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PERSPECTIVE

Medication-assisted treatment for youth with opioid use disorder: Current dilemmas and remaining questions

Derek C. Chang[a,b], Jan Klimas [a,c], Evan Wood[a,d], and Nadia Fairbairn[a,d]

[a]British Columbia Centre on Substance Use, British Columbia Centre for Excellence in HIV/AIDS, St. Paul's Hospital, Vancouver, BC, Canada; [b]Department of Family Medicine, University of British Columbia, St. Paul's Hospital, Vancouver, BC, Canada; [c]School of Medicine, University College Dublin, Belfied, Dublin, Ireland; [d]Department of Medicine, University of British Columbia, St. Paul's Hospital, Vancouver, BC, Canada

ABSTRACT

The prevalence of risky opioid use, opioid use disorder, and related harms continue to rise among youth (adolescents and young adults age 15–25) in North America. With an increasing number of opioid overdoses, there remain significant barriers to care for youth with opioid use disorder, and there is an urgent need to expand evidence-based care for treatment of opioid use disorder among this population. Based on the extensive literature on treatment of opioid use disorder among adults, medicated-assisted treatment is likely to be an important or even essential component of treatment of opioid use disorder for most youth. In this article, we outline the current dilemmas and questions regarding the use of medication-assisted treatment among youth with opioid use disorder and propose some potential solutions based on the current evidence.

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The prevalence of risky opioid use, opioid use disorder (OUD), and related harms continue to rise among youth (adolescents and young adults age 15–25) in North America (1,2). According to the Centers for Disease Control and Prevention, heroin use has more than doubled among 18–25-year-olds in the past decade (1). Overdose rates in this population are also on the rise: 33 states had fatal drug overdose rates above 6 per 100,000 youth by 2011–2013, higher than previous rates (less than 4 per 100,000) among youth in the same states at the turn of the 21st century (2). These growing harms, combined with evidence indicating that onset of substance use disorder is mainly concentrated during adolescence and young adulthood (3), point to an urgent need to expand and scale-up early access to evidence-based treatments for OUD in youth. In addition, neurodevelopment of brain regions associated with motivation and impulsivity, which primarily occurs during adolescence and young adulthood (3), suggests that treatment engagement and prognosis, and strategies to optimize treatment of OUD, may differ in youth compared with their adult counterparts. Strategies that reduce barriers to treatment commonly experienced by youth and address clinical care dilemmas when treating youth with OUD are urgently needed.

A number of agencies have supported the use of pharmacologic therapies such as buprenorphine/naloxone and methadone opioid agonist therapies (OAT) for youth, including the recent policy statement of the American Academy of Pediatrics (4). Though the efficacy of methadone and buprenorphine/naloxone has been well demonstrated in adult populations (5), there are few studies examining the efficacy of OAT among youth. The extant literature has primarily examined the feasibility and efficacy of buprenorphine/naloxone among youth, including a recent randomized controlled trial which found that longer duration (i.e., 56 days) of buprenorphine/naloxone was more effective in preventing relapse among youth compared with a shorter duration (i.e., 28 days) of therapy (6). In addition to improving treatment outcomes, buprenorphine/naloxone has also been found to be a cost-effective treatment for youth with OUD (7). From youth's perspective, buprenorphine/naloxone was perceived to be more effective than methadone for reducing cravings and eliminating withdrawal symptoms, and it was also perceived to be a less-stigmatizing medication than methadone (8). Based on the strong evidence in the adult population and available evidence to date among youth, combined with its superior safety profile compared to methadone, first-line OAT for youth should be buprenorphine/naloxone, with methadone as an

CONTACT Nadia Fairbairn nfairbairn@cfenet.ubc.ca Department of Medicine, University of British Columbia, St. Paul's Hospital, 608-1081 Burrard Street, Vancouver, BC V6Z 1Y6, Canada.

alternative treatment option when buprenorphine/naloxone cannot be used, such as with challenging inductions or ongoing cravings on maximal doses of buprenorphine/naloxone (9,10).

While prescribing OAT to youth, there is still inconsistency regarding the minimal age requirement to prescribe OAT. For instance, buprenorphine/naloxone is currently approved for OUD at age 16 in the United States and at age 18 in Canada (11,12). While methadone can be prescribed to youth under the age of 18, the United States Code of Federal Regulations requires documentation that the patient has failed two previous drug-free or withdrawal management attempts and written consent from a parent or guardian (13). This policy warrants re-evaluation, given that overdose risk is increased with withdrawal management alone due to reduced tolerance to opioids in the event of relapse (10). In addition, only 2.4% of adolescents in treatment for heroin addiction received medication-assisted treatment, as compared with 26.3% of adults (14). This underscores the urgent need to improve medication-assisted treatment access for youth. Though further safety data regarding use of OAT among youth are warranted, due to the lethality and multiple harms associated with OUD, the benefits of OAT are likely to be greater than risks associated with the treatment.

Another critical treatment dilemma in caring for youth with OUD is duration of treatment and strategies for optimizing success of OAT tapers. While the question regarding tapers still requires further exploration among adults, it is particularly critical for youth to determine the duration of OAT and how to minimize relapse rates as many youth will have had shorter periods of exposure to opioids compared with the adult population (15). Studies to date have shown that longer tapers are more effective to reduce opioid use and prevent relapse (15,16), with the aforementioned randomized controlled trial by Marsch et al. (2016) demonstrating that longer tapers (56 days) are more efficacious than shorter tapers (28 days) for relapse prevention and treatment retention (6). For this reason, our provincial guidelines in British Columbia, Canada, recommend that tapers for adults, if undertaken, occur over a minimum 52 weeks duration and with close monitoring during and after the taper given overdose risk is increased (10).

In addition, studies to evaluate the effectiveness of the opioid antagonist medication naltrexone for treatment of OUD in youth are needed as naltrexone may be preferred over OAT by some patients and their families (17). Oral naltrexone is known to be associated with low compliance rates and increased risk for relapse and fatal overdose due to loss of tolerance to opioids (18); thus, we do not recommend oral naltrexone. One study evaluating extended-release injectable naltrexone demonstrated feasibility in youth (17), and this treatment may have the potential to prevent overdose in the event of relapse (18), in particular for youth who have tapered off OAT. More studies are needed to compare the effectiveness of OAT to extended-release injectable or implantable naltrexone in youth in order to help guide clinicians on selection of treatment for OUD in this population.

Psychosocial interventions are common for treating OUD among youth, consisting predominantly of short-term detoxification with subsequent referral to individual or group therapy in residential or outpatient settings (16). However, there is a paucity of research on the efficacy of psychosocial approaches among youth. Psychosocial intervention alone has been associated with high rates of treatment dropout among youth (19). A Cochrane systematic review by Minozzi et al. (2014), which included only two trials comparing OAT alone or in combination with psychosocial interventions compared to no intervention, found that OAT seems more efficacious in retaining youth in treatment (20). However, it should be noted that retention on OAT remains a challenge. For example, one study found that only 56% of youth aged 18–25 years were retained on buprenorphine at 6 months, compared with a 78% retention rate among older adults (21). Retention on extended-release naltrexone for OUD in adults is even lower, estimated around 50% at 6 months in adults, and may be even lower among youth (22). The systemic review also indicated a need for more trials involving youth, in particular comparing OAT with psychosocial treatments alone (20); however, it is important to consider the safety of psychosocial treatment alone and if it would be ethically acceptable to design a study with an arm of psychosocial treatment alone due to the aforementioned high risk of treatment dropout and relapse. Thus, we do not necessarily think more studies on psychosocial treatment alone are warranted.

Drawing on findings from the adult population, the Prescription Opioid Addiction Treatment Study (POATS) demonstrated that tapering off buprenorphine/naloxone OAT, even after 12 weeks of buprenorphine/naloxone treatment, was associated with a 90% relapse rate following buprenorphine-naloxone taper, regardless of receipt of ongoing counseling in addition to OAT (23). Given the adult literature, we argue that treatment of OUD with OAT taper followed by psychosocial intervention alone is not recommended, and perhaps even dangerous, given the risk of overdose and the protective effect of buprenorphine/naloxone against it (10). The use of psychosocial interventions may provide some benefit for patients maintained on OAT,

with contingency management offered in combination with buprenorphine/naloxone treatment having the strongest evidence base among adults (24). Further studies should be conducted in youth examining the efficacy of psychosocial interventions used in combination with OAT, and in particular contingency management with buprenorphine/naloxone given findings in the adult population.

Based on the above, we need more research to better understand optimal treatment approaches for OUD in youth. Based on the current evidence, buprenorphine/naloxone appears to be a safe and efficacious option for youth and we propose this should be first-line treatment for OUD. More studies comparing OAT and extended-release naltrexone are needed in this population. When treatment is initiated, longer duration (>52 weeks) of OAT is recommended. Decision to taper should be governed by the principle "when in doubt, do not taper" while taking into account the potential risks of relapse and overdose as well as access to chronic relapse prevention care; close monitoring is essential during and after the taper completion. We suggest psychosocial interventions be routinely offered in combination with OAT. Lastly, given the efficacy of OAT, we recommend these medications be provided based on the risk and benefit assessment of each case, regardless of age.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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ORCID

Jan Klimas http://orcid.org/0000-0002-5179-0052

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