Improving Outcomes for Youth OUD Treatment

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Disclosures

- Kaliamurthy
 - None
- Wenzel
 - Indivior (medications for studies and current research funding)
 - Alkermes (medications for studies and previous research funding)
 - Braeburn (medications for studies)
 - US WorldMeds (current research funding)
 - National Institutes of Health (current and previous research funding)

Fishman

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- US WorldMeds (consultant, current research funding)
- Indivior (consultant, medications for studies and current research funding)
- Alkermes (medications for studies and previous research funding)
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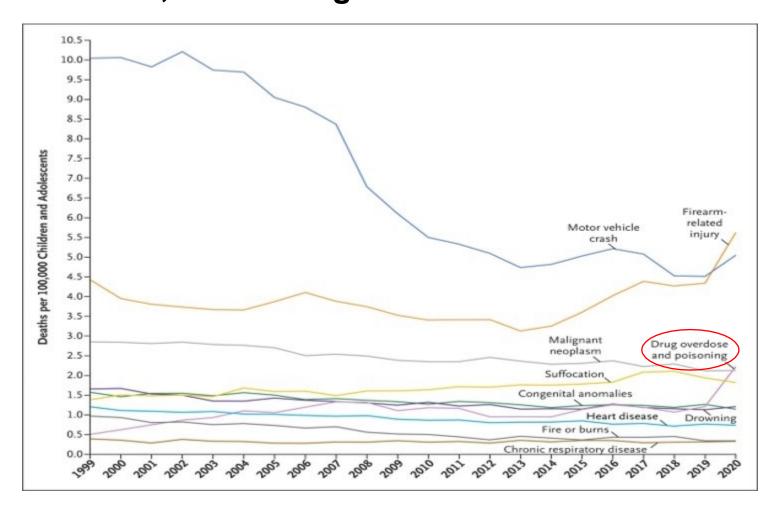
Improving Outcomes for Youth OUD Treatment: XR-MOUD

Sivabalaji Kaliamurthy MD FASAM Howard University School of Medicine Children's National



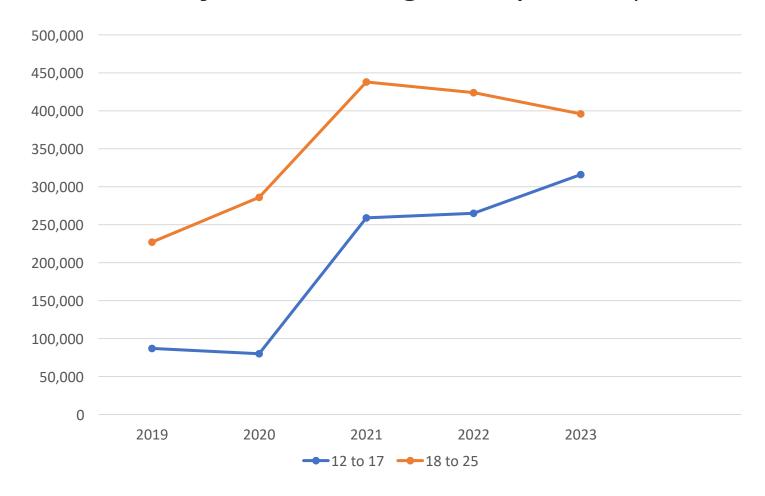


Why? Leading Causes of Death among Children and Adolescents in the United States, 1999 through 2020.



JE Goldstick et al. N Engl J Med 2022;386:1955-1956.

Past year OUD diagnosis (NSDUH)

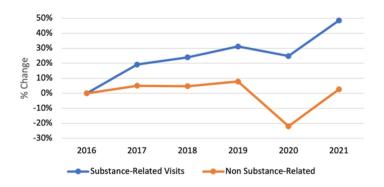


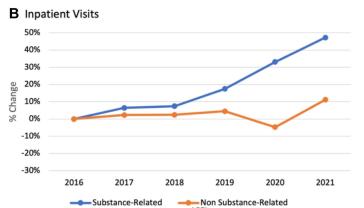
Substance Abuse and Mental Health Services Administration. (2024). Key substance use and mental health indicators in the United States: Results from the 2023 National Survey on Drug Use and Health (HHS Publication No. PEP24-07-021, NSDUH Series H-59). Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/report/2023-nsduh-annual-national-report

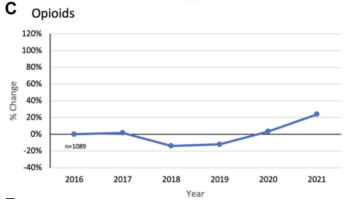
Where do youth seek help? Children's Hospital data *Ball et al.*, (2024)

- 2016–2021: 50% rise in substance-related visits and 50% increase in inpatient admissions.
- Increased for all demographics, regions, and encounter types.
- COVID-19 pandemic; more than expected rise in visits among publicly insured females, NH Black, and Hispanic youth.
- Hispanic youth experienced the greatest percentage growth of all substance-related encounters when compared to NH White youth and NH Black youth.
- Opioids contributed to 23.6% increase overstudy period after decreasing between 2017 to 2019.

A Emergency Department Visits







Challenges in Treatment

Access to medications for opioid use disorder (MOUD)

- Less than one third of youth (13 to 22 yrs) received timely addiction treatment after an opioid overdose. Only 1 in 54 youth received evidenced based pharmacotherapy. *Alinsky et al.*, (2020)
- In 2023, 712 000 adolescents and young adults aged 12 to 25 years had opioid use disorder. 38 907 adolescents and young adults aged 10 to 24 years were dispensed buprenorphine in 2023. Lee et al., (2024)

What next once you initiate MOUD?

- How long do adolescents stay in care? Are there differences between MOUD? Methadone > Buprenorphine and Naltrexone in pre fentanyl era. Hadland et al., (2018)

Resource Limitation

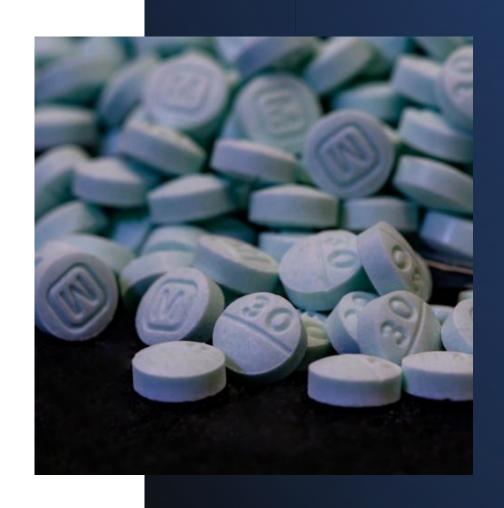
- Only one in four residential addiction-treatment facilities for adolescents offer buprenorphine. *King et al., (2023)*



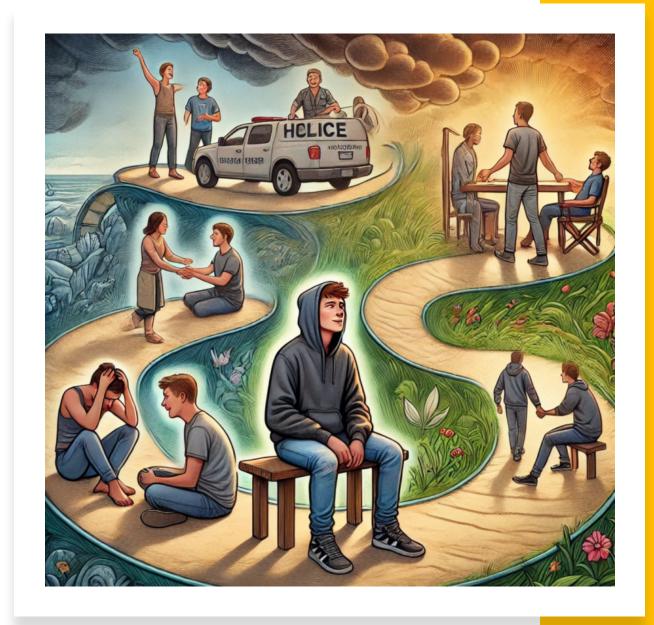
In the era of Fentanyl

Office based opioid treatment for adolescents(< 18 yrs) with opioid use disorder. *Kaliamurthy et al.*, (2024)

- Mean age at intake, 16.8 (1.0) yrs
- Age at first use of opioids, 15.4 (1.2) yrs
- Smoking identified as preferred method.
- Age at first use of any substance. 13.2 (1.6) yrs
- High rates of co-occurring substance use disorder. (50% reported using psychedelics)
- All of them had family involvement. High acceptance of MOUD.
- Approximately 60% retention at three months.
- Low utilization of psychosocial services.



• The journey begins!



Why Use Extended-Release Buprenorphine in Youth with OUD?

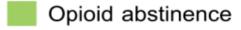
- Improved Treatment Adherence: Adolescents and young adults often face challenges with daily adherence to sublingual buprenorphine/naloxone. XR-BUP, administered weekly or monthly, ensures continuous therapeutic coverage and avoids the need for daily dosing. This reduces the risk of missed doses and potential return to use.
- Stabilization During High-Risk Periods: Early recovery is a period of high risk for overdose and dropout. XR-BUP provides consistent plasma levels, minimizing cravings and risk of relapse during that critical time.

RCT of XR-Bup vs Standard of Care (SoC)

- N=314 adult patients in SoC maintenance treatment, daily SL Bup (mostly) or daily methadone, randomized to stick or switch to XR-Bup
- Stable in-treatment population, mean 50 wks retention at enrollment

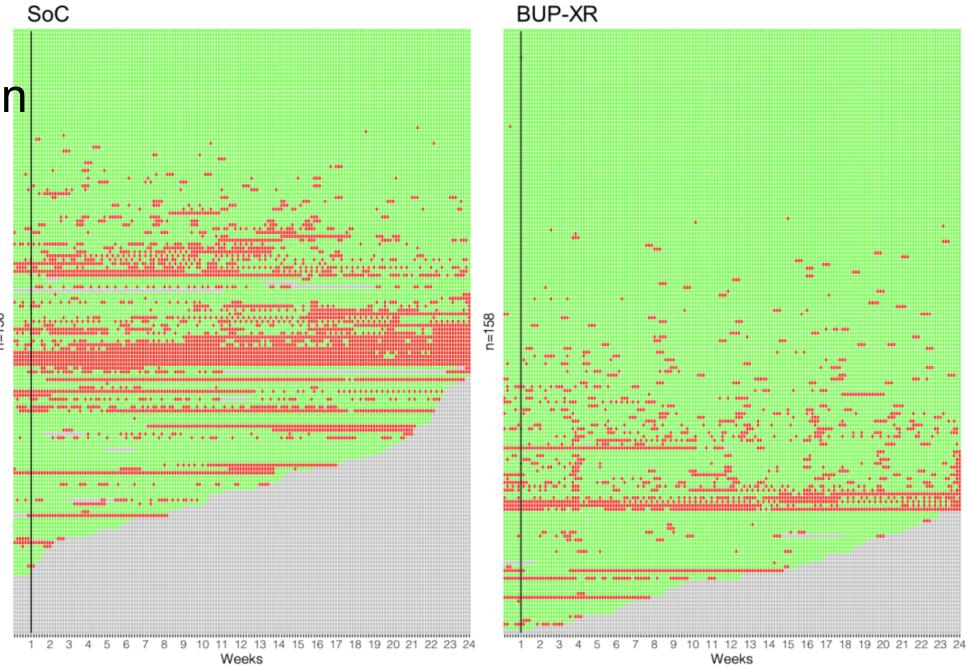
	XR- Bup	SoC
Days opioid abstinent (out of 161d)	123d IRR = 1.18	104d
Max continuous opioid abstinence	95d	77d
Retention in study treatment	145d	129d
Rate of OUD "remission" over 24 wks	75% 0R = 1.9	62%
Days to treatment discontinuation	154d	138d

Visual representation of results



- Opioid use
- No data on opioid us

Marsden et al. Lancet. 2023



XR-Bup in the Real World (Adults)

- Retrospective naturalistic cohort, NJ specialty clinic
- 233 patients Rx'd XR-Bup
- Comparison between groups received ≥1 dose (50%) vs not

	Started XR-Bup	No XR-Bup
6-month retention	70%	37%
Opioid neg UDS over 6m	67%	36%
OR for 6-month retention	5.4	ref

Challenges in patients younger than 18

No data on safety or efficacy.

Insurance barriers to prescribing.

Lack of pediatric facilities offering this intervention.

The Use of Extended-Release Buprenorphine in the Treatment of Adolescent Opioid Use Disorder: A Case Series *Neptune & Kaliamurthy* (2025)

Pt	Age	Sex	Ethnicity	Opioid Use	Method	XR-BUP Regimen	Side Effects	Psych Dx & Notes	* One year later
1	15	М	Hispanic	Fentanyl	Smoking	300mg x3, 100mg x5	Constipation	Anxiety, CUD; nonadherence to SL BUP/NX; ongoing cannabis use	Still in care, stopped XR BUP after one year
2	16	F	Hispanic	Fentanyl	Smoking	300mg x2, 100mg x1	Withdrawal (Day 24)	PTSD, MDD, CUD; prior OD; withdrawal after 1st dose	Still in care, continues XR BUP, had a return to use episode, increased XR BUP to 300 mg and is back in recovery.
3	16	F	White, Hispanic	Fentanyl	Snort & Smoke	Brixadi 96mg x3	Headache, site pain	MDD, GAD, SAD, SI, CUD; SL BUP/NX issues at home	Still in care, continues on XR BUP
4	17	F	Hispanic	Fentanyl	Snort & Smoke	300mg x2, 100mg x3	None	CUD, NUD, grief; prior OD, started XR-BUP after failed naltrexone	Still in care, continues on XR BUP
5	17	F	Hispanic	Fentanyl	Oral & Smoke	300mg x1, 100mg x12	None	Anxiety, CUD, NUD, PTSD, HUS; residential/IOP care	Still in care, continues on XR BUP
6	17	М	Hispanic	Fentanyl	Snort & Smoke	300mg x2	Vomiting, Withdrawal (Week 2-3)	Anxiety, psychosis, CUD; withdrawal, ongoing fentanyl/bath salt use	Not in care anymore. Dropped out after two injections.

^{*} Not in manuscript

Unanswered questions



DURATION OF TREATMENT



WEANING OFF STRATEGIES



LONG TERM CONSEQUENCES



YOUTH OPIOID RECOVERY SUPPORT (YORS):

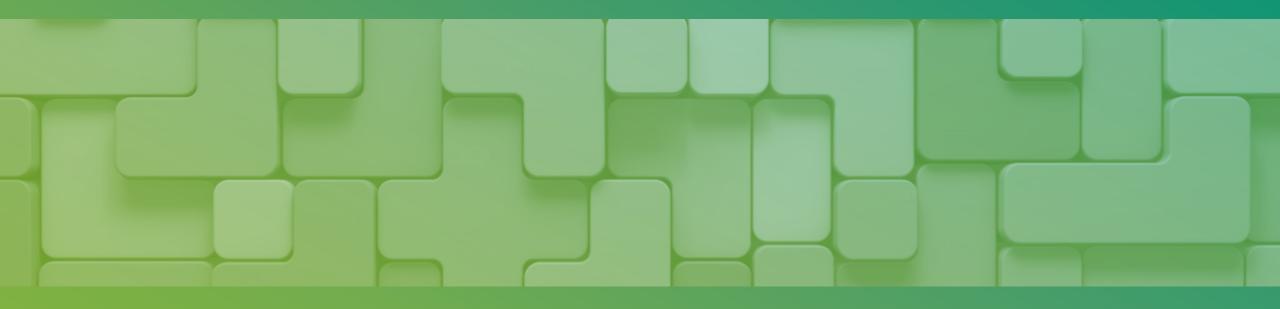
Assertive, Family-Based Treatment for Youth with OUD

Kevin Wenzel, PhD

Psychologist and Director of Research

Maryland Treatment Centers

Baltimore, MD



YOUTH OPIOID RECOVERY SUPPORT (YORS): BACKGROUND AND OVERVIEW

Relapse & dropout

Overdose deaths

Limited family help

Episodic care

What's the problem with treatment as usual for youth with OUD?

They think they're invincible

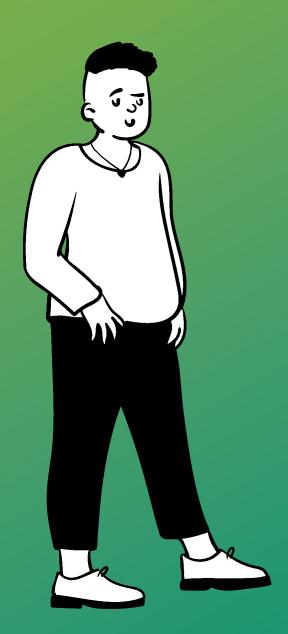
Hard-tonavigate treatment system Underutilization of MOUD

Comorbiolist.

About Youth OUD

- Opioid use disorder (OUD) is an advanced, malignant form of substance use disorder (SUD), usually beginning in youth
- Young adults are disproportionately affected by the opioid epidemic and their developmental vulnerability is prominent. Youth have worse outcomes than mature adults. Fatal overdose rates have increased faster among youth than older adults.
- There is evidence and consensus for medications in OUD (MOUD) in youth, but dissemination is poor due to problems with capacity, misinformation, and prejudice. Problems with initiation and retention.

HOW TO HELP THIS YOUNG PERSON?



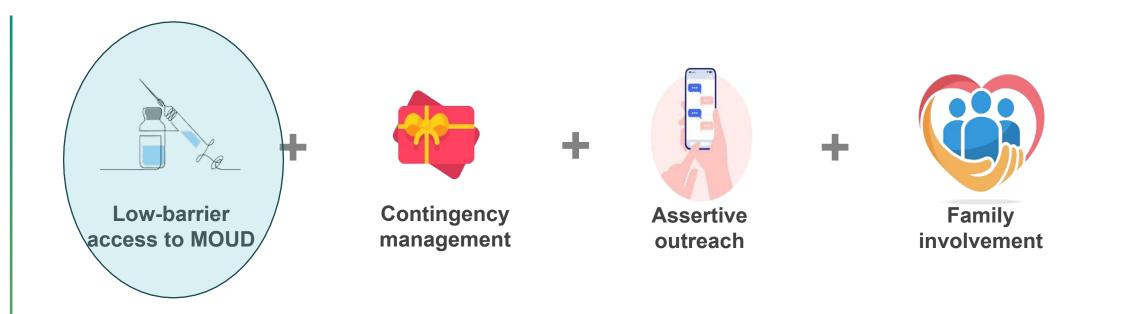
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Youth Opioid Recovery Support (YORS) Intervention

- Developmentally-informed, multi-component intervention and service delivery model to support MOUD adherence
- Emphasis on extended-release (XR) MOUD
- Focus on young adults aged 18-28
- Multidisciplinary treatment team: therapist, care coordinator, prescriber, nurse





Literally meeting them where they are

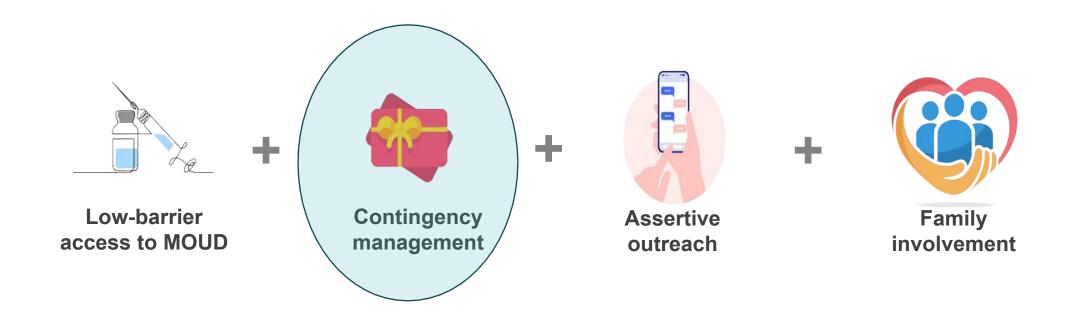
- At home, work, recovery house, jail, hospital
- Indoors or in mobile van
- Rideshare to clinic

Low barrier access in general

- Multiple reminders, logistical help from care coordinators
- Evening, weekend hours
- Same/next day provider appointments

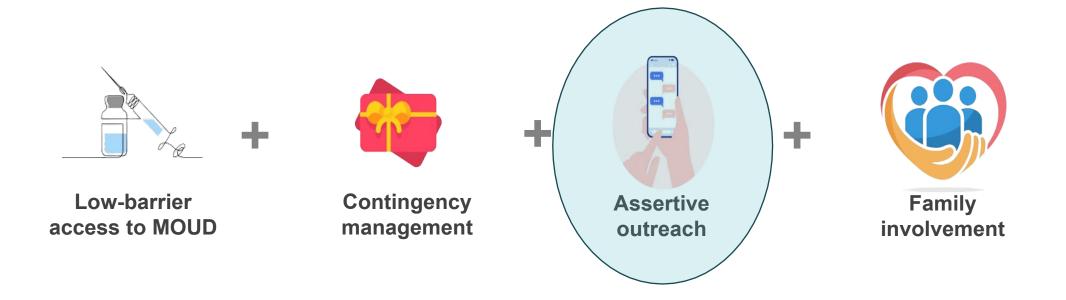


Wenzel & Fishman. Mobile van delivery of extended-release buprenorphine and extended-release naltrexone for youth with OUD: An adaptation to the COVID-19 emergency. *JSAT*. 2021



Contingency management

- Well-established in research (e.g., for negative UDS) but little uptake in real-world care
- YORS' concrete, actionable, behavioral target = XR-MOUD shot
- \$20 for first dose, \$25 for second, \$30 for third, etc. up to \$50
- Additional \$50 bonus for getting all doses



Proactive engagement

- Frequent flexible contacts
 - Offer weekly scheduled individual sessions
 - Provide impromptu therapeutic encounters
- Calls, texts, email, social media, telehealth, in-person

Case management support

- Facilitate care continuity across settings
- Advocate for timely MOUD
- Problem-solve medication receipt



Families have core competence and natural leverage to support recovery. Youth autonomy and self-efficacy are compatible with family empowerment. YORS offers:

- Family involvement in treatment planning, engagement
- Family support through a weekly family support group and individual services from a family peer recovery coach
- Family education and coaching on MOUD, navigating the treatment system



YOUTH OPIOID RECOVERY SUPPORT (YORS): CASE ILLUSTRATIONS VIA TEXT

Discussing Relapse

Young Adult

hey so I tested positive for fentanyl. i just wanted to let you know before you found out from anyone first. on sunday when my friend was over I took one from him because my tooth. was hurting really bad but overall it didn't work. the whole reason why idid it is cause my tooth was hurting really bad and I was in a situation where it was right in my face and everything that I usually do to fix the tooth pain wasn't working so I tried doing that but it had not affect on me cause the shot I guess so I basically did it for no reason. but anyway my mom knows thats why im saying it in the chat and also they still gave me the shot today. I just wanted to get out in front of it and let you know before anyone else tells you. also if I don't respond its casue im at work.

Thanks for letting me know! Really appreciate it. Glad your mom knows and I'm deeply glad you still got the shot.

We will talk more about it next week but you have taken all the right steps, transparency with your mom and me and still getting the shot.

Mom

I'm so grateful he got the shot. I was really shocked and upset at first but after processing it, it was one time, it didn't work & he doesnt crave to do it again. he has his dentist appointment in 6 days. I know he's been in pain. What this comes down to from my pov is boundaries w his friend. I'm not saying he cant come here bc they are best friends but we gotta lay some rules on using in front of [Young Adult].

Completely agreed with everything you said. Sounds like a good plan!

well am not home y'all goin to have to stop doing that... when am post to get it on the 3rd of every mouth y'all just be showing up







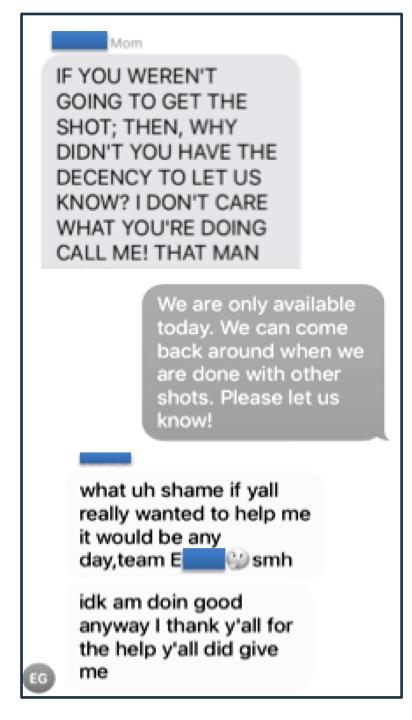
am at the hospital taking care of my son

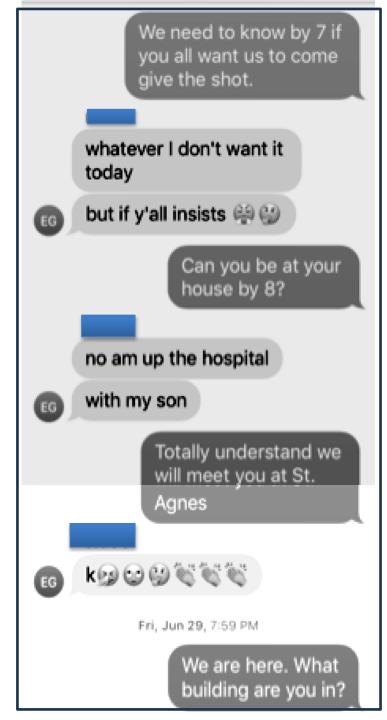
> We scheduled this look at the texts. We can come to the hospital to give you the shot.

and I didn't plan on getting shot today anyway

I didn't schedule nothing

so don't say we





Tues, Dec. 20, 2022 at 10:16 AM

It's Ms. Kamala. Texting you privately. Did you have a chance to share UA results with your mom? Your UA plus the missed session are red flags. Remember that we made a family agreement that I would share any red flags with your mom? My policy is to give you a chance to tell first, and then follow up with mom. Please let her know by this afternoon. I plan to follow up with her after 3 today.

If u want to u can tell her idc regardless nobody gone respect what I say anyways so go head.

I'm grown so I don't get if I say I don't want to tell her it should nd respect.

When you and I and your mom made the family agreement, we agreed no secrets. You can choose how to tell her and you have some time.

Like I said I don't want to worry her we be having enough going on right now and I don't want to put more stress on her . So therefore I rather not .

> I understand your not wanting her to worry. What are your ideas for dealing with the underlying problem of using?

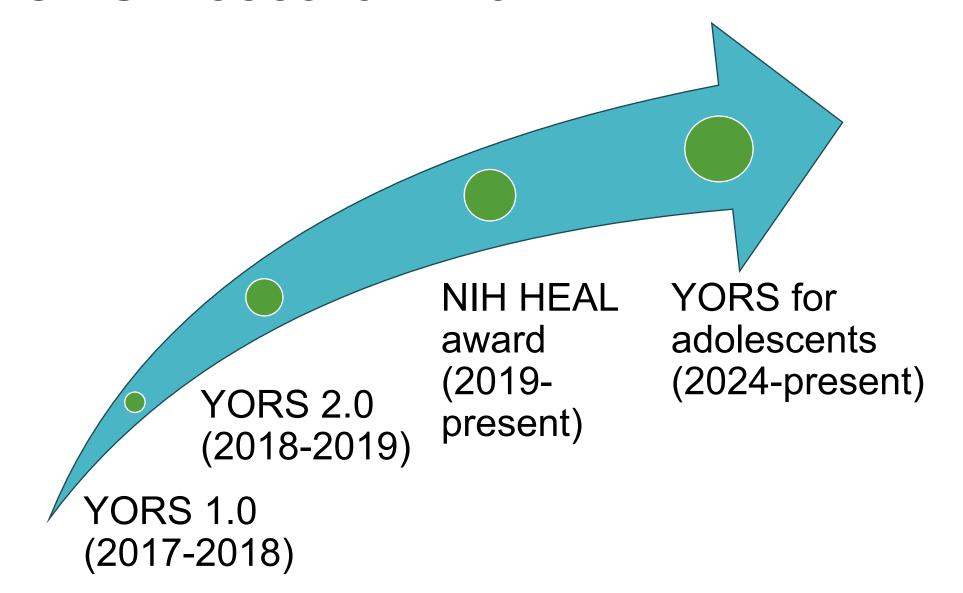
There is no problem I did that on my birthday. That's it that's all.

I agree you've been pretty consistent about not using percocets. But everytime there's been a slip, the other thing has contained fentanyl.



YOUTH OPIOID RECOVERY SUPPORT (YORS): WHAT DOES THE DATA SAY?

YORS Research Arc



YORS 1.0

- N=38 young adults (18-26)
 seeking treatment with XR-NTX
 through usual care
- Randomized to YORS or TAU (1:1) for 24-weeks
- 66% male; 94% White
- Mean Age = 23.4
- 84.2% Medicaid
- 100% history of heroin use
- 71.1% history of injection use

	YORS mean (SD) or % (n)	TAU mean (SD) or% (n)
Number of XR-NTX doses	4.3 (2.3)	0.7 (1.2)
	(n = 18)	(n = 20)
Opioid relapse (yes/no)	61.1% (11)	95.0% (19)
	(n = 18)	(n = 20)
Received all prescribed	44.4% (8)	0.0% (0)
doses (yes/no)	(n = 18)	(n = 20)

YORS 2.0

- N=22 young adults (18-26) seeking treatment with XR-NTX or XR-BUP through usual care
- Uncontrolled trial; used historical TAU from YORS 1.0 for comparator
- 12-24 weeks of intervention/ follow up
- 73% male; 86% White
- Mean Age = 23.9
- 86.4% Medicaid
- 100% hx heroin use
- 64% hx injection use

XR-MOUD receipt and opioid relapse.

	Current YORS	N	Historical TAU	N	p- Value
Doses received at 12- weeks	1.91	22	0.40	20	<0.001
Doses received at 24- weeks	3.76	17	0.70	20	<0.001
% relapsed at 12-weeks	27.3%	22	75.0%	20	< 0.01
% relapsed at 24-weeks	52.9%	17	95.0%	20	< 0.01

NIH HEAL Phase 1 (2019-2021)

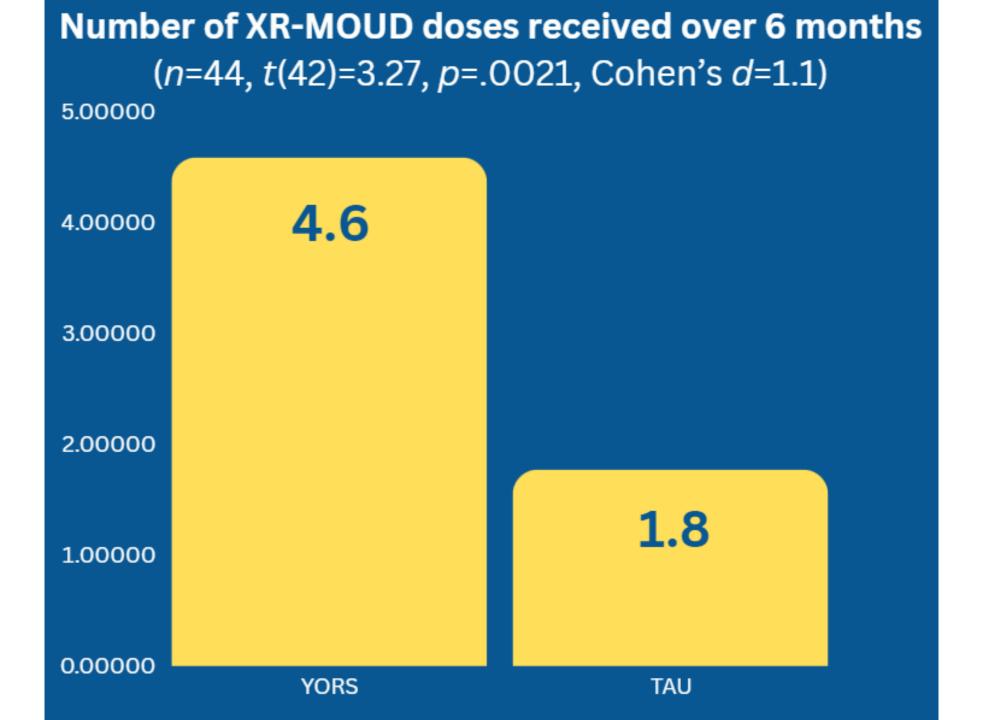
- Choice of XR-MOUD no brainer!
- Mobile Van Delivery 2 thumbs up!
- Telehealth 3 thumbs up!
- Parent peer support group (telehealth)- strong endorsement from sub-group
- mHealth app- lukewarm
- Written feedback- mixed recover





NIH HEAL Phase 2 (2021-present)

- Larger RCT underway (75% recruited)
- Primary Outcome: number of XR-MOUD doses received
- Key secondary Outcome: opioid relapse
- Intervention period = 26 weeks; additional follow-up at 32 weeks
- Interim analysis of RCT data on primary outcome replicates previous findings



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Next Steps:

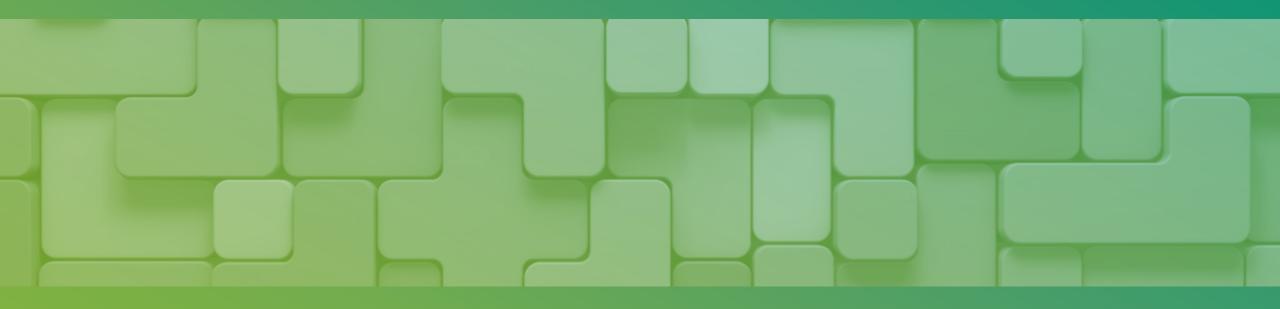
YORS for adolescents

YORS using daily SL Bup

Stay tuned!

Summary: What does the data say?

- YA OUD patients do poorly: Few return for subsequent XR-MOUD injections and most relapse quickly after inpatient discharge
- YORS has shown large, clinically meaningful effects in small, replicated samples
- YORS has been tested on patients choosing different types of XR-MOUD without apparent differences in outcomes (although underpowered)
- YORS has been vetted with young adults, providers and families and refined accordingly
- YORS has embraced telehealth culture and results appear to stay the same
- YORS should be tested in other populations: adolescents and youth choosing SL-bup



YOUTH OPIOID RECOVERY SUPPORT DISCUSSION AND Q&A

Assertive MOUD treatment for Adolescents

Marc Fishman MD Maryland Treatment Centers Johns Hopkins University School of Medicine

Youth Opioid Recovery Support (YORS)





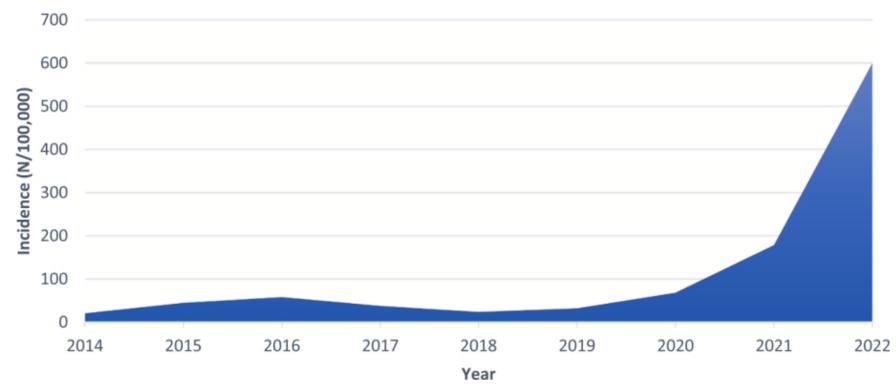


Background

An escalating problem



Incidence of opioid-related presentations

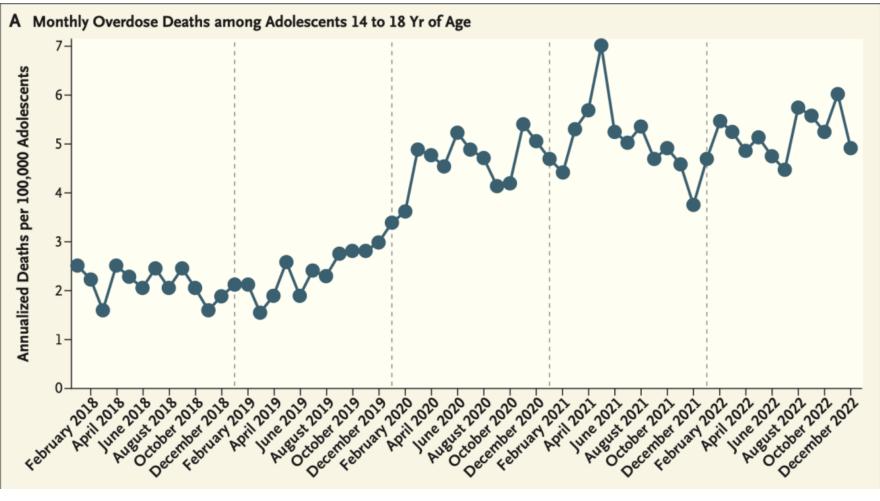


Adolescent OUD presentations to ED across 13 sites. Sidlak et al. *DAD*. 2024.

Background

An escalating problem





US adolescent OD deaths, CDC data. Friedman et al. NEJM. 2024

Background

Problematic Adolescent Treatment



Prior studies (e.g., CTN-0010) show efficacy of SL Bup in adolescents, but still insufficient study of MOUD in this critical target population

- All short term (≤12 wks)
- None with XR Bup
- None in the era of fentanyl



Bup should be standard of care, but has poor uptake

- <5% of adolescent OUD patients get MOUD
 - (Hadland. JAMA Peds. 2018; Woody and Fishman. JAH. 2020)

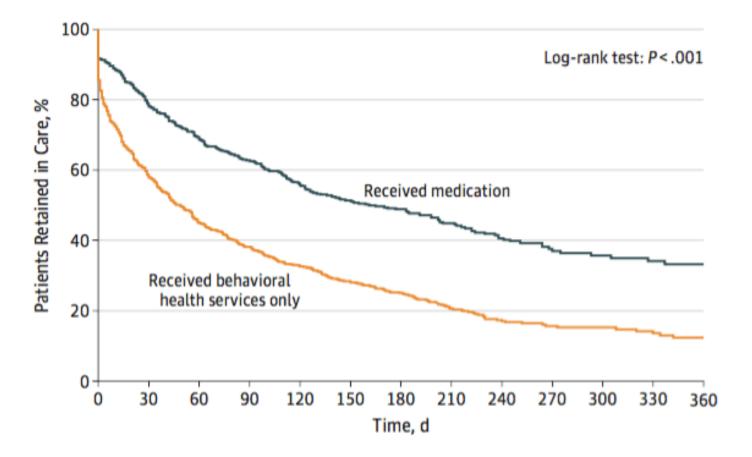


Limited by lack of capacity, practitioner confidence, adequate evidence of efficacy, FDA labeling

Medications promote retention for youth (But poor uptake)

Youth 13-22, Medicaid claims 26% received any medication

(5% for age <18 yrs).



MOUD feasible for youth in real world But poor adherence in community treatment

- Treatment received in acute residential followed by multiple community providers, youth 15-21, N=288
 - XRNTX 28%, Bup 33%, No meds 39%
- Over 6 months following residential discharge low rates of MOUD use:
 - XRNTX: mean doses 1.3
 - 41% 1st OP dose
 - 12% 3rd OP dose
 - 2% 6th OP dose
 - Bup: mean days 57

YORS PILOT EXPANSION TO ADOLESCENTS

RCT

- Young adults aged 18-28
- •6-month intervention period
- Randomized controlled trial to assess efficacy of YORS intervention
- MOUD: XR-NTX or XR-BUP
- **-**79 randomized as of 1/17/25

ADOLESCENT PILOT

- Adolescents aged 13-17
- 4-month intervention period
- Single-arm pilot to explore feasibility of YORS intervention
- MOUD: XR-NTX, XR-BUP, or SL-BUP
- ■10 enrolled as of 1/17/25
- Parent must provide informed consent

PARTICIPANT OVERVIEW

- N=11 adolescent participants
 - 4 female, 7 male
 - Ages 15-17
 - Race/ Ethnicity: 3 Black, 5 Hispanic, 2 Black/Hispanic, 1 White
 - O TSOs = parents (7 mothers, 4 fathers)
- 10 participants have completed the 4-month YORS intervention
- MOUD
 - 7 initiated on SI-Bup
 - 4 transitioned to XR-MOUD during intervention (1 XR-NTX, 3 XR-BUP)
 - 4 initiated on XR-MOUD (3 XR-NTX, 1 XR-BUP)

MOUD OUTCOMES

- 10 adolescent participants completed the YORS intervention:
 - ○68.5% average time (days) on MOUD across 4 months
 - Measured by recorded days of observed or self-reported sl-bup adherence and documented XR adherence
 - 4 patients had an adherence rate greater than 90%
 - 3 initiated on XR-MOUD, 7 initiated on SL-BUP (4 transitioned to XR)
- 1 adolescent participant is currently in the YORS intervention period:
 - Initiated on XR-NTX: 3/3 doses received

SAFETY

- ■3 SAEs 2 psychiatric hospitalizations and extended ED stay for single patient with high severity pre-existing co-morbidity
- Other AEs
 - Injection site discomfort
 - Dizziness, fatigue
 - Psychological distress over offer of substances by another adolescent patient
 - Kicked out of mother's home due to relapse

New YORS R34 PROJECT: EXPANDING YORS TO ADOLESCENTS STUDY AIMS

Specific Aim 1. Adapt and enhance the YORS intervention for new target populations by:

- Adapting existing YORS strategies and techniques to be more developmentally appropriate for adolescents and their TSOs,
- Adapting the YORS intervention components for adolescents on sublingual buprenorphine (e.g., adjusting the contingency management schedule of reinforcement for MOUD adherence component to include sublingual buprenorphine)
- Training a Spanish speaking YORS therapist and translating YORS materials into Spanish to allow the intervention to be used with Spanish speaking family TSOs.

Specific Aim 2. Conduct a single-arm pilot feasibility study of YORS delivered over 6 months for N=40 adolescents and N=40 TSOs presenting for treatment for OUD.

Specific Aim 3. Conduct qualitative interviews in a subset of adolescent-TSO YORS dyads to gain insights into barriers and facilitators to care, including Spanish-speaking dyads, to inform future cultural and linguistic adaptations and refinements in preparation for a future larger scale RCT.

CHANGES & ADDITIONS TO YORS

Same primary components:



- Lower threshold for enrollment: "Considering treatment with XR-NTX, XR-BUP, or SL-BUP OR has begun SL-BUP maintenance within the past two weeks"
 - Original threshold: "Willing to receive treatment with..."
 - In this iteration of YORS, we are making a concerted effort to begin the intervention earlier in the treatment episode

New CM schedule

- o All participants get a raise
- o Adapted for participants for SL-Bup with escalating reinforcement schedule

Formalization of TSO support components

- o Individual outreach from family peer
- Weekly support group standard feature for TSOs
- Home delivery expanded to "low barrier MOUD" which will include home delivery as an option but also things like rides to the clinic or pharmacy, and facilitating communication with prescriber

NEXT STEPS

- Recruiting for new R34 trial since March '25
- Collaboration with the treatment team for new inpatient adolescent program
- •Inclusion of Spanish-speaking families:
 - Hired and training bilingual staff
 - Translation of study materials
- Develop materials for qualitative interviews of R34 patients and TSOs
- Continue assessing safety and feasibility of the YORS components among adolescents
- Expanded experience with XR-Bup



BOND:

Moving upstream to increase the funnel of youth with OUD into care -- recruiting concerned significant others as a target of family coaching

MARYLAND RESIDENTS: DO YOU WORRY ABOUT SOMEONE'S OPIOID USE?



Questions? Discussion?

Therapeutic optimism remains one of our best tools!



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