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A pilot randomized controlled trial of assertive treatment including family involvement and home delivery of medication for young adults with opioid use disorder

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ABSTRACT

Background and Aims Although medications for opioid use disorder (OUD), including extended-release naltrexone (XR-NTX), have demonstrated effectiveness, adherence is often low. We tested the preliminary efficacy of youth opioid recovery support (YORS), a multi-component intervention designed to improve engagement and medication adherence for young adults with OUD. **Design** Single-site randomized controlled trial with 24-week follow-up. **Setting** Community substance use disorder treatment program in Baltimore, MD, USA. **Participants** Young adults aged 18–26 years enrolled in inpatient/residential OUD treatment intending to pursue outpatient OUD treatment with XR-NTX. Twenty-one participants were randomized to YORS and 20 to treatment as usual (TAU). The analyzed sample was 65.8% male. **Intervention and comparator** Components of YORS include: (1) home delivery of XR-NTX; (2) family engagement; (3) assertive outreach; and (4) contingency management for receipt of XR-NTX doses. The comparator was TAU, which consisted of a standard referral to outpatient care following an inpatient stay. **Measurements** Primary outcomes were number of XR-NTX doses received over 24 weeks and relapse to opioid use (defined as ≥ 10 days of use within 28 days) at 24 weeks. **Findings** Participants in the YORS condition received more XR-NTX doses [mean = 4.28; standard deviation (SD) = 2.3] compared with those in TAU (mean = 0.70; SD = 1.2), $P < 0.01$. Participants in the YORS group compared with TAU had lower rates of relapse (61 versus 95%; $P < 0.01$). Survival analyses revealed group differences on time to relapse with participants in TAU being more likely to relapse sooner compared with participants in the YORS condition [hazard ratio (HR) = 2.72, 95% confidence interval (CI) = 1.26–5.88, $P < 0.01$]. **Conclusions** The youth opioid recovery support intervention for extended-release naltrexone adherence and opioid relapse prevention among young adults with opioid use disorder appeared to improve treatment and relapse outcomes compared with standard treatment.

Keywords Assertive outreach, contingency management, family therapy, home delivery, opioid use disorder, young adults.

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INTRODUCTION

Opioid use disorder (OUD) has devastating consequences for young adults and their families. Young adults, typically aged from 18 to 24–26 years, in the United States are disproportionately affected by the current opioid crisis, with the highest per-capita rates of prescription opioid misuse and heroin misuse [1]. Approximately two-thirds of all overdose deaths involved opioids among US young adults in recent years, and there is growing concern concerning the lethality of increasingly widespread fentanyl analogs [2].

Medications for OUD (MOUD: methadone, buprenorphine and extended-release naltrexone) are the standard of care [3,4]. Despite the evidence, uptake of MOUD in youth remains alarmingly low, and compared to older adults, adolescents and young adults with OUD tend to have poorer engagement in and response to MOUD [5–11], due probably to developmental vulnerabilities [6,12–19].

Strategies such as extended-release medication formulations may help to overcome some of the adherence challenges presented by daily medications. However, even with this advantage, many barriers to retention remain [20,21]. Several studies have examined the impact of extended-release naltrexone (XR-NTX) on youth treatment. In a small case–series of young adults receiving XR-NTX for OUD [22], participants received only 1.5 outpatient doses on average over 4 months and 25% dropped out before receiving any outpatient doses. A larger study showed that among 82 youth OUD inpatients who selected XR-NTX as their desired treatment and received a first dose prior to inpatient discharge, only 17% received a third dose and only 7% received a sixth dose [23,24]. Clearly, there is considerable room for improvement in addressing barriers to engagement, retention and adherence in this vulnerable population.

Family treatments have well-known effectiveness in youth substance use disorders (SUDs) [25,26]. Involvement of family or other significant others has shown promise in improving adherence to SUD medications, such as disulfiram in Network therapy [27,28] and oral naltrexone in couples therapy [29]. However, such strategies have been poorly applied in treatment of young adults because of inadequate training, concerns about confidentiality and the developmentally normative push-back by youth against their subjective sense of family 'intrusiveness'.

Assertive outreach and home delivery of medications are also well-established strategies to improve treatment engagement, especially medication adherence. The concept is to bring treatment to patients assertively rather than waiting passively for patients to present to institutional settings. The assertive community treatment (ACT) approach for severe psychiatric illness focuses on contact with patients in their communities rather than clinic-based appointments, and shows benefit over traditional approaches [30–32]. ACT has become a standard treatment in many arenas and some features have been used effectively with cannabis use disorder [33], but little work has been conducted to adapt this model to youth with OUD.

Contingency management (CM) is a highly effective intervention that relies upon the principles of operant conditioning to incentivize desired outcomes. A substantial literature supports CM for SUD treatment among adults [34,35] and youth [36]. CM has also been used effectively to promote medication adherence to oral naltrexone in OUD [29,37,38] as well as medication adherence in other chronic health conditions [39–41].

Although each of these components has shown promise, they have not been combined to promote medication adherence for OUD in this difficult-to-treat population. The youth opioid recovery support (YORS) model includes: home delivery of XR-NTX, family engagement with an emphasis on promotion of medication adherence, assertive outreach to patients and families and CM for receipt of medication doses. One promising case–series [42] demonstrated the benefit of the YORS model compared to a historical control group who received standard care; however, no randomized study has been conducted. The purpose of this study is to further test the YORS intervention in a pilot randomized controlled trial (RCT).

METHODS

Design

This study was a 24-week, open-label, single-site, RCT to test the efficacy of the YORS intervention compared to treatment-as-usual (TAU). Randomization to YORS or TAU (1 : 1) followed eligibility determination, and occurred at varying points during usual care after patients had completed withdrawal management (detoxification) and before they received a first dose of XR-NTX. An on-line random number generator was used to assign participants to treatment condition. This open-label trial involved no masking of treatment or outcomes. Study flow is presented in Fig. 1.

Primary outcomes for this study were: (1) number of outpatient XR-NTX doses received and (2) relapse to opioid use over 24 weeks. Sample size was chosen using a power level of 0.8 and an estimated large effect size based on pilot data with a historical comparison group [42]. Relapse to opioid use was defined as at least 10 days of opioid use within a 4-week period, using a well-established and clinically meaningful measure [43,44] that amalgamates self-report and urine drug screen (UDS) data to calculate days of opioid use. Missing (even in the presence of available self-report data) or positive UDS results were imputed as positive for 5 days of opioid use per 2-week period as a conservative approximation of actual use.

Participants

We recruited patient participants (n = 41) aged 18–26 years seeking treatment for OUD with XR-NTX from a community SUD treatment program (Mountain Manor Treatment Center in Baltimore, MD, USA) during an acute inpatient/residential treatment episode. Patient participants had DSM-5 OUD and endorsed using illicit opioids within the 30 days prior to study enrollment. We excluded patients if they had other unstable medical or psychiatric disorders, transaminase concentrations more than five times the upper limit of normal, chronic pain requiring opioids, homelessness or an anticipated living situation greater than 60 miles away. We also excluded women if they were pregnant, breastfeeding, planning conception or unwilling to use birth control. For patient participants randomized to the YORS condition, we also recruited patient-selected treatment significant others

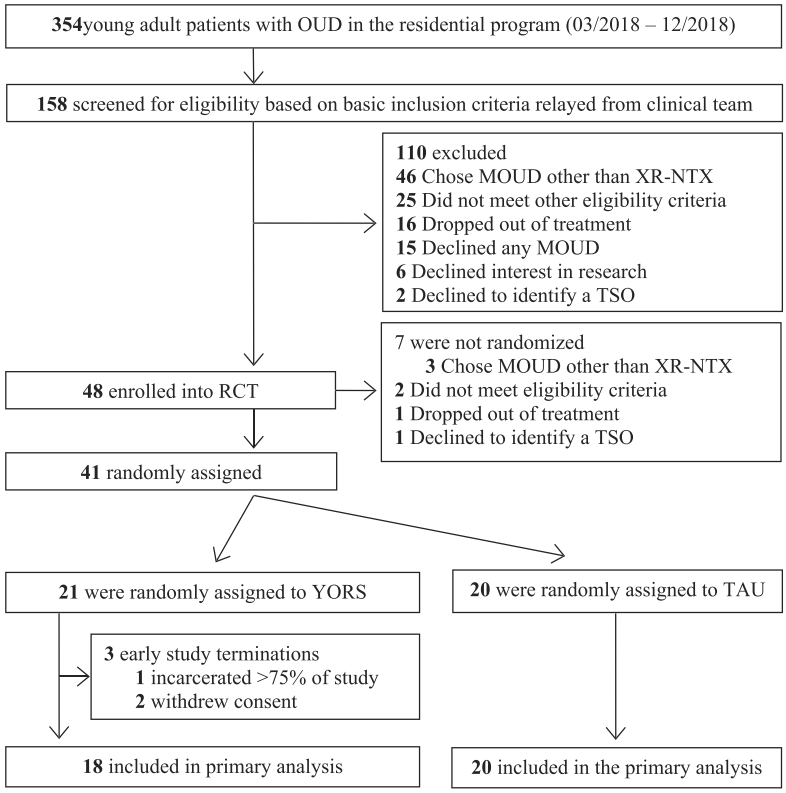

Figure 1 Trial profile

(TSOs; $n = 23$). All study procedures were approved by the Johns Hopkins Institutional Review Board, and all participants provided informed consent.

Measures

Urine drug screens (UDS). Commercially available instant tests, including the synthetic opioids oxycodone and fentanyl, were administered at 2-week intervals.

Time-line follow-back (TLFB) [45]. Interview-based assessment administered by trained study staff to measure opioid and other substance use at baseline and at 2-week intervals.

Demographics/clinical characteristics form. Chart abstraction from inpatient clinical record.

Treatment utilization tracking form. Investigator-created form used to track receipt of XR-NTX, clinical services and outreach contacts. Information was taken from clinical record abstraction, patient interviews and contact with other providers.

Intervention/comparator. Participants in both groups were prescribed a first dose of XR-NTX prior to inpatient discharge, following standard clinical procedures that included withdrawal management, a 7–10-day opioid-free period and at least one lead-in dose of oral naltrexone. Participants in TAU received standard referrals to continuing SUD care, including specific arrangements for ongoing treatment with XR-NTX. Participants in the YORS group also received standard referrals to TAU continuing SUD counseling, but with medication treatment delivered through YORS together with its other components.

Research follow-ups were conducted in person or by telephone when participants were not able to attend in person, and supplemented through patient clinical records with permission. The following components were included in the YORS intervention:

1 Home-delivery of XR-NTX: home visits were scheduled every 3–4 weeks to allow a margin of error for monthly dosing, and conducted by a team consisting of a nurse, therapist and/or treatment assistant. Medication was brought to the patient's home or other community location. A private, convenient location was selected for administration of the gluteal injection. A brief counseling session based on typical medication management [46] was conducted with the patient (and the family if available) or a longer counseling session if the patient had not been attending clinic-based treatment, with increased emphasis on achieving XR-NTX dosing as a primary treatment goal.
2 Family: the family component was delivered by a specially trained and supervised study therapist, beginning during the inpatient stay. It consisted of three primary sessions focused on OUD education and family treatment planning, development of a written family

treatment agreement with strategies to be pursued in the event of non-adherence or relapse, strategies for family promotion of medication adherence, progress assessment and behavioral skills relevant to family goals. Sessions were designed for in-person delivery, with the first session during the inpatient episode and subsequently spaced out over several weeks during the outpatient period, but could be delivered opportunistically whenever participants were available, including by telephone. Brief family coaching communications by telephone or text continued throughout the intervention.

3 Contingency management: gift cards with cash value were given according to the following escalating reinforcement schedule: dose 0 (inpatient, as a 'priming' reinforcer): $20; outpatient dose 1: $25; dose 2: $30; dose 3: $35; dose 4: $40; dose 5: $45; dose 6: $50; bonus for receiving all seven doses: $50. Due to the infrequent opportunities for reinforcement, a 'reset' protocol was not used; that is, if a dose was missed, then the incentive schedule resumed at the level at which it was interrupted.

4 Assertive outreach: this incorporated frequent outreach to patients and families with treatment reminders, progress check-ins, scheduling for medication and other sessions and case-management regarding insurance and other logistics. Staff members used the patient's preferred mode of communication (typically telephone or text messaging), and were persistent until contact was made. Group texts were used as a way to promote open communication with patients and TSOs. Patients were contacted at least weekly and TSOs at least every other week with more intensive engagement at any sign of non-adherence or relapse.

The components were often synergistic (e.g. trying to schedule home visits for times when TSOs would be present in order to utilize their influence, and using text communication to remind participants of available CM incentives). For further details, see the treatment manual in the Supporting information.

Data analyses. Primary and secondary outcomes were calculated using multiple, binary logistic or Cox proportional--hazards regression models. Inclusion of covariates was determined by entering baseline characteristics into individual regression models. Variables with $P < 0.30$ were included in an aggregate model with group assignment. Variables with $P < 0.10$ were included as covariates in the final regression model and were considered significant at $P < 0.10$. In cases where a zero cell count in contingency tables violated the assumption of binary logistic regression, data modification procedures suggested by Dureh [47] were used. Missing UDS data was imputed as positive, and missing XR-NTX doses (e.g. unable to verify delivery by other providers) or intensive outpatient (IOP) sessions were imputed as not received. Missing baseline data were excluded from sample characteristic analyses.

RESULTS

Three participants were excluded from the analyses for withdrawing consent or incarceration for more than 75% of the study window (see Fig. 1). Characteristics of the analyzed sample ($n = 38$; 18 YORS, 20 TAU) are presented in Table 1. Baseline characteristics did not vary significantly by group assignment, except for self-reported days of cocaine use.

YORS intervention delivery

Patient-designated TSOs ($n = 21$) were primarily parents (81%), and less frequently other family members, romantic partners or sponsor/mentors. On average, YORS participants received 2.5 family sessions total and 1.6 contacts/week and TSOs received 1.1 contacts/week.

Receipt of XR-NTX doses

Six participants did not receive a dose of XR-NTX as inpatients because of leaving prematurely against advice. Of those that did not, one of one in the YORS condition and none of five in TAU subsequently received at least one dose as outpatients. Participants in the YORS condition received a greater number of outpatient XR-NTX doses (mean = 4.28) compared to those in TAU [mean = 0.70, $P < 0.01$ (see Table 2 for summary of main outcomes)]. Results of the linear regression indicated a main effect of treatment group on receipt of outpatient XR-NTX doses ($P < 0.001$). Similarly, results of a binary logistic regression indicated a main effect of group assignment on receiving all prescribed doses ($P < 0.01$). Figure 2 shows the distribution of receipt of doses. Overall missing/unconfirmed data of XR-NTX receipt was 10.53% (YORS = 11.11% versus TAU = 10.00%), imputed as not received.

Opioid relapse

Participants in the YORS group compared to those in TAU had lower rates of relapse at 24 weeks (61 versus 95%, $P < 0.01$). Results of a binary logistic regression indicated a main effect of group on opioid relapse ($P < 0.05$). Overall rates of missing data for opioid use were 44% for UDS (YORS 26% versus TAU 60%) and 12% for self-report (11% for both UDS and self-report in the same reporting period). Survival analyses revealed group differences in time to opioid relapse with TAU participants being more likely to relapse over time compared to YORS participants [hazard ratio (HR) = 2.72, 95% CI = 1.26–5.88; see

Table 1 Baseline sample characteristics.

	Overall (n = 38)	*YORS (n = 18)*	*TAU (n = 20)*	*P*
Demographics	Presented as mean (SD) or percentage (*n*)			
Age, years	23.4 (2.3)	23.1 (2.3)	23.7 (2.4)	0.40
% Males	65.8% (25)	66.7% (12)	65.0% (13)	0.91
African American/black	5.3% (2)	5.6% (1)	5.0% (1)	0.96
Caucasian/white	94.7% (36)	94.4% (17)	95.0% (19)	0.96
Hispanic/Latin	7.9% (3)	5.6% (1)	10.0% (2)	0.61
Subjective SES rank[a]	3.9 (1.4)	3.9 (1.3)	3.9 (1.5)	0.99
Months worked in past year	7.1 (4.0)	6.6 (4.4)	7.5 (3.7)	0.49
% Medicaid (public insurance) coverage	84.2% (32)	94.4% (17)	75.0 (15)	0.10
Severity measures				
No. overdoses	3.1 (5.8)	4.2 (8.1)	2.2 (2.5)	0.29
Years of opioid use	5.4 (2.6)	5.3 (2.8)	5.5 (2.4)	0.75
% Began using under 18 years old	39.5% (15)	38.9% (7)	40.0% (8)	0.94
% Life-time heroin use	100% (38)	100% (18)	100% (20)	1
% With history of injection drug use	71.1% (27)	61.1% (11)	80.0% (16)	0.20
Past treatment				
No. of prior residential treatment episodes	2.8 (2.7)	1.9 (2.6)	3.7 (2.6)	0.052
% Previously treated with XR-NTX[b]	44.4% (16)	38.9% (7)	50.0% (9)	0.50
% Previously treated with buprenorphine	55.3% (21)	38.9% (7)	70.0% (14)	0.054
% Previously treated with methadone	15.8% (6)	22.2% (4)	10.0% (2)	0.30
Patient use at baseline				
% Who self-reported use in the past 28 days				
Heroin	92.1% (35)	88.9% (16)	95.0% (19)	0.48
Other illicit opioids	23.7% (9)	27.8% (5)	20.0% (4)	0.57
Cannabis	47.4% (18)	61.1% (11)	35.0% (7)	0.11
Cocaine	63.2% (24)	61.1% (11)	65.0% (13)	0.80
Alcohol	23.7% (9)	27.8% (5)	20.0% (4)	0.57
Benzodiazepines	21.1% (8)	33.3% (6)	10.0% (2)	0.08
No. of self-reported days of use in the past 28 days				
Heroin	21.2 (8.6)	19.1 (9.7)	23.1 (7.1)	0.15
Other illicit opioids	3.4 (7.9)	5.1 (10.3)	1.9 (4.8)	0.22
Cannabis	7.6 (11.2)	10.6 (12.7)	5.0 (9.2)	0.13
Cocaine	9.4 (11.6)	5.4 (10.0)	12.9 (12.0)	0.045
Alcohol	1.7 (5.2)	2.1 (6.6)	1.4 (3.6)	0.72
Benzodiazepines	1.4 (4.7)	1.2 (2.0)	1.6 (6.3)	0.78

SES = socio-economic status; XR-NTX = extended-release naltrexone; UDS = urine drug screen; MOUD = medications for opioid use disorder: methadone, buprenorphine and extended-release naltrexone; YORS = youth opioid recovery support; TAU = treatment-as-usual; SD = standard deviation. Five participants reported treatment with MOUD in the 28 days before coming inpatient (three buprenorphine and two methadone), who were not included in this table. Use of illicit buprenorphine ($n = 3$) and methadone ($n = 4$) was counted as other illicit opioids. [a]Four participants were excluded from analysis on baseline subjective SES due to missing data. [b]Two participants excluded on previous XR-NTX treatment due to missing data.

Fig. 3]. No covariates were identified for inclusion. The relative hazard assumption was not violated; that is, there was no significant treatment × time interaction and the HR was constant over time. In a Kaplan–Meier analysis of estimated time to relapse, the YORS group had greater estimated median survival time (9.0 weeks, 95% CI = 2.1–5.9) compared to the TAU group (3.0 weeks, 95% CI = 1.5–4.5).

Other treatment outcomes

Participants in the YORS condition had fewer days of opioid use over 24 weeks [mean = 23.61, standard deviation (SD) = 21.34] compared to TAU (mean = 51, SD = 35.21, $t_{(36)} = 2.86$, $P < 0.01$). Results of a linear regression testing the effect of group on days of opioid use was significant ($F_{(2,\ 35)} = 6.19$, $P < 0.01$, $R^2 = 0.26$) after controlling for days of cocaine use at baseline as a covariate. However, survival analyses revealed no group differences on opioid abstinence over time (that is, time to first opioid use), and only one participant maintained total opioid abstinence by 24 weeks. Receipt of XR-NTX correlated both with opioid relapse ($r = -0.60$, $P < 0.001$) and days of opioid use ($r = -0.49$, $P = 0.002$), such that as medication receipt increased, opioid relapse and overall days of use decreased.

Group status did not significantly predict utilization of IOP treatment, self-reported cannabis, cocaine,

Table 2 Summary of outcomes at 24 weeks.

	YORS mean (SD) or % (n)	*TAU mean (SD) or % (n)*	*Unadjusted regression (IV = group assignment)*				*Adjusted regression (IV = group assignment)*			
			B	*SE B*	*β*	*P-value*	*B*	*SE B*	*β*	*P-value*
Number of XR-NTX doses	4.3 (2.3) (n = 18)	0.7 (1.2) (n = 20)	−3.58	0.58	−0.72	< 0.001	–	–	–	–
Opioid relapse (yes/no)	61.1% (11) (n = 18)	95.0% (19) (n = 20)	−2.49	1.13	–	< 0.05	–	–	–	–
Received all prescribed doses (yes/no)	44.4% (8) (n = 18)	0.0% (0) (n = 20)	3.46	1.12	–	< 0.01	–	–	–	–
Number of relapses events per individual	1.6 (2.1) (n = 18)	4.2 (2.7) (n = 20)	2.64	0.79	0.49	< 0.01	2.17[c]	0.81[c]	0.40b[c]	< 0.05[c]
Opioid days of use (using imputation rule)	23.6 (21.3) (n = 18)	51.0 (35.2) (n = 20)	27.39	9.58	0.43	< 0.01	21.30[c]	9.79[c]	0.34[c]	< 0.05[c]
Days of IOP attendance	15.2 (18.7) (n = 18)	18.3 (21.0) (n = 20)	3.13	6.49	0.08	0.63	–	–	–	–
Self-reported days of cannabis use	13.4 (16.5) (n = 16)	9.8 (22.7) (n = 19)	−3.56	6.83	−0.09	0.60	0.30[d]	6.43[d]	0.01[d]	0.96[d]
Self-reported days of cocaine use	8.8 (14.9) (n = 16)	15.1 (37.0) (n = 17)	6.31	9.94	0.11	0.53	−11.67[e]	9.50[e]	−0.21[e]	0.53[e]
Self-reported days of benzodiazepine use	3.8 (10.9) (n = 16)	0.3 (0.7) (n = 17)	−3.52	2.64	−0.23	0.19	−3.14[f]	2.14[f]	−0.21[f]	0.15[f]
Self-reported days of alcohol use	6.1 (8.3) (n = 16)	6.5 (21.2) (n = 17)	0.41	5.66	0.01	0.94	1.24[g]	5.37[g]	0.04[g]	0.82[g]

TAU = treatment-as-usual; XR-NTX = extended-release naltrexone; IV = independent variable; IOP = intensive outpatient; YORS = youth opioid recovery support. [a]Alternatively, months of high severity use (≥ 10 days within a 28-day period). [b]All baseline characteristics listed in Table 1 were entered into the regression model as possible covariates. Only regressions for which covariates were identified (i.e. $P < 0.1$) were adjusted. [c]Adjusted for baseline cocaine use; [d]adjusted for baseline marijuana use; [e]adjusted for baseline cocaine use and insurance status; [f]adjusted for baseline benzodiazapine use and ethnicity; [g]adjusted for baseline alcohol use;

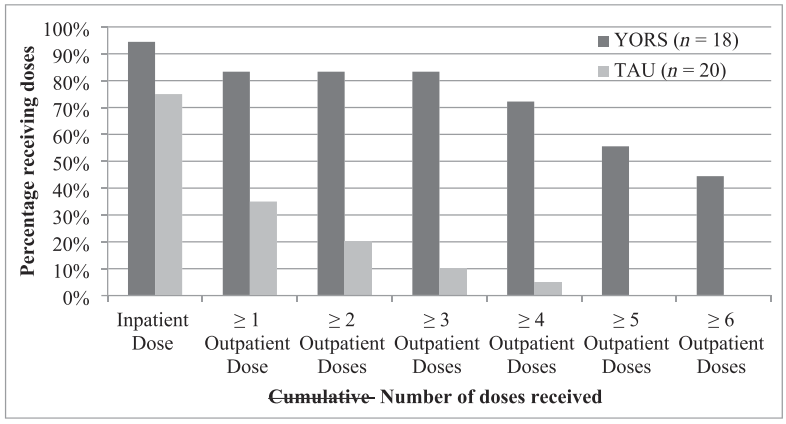

Figure 2 Histogram of cumulative extended-release naltrexone (XR-NTX) dose receipt. TAU = treatment-as-usual; YORS = youth opioid recovery support

benzodiazepine or alcohol use. Fourteen patients (36.7%) were readmitted to residential/inpatient SUD treatment (nine YORS, five TAU).

DISCUSSION

This small pilot RCT supports the efficacy of YORS, a multi-component assertive intervention for OUD in young adults. Positive outcomes were observed for the primary targets of medication adherence and opioid relapse. Compared to TAU, YORS participants received significantly more doses of XR-NTX, lower rates of opioid relapse at both 12 and 24 weeks and fewer overall days of opioid use. Although the majority of YORS participants had relapsed by the end of the 24 weeks, their trajectory of time to relapse was substantially delayed compared to TAU.

A number of factors seemed to play a role in the success of the YORS intervention. Home delivery often helped to

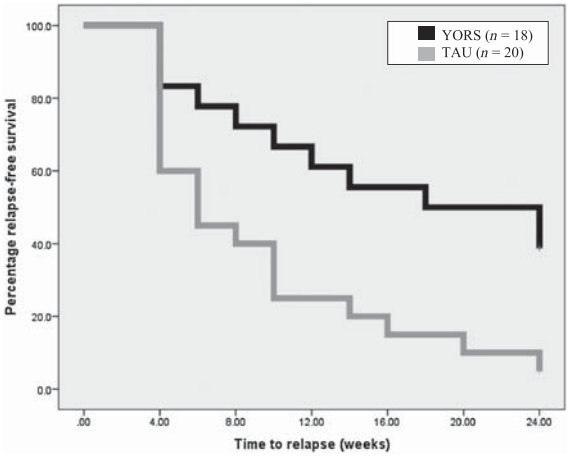

Figure 3 Kaplan–Meier survival curve of opioid relapse. TAU = treatment-as-usual; YORS = youth opioid recovery support

overcome the multiple barriers to clinic-based care, such as lack of transportation, fixed scheduling, competing activities and lack of participation in SUD treatment programming. Home delivery also seemed to lower the threshold of needed motivation and helped to overcome ambivalence, especially after missing a scheduled dose date or after a lapse to opioid use.

The impact of family involvement (i.e. TSOs) was often quite dramatic. These influences were emphasized in the family sessions. Depending on the clinical status of the individual patient, these included: communication skills, applying leverage strategically, prioritizing medication adherence, prioritizing swift return to treatment after relapse and others. For the most part, young adults agreed to open and collaborative communication between themselves, treatment staff and TSOs. With expectations and agreements in place from the beginning, the therapist was poised to navigate circumstances in which the short-term stated intentions of patients (e.g. avoiding or declining XR-NTX doses) and the natural parental guidance of families (e.g. insistence on XR-NTX doses) conflicted. When family influence prevailed, as it often did, the young adult patients would usually acknowledge in retrospect, perhaps reluctantly, that things had turned out for the better. Our conclusion is that, although nuanced, respecting the confidentiality of youth, promoting youth self-efficacy and emerging autonomy and engaging families are all actually quite compatible with one another.

Although we encouraged young adult patients to engage in other treatment/recovery services and activities, we emphasized the primary goal of treatment as achieving medication doses. Promoting medication adherence as the 'bottom line' provided a simple, concrete objective so that families were able to apply their leverage in a more targeted manner. Patient trajectories were markedly non-linear, with waxing/waning levels of motivation and treatment engagement as the rule. For TAU participants, flagging treatment engagement often led to dropout and relapse, whereas for YORS participants the assertive outreach approach to engagement was frequently able to re-establish care, prevent a lapse from progressing to a full relapse and prevent disaster. Just as important as preventing relapse, or perhaps even more important, was return to treatment following relapse. Encouraging frustrated family members to conceptualize OUD as a chronic remitting/relapsing illness was helpful during chaotic trajectories. By coaching TSOs to play the 'long game' and 'pick your battles', they were able to stay more focused on re-engagement rather than giving in to their exasperation and giving up.

It is particularly notable how poorly the TAU group performed. During the course of 24 weeks they received very few outpatient XR-NTX doses (mean = 0.7), with nearly 75% relapse to opioids at 12 weeks and 95% relapse at 24 weeks. These outcomes seem considerably worse than those previously reported in standard treatment conditions [22]. One possibility is that these participants overall comprised a very high-severity cohort, as characterized by high rates of heroin and injection use, early onset of use, histories of relapse following prior treatment episodes including MOUD trials and with lower resources compared to other cohorts (e.g. 84% on Medicaid). Another consideration is that most previous reports have used cohorts recruited after outpatient treatment had been initiated, presumably indicating a substantially better prognosis, but the current TAU results were more similar to our previously reported outcomes among less selectively recruited 'all-comers' in acute residential treatment [23,24]. Many of these TAU patients never linked to any OP treatment at all, and those that did had poor retention. While the same was true for many YORS participants regarding clinic-based care, as an assertive, home-delivered intervention, YORS presumably helped to bridge that gap. Also of note is that despite the strong benefit of YORS in reducing opioid relapse and total days of use the rates of continuous opioid abstinence was very low in both groups, without significant difference, and although the relapse rate for YORS was much lower than for TAU it was still 61%. The results compare favorably to our previous small non-randomized case–series of home-based XR-NTX delivery, with mean = 4.3 doses over 6 months versus 2.3 doses over 4 months, but remain inferior to typical results of general adult treatment [48]. This highlights the particular vulnerability of this high-severity population of young adults for whom there is still considerable room for improvement.

Strengths of the study included randomization, comparison to a usual-care control group, focus upon the critical young adult target population and use of innovative programming to support MOUD adherence. Major limitations of the study include small sample size and extent of missing UDS data. As the missingness of UDS data was

imbalanced by group, the use of imputation probably biased the results in favor of the intervention. We limited assertive outreach for data collection in the TAU group so as not to create a confounding potential treatment effect. However, missingness of data in OUD research tends to correlate with negative outcomes. Further work is also needed to understand the relative contribution of the intervention's various components to determine whether all are needed for all patients. For example, CM anecdotally seemed to play more of a role for some patients than for others—some said that the incentives were small and not especially motivating, while others seemed to respond to reminders of monetary rewards with renewed motivation. If YORS continues to demonstrate efficacy over TAU in larger trials, it would be useful to perform economic analysis to assess the value of the intervention as a path to sustainability and dissemination outside research funding. It remains unclear whether successes can be sustained over the longer term, and whether a subset of patients could be stepped down successfully from the high-intensity intervention to more standard care, once stabilized. Future directions should include exploration of intervention fidelity, dose of contact, family-level outcomes and also incorporate the newly available extended-release buprenorphine to increase patient choice of treatment options and broaden appeal.

In summary, this pilot RCT provides preliminary evidence that an assertive community treatment model, including home delivery of XR-NTX, family engagement, assertive outreach and CM incentives for receipt of medication doses, is feasible and effective for the critical target population of young adults with OUD. It further highlights the importance of linkage from episodes of acute care to more enduring continuing care, and the need for expanded efforts to improve MOUD adherence.

Registration

This pilot randomized controlled trial is registered on clinicaltrials.gov (Identifier: NCT03306368; https://clinicaltrials.gov/ct2/show/NCT03306368).

Declaration of interests

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Author Contributions

Marc Fishman: Conceptualization; funding acquisition; investigation; methodology; project administration; resources; supervision. **Kevin Wenzel:** Conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources. **Hoa Vo:** Conceptualization; data curation; funding acquisition; investigation; methodology; project administration; resources; supervision. **Jared Wildberger:** Data curation; formal analysis; investigation. **Rachael Burgower:** Investigation; project administration.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Data S1. Supporting information.

