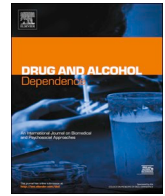




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Evaluation of a personally-tailored opioid overdose prevention education and naloxone distribution intervention to promote harm reduction and treatment readiness in individuals actively using illicit opioids

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ABSTRACT

Background: Opioid overdose prevention education and naloxone distribution (OEND) programs include information on general risk factors, overdose recognition, and naloxone utilization. This study evaluated a personally-tailored OEND (PTOEND) intervention designed to promote harm reduction and treatment readiness for illicit opioid users by also including education about personal overdose-risk factors and medication for opioid use disorder (MOUD).

Method: A secondary analysis of a randomized controlled trial testing a Peer recovery support service (PRSS) intervention, relative to Control, in adult illicit opioid users reporting treatment for an overdose in the prior 6 months. PTOEND, a 30-minute computer-guided intervention, was administered by a research assistant at the randomization visit to all participants (N = 80). Participants completed a telephone visit 3 weeks post-randomization (n = 74) to assess changes in opioid overdose/MOUD knowledge and treatment readiness. Participants completed in-person visits at 3 (n = 66), 6 (n = 58), and 12 (n = 44) months post-randomization to assess illicit opioid use and naloxone utilization (all time points) and overdose-risk behaviors (12 months). We conducted pre-post analyses of the impact of PTOEND controlling for the PRSS effect.

Results: PTOEND increased knowledge of overdose (79.8% to 81.5%, $p < 0.05$) and MOUD (66.9% to 75.0%, $p < 0.01$) and decreased perceived treatment barriers (2.1 to 1.9, $p < 0.01$); desire to quit all substances increased (7.2 to 7.8, $p = 0.05$). Self-reported opioid use was significantly decreased at each follow-up (all $p < 0.01$). Self-reported overdose-risk behaviors decreased significantly (6.2 to 2.4, $p < 0.01$). A majority of participants (65 %) reported naloxone utilization.

Conclusions: PTOEND may be effective for promoting harm reduction and treatment readiness.

1. Introduction

The majority of opioid overdose prevention education and naloxone distribution (OEND) programs reported in the literature have emphasized training participants in the recognition of, and appropriate response to, overdose, especially the use of naloxone to rescue people experiencing an overdose (Clark et al., 2014). Training on the administration of naloxone was necessary partly because the products available at the time required either syringe injection or assembly of an after-market intra-nasal atomization device. In recent years, the FDA has approved several naloxone delivery systems specifically designed for use by untrained people (e.g., Narcan® nasal spray, Evzio® auto-

injector) (Lewis et al., 2017; Strang et al., 2019), reducing the need for training on naloxone administration. Research suggests that naloxone is most likely to be utilized when distributed to individuals actively using opioids (Bennett et al., 2018). Because naloxone administration is no longer a complicated, multi-step process, we developed a personally-tailored (PTOEND) intervention for active illicit opioid users with less emphasis on the specifics of naloxone administration and more on education that could enhance the harm reduction effect and promote treatment readiness.

The PTOEND was designed to expand harm reduction by not only encouraging the use of naloxone but also educating the individual about his/her personal factors that increase risk for opioid overdose

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(OOD), including modifiable behaviors that increase risk. In addition, the PTOEND was designed to promote readiness for medication for opioid use disorder (MOUD), which is effective for preventing OODs (Laroche et al., 2019; Sordo et al., 2017) but is underutilized (Volkow and Wargo, 2018), in part due to inaccurate perceptions including misconceptions about its side effects and lack of efficacy (Peterson et al., 2010; Uebelacker et al., 2016; Zaller et al., 2009). Specifically, the PTOEND is designed to assess for, and correct, an individual's negative beliefs about MOUD. In a recent randomized trial comparing a Peer recovery support service (PRSS) to a Control condition (Winhusen et al., 2020), PTOEND was provided to all study participants. The present study is a secondary analysis of that randomized trial, designed to evaluate the impact of PTOEND on overdose/MOUD knowledge, treatment readiness, and harm reduction, controlling for the impact of the randomized PRSS intervention.

2. Methods

2.1. Participants

Participants were enrolled in a randomized trial evaluating the effect of a 20-minute telephone PRSS intervention relative to a Control condition; all participants (N = 80) received PTOEND (Winhusen et al., 2020). Participants for the trial were recruited through various methods including advertisements, flyers, and word-of-mouth in Cincinnati, Ohio. All participants were given a thorough study explanation and signed an informed consent form that was approved by the University of Cincinnati (UC) Institutional Review Board. Eligible participants were at least 18 years of age and reported treatment for an OOD within the past 6 months. To be eligible, participants were required to have an opioid-positive urine drug screen (UDS), score as "high risk" for heroin and/or non-medical use of prescription opioids on the NIDA modified ASSIST (i.e., ≥ 27), be willing to have their PRSS intervention audio recorded and rated, and have access to a phone. Participants were excluded from the study if they were currently engaged in substance use disorder treatment or unlikely to complete the study (e.g., probable incarceration, residence > 40 miles from site, unable to provide reliable locators, etc.).

2.2. PTOEND

2.2.1. Intervention

PTOEND is a computer-guided intervention which utilizes REDCap (Harris et al., 2019) to complete assessments and automatically generate personally-tailored feedback reports; the use of REDCap, which is an NIH-supported, secure, web-based research data platform, limits the technological costs of the intervention to the cost of an internet connection and a computer tablet. PTOEND is a 30-minute intervention in which an interviewer: 1) administers REDCap surveys to assess an individual's OOD/MOUD knowledge and opioid overdose risk factors; and 2) reviews the personal feedback reports with the recipient. OOD/MOUD knowledge was assessed with the Opioid Overdose and Treatment Awareness Survey (OOTAS); information about the survey is published elsewhere (Winhusen et al., 2016). In brief, the OOTAS assesses knowledge about OOD and MOUD. The OOTAS is comprised of 4 sections: 1) OOD risk factors; 2) signs of an OOD; 3) how to respond to an OOD; and 4) misconceptions about MOUD (Winhusen et al., 2016). The first 3 sections include only evidence-based items supported by a literature review, while items for the fourth section were based on both a literature review and on input from the medical staff of the UC-affiliated methadone program. The reports generated from the OOTAS, the "Opioid Overdose Information Report" (see Supplemental Figure 1 for an example report) and the "Medication Assisted Treatment Report" (see Supplemental Figure 2 for an example report) provide feedback on the questions answered incorrectly by the participant to provide

targeted knowledge enhancement, including the correction of misconceptions about MOUD.

The individual's opioid overdose risk factors were assessed with the Personal Opioid-Overdose Risk Survey (PORS); information about the survey is published elsewhere (Winhusen et al., 2016). In brief, the PORS includes risk factors for which there is documented evidence and scoring for each item was based on the strength of the evidence that the factor increases OOD risk (Winhusen et al., 2016); the "Personal Overdose Risk Factors Report" (see Supplemental Figure 3 for an example report) is generated from the participant's responses to the PORS. All three personally-tailored feedback reports were reviewed with the participant by a trained research assistant. All participants also received a Narcan® Nasal Spray kit (which includes two single-dose spray bottles), information about local MOUD providers, and standard information about overdose and MOUD which included the SAMHSA publications "Opioid Overdose Prevention Toolkit: Safety Advice for Patients and Family Members" (Substance Abuse and Mental Health Services Administration, 2016b), "Recovering from Opioid Overdose" (Substance Abuse and Mental Health Services Administration, 2016a), and "Medication-Assisted Treatment for Opioid Addiction: Facts for Families and Friends" (Substance Abuse and Mental Health Services Administration, 2011).

2.2.2. Training

One of the authors (F.K.) trained bachelor's-level research staff on the administration of all study assessments, including those used to tailor the intervention (PORS, OOTAS). Trainees received a comprehensive training manual. Training sessions provided didactic training on the background and rationale of the study, basic listening strategies, a review of the three personalized reports provided to participants, and specific instruction on delivery of the PTOEND. Training also included role playing sessions with immediate feedback from the trainer and recorded slide presentations for review prior to the live training session. Training on the PTOEND took approximately 2.5 h to complete.

2.3. Procedures

All in-person visits were completed at the research site, which was physically co-located with a substance use disorder treatment program. After signing the informed consent form, the study candidate completed screening and baseline assessments. Eligible participants were randomized to the PRSS or Control condition in a 1:1 ratio. All participants received the PTOEND intervention during the randomization visit. Participants in the PRSS arm were scheduled to complete the telephone intervention within 2 weeks of randomization. Participants completed a telephone visit 3 weeks after randomization and in-person visits at 3, 6, and 12 months after randomization. Study participants completing screening and attending all three in-person follow-up visits were reimbursed \$200 for their time and travel. Participants completing the telephone visit 3 weeks post-randomization received an additional \$20 reimbursement.

2.4. Measures

2.4.1. Knowledge about OOD and MOUD

As described above, the OOTAS knowledge evaluation (Winhusen et al., 2016) was administered at baseline to generate the personally-tailored Opioid Overdose Information and MOUD Reports. The OOTAS was also administered during the Week 3 follow-up call to evaluate the degree to which participants gained and retained knowledge about the information presented in the reports. The difference from Baseline to Week 3 in OOD knowledge (including OOD risk factors, signs of an OOD, and how to respond to an OOD) and MOUD knowledge (misconceptions about MOUD) were the measures of interest.

2.4.2. Treatment readiness

The Barriers to Treatment Inventory (BTI) is a 25-item, 5-point Likert-scale questionnaire with 7 internally consistent subscales relating to Absence of Problem, Negative Social Support, Fear of Treatment, Privacy Concerns, Time Conflict, Poor Treatment Availability, and Admission Difficulty (Kelly et al., 2014; Rapp et al., 2006). Greater BTI scores represent a higher degree of barriers to starting treatment (range: 1–5). The BTI was administered at baseline and during the Week 3 follow-up call; change in average score of all items was the outcome of interest. Participants' commitment to abstinence from illicit substances was assessed with the Thoughts About Abstinence (TAA) measure (Hall et al., 1991). This measure assesses the participant's desire to quit drugs (0 = "No Desire to Quit" to 9 = "Greatest Desire to Quit"), expected success in quitting (0 = "Very Low Chance of Success" to 9 = "Very High Chance of Success"), and estimated difficulty in avoiding relapse (0 = "Very Easy" to 9 = "Very Difficult"). The TAA was completed at baseline and during the Week 3 follow-up call to evaluate the change in each of the 3 subscale scores.

2.4.3. Harm reduction

2.4.3.1. Illicit opioid use. At 3-, 6-, and 12-month follow-up visits, urine samples were collected using temperature monitoring and the validity of urine samples was checked with the use of a commercially available adulterant test. Urine samples were tested for the following opioids: buprenorphine, fentanyl, opiates, methadone, and oxycodone; a positive buprenorphine/ methadone result was not scored as illicit opioid use for individuals with verified MOUD enrollment. Self-report of past month opioid use was assessed using the Timeline Follow-back (TLFB) method (Fals-Stewart et al., 2000), which is a widely employed and well-validated method.

2.4.3.2. Modifiable overdose-risk behaviors. As described above, the PORS was administered at baseline to generate the Personal Overdose Risk Factors Report. The PORS was administered again at the 12-month follow-up visit to evaluate change in the participant's risk of opioid overdose. The 13-item PORS includes 4 risk factors that are not readily modifiable by the individual (i.e., decreased liver function, depressive symptoms, years of opioid use, number of prior overdoses); the change in overdose-risk behaviors was based on the total of the 9 items that were potentially modifiable.

2.4.3.3. Naloxone utilization. At 3-, 6-, and 12-month follow-up visits, participants were asked whether the Narcan® Nasal Spray kit provided at randomization had been used, and if so, whom it had been used for (self and/or somebody else).

2.5. Data analysis

We used linear mixed model regression analyses to evaluate whether follow-up data demonstrated improvement from baseline. Random intercept mixed models were used in order to account for between-participant and within-participant variability. The analyses included the randomized treatment group (PRSS vs. Control) as a covariate, to account for the PRSS effect. Because of the relatively small sample size in this pilot trial, we did not attempt to control for additional covariates. Pre-post analyses could not be conducted for illicit-opioid positive UDS results because an opioid-positive UDS was required for study eligibility (i.e., 100 % of participants were in the category of UDS positive at baseline). Because there were non-completers for each of the research visits, we conducted analyses to evaluate the degree to which the 3-week, 3-month, 6-month, and 12-month completer samples differed at baseline from the respective non-completer samples in order to help determine whether any changes from baseline were due to baseline differences between completers and non-completers. These analyses used Pearson's chi-squared tests, Fisher's exact tests, and Wilcoxon

rank-sum tests, depending on the data type and the compatibility of the data with test assumptions.

3. Results

3.1. Participants

Over 90 % of participants were recruited from flyers handed out at a syringe exchange program and 91 % of randomized participants reported intravenous opioid use. The sample was approximately 55 % male and 12.5 % African American; participants were 39 years of age on average (SD = 11.4). On average, the participants reported 14.3 years of lifetime opioid use (SD = 11.4), 6.7 lifetime overdoses (SD = 7.2), and 26.5 days of opioid use (SD = 4.3) in the prior 28 days. The completer and non-completer samples did not differ significantly on these baseline characteristics. The Week 3 follow-up call was completed by 74 (93 %) participants, the Month 3 visit was completed by 66 (83 %) participants, the Month 6 visit was completed by 58 (73 %) participants, and the Month 12 visit was completed by 44 (55 %) participants. Of the 44 participants who completed the 12-month visit, one participant missed month 3 and one participant missed month 6.

3.2. OOD/MOUD knowledge

Week 3 completers and non-completers did not differ significantly on OOD/MOUD knowledge at baseline (Supplemental Table 1). As can be seen in Table 1, there was a statistically significant increase from baseline to the Week 3 follow-up call in OOD knowledge, from a mean baseline score of 79.8 % to a mean week 3 score of 81.5 % correct ($p = 0.03$), and MOUD knowledge from a mean baseline score of 66.9 % to a mean week 3 score 75.0 % correct ($p < 0.01$).

3.3. Treatment readiness

Week 3 completers and non-completers did not differ significantly on treatment readiness as measured by the BTI or TAA at baseline (Supplemental Table 1). From baseline to the Week 3 follow-up call, there was a statistically significant reduction in overall BTI score from 2.1 to 1.9 ($p < 0.01$) indicating a decrease in the perceived barriers to treatment. As can be seen in Table 1, there was a significant decrease in four of the seven BTI subscales, including: Fear of Treatment (from 2.1 to 1.8, $p = 0.02$), Time Conflict (from 2.4 to 2.1, $p = 0.01$), Poor Treatment Availability (from 2.2 to 1.9, $p < 0.01$), and Admission Difficulty (from 2.9 to 2.6, $p < 0.01$). From baseline to the Week 3 follow-up call, there was an increase in the TAA Desire to Quit All Drugs subscale that did not reach statistical significance (from 7.2 to 7.8, $p = 0.05$). A significant increase was observed in expected success in quitting (from 6.6 to 7.5, $p < 0.01$) and a significant decrease was found in expected difficulty in avoiding relapse (from 7.5 to 6.8, $p = 0.02$).

3.4. Harm reduction

3.4.1. Illicit opioid use

Completers and non-completers did not differ significantly on baseline days of opioid use (Supplemental Table 2). Self-reported past-28-day opioid use was significantly decreased from baseline at the 3 month (26.6 to 19.33, $p < 0.0001$), 6 month (26.4 to 19.2, $p < 0.0001$) and 12 month (26.1 to 16.8, $p < 0.0001$) follow-ups. Opioid-positive UDS results remained high (≥ 85 %) throughout the study; as noted in data analysis, the UDS data could not be analyzed due to study eligibility criterion requiring an opioid-positive UDS at baseline.

3.4.2. OOD-risk behaviors

Completers and non-completers did not differ significantly on baseline OOD-risk behaviors (Supplemental Table 3). As can be seen in

Table 1
Knowledge and treatment readiness results pre- and post-PTOEND intervention, with regression estimates and 95 % confidence intervals.

	Pre-intervention (n = 74)	Post-intervention (n = 74)	Intercept	Time (95 % confidence interval), p-value	PRSS* group (95 % confidence interval)
Knowledge (% answers correct)					
Opioid Overdose	79.8 % (6.6 %)	81.5 % (7.1 %)	0.790	0.018 (0.001, 0.034), p = 0.03	0.014 (-0.012, 0.040)
MOUD ^a	66.9 % (24.2 %)	75.0 % (19.6 %)	0.679	0.080 (0.035, 0.126), p < 0.01	-0.017 (-0.107, 0.072)
Treatment Readiness					
BTI ^b – Absence of Problem	1.6 (0.6)	1.4 (0.5)	1.61	-0.13 (-0.27, 0.000), p = 0.05	-0.13 (-0.32, 0.06)
BTI ^b – Negative Social Support	1.8 (0.6)	1.6 (0.6)	1.81	-0.12 (-0.27, 0.04), p = 0.14	-0.12 (-0.33, 0.10)
BTI ^b – Fear of Treatment	2.1 (0.7)	1.8 (0.7)	2.15	-0.21 (-0.38, -0.03), p = 0.02	-0.25 (-0.52, 0.02)
BTI ^b – Privacy Concerns	3.0 (1.2)	3.0 (1.2)	3.10	0.03 (-0.20, 0.25), p = 0.80	-0.14 (-0.62, 0.34)
BTI ^b – Time Conflict	2.4 (1.0)	2.1 (1.0)	2.46	-0.29 (-0.53, -0.06), p = 0.01	-0.23 (-0.61, 0.16)
BTI ^b – Poor Treatment Availability	2.2 (0.7)	1.9 (0.7)	2.24	-0.26 (-0.44, -0.09), p < 0.01	-0.15 (-0.42, 0.12)
BTI ^b – Admission Difficulty	2.9 (0.9)	2.6 (1.1)	2.84	-0.31 (-0.55, -0.07), p < 0.01	0.07 (-0.31, 0.45)
BTI ^b Total	2.1 (0.5)	1.9 (0.5)	2.15	-0.16 (-0.28, -0.05), p < 0.01	-0.14 (-0.32, 0.03)
TAA ^c -Desire to quit drugs	7.2 (2.4)	7.8 (2.0)	7.40	0.56 (-0.01, 1.13), p = 0.05	-0.36 (-1.19, 0.48)
TAA ^c - Expected success	6.6 (2.4)	7.5 (1.9)	6.53	0.90 (0.28, 1.53), p < 0.01	0.12 (-0.67, 0.90)
TAA ^c - Expected difficulty	7.5 (2.3)	6.8 (2.6)	7.33	-0.72 (-1.32, -0.12), p = 0.02	0.44 (-0.49, 1.36)

^a Medication for Opioid Use Disorder; ^b Barriers to Treatment Inventory (range: 1–5); ^c Thoughts about Abstinence (range: 0–9); ^d W = Wilcoxon; *randomization to Peer Recovery Support Service group was considered a nuisance covariate; the estimate of interest is “time”.

Table 3, participants scored significantly higher on overdose-risk factors at baseline relative to the 12-month visit (6.2 vs. 2.4, $p < 0.0001$). As can also be seen, there was a significant decrease in five risky behaviors including: escalating opioid dosage (86.4 % vs. 15.9 %, $p < 0.001$), injecting opioids (88.6 % vs. 61.4 %, $p < 0.001$), benzodiazepine co-use (31.8 % vs. 16.3 %, $p = 0.04$), alcohol co-use (27.3 % vs. 11.4 %, $p < .001$), and following abstinence with the same level of use (27.3 % vs. 9.3 %, $p < 0.001$).

3.5. Naloxone utilization

By the 12-month follow-up visit, the majority of participants reported utilizing the study-provided naloxone kit. Of the 66 participants who provided naloxone utilization data, 43 (65 %) reported that the kit had been used; 37 (86 %) of those reporting kit use reported that the kit was used on someone else and 7 (16 %) of those reporting kit use reported that the kit had been used on themselves.

4. Discussion

This secondary analysis evaluated the impact of a PTOEND intervention for individuals with active illicit opioid use who reported having experienced an OOD within the prior 6 months. The study results suggest that the 30-min, computer-guided PTOEND may be effective as a harm reduction intervention and in increasing OOD/MOUD knowledge and treatment readiness.

Similar to OEND programs in the published literature, PTOEND was designed to increase knowledge about OOD risk factors, signs of an OOD, and how to respond appropriately to an OOD including naloxone utilization (Clark et al., 2014). Consistent with results evaluating other OEND programs, PTOEND significantly increased OOD knowledge (Clark et al., 2014). In the present study, 65 % of participants reported

utilizing the study-provided Narcan® Nasal Spray kit during the 1-year follow-up period. This proportion is higher than the proportion reported in prior research. An analysis of data from 2006 to 2015 found a 1-year naloxone refill rate of 11–23 % (Bennett et al., 2018). A systematic review of studies evaluating naloxone distribution programs reported that kit utilization ranged from 0% to 67 % with a median of 11 % (McDonald and Strang, 2016). The higher proportion of kit use reported in the present study could be due to several factors. First, the present study included systematic follow-up visits during which utilization of the Narcan® Nasal Spray kit was assessed whereas many prior studies have relied upon participants spontaneously returning for naloxone refills (McDonald and Strang, 2016). Second, the present study provided Narcan® Nasal Spray kits, which are easier to administer relative to earlier incarnations of take-home naloxone, which required intramuscular injection or assembly of an “improvised” (not FDA-approved) nasal atomizer device. Third, the PTOEND intervention may be more effective in promoting naloxone utilization relative to other OEND programs.

The PTOEND intervention evaluated in the present study differed from OEND programs in the published literature by expanding OEND for active illicit opioid users to include information about MOUD and educating the individual about his/her specific OOD risk factors. The study results suggest that the intervention significantly increased MOUD knowledge and reduced OOD risk behaviors. This is a potentially important finding given that the study participants were at heightened risk for OOD, with 100 % having experienced a prior OOD and 91 % being active injection opioid users. Pre-post analyses performed on seven OOD risky behaviors revealed significant decreases in five (escalating opioid dosage, injecting opioids, benzodiazepine co-use, alcohol co-use, and following abstinence with the same level of use) but not in two others: other drug co-use, for which there was a decrease that did not reach statistical significance, and testing opioids before use, for

Table 2
Self-reported illicit opioid use in prior 28 days results pre- and post-PTOEND intervention, with regression estimates and 95 % confidence intervals.

Baseline use days, m(SD)	Endpoint use days, m(SD)	Intercept	Time (95 % confidence interval), p-value	PRSS* group (95% confidence interval)
Month 3 Endpoint (N = 65^a)				
26.6 (4.5)	19.3 (11.7)	25.48	-7.17 (-9.71, -4.64), p < 0.0001	2.12 (-0.89, 5.13)
Month 6 Endpoint (N = 58)				
26.4 (4.7)	19.2 (10.7)	26.43	-7.36 (-9.97, -4.76), p < 0.0001	0.21 (-2.47, 2.90)
Month 12 Endpoint (N = 44)				
26.1 (5.4)	16.8 (12.9)	26.04	-9.77 (-12.83, -6.71), p < 0.0001	0.99 (-2.16, 4.14)

^a 1 of the 66 participants attending the Month 3 visit did not provide self-report substance use data.

* randomization to Peer Recovery Support Service group was considered a nuisance covariate; the estimate of interest is “time”.

Table 3
Opioid overdose-risk behaviors as a function of time.

	Baseline	Month 12	Statistical Test from Pre-Post Regression
Escalating Opioid Dosage, n, %	38 (86.4 %)	7 (15.9 %)	$\chi^2(1) = 47.14, p < 0.0001$
Injecting Opioid, n, %	39 (88.6 %)	27 (61.4 %)	$\chi^2(1) = 15.87, p < 0.0001$
Benzodiazepines Co-Use, n, %	14 (31.8 %)	7 (16.3 %)	$\chi^2(1) = 4.45, p = 0.0349$
Alcohol Co-Use, n, %	12 (27.3 %)	5 (11.4 %)	$\chi^2(1) = 12.72, p = 0.0004$
Other Drug Co-Use, n, %	34 (77.3 %)	30 (68.2 %)	$\chi^2(1) = 2.60, p = 0.11$
Testing Opioid before Use ^a , n, %	13 (29.5 %)	13 (29.5 %)	$\chi^2(1) = 0.13, p = 0.72$
Following Abstinence with Same Level of Use, n, %	12 (27.3 %)	4 (9.3 %)	$\chi^2(1) = 19.47, p < 0.0001$
Enrolled in Methadone or Suboxone Treatment ^a , n, %	0 (0.0 %)	14 (31.8 %)	– ^b
> 4 Alcoholic Drinks/Day, n, %	5 (11.4 %)	0 (0 %)	– ^b
Total Score (0–14), mean (SD)	6.2 (2.8)	2.4 (2.1)	$\chi^2(1) = 85.50, p < 0.0001$

^a Item represents protective factor, rather than risk factor.

^b Analysis could not be conducted due to extreme values.

which there was no change. The significant decrease in benzodiazepine and alcohol, but not other drug, co-use may reflect the degree to which co-use of these substances directly increase the likelihood of opioid overdose (i.e., alcohol and benzodiazepines increase respiratory depression whereas other drugs impact judgement that could lead to risky behavior) with participants accordingly modifying their behavior to reduce the most risky co-used substances. The lack of change in testing the strength of opioids suggests that an additional intervention may be needed to encourage the behavior. Several studies have found that participants report an increase in using “testing doses” when the use of a fentanyl test strip indicates the presence of fentanyl (Allen et al., 2020; Goldman et al., 2019; Peiper et al., 2019); thus, the provision of fentanyl test strips might increase the use of testing doses although some research has reported that utilization of provided fentanyl test strips is low (Karamouzian et al., 2018; McGowan et al., 2018), which would limit their potential benefit.

The study results suggest that the PTOEND intervention significantly increased readiness for treatment and decreased self-reported opioid use. A significant decrease was observed in the Barriers to Treatment total score and in four of the seven subscales (Fear of Treatment, Time Conflict, Poor Treatment Availability, and Admission Difficulty). Two of the subscales, Absence of Problem and Negative Social Support, had low baseline values and, thus, the lack of significant change could reflect a floor effect. No significant change was observed for the final subscale, Privacy Concerns, which may be due to the fact that the MOUD knowledge section of the PTOEND intervention did not include information about the degree to which MOUD health information is protected; the intervention might be strengthened by including this information. To our knowledge, there are no published intervention studies reporting pre-post changes for Barriers to Treatment and, thus, there are no studies with which to compare these results. The participants’ reported desire to stop using drugs, from the Thoughts About Abstinence measure, was relatively high at baseline and the observed increase did not reach statistical significance. In contrast, there was a significant increase in the expected likelihood of a quit attempt being successful and a significant decrease in the estimated difficulty of avoiding a relapse; it is speculated that these changes were related to the information provided about the effectiveness of MOUD. These changes compare favorably to pre-post changes found in a trial conducted by our team on motivational enhancement therapy (MET) for pregnant women (Winhusen et al., 2008). While it should be noted that the study populations were very different (i.e., MET included pregnant women enrolled in treatment at baseline), the results from the present trial compare favorably to unpublished data from the MET arm of the MET trial with greater mean changes for desire to quit drugs (0.6 vs. 0.3), expected success of quitting (0.9 vs. 0.5) and expected difficulty of avoiding relapse (–0.7 vs. –0.5). A review of the published literature revealed two additional studies providing pre-post data for the Thoughts About Abstinence instrument, both focused on smoking cessation (Manuel et al., 2013; Shmueli et al., 2008). The results of the

present trial compare favorably with the mean pre-post changes reported by the smoking cessation studies for desire to quit (0.6 vs. –0.7 and 0.2) and expected success of quitting (0.9 vs. 0.5 and 0.7) but were somewhat smaller in magnitude for expected difficulty of avoiding relapse (–0.7 vs. –1.4 and –1.1) (Manuel et al., 2013; Shmueli et al., 2008). The study results also suggest that PTOEND may be effective in reducing illicit opioid use, with a significant decrease found for self-reported illicit opioid use days. However, it should be noted that illicit opioid-positive UDS results remained high ($\geq 85\%$) throughout the study. The discrepancy between the self-report and UDS results could be due to response bias and/or the different constructs being assessed (i.e., days of use by self-report and abstinence by UDS).

The results from the present pilot trial should be considered in light of several limitations. First, there was no control group and, hence, the observed results could be due to factors other than PTOEND, for example the impact of having their substance use and naloxone utilization assessed during the three in-person follow-up visits. Second, the positive study findings are based on self-report measures, which are open to a number of potential biases. Third, the study sample was relatively small ($N = 80$) and the study was conducted at a single site, thus the degree to which the findings are generalizable is unclear. Finally, it is important to note the relatively low level of study visit attendance at Month 12 (55 %). Despite being similar at baseline to those that completed, the unobserved outcomes of participants who failed to attend follow-up visits may have been worse than the observed outcomes of the completers. If that is the case, then the results presented in this study would tend to overestimate the benefits of the PTOEND intervention.

Despite the study limitations, the results suggest the potential promise of a 30-min, computer-guided PTOEND intervention for promoting harm reduction and treatment readiness in individuals actively using illicit opioids who are at heightened risk for OOD. If found effective in future studies, PTOEND would likely be sustainable given its relatively low cost and ease of interventionist training. PTOEND utilizes REDCap (Harris et al., 2019) to complete assessments and automatically generate personally-tailored feedback reports; hence the technological costs of the intervention are limited to the cost of an internet connection and a computer tablet. In the present study we utilized bachelor’s level research assistants as the interventionists with training on the intervention taking approximately 2.5 h; other bachelor’s level staff (e.g., counselors, nurses, etc.) could be utilized as interventionists outside the research context. In addition, in the current era of COVID-19, it is notable that this intervention could easily be implemented via phone or telehealth. Research to further develop and test the PTOEND seems warranted. Still, the elements of the PTOEND have been tested in a prior small acceptability study (Winhusen et al., 2016) and a self-administered version was developed and tested in a small pre-post pilot study ($N = 20$) which found a significant increase in OOD and MOUD knowledge and in which 90 % of participants accepted a MOUD provider list (data not published). Taken together,

these findings suggest that the PTOEND could benefit individuals who misuse opioids. Thus, starting in October of 2020, individuals in need of opioid overdose prevention education will be able to access the self-administered version on-line through the UC College of Medicine Center for Addiction Research website at no charge.

Contributors

Dr. Winhusen was the principal investigator for this study, conceptualized the intervention and the study design, contributed to the analysis and interpretation of the data, and led the drafting of the manuscript. Drs. Wilder and Lyons contributed to the study design, contributed to interpretation of the data, and critically reviewed the manuscript. Mr. Theobald contributed to the interpretation of the data and critically reviewed the manuscript. Ms. Kropp developed the training package, contributed to the interpretation of the data, and critically reviewed the manuscript. Mr. Lewis conducted analyses, contributed to the interpretation of the data, and critically reviewed the manuscript. All authors contributed to and have approved the final manuscript.

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Declaration of Competing Interest

The authors have no potential conflicts of interest to report.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2020.108265>.

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