

Comment on: Kleinman RA, Larney S, Sule NO, Ma C, Szatmari P, Kurdyak P. Comparative Effectiveness of Buprenorphine-Naloxone and Methadone for Opioid Overdose Among Youths. JAMA Pediatr. 2026 May 1;180(5):577-579. doi: 10.1001/jamapediatrics.2026.0041. PMID: 41801220; PMCID: PMC12973210.

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Reply to Kleinman et al: Buprenorphine and Methadone for Opioid Overdose Among Youths

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We commend Kleinman et al. for their retrospective study comparing methadone and buprenorphine naloxone for reducing opioid overdoses among Ontario youths aged 15 to 24 with opioid use disorder (OUD). [1] Over 1 year, there was a 16% reduced hazard of opioid overdose among buprenorphine naloxone initiators, although the CIs included the possibility of no association. Notably, eight youths died during methadone treatment compared with none during buprenorphine naloxone treatment. Against this backdrop, several issues warrant attention.

An OUD indication for buprenorphine in adolescents (12–18 years) is urgently needed. Despite statements to the contrary, buprenorphine is not indicated for treating OUD in adolescents. For example, the ASAM 2020 guideline states “Buprenorphine has been approved by the FDA for the treatment of patients aged 16 years and older,” a misstatement that has propagated through derivative guidance and secondary sources. [2]

In this study, youths ≤ 18 years represented only 2.7% of the cohort, indicating persistent hesitancy to prescribe medications for OUD (MOUD) to adolescents. National data reflect the same pattern: buprenorphine treatment rose more than threefold among adults over 55 yet declined among youth under 18, even as adolescent overdose deaths surged. [3] Similarly, Welsh, analyzing TEDS data, found MOUD planned at admission for 93% of adults ≥ 25 , 56% of those 18–24, and only 2% of youth 12–17. [4] These gradients highlight a structural reluctance to offer evidence based treatment to adolescents despite escalating need.

Kleinman et al. also note the importance of evaluating extended release (ER) buprenorphine. Transmucosal buprenorphine requires safeguards, including daily observed dosing, slow progression to carries, and pharmacy monitoring to limit diversion, while methadone demands even stricter supervision. In contrast, ER buprenorphine eliminates diversion risk, improves adherence, and reduces pharmacy burden, making it a potentially safer and more practical option for adolescents.

Two ER buprenorphine formulations are available in the U.S. and one in Canada, with differing dosing flexibility. One product provides monthly dosing in 100 mg and 300 mg strengths; another offers weekly (8, 16, 24, and 32 mg) and monthly dosing (64, 96, and 128 mg). Importantly, a large NIH supported trial (CTN 0158) proposes to evaluate ER buprenorphine versus daily transmucosal buprenorphine in youths aged 14–21. The absence of a placebo or detoxification arm in the study reflects growing consensus that withholding MOUD from adolescents is no longer ethically defensible. [5]

Kleinman et al. underscore the need to expand adolescent access to buprenorphine and to rigorously evaluate ER buprenorphine in adolescents.

References:

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