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**OPIOID AGONIST THERAPY FOR YOUTH WITH OPIOID USE DISORDER:  
CURRENT DILEMMAS AND REMAINING QUESTIONS**

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### **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 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. In this article, we outline the current dilemmas and questions regarding the use of opioid agonist therapy among youth with opioid use disorder and propose some answers based on the current evidence.

**Key words: Youth — adolescent — opioid agonist therapy — opioid use disorder — buprenorphine — methadone**

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 21<sup>st</sup> century [2]. These growing harms, combined with evidence indicating that experimentation with substances and onset of substance use disorder is mainly concentrated during adolescence and young adulthood, when neurodevelopment in brain regions associated with motivation, impulsivity and addiction takes place, youth represent a critical period for intervention [3]. Despite these factors, there remain significant barriers to care for OUD among youth and there is an urgent need to expand evidence-based care for treatment of OUD among youth.

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 [4]. However, there is a paucity of research on the efficacy of psychosocial approaches among youth. A Cochrane systematic review by Mengzi et al. (2014), did not identify any trials comparing opioid agonist therapies (OAT) with psychosocial treatments alone in youth [5] and, to our knowledge, there have been no subsequent studies conducted. A previous study by Weiss et al. (2011) conducted in adults demonstrated a 90% treatment failure rate

following buprenorphine-naloxone taper, with no significant difference between groups treated with buprenorphine/naloxone in combination with counseling and buprenorphine/naloxone basic medical management [6]. Thus, the benefits of psychosocial intervention alone remain debatable. It is also worth noting that among youth, psychosocial intervention alone has been associated with high rates of treatment dropout [7]. While the duration of exposure to opioids among youth will often be shorter compared to the adult population at the time of seeking treatment [8], which may convey increased likelihood of successful treatment with psychosocial interventions alone, evidence to date suggests that psychosocial interventions should be routinely offered in combination with OAT.

A number of agencies have recently supported the use of OAT among youth, including the policy statement of the American Academy of Pediatrics [9]. Though the efficacy of OAT including methadone and buprenorphine/naloxone has been well demonstrated in adult populations [10], there are few studies examining the efficacy of OAT among youth. Despite limited studies of OAT in the youth population, buprenorphine/naloxone has been studied the most, including a recent randomized controlled trial (RCT) which found that longer duration (56 days) of buprenorphine/naloxone was more effective in preventing relapse among youth compared with a shorter duration (28 days) [11]. In addition to improving treatment outcomes, buprenorphine/naloxone has also been found to be cost-effective in treating youth with OUD [12]. From youth's perspective, buprenorphine/naloxone has been found 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 [13]. 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 alternative treatment option when buprenorphine/naloxone cannot be used such as with challenging inductions or ongoing cravings despite the maximum dose of buprenorphine/naloxone [14,15].

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 [16,17]. Though further safety data regarding use of OAT among youth is warranted, since adolescence is a constantly evolving state of maturation, it is likely most important to consider the duration and the severity of OUD, rather than using fixed age requirements, to match severity of OUD with intensity of treatment and clinical decision-making regarding use of OAT in this population.

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 [8]. Studies to date have shown that longer tapers are more effective than short-term tapers to reduce opioid use and prevent relapse [4,18], with the

aforementioned randomized controlled trial by Marsch et al. (2016) demonstrating that longer tapers (56 days) are more efficacious than shorter taper (28 days) for relapse prevention and treatment retention [11]. For this reason, our provincial guidelines in British Columbia, Canada, recommend tapers if undertaken occur slowly, over minimum 52 weeks duration in adults [15].

Based on the above, we need more research to answer those questions and to better understand the optimal approaches for this population. Based on the current evidence, we suggest psychosocial interventions should be routinely offered in combination with OAT. Furthermore, buprenorphine/naloxone appears as a safe and efficacious option for youth. We propose buprenorphine/naloxone be the first-line pharmacotherapy for OUD. We recommend slow tapers (>52 weeks) over short tapers after stabilization has occurred on OAT. Lastly, given the efficacy of OAT, we recommend these medications be provided at any age if the severity of OUD warrants initiation of pharmacotherapy.



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