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Review article

A Scoping Review of Evidence-Based Interventions and Health-Related Services for Youth Who Use Nonmedical Opioids in Canada and the United States

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A B S T R A C T

Purpose: This scoping review synthesizes the characteristics and outcomes of recent evidence-based treatments and services for youth with nonmedical opioid use/opioid use disorder in the context of the ongoing opioid crisis in Canada and the United States.
Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - Extension for Scoping Reviews guidelines, empirical health databases were searched for literature describing treatments or health-related services for nonmedical opioid use/opioid use disorder among youth (ages 12–25). Two independent reviewers conducted study screening, selection, and data extraction. A deductive content analysis further synthesized the interventions' characteristics following the Consolidated Framework for Implementation Research and an inductive content analysis synthesized the interventions' efficacy/effectiveness outcomes.
Results: Twenty-five articles met inclusion from 2,761 screened; 88% described opioid agonist treatment (alone or in combination with nonpharmacological treatment). Following the Consolidated Framework for Implementation Research, commonly identified adaptable characteristics

IMPLICATIONS AND CONTRIBUTION

This scoping review identifies and synthesizes key characteristics and outcomes of pharmacological and nonpharmacological interventions for nonmedical opioid use/opioid use disorder among youth in Canada and the United States. At the pinnacle of the ongoing opioid crisis, this research

Conflicts of interest: Author's Hui, Gunn, Doug Wright, and Marshall received consulting fees from Changemark Research + Evaluation for their methodological expertise and work performed on the protocol registration, search strategy, screening, and extraction. Author Marshall also received consulting fees for research done for the Canadian Centre on Substance Use and Addiction and is a current employee of the Government of Alberta. The first draft of the manuscript was written by author K. Marchand, and no honorarium or payment was given to anyone to produce the manuscript. The remaining authors have no potential conflicts of interest.

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included treatment decision-making processes, integrated health and social services, and treatment settings. Efficacy/effectiveness outcomes most frequently included substance use and treatment engagement.

Discussion: This study informs future development, implementation, and evaluation of practices and policies that could be tailored to improve the quality of opioid agonist treatment for youth at risk of significant harms from nonmedical opioid use.

is urgently needed to inform youth-centered practices and policies to treatment and services.

Widespread harms related to nonmedical opioid use and opioid use disorder (OUD) are leading public health issues in Canada and the United States [1,2]. Adolescents and young adults (collectively referred to as "youth" hereafter, typically aged 12–25) [3,4] are a particularly important population to support. Evidence in both Canada and the United States indicates that rates of opioid-related emergency department visits, hospitalizations, unintentional opioid-related poisonings, and OUD diagnoses have dramatically increased among youth in the last 2 decades [5–9], with years of life lost now surpassing that of cancer [10].

Accordingly, it remains crucial that youth have timely access to evidence-based interventions to reduce the escalating harms of nonmedical opioid use/OUD. Current clinical guidance in both Canada [11] and the United States [12,13] have focused on youth meeting the criteria for moderate/severe OUD. These guidelines recommend delivery of opioid agonist treatment (OAT) with full opioid agonists (e.g., methadone), partial agonists (i.e., buprenorphine), and antagonists (i.e., naltrexone, in the United States only) [11,13]. It is also recommended that youth be offered comprehensive health and psychosocial supports, such as harm reduction, referrals for health (e.g., infections related to injecting practices) and social (e.g., family involvement, housing) needs, and nonpharmacological (e.g., counseling) interventions [11,13]. However, these guidelines acknowledge that research on OAT among youth is still ongoing, and the efficacy of nonpharmacological interventions and comprehensive supports (alone and in combination with OAT) remains to be determined [11,14–16].

There is also mounting evidence that youth are less likely to access OAT compared to adults and do not receive the same quality of OAT nor experience the same improved outcomes [7,9,17–22]. There are several possible mechanisms that may explain these disparities. Research suggests that youths' OAT goals may not be compatible with how OAT is delivered and how effectiveness is measured [23–25]. For example, recent qualitative research with street entrenched youth has revealed that some youth view OAT as a short-term solution to manage opioid withdrawal and cravings rather than a long-term treatment option as recommended for adults with OUD [23,25]. Research also indicates that structural and systems-level barriers, such as substance-related stigma, adult-oriented settings, restrictive titration and dosage protocols, daily witnessed dosing, and rural/remote geographic location, hinder youth from engaging in OAT [25–27]. These barriers may be even greater among subgroups of equity-deserving youth. For instance, a recent systematic review reported that Black, Hispanic, and/or Latino youth and youth with lower socio-economic status may be less likely to access OAT relative to non-Black, non-Hispanic, and/or non-Latino youth [20].

Thus, there is an urgent need to develop and implement OAT service delivery and measurement frameworks that are centered on the needs and preferences of youth with nonmedical opioid use/OUD. We conducted a scoping review to inform this framework by identifying and summarizing the breadth of evidence-based intervention(s) that aim to improve the health-related outcomes of youth with nonmedical opioid use/OUD in Canada and the United States. Specifically, this scoping review was guided by the following research questions:

(1) What treatment interventions and health-related services have been investigated in empirical literature among youth with nonmedical opioid use/OUD in Canada and the United States?
(2) What are the characteristics of those evidence-based interventions?
(3) What health-related outcomes have been described or selected to measure intervention efficacy/effectiveness?

Prior reviews have been published on OAT effectiveness [28–31] and OAT access and retention [20,21] among youth. However, these reviews did not include the full range of interventions for nonmedical opioid use/OUD (e.g., harm reduction, OAT, psychosocial services) or synthesize the characteristics of the interventions (e.g., settings, provider types) and health-related outcomes measured. Additionally, our scoping review uniquely applied the Consolidated Framework for Implementation Research (CFIR) [32,33], a meta-theoretical framework that guides the implementation process and outcomes of evidence-based practices and interventions, including those for substance use [33,34]. Therefore, this scoping review presents an original synthesis of the full range of recent evidence-based interventions for youth using nonmedical opioids/OUD that can inform the characteristics of youth-centered OAT frameworks and their future implementation.

Methods

Study design

Our review protocol followed the Arksey and O'Malley framework [35] and the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses - Extension for Scoping Reviews [36]. The protocol was registered with the Open Science Framework Generalized Systematic Review Registry before the review was completed [37].

Search strategy

The search strategy was developed as a broad framing of the population, intervention, comparator, and outcomes (see below).

Search terms were developed in English by a medical librarian (author M.D.W.) using subject headings, related terms, and keywords. Boolean logic and operators (i.e., "and," "or," "not") were used to combine and refine search terms and concepts. The search was conducted in five electronic health and social science databases: 1) Medline, 2) Embase and 3) Cochrane Central Register of Controlled Trials, which were searched via Ovid, and 4) American Psychological Association PsycINFO and 5) Cumulative Index to Nursing and Allied Health Literature databases, which were searched via EBSCOhost. Before finalization, the search strategy was pilot tested by two reviewers. All searches were conducted on July 19, 2023, for entries published in English between January 1, 2015 and July 18, 2023 (Appendix A Search Strategy). This date range was selected to align with recent shifts in the unregulated drug market to fentanyl-contaminated opioids [38–40], significant increases in morbidity and mortality among youth [5–7], and emerging harm reduction and public health interventions and calls to action for the opioid-related drug poisoning emergency [41–44].

Selection criteria

Given our interest in evidence-based interventions, we included primary empirical studies with original peer-reviewed data, including clinical trials (randomized or nonrandomized), observational studies (e.g., cohort, case-control studies), qualitative studies, and case series or case reports. Prior empirical reviews (e.g., systematic reviews) that met eligibility criteria besides the study design were screened for potentially relevant articles, which were then included. Gray literature (clinical guidelines, reports) was excluded. The following criteria were used to determine eligibility:

Population

- Included youth ages 12–25 years and/or reported stratified data for youth in this age range.
- Included youth with nonmedical opioid use/OUD, as determined by over 50% of the sample having self-reported or validated use of nonmedical opioids or having a formal diagnosis of OUD (based on the Diagnostic and Statistical Manual (version III or newer) or International Classification of Diseases (version seven or newer) or being enrolled in a substance use treatment for nonmedical opioid use/OUD.
- Studies with mixed populations that included youth who used substances other than opioids (e.g., stimulants) were considered for inclusion if they reported relevant data separately for youth with nonmedical opioid use/OUD.

Intervention

- Delivered or investigated an intervention or health-related service, including any harm reduction (e.g., supervised consumption sites, drug checking), pharmacological (i.e., OAT), nonpharmacological (e.g., counseling, peer support, family-based interventions), or a combination of approaches.
- Delivered or investigated tailored interventions for equity-deserving youth (e.g., racialized youth, 2SLGBTQIA + youth, immigrant, or refugee populations).
- Delivered or investigated interventions in inpatient (e.g., hospitals, residential treatment centers), outpatient (e.g., emergency departments, primary care, outreach), and virtual service delivery settings.
- School- and community-based prevention and psychoeducational programs that were not specifically tailored for youth actively engaged in nonmedical opioid use were excluded.

Comparator

- Studies with or without a comparison group were eligible for inclusion.

Outcome(s)

- Aligning with prior reviews [15,21,28,30,31], studies on youth-reported preferences and outcomes of interventions for nonmedical opioid use/OUD [23,25], and recent international guidance on patient-centered OAT outcomes monitoring [45], studies were considered if they reported at least one health-related efficacy/effectiveness outcome, such as treatment engagement (e.g., retention, adherence), substance use (e.g., frequency of substance use, craving/withdrawal), and health (e.g., mental health, health-related quality of life).
- Qualitative studies were considered if they described a youth-reported health-related outcome or experience in relation to an intervention, as defined above.

Screening and study selection

After reaching an interrater reliability coefficient of $\geq$0.80, two independent reviewers (authors D.H. and H.G.) screened deduplicated titles and abstracts and selected relevant full-text publications. They also searched the reference lists of reviews that met eligibility criteria besides the study design. Full-text publications were retrieved if both reviewers considered it to be potentially relevant. Final inclusion required both reviewers to agree on eligibility. Conflicts between reviewers were discussed at the title/abstract and full-text review stages and were resolved via discussion or by a third reviewer (author T.M.) when consensus between the two reviewers could not be reached. Study selection was facilitated using Endnote (deduplication) and Covidence (screening).

Data extraction and analysis

Data were extracted into templates prepared by the study team, focusing on study characteristics, methodology, population, intervention, comparator, and outcomes. From these extracts, tabular and graphical summaries were used to describe the included studies (Appendices B and C).

For research questions two and three, a content analysis was performed for a more in-depth synthesis of the interventions' characteristics and outcomes [46]. This approach was deemed beneficial to distill similarities and differences across the breadth of original study designs. The content analysis was conducted in NVivo (Luminervo, Denver, CO) [47] and led by author K.M. upon regular debriefs with the analysis team (authors R.T. and S.B.). These authors have extensive experience with qualitative data analysis [24,48,49], including content analysis and qualitative syntheses [50]. For research question two, a deductive coding scheme was developed using the 2009 CFIR, which includes five

major domains: (1) Intervention Characteristics (e.g., adaptability); (2) Outer Setting (e.g., patient needs and resources); (3) Inner Setting (e.g., readiness for implementation); (4) Individuals Involved (e.g., knowledge and beliefs about the intervention); and (5) Implementation Process (e.g., executing the intervention) [32,33]. The CFIR's Inner and Outer Setting domains and Adaptable Characteristics construct were particularly relevant to the study's aims of synthesizing characteristics (e.g., adaptable elements, settings, provider characteristics) of the interventions that could be adapted to inform the development of youth-centered OAT service delivery frameworks. Therefore, the coding scheme focused on a subset of constructs from the Intervention Characteristics, Inner and Outer Setting, and Characteristics of Individuals domains. Upon careful review and discussion with the analysis team, author K.M. entered the selected 2009 CFIR domains, constructs, and their definitions to the coding scheme and NVivo. Content from the original studies was coded using this coding scheme and open codes were used to capture content that did not fit the predetermined coding scheme. For research question three, inductive and open codes were used to capture the primary and secondary health-related outcomes measured or described in the studies. After all studies were coded, the open codes were synthesized by the analysis team to identify and define new categories.

Given the noted age-related disparities in intervention access and outcomes for nonmedical opioid use/OUD, a sensitivity analysis was conducted for research question 1–3 to explore findings by adolescent, young adult and mixed age subgroups. These results are summarized in the results section and further detailed in Appendix D.

Results

Overview of included studies

The search yielded 4,368 articles from the database search and 13 articles from searching citations (Figure 1). Initial screening was performed on 2,761 deduplicated records, and 100 records underwent full-text screening (87 from the database search and 13 from citation search). A final set of 25 articles was included.

Table 1 presents descriptive characteristics of the included studies (n = 25). A high proportion of the studies were published between 2020 and 2023 (64%), in the United States (68%), and included both adolescent and young adult samples (44%; age 12–19 and 20–24 years of age, respectively), and samples using opioids only (60%). Most of the studies investigated at least one pharmacological intervention (i.e., studies focused on OAT medications; 48%) or a combination of pharmacological and nonpharmacological interventions (e.g., studies focused on behavioral, psychological, psychosocial treatments; 40%). Three studies (12%) investigated a nonpharmacological intervention alone. The proportion of studies investigating each intervention type was similar across study samples; for instance, 80% of

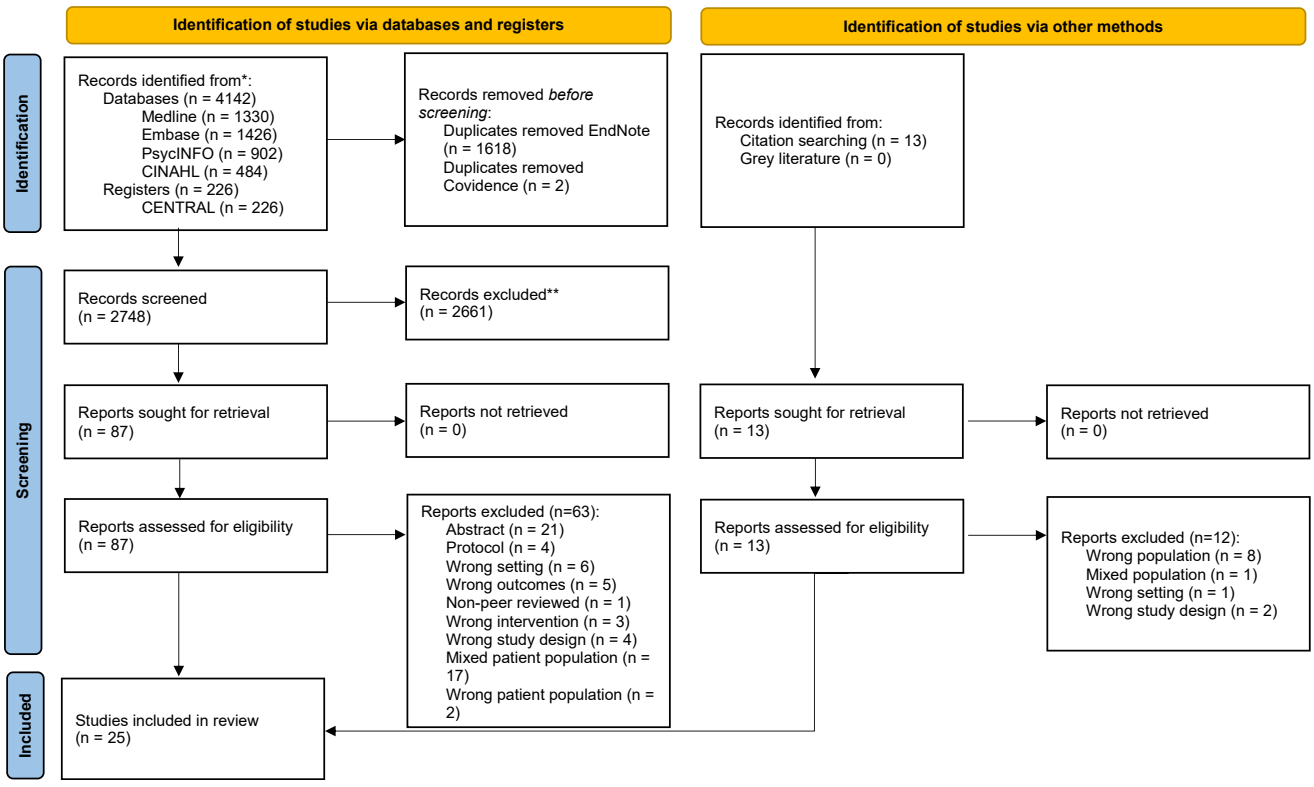

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram for searches in databases, registers, and other sources. Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021; 372:n71. https://doi.org/10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org.

Table 1
Overview of studies included in the scoping review (n = 25)

	Overall
	N = 25
	N (%)
Publication year[a]	
2015-2019	9 (36)
2020-2023	16 (64)
Geographic location	
Canada	8 (32)
United States	17 (68)
Study design	
Controlled trial	7 (28)
Observational study[b]	9 (36)
Case series/case report	5 (20)
Qualitative study	4 (16)
Youth sample[c]	
Adolescents	5 (20)
Young adults	4 (16)
Adolescents and young adults	11 (44)
Youth and adults	5 (20)
Target substance type	
Opioids only	15 (60)
Opioids and other substance(s)	10 (40)
Intervention type[d]	
Pharmacological	12 (48)
Nonpharmacological	3 (12)
Combined	10 (40)

[a] 2020 marks the period following the release of two important United States (2020 publication year) [13] and Canada (2018 publication year) [11] clinical practice guidelines on opioid agonist treatment for youth.
[b] Includes eight cohort studies and one cross-sectional study.
[c] This period typically includes adolescents and young adults between the ages of 12–25 years [3,4], spanning the periods of middle- and late-adolescence and early adulthood. Accordingly, adolescents were aged 12–19 and young adults were aged 20–25.
[d] Includes pharmacological (i.e., opioid agonist treatment medications) and nonpharmacological interventions (i.e., behavioral, psychological, counseling, psychosocial, harm reduction).

studies among adolescent only samples investigated a pharmacological intervention alone or in combination with nonpharmacological interventions and 100% did so among young adult only samples (Appendix D, Table 1).

Aligning with our aim to synthesize the breadth of interventions and services that have been investigated across original studies, the remaining sections summarize the results by the broader intervention categories. For a detailed summary of each study's findings and outcomes by study design, see Appendix B-C.

Identification of evidence-based treatment interventions and health-related services for youth with nonmedical opioid use

Table 2 summarizes the breadth of pharmacological and nonpharmacological interventions identified across all study designs. Among the studies that delivered or investigated any pharmacological interventions (n = 22), buprenorphine was the predominant medication investigated (mainly buprenorphine-naloxone or extended-release buprenorphine alone, n = 11, 50%), and a smaller number of studies investigated naltrexone (in the United States only), methadone, slow-release oral morphine, or hydromorphone tablets (in Canada only). Among the six (27%) studies where multiple OAT medications were investigated, three were large secondary analyses of administrative health records data [22,51,52], and three were qualitative studies where youth described encountering a range of medication types in their interactions with service providers [23,25,53]. Of note, 19 (54%) studies investigated adaptable components (e.g., titration schedules, duration of treatment, home dosing, tapering protocols) of pharmacological interventions, which are further summarized in section 3.3.

Among the studies describing any nonpharmacological interventions (n = 13), cognitive behavioral therapy (CBT) or counseling in general, without specification of the manualized approach used, were frequently described. Generally, CBT and counseling were offered in individual and/or group formats. Three studies provided more than one nonpharmacological intervention [54–56], with one study comparing outcomes among four interventions, Adolescent Community Reinforcement Approach, Motivational Enhancement Therapy + CBT, CBT alone, or treatment as usual [57]. Other interventions included 12-Step Facilitation, Family Therapy, Individual Relapse Prevention, and Community Reinforcement Approach. Two studies investigated novel interventions, one of which was a body motion-activated game aimed at relapse prevention [58], and another investigated repetitive transcranial magnetic stimulation [59]. The range of pharmacological and nonpharmacological interventions was similarly distributed across study samples. For example, buprenorphine was the most frequently identified pharmacological intervention amongst studies involving adolescent only and young adult only samples (60% and 75%, respectively) (Appendix D, Table 2).

Characteristics of evidence-based interventions following the CFIR

Table 3 summarizes the deductive content analysis following the selected CFIR domains/constructs. From the Intervention Characteristics domain, the CFIR's "Adaptability" construct was deemed most relevant as it identified elements of the interventions that could be tailored or refined. Nineteen studies (54 coding references) were coded at this construct, 16 of which involved a pharmacological intervention. Five categories of adaptable elements were identified through open coding, including: 1) titration/induction schedules and dosing; 2) maintenance dosages; 3) duration of treatment delivery; 4) traditional clinic-based versus alternative dispensation procedures; and 5) tapering schedules and dosing. One study [56] considered medication type as an adaptable element of pharmacological intervention delivery. For the nonpharmacological interventions, adaptable elements included the duration of treatment delivery (2 studies; [58,60]) and treatment modality, where in one study, youth were referred to one of four treatment modalities after initial assessment [57].

From the Outer Setting domain, the "Patient Needs & Resources" construct was important to identifying youths' needs, barriers, and facilitators to engaging in interventions. Six studies (73 coding references) were coded at this construct, including two case reports [61,62] and four qualitative studies [23,25,53,63], all of which focused on pharmacological interventions. The case reports identified additional health and psychosocial service needs that were considered in youths' engagement with buprenorphine-naloxone. For instance, one case report acknowledged that unaddressed underlying mental health conditions impacted the youth's continuation on buprenorphine-naloxone following a rapid induction protocol [61]. Across the four qualitative studies, commonly identified barriers included the misalignment between youths' treatment

Table 2
Summary of the range of pharmacological and nonpharmacological interventions identified from all study designs (n = 25)

Intervention	N (%)[a]	Summary
Any pharmacological intervention(s) (n = 22)[b]		
Buprenorphine	11 (50)	• Studies investigating buprenorphine (e.g., Subutex), extended-release buprenorphine (e.g., Sublocade) and/or buprenorphine-naloxone (e.g., Suboxone). • Studies investigating variations in buprenorphine titration (e.g., low dose induction) and tapering protocols (e.g., 28-day vs. 56-day). • Studies investigating different durations of buprenorphine treatment (e.g., short-term buprenorphine detoxification, short-term vs. extended term buprenorphine-naloxone). • Studies investigating the benefits of buprenorphine when combined with adjunct pharmacological treatments (e.g., buprenorphine-naloxone + memantine vs. buprenorphine alone). • Study investigating a novel low-barrier, technology-assisted Interim Buprenorphine Treatment (IBT) regimen as a bridge while waiting for comprehensive OAT.
Naltrexone	3 (14)	• Studies from the United States only. • Studies investigating monthly extended-release naltrexone versus treatment as usual (daily buprenorphine maintenance or medically managed opioid withdrawal). • Study investigating home-based delivery of extended-release naltrexone versus clinic-based delivery.
Methadone	1 (4)	• Study describing a youths' preference to transition from buprenorphine-naloxone to methadone.
Slow-release oral morphine	1 (4)	• A qualitative study where a youth describes their preference for this medication over methadone.
Hydromorphone tablets	2 (9)	• Qualitative studies where youth and service providers' experiences accessing hydromorphone tablets made available during the COVID-19 pandemic through a novel program in Canada (Risk Mitigation Guidelines).
Multiple OAT medications	6 (27)	• Studies where >1 medication type from the above types was delivered or investigated. • Two studies investigated buprenorphine and naltrexone in either residential or outpatient setting, with the medication choice based on youth preference. • Studies conducting population-level administrative health database analyses of youths' receipt of OAT medications available in their respective setting. In Canadian studies, this included buprenorphine-naloxone, methadone, slow-release oral morphine, and injectable OAT (with hydromorphone or diacetylmorphine). In US studies, this included buprenorphine, buprenorphine-naloxone, naltrexone, or methadone. • Qualitative studies of youth (and/or service providers) experiences engaging with (or delivering) OAT or their perceptions of OAT (for those who have not accessed it). In these studies, youth described encountering all medication types at some point in their OAT trajectory, with most discussing experiences with buprenorphine-naloxone or methadone, and a small number referencing experiences with slow-release oral morphine or oral hydromorphone tablets (Canadian studies only). • Study of the novel risk mitigation policy in Canada where OAT was expanded to include hydromorphone tablets and youth could get easier access to take home OAT in response to COVID-19 and drug toxicity crisis.
Any nonpharmacological intervention(s) (n = 13)[c]		
Cognitive behavioral therapy	4 (31)	• Group or individual cognitive behaviorall therapy (CBT) provided alone or in combination with other behavioral interventions (e.g., motivational enhancement therapy) or pharmacological interventions (e.g., buprenorphine-naloxone). In the latter studies, CBT was offered to all participants and is not a comparator intervention against pharmacological interventions.
Counseling—general	3 (23)	• Studies describing group or individual counseling as being offered or engaged in by youth, but without further specification of the manualized approach used.
Multiple nonpharmacological interventions	3 (23)	• Studies where >1 nonpharmacological intervention is offered. • In two studies, there were no comparisons made between the different interventions, rather the interventions were required as part of treatment or youth could choose which to engage in based on their preference. • One study compared outcomes and potential moderators of four interventions − A-CRA, MET + CBT, CBT alone, TAU.
Novel interventions	2 (16)	• A-CRA • Studies investigated novel interventions for youth opioid use disorder. • One study investigated an intervention called "Recovery warrior game play"—a body motion-activated game aimed at relapse prevention. • A second study investigated "Repetitive Transcranial Magnetic Simulation"—a noninvasive method of neuromodulation of the dorsolateral prefrontal cortex.
Other interventions	6 (46)	• Family therapy • MET • Relapse prevention • 12-step facilitation

A-CRA = Adolescent Community Reinforcement Approach; MET = motivational enhancement therapy; OAT = opioid agonist treatment; TAU = treatment as usual.
[a] A study could describe more than one intervention; therefore, categories are not mutually exclusive and may not sum up to their respective totals.
[b] Pharmacological interventions were identified from studies investigating only pharmacological interventions (n = 12) or a combination of pharmacological and nonpharmacological interventions (n = 10), for a total of 22 individual studies.
[c] Nonpharmacological interventions were identified from studies investigating only nonpharmacological interventions (n = 3) or a combination of pharmacological and nonpharmacological interventions (n = 10), for a total of 13 individual studies.

goals and the medicalization of OAT, long-term treatment expectations, daily witnessed dispensation, and inflexible missed dose guidelines. In contrast, facilitators to OAT predominantly focused on interactions where youth and service providers collaborated on decisions regarding OAT medications and adjunct health and social services and developed trusting relationships.

From the Inner Setting domain, a new category for "Service Delivery Settings" was created to meet the study's objectives. A total of 18 studies (25 coding references) were coded in this new category. Across those studies, interventions were commonly delivered in community-based outpatient substance use programs (n = 7), child or youth-specific inpatient hospital settings (n = 3), residential substance use treatment settings (n = 3), and

Table 3
Results from the deductive content analysis of empirical content coded at the select domains and constructs of the 2009 Consolidated Framework for Implementation Research (n = 25)

Selected 2009 CFIR domain/constructs[a]	N of studies coded (n of coding references)	Summary of key findings
Intervention characteristics:		
*Adaptability:*Degree to which an intervention can be adapted, tailored, refined, reinvented to meet local needs	19 (54)	• For studies of pharmacological interventions, adaptable elements included: ○ Titration/induction schedules and dosing, ranging from low dose induction to rapid micro induction to traditional induction schedules. ○ Maintenance dosages for studies with buprenorphine, which ranged from 8 mg–32 mg per day. Dosage detail not described in studies administering other OAT medications. ○ Duration of intervention delivery, which were predominantly classified as short-term (<3 months); three studies included >3 months observation, with one study reporting retention rates beyond this period. ○ Adaptable elements of pharmacological treatment dispensation procedures, which were described in four studies as clinic attendance frequency (from daily to 2–3 times weekly), take home doses, and home-based versus clinic-based delivery of extended-release naltrexone. ○ Tapering schedules and dosing, which were described in three studies, with tapering schedules ranging from 7 days to 30 days and dosing ranging from max of 8 mg–12 mg per day, tapering weekly until medication stopped. • For studies of nonpharmacological interventions, adaptable elements included different definitions of treatment as usual and mandatory versus voluntary treatment.
Trialability: Ability to test an intervention on a small scale and reverse course if warranted	1 (3)	• Pilot initiative to deliver doses of extended-release naltrexone at home to patients enrolled in a youth opioid-specific treatment program. The case series study reported on the feasibility of the pilot with the first 14 patients enrolled.
Complexity: Perceived difficulty of the intervention, reflected by duration, scope, radicalness, etc.	0	
Cost: Costs of the intervention and costs associated with implementing it.	0	
Outer setting:		
Patient needs and resources: Patient needs; barriers and facilitators to meet those needs are known and prioritized by the organization	6 (73)	• Four qualitative studies and two case reports described youths' needs, and barriers and facilitators to meeting those needs, all in the context of pharmacological interventions. • Common barriers to meeting youths' needs on pharmacological interventions included: ○ Daily witnessed dispensation/lack of take home-dosing and missed dose guidelines. ○ Unmet medication preferences (e.g., methadone or slow-release oral morphine). ○ Inadequate dosing (especially in the context of fentanyl use). ○ Uncertainty about how and when to taper off OAT. ○ Underlying mental health concerns. • Common facilitators to meeting youths' needs on pharmacological interventions included: ○ Being discharged from residential treatment with a pharmacological treatment plan. ○ Being actively involved in decision-making on aspects of treatment (e.g., OAT duration, finding the right treatment or solution). ○ Receiving supports for health and social concerns. ○ Developing and being able to maintain trusting relationships with service providers. • No studies were identified that investigated youths' treatment needs (e.g., those identified through a comprehensive assessment) or how to match services to those needs.
Cosmopolitanism: Degree to which an organization is networked with other external organizations	6 (6)	• These studies described delivering services as part of a network of organizations, commonly involving community-based outpatient centers, most of which operated as specialty substance use disorder treatment sites that collaborated with or shared resources (e.g., electronic medical records) with other inpatient or hospital-based settings.
External policies and incentives: External strategies to spread interventions, including policy and regulations, external mandates, etc.	0	

(*continued on next page*)

Table 3
Continued

Selected 2009 CFIR domain/constructs[a]	N of studies coded (n of coding references)	Summary of key findings
Inner setting:		
Structural characteristics: Social architecture, age, maturity, and size of an organization	4 (4)	• Structural characteristics identified in the studies when they described their intervention primarily reflected the size of the organization and the internal networks that supported coordination of service delivery. • Two studies described delivering interventions as part of a large single hospital-based healthcare system that also provided community-based outpatient services and worked with those teams to ensure closed loop referrals. • Two studies described intervention development, delivery, and research being done through the national coordinating center of community outpatient treatment.
Service delivery setting (open codes)	18 (25)	• This construct was not part of the CFIR but added to capture information about the intervention setting as described most in the study's methods section. • The most common settings identified were community-based outpatient substance use programs (n = 7) and residential substance use treatment settings (n = 3). • Four studies described interventions being delivered in child/youth-specific settings, including a pediatric hospital (n = 3) and a pilot youth-specific initiative involving delivering of extended-release naltrexone. • One study described a school-based OAT program, delivered in the high school medical clinic, which was attended by 23 remote First Nations students. • Other settings included general community outpatient setting (n = 2) and hospital outpatient (n = 1).
Culture: Norms, values, and basic assumptions of the organization	0	
Characteristics of individuals involved:		
Other personal attributes: Broad construct of other personal traits, such as competence, capacity, values, etc.	12 (20)	• Captures the diverse types of service providers that were identified in the study's descriptions of their intervention delivery. • Common service provider types included counselors, nurses, physicians, and psychologists. • One study described a multidisciplinary team. • No studies described service delivery by peers.
Knowledge and beliefs about the intervention	4 (4)	• Open code for provider's skills, training, and competencies, including therapists training in nonpharmacological intervention delivery, fidelity assessment, ongoing coaching, and trauma-informed OUD care.

CFIR = Consolidated Framework for Implementation Research; OAT = opioid agonist treatment; OUD = opioid use disorder.

[a] Following the 2009 Consolidated Framework for Implementation Research [32,33], a subset of domains and constructs were selected as they relate to the overarching goal of the project to inform development and implementation of a youth-centered framework for OAT models of care and the specific research question to synthesize the original evidence on the characteristics of the pharmacological and nonpharmacological interventions.

hospital outpatient settings (n = 2). One study uniquely described an OAT program that was delivered as part of a high school medical clinic [64], and one study described a pilot initiative delivering youth extended-release naltrexone at home [56]. No studies were identified from virtual care settings. Studies of pharmacological and/or nonpharmacological interventions were similarly distributed across all settings identified.

Few studies were coded at predetermined codes from the Characteristics of Individuals Involved domain. However, 12 studies (20 coding references) identified the professional designation of service providers involved in the interventions' delivery. This most frequently included counselors, nurses, physicians, and psychologists. Of note, only one study [65] described pharmacological intervention delivery by a multidisciplinary team of pediatric hospitalists, outpatient OAT providers, juvenile detention OAT providers, and substance use therapists. No studies involving peers as part of the service delivery team were identified.

There were minimal differences in the proportion of studies coded at the CFIR domains/constructs and their characteristics across study samples, with the exception of the adaptability construct, which was coded at fewer studies among mixed adolescent and young adult samples (Appendix D, Table 3).

What outcomes have been described or selected to measure intervention efficacy/effectiveness?

Figure 2 displays the types of primary and secondary efficacy/effectiveness outcomes that were identified from across the studies (n = 21, excluding the qualitative studies). Three categories of primary outcomes were identified, including substance use (n = 13; e.g., self-reported opioid use, withdrawal, and craving symptoms), treatment engagement (n = 7; e.g., induction status, timely receipt of treatment, retention rates), and health and/or social outcomes (n = 2; e.g., self-reported anxiety, depression, incarceration). These categories were also predominant among the secondary outcomes measured in the studies, though two studies measured adverse events [65,66], and one study measured self-efficacy and perceived helpfulness of the intervention [58]. No studies measured treatment satisfaction or other measures of treatment perceptions as primary or

secondary outcomes. However, one study measured treatment satisfaction as a predictor of "problematic opioid use" [60] and another measured therapeutic alliance as a potential mediator between treatment assignment (buprenorphine-naloxone vs. detox) and opioid use outcomes [67]. No clear patterns were observed when comparing the primary or secondary outcomes across study samples (Appendix D, Table 4).

Discussion

This scoping review summarized the breadth and characteristics of published interventions for youth with nonmedical opioid use/OUD in Canada and the United States. Our content analysis further synthesized attributes of the interventions that could be adapted to inform the development, implementation, and evaluation of future youth-centered OAT frameworks. Accordingly, our discussion focuses on these adaptable attributes and directions for future research, practice, and policy.

A total of 25 empirical studies were included in our review, with most published in the United States and since 2020. Across studies, pharmacological interventions with OAT alone or in combination with nonpharmacological interventions were most investigated. While a recent systematic review found that adolescents were more likely to receive opioid antagonists and partial agonists (i.e., naltrexone and buprenorphine-naloxone) compared to young adults [20], our sensitivity analysis suggested minimal age-related patterns in the breadth of interventions identified, their characteristics and outcomes. This difference may be explained by our narrower selection of studies published since 2015. Indeed, we found a higher proportion of studies involving adolescents have been published since 2020. Therefore, our findings suggest an increasing empirical focus on pharmacological interventions among youth. This is an encouraging finding given the recommendations of leading addiction and pediatric health agencies in both Canada [11] and the United States [12,13] to offer OAT to adolescents and young adults with moderate or severe OUD.

Our review found that buprenorphine (e.g., buprenorphine-naloxone, extended-release buprenorphine) was the most frequently investigated form of OAT. These findings may be reflective of the clinical guidelines in both Canada and the United States where buprenorphine has been recommended to youth due to its safety, effectiveness, and potential flexibility for take-home dosages [11,12]. However, our in-depth synthesis of the barriers and facilitators to treatment showed that youth have diverse preferences toward medication types. Based on the four qualitative studies [23,25,53,63], these preferences may be influenced by youths' prior OAT experiences (their own and those of their peers), immediate treatment needs (e.g., addressing withdrawal and craving), long-term goals (e.g., vocational opportunities), and expectations for treatment duration. For example, in one qualitative study, some youth preferred methadone because of its ability to address physical and mental health concerns [23]. In another, methadone was not preferred by some youth due to undesirable side effects seen among their peers [25]. Across both studies, youth experienced pressure to initiate buprenorphine-naloxone over other medications and emphasized the positive impact of receiving their preferred medication type on OAT engagement [23,25].

These results suggest that OAT medication type and preference are key attributes for youth-centered OAT frameworks and encourage service providers to offer youth the full range of medications. However, the operationalization of these attributes and processes to support shared decision-making is an area that requires further research in real-world settings. In our review, we identified three large retrospective cohort studies using administrative health records where youth could access all approved medications in their context (e.g., buprenorphine-naloxone, methadone, naltrexone) [22,51,52]. Unfortunately, study outcomes were not disaggregated by medication type, nor were the studies able to consider medication choice or preference in their designs. This precludes an understanding of the relative effectiveness of the different OAT medications for youth and how medication preferences relate to youth-reported outcomes and experiences.

Medication dosage, treatment duration, and titration/induction and tapering processes may also be key modifiable attributes to consider in youth-centered OAT frameworks. These attributes were salient among the qualitative studies where youth expressed their important role in OAT engagement and outcomes, such as relapse [23,25]. Several of the quantitative studies and case reports also investigated OAT titration/induction and tapering protocols. These studies generally concluded the feasibility of rapid microinduction protocols [61,62], brief hospital-based induction protocols [68], low barrier interim buprenorphine delivery [69], and the benefits of longer tapering protocols [55]. While many studies in our review described the range of medication dosages as part of their study procedures, few tested the relationship between dose/dose adequacy and outcomes. This is an important gap as perceived dose adequacy during induction, treatment, and tapering is a predictor of outcomes such as withdrawal, craving, relapse, adherence, and satisfaction [70–73]. Consequently, further research on the impact of medication preference, medication received, and dose adequacy on youths' OAT engagement patterns and outcomes is crucial. To support the implementation of these attributes, research might also consider developing shared decision-making processes and tools, such as decision aids, which help patients and service providers make informed, systematic medical decisions when there is no clear superior intervention [74–76].

Beyond medication-related attributes of OAT, our review reinforces the continued need for research on the benefits of nonpharmacological interventions in OAT for youth. Despite guidelines recommending a comprehensive set of interventions for youth with OUD and other substance use disorders [11–13], gaps remain regarding effective psychosocial interventions (alone or in combination with OAT). Ten studies described nonpharmacological interventions as being offered to all participants on a voluntary basis in combination with OAT, which inhibits conclusions on the independent effects of those interventions on outcomes. However, in one noteworthy study, Hammond et al. [67] found that "therapy dose" (i.e., number of individuals, group, family counseling sessions attended) and therapeutic alliance (perceived degree of patient-provider alliance) mediated the effect of the treatment arm (2 weeks buprenorphine-naloxone detox vs. 12 weeks buprenorphine-naloxone treatment) on opioid abstinence outcomes. These results suggest that OAT outcomes may be optimized via behavioral interventions. However, it is still uncertain which behavioral interventions are effective for youth and whether effectiveness is impacted by their characteristics, contexts, and treatment goals.

To inform future research and evaluation of youth-centered OAT delivery, our review also synthesized the primary and secondary efficacy/effectiveness outcomes across the quantitative

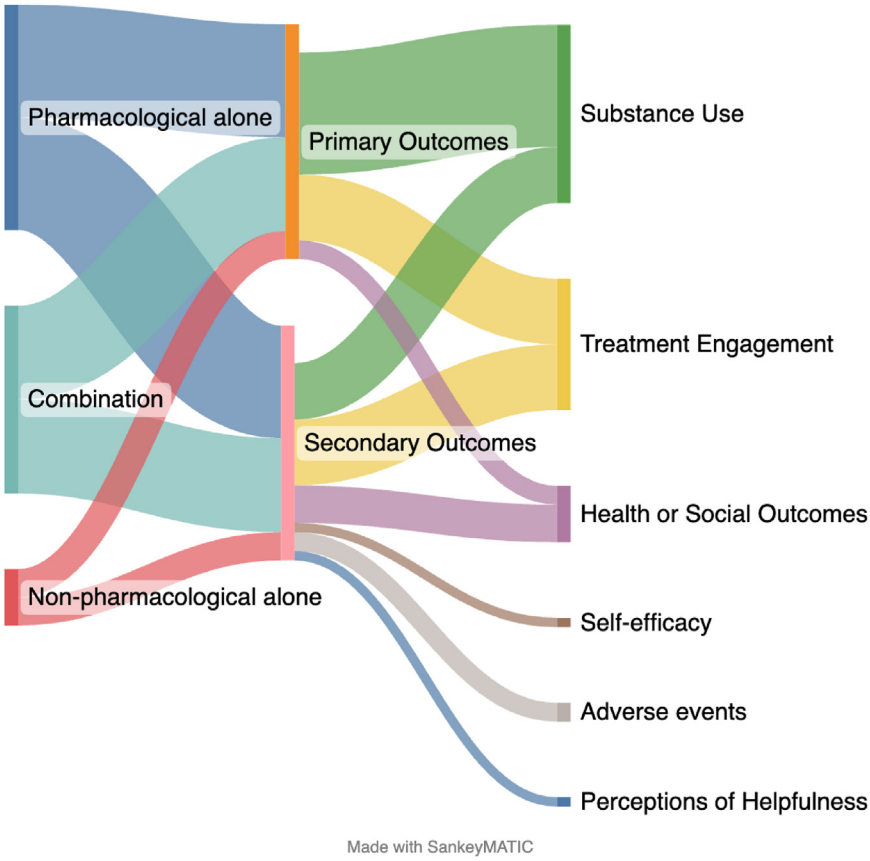

Figure 2. Sankey diagram of primary and secondary outcomes used in studies to measure intervention efficacy or effectiveness by intervention type. Sankey Diagram interpretation: Sankey diagram of the specific primary and secondary outcomes from studies involving pharmacological, non-pharmacological or combined interventions. The width of each band represents the relative number of references that were coded at the outcome sub-category. Outcome categories were not mutually exclusive, such that a reference may have described more than one primary and/or secondary outcome. The four qualitative studies were not included in this analysis, which is why the band for the pharmacological interventions' node is wider than the band for primary and secondary outcomes nodes.

studies. Aligning with OUD treatment aims (i.e., to reduce opioid use and its related harms), we found that substance use was a common primary and/or secondary outcome. Interestingly, treatment engagement was also frequently defined as a primary or secondary outcome, with measures such as treatment initiation and retention commonly applied and defined according to the study design (e.g., 12-week retention). The choice of this outcome among studies with youth may have been influenced by research among adults where OAT engagement (adherence and retention) remains one of the most important predictors of mortality, substance use, and health outcomes [21,45,77,78]. While efforts to promote OAT engagement remain crucial, it may be relevant to acknowledge that this outcome is premised on addiction being defined as a chronic medical condition that requires "long-term" retention in treatment, with thresholds for variable definition often determined by study design (e.g., 12 weeks, 1 year, time to dropout) [21,79–81]. However, this conceptualization of treatment retention appears to conflict with youths' OAT goals. As shown in one of the included qualitative studies [23] and other research [82], some youth have goals to make a "full recovery" from nonmedical opioid use/OUD and prefer to taper or engage in OAT short-term. This suggests that treatment engagement outcomes may be a complex concept to operationalize among youth and that additional outcome measures may be needed. To reduce possible bias in future research on youth-centered OAT, youths' OAT goals/preferences on treatment duration, reasons for discontinuation, and longitudinal outcomes (e.g., relapse, health, and social functioning) should be collected. Additionally, youth, service providers, and researchers may consider collaborating to develop a minimal set of patient-reported outcome and experience measures that can inform ongoing service delivery, program evaluation, and research.

Limitations

There are four important limitations to our scoping review that should be considered. First, our search strategy was refined to studies published since 2015. This decision was made to ensure that interventions were investigated in the context of changes to the unregulated drug markets in the United States and Canada. However, interventions such as methadone and CBT have been available and delivered to youth using opioids for much longer, and thus, we may have excluded earlier publications that could inform a youth-centered response to nonmedical opioid use/OUD. Secondly, despite that our search strategy included a variety of key terms for nonmedical opioid use (e.g., opioid use, abuse, misuse, etc.), our review yielded studies that

predominantly focused on youth meeting OUD criteria. This may explain the distribution of studies focused on treatment instead of prevention, early intervention, and harm reduction. For readers in the United States, a recent report on evidence-based prevention, early intervention, and treatments for adolescents with OUD may be of interest [83]. Third, although there are potential disparities in OAT access among equity-deserving youth (e.g., racialized youth, youth with lower socioeconomic status, youth living in rural and remote regions), we were unable to conduct sensitivity analyses beyond those related to age due to limited information in the original studies (e.g., sampling frame focused on youth with opioid use/OUD broadly, no stratified results). This is a crucial research direction as it is possible that youths' OAT preferences and outcomes may be influenced by this diversity. Thus, efforts to develop youth-centered OAT practices and policies, such as those relating to medication types and dosage and treatment settings, should consider this diversity carefully. The final limitation relates to our exclusion of gray literature or empirical literature where health-related efficacy/effectiveness outcomes were not measured (e.g., protocols). The decision to exclude these documents was made considering project resources and our interest in synthesizing the range of efficacy/effectiveness outcomes measured in empirical research. As a result, it is likely that studies initiated by nonacademic professionals or studies of emerging interventions and their implementation process and outcomes were excluded from this review. This may explain why our review did not identify any studies of innovative harm reduction interventions or interventions tailored to equity-deserving groups. This also explains our review's limited synthesis of CFIR domains and constructs that could more directly inform the implementation of future youth-centered OAT frameworks, such as 'Implementation Process' domain and constructs, such as 'Peer Pressure' and 'Implementation Climate.' As future youth-centered OAT frameworks are implemented, studies on the implementation process and outcomes are needed.

Conclusions

This scoping review synthesizes empirical research on evidence-based interventions and outcomes for youth using unregulated opioids in Canada and the United States. Our review found that there has been increased attention towards OAT for youth in research since 2020, which aligns with recent recommendations for the use of OAT in youth. Our review has also identified key considerations for developing, implementing, and evaluating youth-centered OAT frameworks, including the importance of medication selection, dosage, treatment induction and tapering processes, comprehensive care, and outcome selection. These findings have considerable implications for future research, clinical care, and policymaking.

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Supplementary Data

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