14]. 30–80% of PO addicts report that they had been prescribed opioids for pain by a provider and that they later went on to abuse the opioids that were prescribed [4, 11, 12]. Also, legitimate opioid prescribing is a key source of drug diversion. The main source of opioid diversion in the U.S. is provider overprescribing for acute pain [13]. The benefits of opioid prescribing need to be carefully weighed against the potential harms of PO addiction and diversion.

Recently, opioid prescribing has received increased scrutiny. As the estimates of misuse and abuse in patients with chronic non-cancer pain are as high as 50%, universal risk assessment and stratification is essential [1]. A personal or family history of substance abuse, substance use disorders (SUDs), euphoria associated with use, mental health diagnoses, male sex and younger age are risks factors for opioid misuse and abuse [1, 2, 5, 6]. Although a number of screening tools have been developed to aid in risk-stratification, research is needed to determine their utility in predicting aberrant behaviors in diverse populations. Further refinement of these tools should be driven by identification of significant predictors of PO misuse, addiction, and diversion.

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Provider fears in response to potential opioid prescribing risks may create a barrier to access for patients with either acute or chronic pain. Concerns about contributing to addiction, diversion, and overdose deaths may cause clinicians to avoid opioid prescribing all together in favor of non-opioid analgesics. Furthermore, the possibility of medical or DEA license revocation in the setting of medical malpractice/negligence, may result in overly conservative opioid prescribing[15]. Also, the threat of criminal prosecution in the setting of alleged reckless prescribing is likely to drive down opioid prescribing. Unfortunately, patients with conditions warranting legitimate PO use may experience impaired access to medications and suboptimal pain relief.

McCabe et al. conducted a study which helps to address these diverse aspects of opioid prescribing [8] They characterized risk of nonmedical use of PO (NMUPO) and SUD symptoms at age 35 based on the context of adolescent PO exposure. PO exposure during adolescence can be used to augment current screening efforts for risk-stratification when initiating opioid therapy in older adults. Also, the study describes the longitudinal follow-up of patients legitimately prescribed opioids during adolescence, and the influence of this exposure on subsequent development of NMUPO and SUD symptoms. These results of this study have important implications for opioid prescribing to adolescents.

The authors present a clear and concise analysis of a prospective cohort study of a nationally representative sample of subjects followed from adolescence to age 35. It is notable that any type of PO exposure during adolescence was significantly associated with NMUPO use at age 35. However, the risk was highest in those with concurrent medical and NMUPO. As NMUPO is significantly and independently associated with pain [10], future research is needed to determine whether uncontrolled pain leads patients legitimately prescribed opioids to nonmedical use of these drugs. One of the study limitations is the sampling of participants over 2 decades. As NMUPOs began to increase in the mid-1990s, high school seniors in earlier cohorts may not be representative of current adolescents, and the effect of adolescent NMUPOs may be underestimated. Similarly, retention was highest amongst females and whites. The context of adolescent exposure to POs may vary based on gender and race/ethnicity differences. Also, as the sample was followed only to age 35, more long-term follow up data are needed to determine how the context of adolescent opioid exposure affects an aging population developing chronic illness and pain conditions, and undergoing surgery, with repeated PO exposure.

The authors do present some reassuring findings. Legitimate PO use during adolescence was not associated with SUD symptoms at age 35. However, those with any NMUPO during adolescence were more likely to have SUD symptoms at age 35. Perhaps, efforts to curb NMUPO amongst adolescents through public education may prevent the future development of PO addiction, diversion, and overdose deaths. This sentiment is reflected in the National Pain Strategy's objective to "develop and implement a national educational campaign encouraging safe medication use, especially opioid use, among patients with pain." With additional resources, screening and brief intervention programs amongst adolescents reporting NMUPO could also be a more targeted strategy. An important caveat was the high prevalence of polysubstance abuse. As polypharmacy of multiple sedatives can promote respiratory depression and death, preventative measures may be more effective in the context

of polysubstance abuse. In addition, polysubstance abuse may be an important confounder of the relationship between adolescent NMUPO and subsequent development of SUDs. This is supported by the author's findings that adolescent NMUPO was more likely to be associated with alcohol rather than a PO use disorder at age 35.

Prior to initiating PO therapy, it is essential for clinicians to weigh the risks and benefits of treatment. McCabe et al. provide valuable insight into the prevalence of legitimate and NMUPO in adolescence [8]. Even more concerning is the high prevalence of polysubstance use amongst adolescents reporting NMUPO, which should be addressed in both public education and more targeted interventions. In addition, the study highlights the risk associated with adolescent PO exposure on the subsequent development of NMUPO or SUD symptoms at age 35. Future longitudinal research is needed to extend the study findings to older and elderly adults, who are more likely to be repeatedly exposed to POs to treat various acute and chronic pain conditions.

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