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A community pharmacy-led intervention for opioid medication misuse: A small-scale randomized clinical trial

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ABSTRACT

Background: Stemming the opioid epidemic requires testing novel interventions. Toward this goal, feasibility and acceptability of a Brief Motivational Intervention-Medication Therapy Management (BMI-MTM) intervention was examined along with its impact on medication misuse and concomitant health conditions.

Methods: We conducted a two-group randomized trial in 2 community pharmacies. We screened patients for prescription opioid misuse at point-of-service using the Prescription Opioid Misuse Index. Participants were assigned to standard medication counseling (SMC) or SMC + BMI-MTM (referred to as BMI-MTM herein). BMI-MTM consists of a pharmacist-led medication counseling/brief motivational session and 8-weekly patient navigation sessions. Assessments were at baseline, 2-, and 3-months. Primary outcomes included feasibility, acceptability, and mitigation of opioid medication misuse. Secondary outcomes included pain and depression. Outcomes were analyzed with descriptive and multivariable statistics (intent-to-treat [ITT] and adjusted for number of sessions completed [NUMSESS]).

Results: Thirty-two participants provided informed consent (74.4% consent rate; SMC n = 17, BMI-MTM n = 15; 3-month assessment retention ≥93%). Feasibility was demonstrated by all BMI-MTM recipients completing the pharmacist session and an average of 7 navigation sessions. BMI-MTM recipients indicated ≥4.2 (5 maximum) level of satisfaction with the pharmacist-led session, and 92.4% were satisfied with navigation sessions. Compared to SMC at 3-months, BMI-MTM recipients reported greater improvements in misuse (ITT: Adjusted Odds Ratio [AOR] = 0.13; 95% CI = 0.05, 0.35, $p < 0.001$. NUMSESS: AOR = 0.05; 95% CI = 0.01, 0.25; $p < 0.001$), pain (ITT: B = 8.8, 95% CI = -0.95, 18.5, p = 0.08; NUMSESS: B = 14.0, 95% CI = 3.28, 24.8, p = 0.01), and depression (ITT: B = -0.44; 95% CI = -0.65, -0.22; $p < 0.001$. NUMSESS: B = -0.64; 95% CI = -0.82, -0.46; $p < 0.001$).

Conclusions: BMI-MTM is a feasible misuse intervention associated with superior satisfaction and outcomes than SMC. Future research should test BMI-MTM in a large-scale, fully-powered trial.

1. Background

Nearly 11.1 million individuals across the US in 2017 reported past year misuse of opioid pain-relievers (SAMHSA., 2018a,b). Within this sizable population, it is estimated that > 36% misused opioid medications prescribed to them (SAMHSA., 2018a,b). Although prescribing has declined nationally in recent years (CDC, 2018), use of these medications often transitions to heroin use embedded in a trajectory of escalating opioid misuse (Al-Tayyib et al., 2017; Harocopos et al., 2016; Lake et al., 2016; Palamar et al., 2016). Continued vigilance is therefore required to identify and provide evidence-based interventions for individuals misusing opioid medications.

The pharmacy is a point of contact for patients receiving and misusing prescription opioids. This setting is thus potentially an important

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location to provide intervention. Notably, pharmacies are not only ubiquitous but are primary locations where patients legally fill opioid prescriptions that are often misused (Cicero et al., 2011; Inciardi et al., 2007; SAMHSA., 2018a,b). More than 90% of US residents live within five miles of a retail pharmacy (Drug Store News, 2016), and there are approximately 60,000 pharmacies employing a workforce of > 170,000 pharmacists (CDC, 2013). Their accessibility is thus a major, albeit underutilized, resource for identifying and providing interventions for misuse of prescribed opioids. Furthermore, it is noteworthy that pharmacists are consistently ranked among the most trusted professionals (Riffkin, 2014), and patients express willingness to receive behavioral health information from pharmacists (Cochran et al., 2016a,b; Cochran et al., 2015; Dhital et al., 2010). Although the importance of pharmacists in treatment of numerous health conditions; such as cancer care, diabetes, and cardiovascular disease; has been documented (Colombo et al., 2017; Hughes et al., 2017; Mekonnen et al., 2016; van der Molen et al., 2017), research is highly limited in this service setting regarding interventions with patients who misuse opioids.

Accordingly, we developed a pharmacy-based integrated care model consisting of a pharmacist-led medication counseling/brief motivational interviewing session in conjunction with 8 patient navigation sessions (Cochran et al., 2016a,b). The pharmacist component targets medication adherence/misuse, and the subsequent navigator sessions focus on treatment adherence and reduction of psychosocial risks factors. This study evaluates this intervention, termed Brief Motivational Intervention-Medication Therapy Management (BMI-MTM), in a single-blinded randomized clinical trial. As the first intervention study involving community pharmacy patients with opioid medication misuse (NIDA R21DA043735; NCT03149718), a main objective pertains to establishing the acceptability and feasibility of the BMI-MTM intervention as well as determining its preliminary effects on reducing opioid medication misuse and concomitant health conditions.

2. Material and methods

Methods for this study have been reported in detail previously (Cochran et al., 2018). Study participants were recruited from 2 community pharmacies located in southwestern Pennsylvania, one associated with an academic medical center and one an independent pharmacy in a rural county.

2.1. Participant identification, inclusion/exclusion, and enrollment

Potential participants were approached if they were currently prescribed an opioid medication and were screened in-person at the community pharmacy sites by the study pharmacist, pharmacy technician, or research staff. The study also advertised within other local pharmacies as well as through a research participant registry.

To be included in the study, patients were required to be English speaking and ≥18 years of age. Study inclusion criteria also required patients to be currently misusing their prescribed opioid medication. To identify misuse, we employed the Prescription Opioid Misuse Index (POMI; see outcomes section for validity/reliability (Knisely et al., 2008). This brief 6-item instrument asks patients about behaviors related to their current usage of their opioid pain medication, with ≥2 positive items indicative of misuse. Specific behaviors screened on the POMI include seeking early refills, taking medications at higher doses or more frequently than prescribed, doctor shopping, and using medication to deal with problems or for psychoactive effects (Knisely et al., 2008). Items in the POMI would be not applicable to those filling opioid medications the first time.

Patients were excluded if they self-reported: pregnancy, solely filling buprenorphine or buprenorphine combination projects, being unable to provide contact information, planning to move residences within the 3 months of recruitment, or having a psychotic or manic episode in the 30 previous days. Psychosis assessment was performed using the subscale from the Behavior and Symptom Identification Scale (Eisen et al., 2004), and mania was assessed using Altman Self-Rating Mania Scale (Altman et al., 1997). Those who self-reported receiving treatment for cancer were also excluded from study participation given limited literature on appropriate use/misuse of opioid medications among this population (Manchikanti et al., 2018; Pinkerton and Hardy, 2017; Sutradhar et al., 2017)—that is to say—it is not fully understood in the field how clinical measures of opioid medication misuse may apply to this population. Patients excluded were provided with information about the risks of opioid pain medication misuse, and the research team helped them to obtain health or psychosocial services if they desired.

Patients who met all study criteria for inclusion were required to provide written informed consent approved by the University of Pittsburgh Institutional Review Board. Following consent and enrollment, participants completed a baseline assessment and were then randomly assigned on a 1:1 ratio to the standard medication counseling (SMC) or SMC + BMI-MTM study conditions (referred to as BMI-MTM herein).

2.2. Standard medication counseling condition

SMC is the Centers for Medicaid and Medicare Services requirement for pharmacists wherein patients who are filling prescriptions receive information for all medications received and are offered counseling (Centers for Medicaid and Medicare Services, 2014). SMC in Pennsylvania requires pharmacists to: (1) offer counseling related to the medication, (2) document counseling has been offered, (3) document patient refusal of counseling, (4) offer a counseling process for patients not present (not applicable in this study), (5) discuss possible generic substitutions, and (6) provide information about the medication (Centers for Medicaid and Medicare Services, 2014). Licensed pharmacists other than the study pharmacists (i.e., those trained in the BMI-MTM intervention) delivered SMC in this project as part of their standard dispensing practice. Those pharmacists who delivered SMC possessed similar level of education and licensing as the pharmacists who delivered BMI-MTM. It is important to note that due to regulatory requirements, all participants received SMC as part of the study—-including BMI-MTM recipients.

2.3. Brief motivational intervention-medication therapy management

2.3.1. Interventionists, training, and administration

BMI-MTM was the intervention condition and was comprised of 4 specific evidence-based practices. The evidence-based practices that constitute BMI-MTM include: (1) medication therapy management (MTM), (2) brief motivational interviewing (BMI), (3) patient navigation (PN), and (4) naloxone training and referral.

Intervention components were delivered sequentially, with the pharmacy-based session delivered by a licensed pharmacist lasting 30–45 min followed by 8 patient navigation sessions delivered telephonically by a patient navigator, a master's level research interventionist. Study pharmacists and navigators underwent approximately 16 h of training in basic motivational interviewing skills (Miller and Rollnick, 2013) by a Motivational Interviewing Network of Trainers (MINT) trainer.

Both pharmacy-based and telephonic sessions were set up on an appointment basis in order to accommodate the pharmacy workflow as well as patients' needs and time constraints. Prior to session initiation with participants, study pharmacists and navigators received a brief report of general physical and behavioral health status of participants based on information collected during the baseline assessment. All sessions were audio-recorded and a subset was selected at random for review using session checklists developed by the study team to assess for protocol adherence and general case management and motivational

interviewing fidelity. Specifically, regarding motivational interviewing fidelity, research staff who reviewed sessions were master's level social workers who underwent at least 16 h of motivational interviewing training, mentioned above, and were provided periodic supervision by the MINT trainer.

2.3.2. Pharmacy-led intervention component

The pharmacy portion of the BMI-MTM intervention involved delivery of MTM combined with brief motivational interviewing. MTM delivery specifically targeted improving adherence to taking the opioid medication as prescribed. A primary objective of MTM is to enable patients to proactively manage medication usage by resolving barriers to regimen adherence (American Pharmacists Association, 2008; Bluml, 2005). MTM in this study involved the study pharmacists: (1) reviewing with participants' opioid medication(s) being actively taken and identifying possible unsafe interactions; (2) speaking with the patient about misuse and specifically identified misuse behaviors; and (3) identifying targets for adherence improvement and encouraging patients to take action toward behavior change. Within the MTM session, brief motivational interviewing was employed to address opioid medication misuse by facilitating a non-directive discussion regarding motivation to change, discussing importance/confidence to avoid misuse, and resolving ambivalence towards stopping misuse. Upon session conclusion, the study pharmacists provided participants with a record of the participant's plans for health behavior change and initiated a warm handoff to the study navigator within 1 business day.

2.3.3. Patient navigation component

The PN model delivered herein employed principles of strengths-based case management (Brun and Rapp, 2001; Saleebey, 2009) and motivational interviewing (Miller and Rollnick, 2013). The PN portion of the BMI-MTM was delivered through 8 weekly telephonic sessions, which lasted 30–45 min per session. Sessions 1–3 involved development of therapeutic alliance/rapport, goal setting for needed services (e.g. mental, physical, behavioral health), identifying barriers, and problem resolution. In sessions 2–3, navigators also focused on aiding patients to enroll in psychosocial services, behavioral health, and/or physical healthcare. Session 4 initiated a discussion with patients around overdose risk, possible need for a naloxone kit (SAMHSA, 2013), and referral to locations where a kits/training could be obtained. Sessions 5–7 continued to focus on service engagement, identifying health needs, and providing referral and enrollment support to any additional service providers. Session 8 included discussion, planning, and commitment for continued self-care.

2.4. Assessment and compensation

Assessments were conducted at baseline, 2-months (upon PN completion for BMI-MTM recipients), and 3-months. Participants who completed the baseline assessment received $20, $30 for the 2-month, and $75 for the 3-month assessments. The baseline assessment took approximately 35 min and follow up assessments lasted about 25 min.

2.5. Outcome measurement

Primary outcomes included feasibility and acceptability of the BMI-MTM intervention. For the assessment of feasibility, we tracked study screening/enrollment rates and session completion rates. We measured acceptability by assessing satisfaction with relevant items from the Patient Satisfaction Survey for Comprehensive Medication Management (PSSCMM; Moon et al., 2016), a reliable and content/factorial valid 10-item self-report instrument (Moon et al., 2016). This instrument measures patient satisfaction with the pharmacist-delivered portion of BMI-MTM. We also assessed acceptability using a modified Patient Satisfaction Questionnaire-18 (PSQ-18; Thayaparan and Mahdi, 2013); a reliable and criterion valid 18-item self-report instrument (Marshall and Hays, 1994; Thayaparan and Mahdi, 2013), which assesses general satisfaction, technical quality, interpersonal manner, quality of communication, time spent with navigator, accessibility, and convenience. This instrument was used to assess satisfaction with the navigator portion of the intervention and was adapted by replacing the "provider" terminology to instead say "patient navigator." Acceptability was also assessed by tracking retention of BMI-MTM recipients at the study assessment time points.

Primary outcomes also included opioid medication misuse. Described above, opioid medication misuse was measured by the Prescription Opioid Misuse Index (POMI). This instrument has criterion validity and is reliable (Knisely et al., 2008).

Secondary outcomes included pain, which was measured by the Short Form (SF)-36; a 36-item content, criterion, and construct valid measure with demonstrated reliability (Ware, 2019). The two-item pain subscale asked about level of bodily pain and pain-related physical functioning and is scored on a 0–200 scale. We assessed depression using the Patient Health Questionnaire (PHQ) depression subscale, a valid mental health assessment with demonstrated reliability (Hides et al., 2007; Smith et al., 2007; Spitzer et al., 1999, 2000). This subscale is scored on a 5-point scale (0 = none-minimal; 1 = mild; 2 = moderate, 3 = moderately severe; 4 = severe).

Other outcomes assessed included a urine toxicology screen to examine cannabis and opiate use. Cannabis screening was particularly important to assess in this project in order to examine whether improvements in pain following reductions in misuse were associated with increased cannabis use—given the popular application of cannabis for pain management. We also tracked self-reported naloxone prescription fills during the study period, given, as part of the intervention, all patients received naloxone referral.

2.6. Participant health and demographic characteristics

We also collected information on mental health, unhealthy alcohol use, type of opioid medication use, and demographic characteristics. These variables informed whether differences existed in patient characteristics by intervention group at baseline. Specifically, Posttraumatic Stress Disorder (PTSD) was measured using the 5-item criterion valid Primary Care-Posttraumatic Stress Disorder assessment, which has test-retest reliability (Ouimette et al., 2008; Prins et al., 2003; van Dam et al., 2010). The anxiety subscale from the PHQ was also administered. Unhealthy alcohol consumption was assessed using the Alcohol Use Disorders Identification Test-C (Han et al., 2017; SAMHSA, 2019). Opioid medication type was captured in an open-ended question format. Age (years), sex (male = 0, female = 1), race (nonwhite = 0, white = 1), education (greater than high school = 0, high school or less = 1), employment (unemployed = 0, employed = 1), marital (not married = 0, married = 1), and insurance status (not insured = 0, insured = 1) were collected to assess participant demographics.

2.7. Analyses

We conducted descriptive analyses of frequencies, proportions, and measures of central tendency to compare participant health and demographic characteristics at baseline. Similarly, we employed descriptive statistical measures to assess our outcome measures. For longitudinal analyses, we developed general estimating equation models. Within these, we tested a time by intervention condition interaction on study outcomes (Twisk et al., 2018). For dichotomous outcomes, we employed the binary distribution with logit link. For continuous outcomes, we employed the Gaussian distribution and identity link. All models utilized the autoregressive correlation matrix to account for repeated observations. We present two sets of multivariable models—one set presenting intent-to-treat (ITT) outcomes adjusted for site and a second set adjusted for site as well as for numbers of sessions (NUMSESS) completed. We estimated robust standard errors

for all models. Analyses were conducted in Stata 15.1 (StataCorp, 2017).

3. Results

From September 2017 through November 2018, we approached a total of 387 patients, of whom 314 agreed to be screened (81.1%). No statistically significant differences were detected in age category (18–25, 26–40, 41–64, and > 64), gender, and insurance status (insured vs. not insured) for those who chose to be screened compared to those that did not ($p > 0.05$). Of those who agreed to participate in screening, 21% (n = 65) were positive for opioid medication misuse. Fourteen of those screening positive did not meet other eligibility criteria, and 8 additional patients were not reachable for recruitment following screening in the pharmacy. Therefore, a total of 43 patients were approached, of whom 32 provided written informed consent (74.4%). Patients were assigned to BMI-MTM (n = 15) or SMC (n = 17) conditions. A total of 14 (93.3%) BMI-MTM recipients and 16 (94.1%) SMC participants completed the 2-month follow up assessment, and a total of 14 (93.3%) BMI-MTM recipients and 17 (100%) SMC participants completed the 3-month follow up assessment.

3.1. Baseline characteristics

No significant differences were detected between conditions in term of demographics, physical health, mental health, or substance use indicators at baseline (Table 1). Participants were: on average 51.9 years old, female, employed, and possessed a high school or less education. Most patients were prescribed oxycodone. Participants also screened positive for depression, anxiety, and PTSD. Approximately one-third of patients screened positive for cannabis use.

We also inspected specific misuse behaviors participants endorsed at baseline to understand their risk profiles, i.e., the individual items asked in the POMI (Table 1). No statistically significant differences in behaviors were detected between intervention groups ($p > 0.05$). The majority of participants acknowledged using more of their medication than prescribed, using the medication more often than directed, getting early refills, getting high/feeling a buzz, and using the medication to cope with emotional problems. The least frequently endorsed misuse behavior was doctor shopping.

3.2. Outcome analyses

BMI-MTM participants reported high level of satisfaction with the pharmacy and PN portions of the intervention (not shown). Specifically, all participants who completed the satisfaction survey (n = 13) agreed/strongly agreed the pharmacist ensured medication safety, increased confidence to manage their medications, and listened to their concerns. Most participants agreed/strongly agreed they would recommend the pharmacist to friends/family (92.4%, n = 12), with 1 patient disagreeing (n = 1). Participants who completed the navigator satisfaction survey (N = 13), on a 5 point scale, gave nearly perfect ratings for general satisfaction (Mean [M] = 4.5, SD = 0.59), technical quality (M = 4.6, SD = 0.56), interpersonal manner (M = 4.8, SD = 0.25), quality of communication (M = 4.7, SD = 0.38), time spent with the navigator (M = 4.7, SD = 0.43), and accessibility and convenience (M = 4.2, SD = 0.46). In addition, all BMI-MTM condition participants received the pharmacist intervention, and 73.3% (n = 11) of BMI-MTM participants received the complete navigation intervention—with an average 7 navigation sessions completed (SD = 2.2; not shown).

In terms of unadjusted changes in opioid medication misuse across time (Fig. 1), at 2 months, 42.9% (n = 6) of BMI-MTM recipients

Table 1
Baseline Participant Characteristics by Intervention Condition (N = 32) [a].

	Total		BMI-MTM		SMC				
Demographics	**n**	**%**	**n**	**%**	**n**	**%**	χ^2	**DF**	**p**
Age (years) [b]	51.9	12.6	53	9.4	50.9	15.1	−0.5	30	0.68
Female	18	56.3	8	53.3	10	58.8	0.1	1	0.76
White	23	71.9	11	73.3	12	70.6	0.0	1	1.00
Employed	10	31.3	7	46.7	3	17.7	3.1	1	0.08
< High school	17	53.1	8	53.3	9	52.9	0.0	1	0.98
Insured	22	68.8	9	60.0	13	76.5	1.0	1	0.32
Married	8	25.0	3	20.0	5	29.4	0.4	1	0.42
Physical health									
Pain [b, c]	27.7	19.6	27.5	16.1	27.8	22.8	0.0	30	0.48
Primary opioid medication									
Hydrocodone	12	37.5	5	33.3	7	41.2	3.3	3	0.35
Oxycodone	17	53.1	9	60.0	8	47.1			
Dilaudid	2	6.3	0	0.0	2	11.8			
Tramadol	3	3.1	1	6.7	0	0.0			
Mental health									
Depression [b, d]	1.6	1.3	1.8	1.2	1.4	1.4	−1.0	30	0.86
Anxiety [c, e]	6	18.8	3	20.0	3	17.7	0.0	1	1.00
Posttraumatic stress disorder [e]	9	29.0	4	26.7	5	31.3	0.1	1	1.00
Substance use and toxicology									
Hazardous drinking [e]	6	18.8	2	13.3	4	23.5	0.5	1	0.46
Positive cannabis toxicology [e]	11	34.4	5	33.3	6	35.3	0.0	1	0.91
Misuse Behaviors									
Using more medication than prescribed	28	87.5	13	86.7	15	88.2	0.02	1	1.00
Using medication more than directed	30	93.8	15	100	15	88.2	1.9	1	0.49
Early refills	13	40.6	8	53.3	5	29.4	1.9	1	0.17
Getting high/feeling a buzz	6	18.8	4	26.7	2	11.8	1.2	1	0.38
Using medication to cope with emotions	6	18.8	4	26.7	2	11.8	1.2	1	0.38
Doctor shopping	4	12.5	3	20.0	1	5.9	1.5	1	0.32

[a] Fisher exact used with n < 5.
[b] Mean, SD, t-value.
[c] Scored on a 0–200 scale.
[d] scored on a 1–5 scale (0 = none-minimal; 1 = mild; 2 = moderate, 3 = moderately severe; 4 = severe).
[e] Number and percent of positive participant screenings.

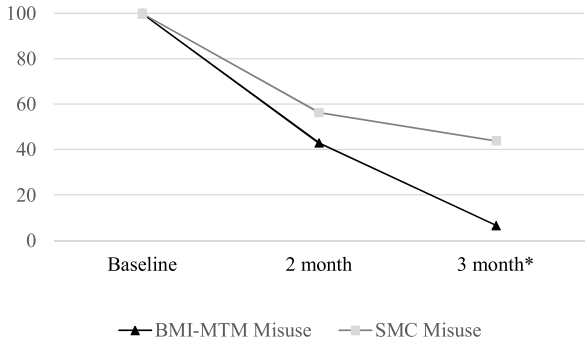

Fig. 1. Unadjusted Percentages of Opioid Medication Misuse by Intervention Condition across Time.

Table 2
Primary and Secondary Outcomes with Treatment By Time Interaction.

Intent-to-Treat Analysis [a]				
Primary outcomes	**AOR**	**SE**	**95% CI**	**p**
Misuse mitigation	0.13	0.07	0.05, 0.35	< 0.001
Secondary outcomes				
Depression [b]	−0.44	0.11	−0.65, -0.22	< 0.001
Pain improvement [b]	8.8	5.0	−0.95, 18.5	0.08
Cannabis toxicology	0.61	0.21	0.28, 1.33	0.21
Opiate use toxicology	0.50	0.18	0.25, 1.01	0.05
Adjusted for Numbers of Sessions Completed [c]				
Primary outcomes				
Misuse mitigation	0.05	0.04	0.01, 0.25	< 0.001
Secondary outcomes				
Depression [b]	−0.64	0.09	−0.81, -0.46	< 0.001
Pain improvement [b]	14.0	5.49	3.28, 24.8	0.01
Cannabis toxicology	0.62	0.27	0.26, 1.47	0.28
Opiate use toxicology	0.52	0.19	0.26, 1.05	0.07

[a] Models adjusted for site.
[b] Continuous indicator with Gaussian distribution and unstandardized Beta value reported.
[c] Models adjusted for site and numbers of sessions completed.

reported continued misuse, and 56.3% (n = 9) of SMC recipients reported continued misuse (p = 0.46). At 3 months, 6.7% (n = 1) of BMI-MTM recipients reported continued misuse, and 43.8% (n = 7) of SMC recipients reported continued misuse (p = 0.02). In terms of our multivariable models (Table 2), participants who received the BMI-MTM intervention were less likely than SMC patients to report continued misuse at 3-months (ITT: Adjusted Odds Ratio [AOR] = 0.13; 95% CI = 0.05, 0.35, p < 0.001. NUMSESS: AOR = 0.05; 95% CI = 0.01, 0.25; p < 0.001).

We also examined unadjusted changes in pain (not shown), which demonstrated improvements for both groups' mean scores across time, with greater improvement for BMI-MTM recipients (Baseline: BMI-MTM = 55, SMC = 55.6; 2-months: BMI-MTM = 85.4, SMC = 74.7; 3-months: BMI-MTM = 85.3, SMC = 79.9; all p > 0.05). For multivariable analyses (Table 2), BMI-MTM participants reported a promising but non-significant trend for improvements in levels of pain compared to SMC recipients (ITT: B = 8.8, 95% CI = -0.95, 18.5, p = 0.08), with significant improvements in session adjusted analyses (NUMSESS: B = 14.0, 95% CI = 3.28, 24.8, p = 0.01). We also examined unadjusted changes in depression (not shown), which showed improvements for both groups' mean scores across time, with greater improvement for BMI-MTM recipients (Baseline: BMI-MTM = 1.8, SMC = 1.4; 2-months: BMI-MTM = 1.7, SMC = 1.4; 3-months: BMI-MTM = 0.5, SMC = 0.3; all p > 0.05). For multivariable analyses (Table 2), participants who received the BMI-MTM intervention were more likely than SMC patients to report decreases in level of depression across time (ITT: B = -0.44; 95% CI = -0.65, -0.22; p < 0.001. NUMSESS: B = -0.64; 95% CI = -0.82, -0.46; p < 0.001). In connection with the improvement in pain, as an ad hoc analysis, we also examined changes in cannabis toxicology should participants have increased use of this drug resulting in pain improvement; no significant changes were detected (ITT: p = 0.21; NUMSESS: p = 0.28).

Finally, we also examined unadjusted changes in percentages of participants with positive opioid toxicology (not shown), which showed improvements for both groups' across time, with greater improvement for BMI-MTM recipients (Baseline: BMI-MTM = 33.3%, SMC = 41.2%, p = 0.65; 2-months: BMI-MTM = 23.1%, SMC = 37.5%, p = 0.40; 3-months: BMI-MTM = 13.3%, SMC = 50%; p = 0.04). For multivariable analyses (Table 2), we detected a promising but non-significant trend for decreases in positive opiate toxicology screens for BMI-MTM recipients (ITT: AOR = 0.50, 95% CI = 0.25,1.01, p = 0.05. NUMSESS: AOR = 0.52, 95% CI = 0.26,1.05, p = 0.07). At the 3-month follow up, 1 SMC patient (6.3%) filled a naloxone prescription, and 3 (23.1%) BMI-MTM recipients filled a naloxone prescription, with no significant proportional differences (p = 0.19).

4. Discussion

These findings suggest community pharmacy may represent an underutilized but potentially valuable resource for identifying and intervening with patients who misuse opioid medications. This single-blinded randomized trial, although relatively small, provides tentative evidence for feasibility, acceptability, and preliminary efficacy of a pharmacy-led integrated model of care at point-of-service.

4.1. Acceptability and feasibility

A main goal of this study was to assess acceptability and feasibility of BMI-MTM. The high level of agreement among participants for satisfaction for both the pharmacist and the navigator delivered portions of the intervention suggests participants found the overall intervention useful and helpful. Further, our screening rate (> 80%), consent rate (74.4%), and high level of intervention completion appear to provide a strong indication that patients can be successfully engaged in the study and most sessions could be delivered to and completed by participants in a future study. Additionally, the navigation portion of the intervention was achieved via telephone (with the exception of 1 session of 1 patient who wished to have the initial visit in person), which could be particularly appealing for future intervention scalability. Our study assessment follow up rates also support study feasibility.

It is important to note with respect to feasibility of patient identification that more than 20% of patients had positive screens for opioid medication misuse, which positive rate approximates our previous research (15.1%; Cochran et al., 2016a,b). It is possible that the current study sample resulted in a slightly higher misuse positive rate than our previous work given our community advertisements soliciting potential participants for participation.

4.2. Opioid medication misuse, pain, and depression

BMI-MTM has more robust preliminary indications for reducing medication misuse and possible improvements for pain with frequently associated depression compared to current standard treatment. Although the comparison is not statistically significant, the BMI-MTM intervention was also associated with better outcome revealed by toxicology screens. Whereas previous research in other health care settings with motivational interviewing focusing on reducing problematic opioid medication consumption has also shown similar improvements (Zahradnik et al., 2009), this study additionally demonstrates superior alleviation of pain and depression among participants who received the BMI-MTM intervention. Although this study was not designed to examine the mechanisms underlying improvements in these latter conditions, it has been shown that misuse of opioid medications is closely related to pain and depression (Fasick et al., 2015; Koyyalagunta et al.,

2013; Li, 2015; Sheng et al., 2017; Vowles et al., 2015). Accordingly, it is important in future research to precisely characterize the clinical phenomenology and the mechanisms through which BMI-MTM effects positive change in patients with varying levels of pain as well as depression. Such additional research would also likely benefit from understanding the effects of the pharmacist compared to the patient navigation portions of the intervention on the study outcomes.

4.3. Naloxone

It is noteworthy that naloxone fills at the 3-month assessment were modestly higher in the BMI-MTM group compared to compared SMC (23.1% vs. 6.3%). Given the critical importance of this medication for overdose prevention, future application of the BMI-MTM should include directly dispensing naloxone by the pharmacist instead of the navigator solely providing education and referral.

4.4. Limitations

Although there are many promising aspects of this study, including its randomized design, the integrated model of care, and preliminary outcomes; one should be mindful of its limitations. We recognize ITT analyses for pain only approached significance ($p = 0.08$), with significant effects for the multivariable model adjusted for numbers of sessions. Possible enhancements to pain measurement in future research may help better elucidate BMI-MTM impact on this important outcome. Our limited number of participants in this study were recruited by convenience from southwestern PA, which limits the external validity of these findings and caution should be taken in interpreting findings. Future research must work to expand the geographical catchment recruitment area to increase generalizability. We also recognize many of our outcome measures were based on participant self-reported behaviors, which could allow attention or social desirability biases to impact the results. While assessors were blinded to study condition in order to help limit some of these threats to internal validity, future investigation into BMI-MTM efficacy will gather more objective outcome information, such as individual-level prescription drug monitoring data or smart pill bottle technology for medication use (Stip et al., 2013; Treskes et al., 2018). However, the noted trends for reductions in positive opiate toxicology for BMI-MTM compared to SMC recipients (ITT: AOR = 0.50, 95% CI = 0.25,1.01, p = 0.05. NUMSESS: AOR = 0.52, 95% CI = 0.26,1.05, p = 0.07) provide modest evidence for the validity of the documented changes for medication use. These more objective data would likely enhance the understanding of the chronicity of the medication prescription/use. Enhanced assessment in future research likely is also merited for opioid use disorder for this population. While this project was focused on misuse, additional information regarding opioid use disorder would likely improve interventionists' insight for session delivery and care planning. In addition, future research and clinical applications of BMI-MTM would likely also benefit from a more thorough/comprehensive assessment of other substance use for possible treatment planning to help ameliorate concurrent drug use that may heighten misuse symptomology.

5. Conclusion

This study provides initial support for the BMI-MTM intervention being acceptable and feasible for delivery, mitigating opioid medication misuse, and improving pain and depression. Future research should build on these preliminary data by further examining this intervention within a fully powered clinical trial framework. Such future research could provide necessary information and evidence to the field that would support possible broader application of this intervention to reduce opioid-related risks and improve public health.

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Contributors

All authors participated in the conceptual development, writing, and revision of this article. Dr. Cochran performed the statistical analyses for this project. All authors approved of the final manuscript before submission.

Declaration of Competing Interest

No conflicts declared.

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