TITLE PAGE

Title of Project:

Preventing Opioid Misuse through Safe Opioid Use Agreements between Patients and Surgical Providers (PROMISE-ME)

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STRUCTURED ABSTRACT

Purpose: The effect of pain agreements to reduce opioid misuse is an accepted practice in many settings, but it has never been applied to the acute care setting. The goal is to assess the effectiveness of a safe opioid use agreement in surgical care on patients' opioid disposal behavior, safe opioid use and storage behavior.

Scope: 1) Create a safe opioid use agreement using the Delphi method. 2) Implement this agreement in a surgical clinic setting to see how effective it would be on patient's disposal, use, and storage behavior.

Methods: The safe opioid use agreement was created using the Delphi method with input from stakeholder panel of 37 members, including patients, surgeons, nurses, anesthesiologists, pharmacists, and quality improvement experts. After this agreement was developed, a randomized, controlled trial was then conducted to implement the agreement in three locations with surgery clinics in the Houston, TX, area.

Results: We found that the safe opioid use agreement that was developed was not effective on a patient's safe disposal, safe opioid use, and storage behavior. However, future studies may need to be done to look at implementation of opioid use agreements.

Key Words: Opioid, Opioid use agreement, safe disposal, opioid use, opioid storage, surgery clinic, implementation

PURPOSE

Our primary objective was to assess the effectiveness of a safe opioid use agreement in surgical care on patients' opioid disposal behavior. Our secondary objective was to assess the effectiveness of a safe opioid use agreement in surgical care on outcomes of patients' safe opioid use and storage behavior. To determine the best way to implement the agreement and test its initial effectiveness, we will conduct a study with these specific aims:

Specific Aim 1: Assess barriers and facilitators to implementing a safe opioid use agreement within the surgical care setting.

Specific Aim 2: Implement the opioid use agreement and assess the acceptability, adoption, appropriateness, feasibility, and fidelity.

Specific Aim 3: Test the effectiveness of a safe opioid use agreement within the surgical care setting using a stepped wedge trial design.

SCOPE

In 2017, 191 million opioid prescriptions were dispensed in the United States, of which a significant portion were prescribed for acute pain management following surgical encounters. In addition, on average, 70% to 90% of prescribed opioid pills following surgery remain unused after the initial pain episode, and over 70% of surgery patients do not dispose of their unused opioids. Unused pills are a common source of nonmedical use; 54% of people obtain their pills for nonmedical use through friends or relatives, and 35% obtain them through their healthcare provider. Nonmedical use of opioids can lead to adverse drug events (ADEs) and frequently is a pathway to use of other, illicit, drugs, such as heroin. Thus, surgical prescription and over-prescription of opioids can result in harm to patients themselves as well as to the surrounding communities. It is not surprising that the increased number of opioid prescriptions in the U.S. is highly correlated with an increase in nonmedical use, abuse, and overdose death rates. In addition to decreasing the number of pills prescribed, effective prevention of harm caused by prescription opioids requires patients to safely use pills—using only the minimum needed to control pain, safely storing them, and appropriately disposing of unused pills after acute pain treatment.

The effect of pain agreements to reduce opioid misuse is an accepted practice in many settings, but it has never been applied to the acute care setting. Pain agreements are considered the standard of care for chronic pain management reliant on opioid prescribing, and they are a mandated component of care in many states. Therefore, the adjunct of safe opioid use agreements into acute pain management offers a logical extension of current practices from chronic pain management.

This study tested the use of agreements to improve safe opioid use to prevent misuse and opioid-related harm. We hypothesized that incorporating the safe opioid use agreement in surgical care will increase the disposal rate of unused prescribed opioid compared to routine care.

Specific Aim 1 was accomplished during the first year of the grant. A Delphi study was conducted to determine the content of the opioid use agreement. A stakeholder panel of 37 members including patients, surgeons, nurses, anesthesiologists, pharmacists, and quality improvement experts was formed.

A formal Delphi process was completed using this panel and achieved consensus for the Safe Opioid Use Agreement that was used for Specific Aims 2 and 3. Specific Aims 2 and 3 were completed in clinics associated with UTHealth Houston through a randomized controlled trial.

Patients were enrolled from three sites: Clinics at Lyndon Baines Johnson General Hospital (LBJ) and UT Physicians Minimally Invasive Surgeons of Texas clinics (MIST) in Bellaire and Sugar Land. Participants were adults (at least 18 years of age), any gender, who spoke English or Spanish and were undergoing a general surgery procedure with a high likelihood of receiving an opioid prescription. The general surgery clinic schedules were screened daily to identify potential patients for the study. LBJ is a community hospital servicing patients in Harris County who mostly are uninsured. These patients also have a lower level of education and lower household income compared to patients at the MIST clinic locations.

METHODS

For Specific Aim 1, we established a stakeholder panel of 37 members, including patients, surgeons, nurses, anesthesiologists, pharmacists, and quality improvement experts. Utilizing this stakeholder panel, we completed a formal Delphi process and achieved consensus for a Safe Opioid Use Agreement (for use in the perioperative period). For this process, we collected detailed qualitative and quantitative data through multiple rounds of iterative improvement in order to achieve consensus agreement for the wording, length, and formatting of an agreement document. We developed a finalized Safe Opioid Use Agreement as well as a checklist indicating major educational topics around perioperative safe opioid use, storage, and disposal to assist implementation of the agreement. This agreement was used for Specific Aims 2 and 3.

For Specific Aims 2 and 3, we conducted a randomized, parallel-group, controlled superiority trial with 1:1 allocation to investigate the effectiveness of a safe opioid use agreement in surgical care. We anticipated enrolling participants for up to 12 months until the enrollment goal of 450 patients was reached. Subject participation was approximately 1 month, starting at their preoperative appointment and ending after their postoperative appointment approximately 30 days after surgery (25-40 days). Patients who did have a postoperative appointment received a follow-up phone call from a study team member to answer the survey questions. Study visits coincided with patients' regularly scheduled clinic visits, and patients did need to attend any additional visits or make any additional trips to the study site.

Patients were randomized following the signing of the consent form into one of two groups: Opioid Use Agreement group (intervention) and Standard Care group (control); 226 patients were randomized to the Opioid Use Agreement group, and 224 were randomized to the Standard Care group. Those randomized to the receive the intervention were administered the opioid use agreement by the research coordinator. Patients randomized to the Standard Care group received standard care which included safe opioid education from the surgical team. Patients, investigators, and data analysts were blinded to the study group assignment. In order for the patients to be kept blinded, patients were told that the study was being done to find out how opioids were prescribed and used at LBJ.

Patients were interviewed using three different patient-reported outcome surveys: PROMIS Pain Interference Short Form 4a, PROMIS Global Health-Physical 2a, PROMIS Global Health-Mental 2a, and PROMIS Emotional Distress-Anxiety-Short Form 4a. These surveys were administered both preoperatively and postoperatively. The patient's medical record was reviewed once the patient's surgical procedure was completed to collect information regarding the surgery as well as medications, in particular pain medications, that were prescribed following the surgery.

During the postoperative interview, information was obtained regarding whether or not the patient filled an opioid prescription as well as if the patient had any leftover opioid medication. Information regarding other methods of pain relief was also obtained from the patient during this interview.

RESULTS

For Specific Aims 1, the Safe Opioid Use Agreement was developed. For the next two aims, this agreement was implemented and studied. The primary outcome was patient self-reported disposal of prescription opioids 25-40 days after surgery. Secondary outcomes included if opioid prescription was filled, number of opioid pills used, if opioid pills were leftover, storage methods, disposal method, diversion, other pain management strategies (all self-reported at 25-40 days).

Figure 1 depicts the flow of patients who were enrolled in the study.

Overall, 450 patients were enrolled from December 2022 to October 2023. Study follow-ups were completed in January 2024. Baseline demographics and patient characteristics of all randomized patients are shown in Table 1. Of all 450 randomized patients, 359 patients underwent surgery and completed their postoperative follow-up. Of these patients, 254 patients were prescribed opioids following their surgery. Only 143 (32% of the randomized patients) were included in the final analysis. These patients had surgery, were prescribed an opioid, and had leftover opioid medication at their final postoperative visit. Table 2 depicts the baseline characteristics of the patients who were included in the final analysis. For the final analyses, 75 patients were from the Opioid Use Agreement group and 68 were from the Standard Care group. Only patients who had leftover opioid medication were included in the final analysis.

Table 3 shows the results for our primary and secondary outcomes between the two groups.

With a difference between types of patients treated at LBJ and MIST clinics, additional analyses were completed to compare the outcomes of patients at these sites. The results are shown in Table 4.

Our study found that the developed opioid use agreement was not effective at improving opioid disposal or safe use habits. Our opioid use agreement was implemented in a similar fashion to how pain contracts are implemented in clinics, where they are required by state law.

We encountered some unanticipated challenges while conducting this study. First, the agreement that was developed in Specific Aim 1 was developed at a different site from where it was implemented (Northwestern University versus UTHealth Houston). Our observed dropout rate was also much higher than our anticipated dropout rate, which led to a lack of patients with leftover opioid medication. Also, during this time, we found that the number of opioid pills being prescribed was much lower than in the past.

Although our opioid use agreement was not effective, this study was the first prospective, randomized clinical trial of integrating an opioid use agreement into surgical clinics. We see this as one step in helping to understand implementation of opioid use agreements in these settings.

Figure 1. Patient flow diagram

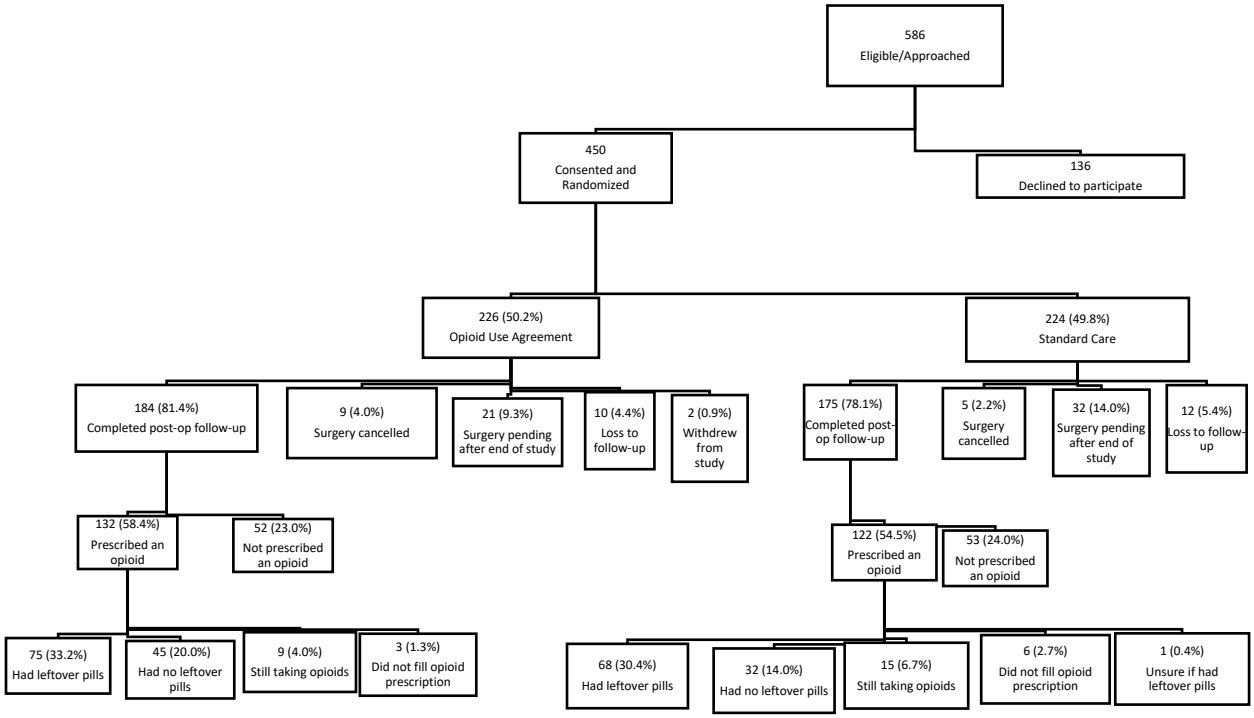

Table 1. Baseline characteristics of randomized patients [[1]Mean (SD); n (%)]

Characteristic	Overall[1]	Opioid Use Agreement, N = 226[1]	Standard Care, N = 224[1]
Age (in years)	48 (13)	48 (13)	48 (13)
Sex			
Male	151 (40%)	78 (40%)	73 (39%)
Female	229 (60%)	116 (60%)	113 (61%)
Race/ethnicity			
Non-Hispanic White	80 (18%)	41 (18%)	39 (17%)
Non-Hispanic Black	85 (19%)	41 (18%)	44 (20%)
Hispanic	264 (59%)	133 (60%)	131 (59%)
Other	17 (3.8%)	8 (3.6%)	9 (4.0%)
Highest level of education			
Did not complete HS	140 (31%)	70 (31%)	70 (31%)
HS or GED	191 (43%)	92 (41%)	99 (44%)
College or graduate degree	117 (26%)	63 (28%)	54 (24%)
Current employment status			
Employed/Self-employed	254 (57%)	134 (60%)	120 (54%)
Unemployed/Retired/Homemaker/Student	194 (43%)	91 (40%)	103 (46%)
Yearly household income			
< $52,500	217 (67%)	105 (66%)	112 (67%)
$52,500-156,600	80 (25%)	36 (23%)	44 (27%)
>156,600	27 (8.3%)	17 (11%)	10 (6.0%)
Prior opioid use	216 (50%)	106 (48%)	110 (52%)
Struggled with drugs or alcohol in the past	22 (4.9%)	13 (5.8%)	9 (4.0%)
Having children or teens in the household	222 (49%)	114 (50%)	108 (48%)
Someone else in the household taking prescribed opioid pain medications	15 (3.4%)	9 (4.1%)	6 (2.7%)
Study site			
LBJ	296 (66%)	149 (66%)	147 (66%)
MIST-Bellaire	80 (18%)	40 (18%)	40 (18%)
MIST-Sugar Land	74 (16%)	37 (16%)	37 (17%)

Table 2. Baseline characteristics of patients in final analysis [[1]Mean (SD); n (%); Ref=reference group]

Characteristic	Overall[1] N = 143	Opioid Use Agreement, N = 75[1]	Standard Care, N = 68[1]	PP(RR>1)
Age (in years)	47 (13)	48 (13)	46 (13)	0.74
Female	95 (66%)	51 (68%)	44 (65%)	0.68
Race/ethnicity				
Non-Hispanic White	40 (28%)	22 (29%)	18 (26%)	Ref
Non-Hispanic Black	20 (14%)	11 (15%)	9 (13%)	0.47
Hispanic	76 (53%)	38 (51%)	38 (56%)	0.32
Other	7 (4.9%)	4 (5.3%)	3 (4.4%)	0.43
Highest level of education				
Did not complete HS	33 (23%)	17 (23%)	16 (24%)	Ref
HS or GED	57 (40%)	29 (39%)	28 (41%)	0.50
College or graduate degree	52 (37%)	28 (38%)	24 (35%)	0.60
Current employment status				
Employed/Self-employed	88 (62%)	47 (63%)	41 (61%)	Ref
Unemployed/Retired/Homemaker/Student	54 (38%)	28 (37%)	26 (39%)	0.41
Yearly household income				
< $52,500	59 (55%)	27 (51%)	32 (59%)	Ref
$52,500-156,600	36 (34%)	18 (34%)	18 (33%)	0.64
>156,600	12 (11%)	8 (15%)	4 (7.4%)	0.87
Prior opioid use				
No	62 (45%)	31 (42%)	31 (48%)	Ref
Yes	76 (55%)	43 (58%)	33 (52%)	0.79
Struggled with drugs or alcohol in the past				
No	138 (97.2%)	73 (98.6%)	65 (95.6%)	Ref
Yes	4 (2.8%)	1 (1.4%)	3 (4.4%)	0.05

Having children or teens in the household				
No	58 (41%)	32 (43%)	26 (38%)	Ref
Yes	85 (59%)	43 (57%)	42 (62%)	0.31
Someone else in the household taking prescribed opioid pain medications				
No	133 (97.8%)	69 (97.2%)	64 (98.5%)	Ref
Yes	3 (2.2%)	2 (2.8%)	1 (1.5%)	0.48
Surgery Procedure				
Minor General Surgery	71 (50%)	37 (49%)	34 (50%)	Ref
Major MIS	59 (41%)	33 (44%)	26 (38%)	0.66
Perianal	6 (4.2%)	1 (1.3%)	5 (7.4%)	0.02
Major Open	7 (4.9%)	4 (5.3%)	3 (4.4%)	0.47
Study site				
LBJ	81 (57%)	41 (55%)	40 (59%)	Ref
MIST-Bellaire	32 (22%)	16 (21%)	16 (24%)	0.44
MIST-Sugar Land	30 (21%)	18 (24%)	12 (18%)	0.78

Table 3. Primary and secondary outcomes b

Outcome b	Overall b	Opioid Use b Agreement, N = l 75 l	Standard Care, N = 68 l	RR (95% Crl) b	PP(RR>1) b
Dispose of leftover[abc]	13 (9.1%) l	5 (6.7%) l	8 (12%) l	0.66 (0.28 – 1.57) l	.17 l
Safe disposal l method[a]	8 (62%) l	3 (60%) l	5 (63%) l	1.00 (0.28 – 3.58) l	.50 l
Safe storage[ab]	9 (6.3%) l	4 (5.3%) l	5 (7.4%) l	. 73 (0.18 – 2.77) l	.32 l
Child-safe container[ab]	141 (99%) l	74 (100%) l	67 (99%) l	1.00 (0.96 – 1.06) l	.61 l
Diversion l	(0%) l	(0%) l	(0%) l	-	-

[a] adjusted for study site l
[b] adjusted for struggled with drugs or alcohol in the past l
[c] adjusted for procedure l
For the primary outcome: RD (95% Crl) = -0.02 (-0.18 – 0.04), PP(RD>0) = 0.17 l

Table 4. Primary and secondary outcomes by clinic location b

Characteristic b	LBJ, l N = 81[1]	MIST-Bellaire, l N = 32[1]	MIST-Sugar b Land, N = 30[1]	RR_B (95%Crl) b	PP_B	RR_S (95%Crl) b	PP_S
Disposed of l leftover opioids l [abc]	5 l (6.2%) l	3 (9.4%) l	5 (17%) l	.90 l (0.11-l 7.42) l	.46 l	2.17 l (0.33– l 14.94) l	.79 l
Safe disposal l method [a]	3 (60%) l	2 (67%) l	3 (60%) l	1.10 (0.20 l –l5.44)l	.56 l	1.00 l (0.27 – l 3.51) l	.50 l
Safe storage [ab]	7 l (8.6%) l	1 (3.1%) l	1 (3.3%) l	.28 l (l.01-l 1.68) l	.09 l	.29 l (l.01-l 1.78) l	.11 l
Child-safe l container [ab]	81 l (100%) l	30 (97%) l	30 (100%) l	.96 l (0.84-l 1.02) l	.11 l	.99 l (0.89-l 1.03) l	.28 l

[a] adjusted for intervention group l

[b] adjusted for struggled with drugs or alcohol in the past l

[c] adjusted for procedure l

RR_B Risk ratio comparing MIST-Bellaire to LBJ Hospital, PP_B Posterior probability that the Risk ratio comparing l MIST-Bellaire to LBJ Hospital is higher than 1, RR_S Risk ratio comparing MIST-Sugarland to LBJ Hospital, PP_S Posterior probability that the Risk ratio comparing MIST-Sugarland to LBJ Hospital is higher than 1. l

LIST OF PUBLICATIONS AND PRODUCTS

The results of the Delphi study were presented at the following conference:

Schäfer W, Iroz C, Johnson J, Shallcross M, Huang R, Balbale S, Stulberg JJ. The Development of a Patient-Provider Opioid Use Agreement for Surgical Care Using the Delphi Method. American College of Surgeons (ACS) Quality and Safety Conference. Virtual, July 2021. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10522037/

At the completion of the project period, we are in the process of submitting a manuscript for publication.

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