Increasing system-wide implementation of opioid prescribing guidelines in primary care: findings from a non-randomized stepped-wedge quality improvement project.

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Abstract

Background: Clinician utilization of practice guidelines can reduce inappropriate opioid prescribing and harm in chronic non-cancer pain; yet, implementation of "opioid guidelines" is subpar. We hypothesized that a multi-component quality improvement (QI) augmentation of "routine" system-level implementation efforts would increase clinician adherence to the opioid guideline-driven policy recommendations.

Methods: Opioid policy was implemented system-wide in 26 primary care clinics. A convenience sample of 9 clinics received the QI augmentation (one-hour academic detailing; 2 online educational modules; 4-6 monthly one-hour practice facilitation sessions) in this non-randomized stepped-wedge QI project. The intervention subjects were volunteer clinic staff. The target patient population was adults with chronic non-cancer pain treated with long-term opioids. The outcomes included the clinic-level percentage of target patients with a current treatment agreement (primary outcome), rates of opioid-benzodiazepine co-prescribing, urine drug testing, depression and opioid misuse screening, and prescription drug monitoring database check; additional measures included daily morphine-equivalent dose (MED), and the percentages of all target patients and patients prescribed ≥90mg/day MED. T-test, mixed-regression and stepped-wedge-based analyses evaluated the QI impact, with significance and effect size assessed with two-tailed $p<0.05$, 95% confidence intervals and/or Cohen's *d*.

Results: Two-hundred-fifteen intervention subjects, a subset of clinical staff, received at least one intervention component; 1,255 patients in the intervention and 1,632 patients in the 17 comparison clinics were prescribed long-term opioids. At baseline, more intervention than comparison clinic patients were screened for depression (8.1% vs 1.1%, p=0.019) and prescribed ≥90mg/day MED (23.0% vs 15.5%, p=0.038). The stepped-wedge analysis did not show statistically significant change in outcomes in the intervention clinics, when accounting for the comparison clinics' trends. The Cohen's *d* values favored the intervention clinics in all outcomes except opioid-benzodiazepine co-prescribing. Subgroup analysis showed that patients prescribed ≥90mg/day MED in the intervention compared to comparison clinics improved urine drug screening rates (38.8% vs 19.1%, p=0.02), but not other outcomes (p³0.05).

Conclusions: Augmenting routine policy implementation with targeted QI intervention, delivered to volunteer clinic staff, did not additionally improve clinic-level, opioid guideline-concordant care metrics. However, the observed effect sizes suggested this approach may be effective, especially in higher-risk patients, under more rigorous implementation conditions.

Background

Chronic non-cancer pain is a common, disabling condition[1] for which opioids have been increasingly prescribed over the past decades, despite a paucity of research on long-term benefits and strong evidence for dose-dependent harm,[2,3] compounded by inappropriate opioid prescribing practices.[4,5] Implementation of evidence- and guideline-based management of opioid therapy in chronic non-cancer pain can reduce inappropriate prescribing and harm from opioids.[4–11] Adopting guideline-concordant management of opioid therapy in primary care is particularly important because primary care clinicians prescribe approximately half of opioid analgesics.[12] However, research on effective dissemination and implementation of opioid practice guidelines is limited, and shows mixed results.[13,14] In general, guidelines with high clinical complexity and low research evidence support, as is the case with opioid guidelines,[3,15–18] show low adoption rates.[13,14]

In February 2016, one academic health system implemented a guideline-driven[15–17] opioid therapy management policy (opioid policy) in primary care via informational sessions for clinicians and clinic teams (routine rollout).[19] Our project goal was to assess if a multi-faceted, clinic-level quality improvement (QI) intervention in addition to routine rollout, compared to routine rollout alone, would improve guideline- and policy-concordant care and associated metrics,[15–17] assessed via de-identified clinic-level electronic health record (EHR) data.

Methods

This report follows the SQUIRE 2.0 standards for QI reporting.20 Details on the routine rollout, QI protocol development, components and implementation are described elsewhere.19 The Institutional Review Board deemed the project a QI initiative, not constituting human subjects research, as defined under 45 CFR 46.102(d). Context and Setting The academic health system included 35 primary care (internal medicine and family medicine) clinics in rural, suburban and urban settings, caring for 200,000 adult primary care patients. In February 2016, it introduced a guideline-driven opioid policy on the management of long-term (≥ 3 months) opioid therapy in primary care adult outpatients with chronic non-cancer pain ("target patients"). The opioid policy provided multiple guideline-concordant recommendations for safety, treatment response monitoring, and management in this target population.19 The system-wide routine rollout of this policy involved a pilot-testing of the rollout methods in 3 clinics in the fall of 2015, followed by the system-wide rollout in February 2016 that consisted of an one-hour in-person meeting for clinicians; an one-hour online training session for clinic staff; and two follow-up tele-meetings to address comments/questions from the clinic staff.19The health system's leadership approved this QI project to determine if augmenting the routine rollout would improve outcomes in this target patient population. Clinic Selection The health system included 35 primary care clinics. Nine of these clinics were involved in other opioid QI initiatives and were excluded from the recruitment pool, yielding 26 clinics eligible for the QI project and included in the analyses. Among these 26 clinics, those with the highest number of target patients were approached first. Three of the approached clinics declined ("too busy for new QI efforts"). The first 9 consenting clinics (convenience sample) were enrolled into a non-randomized stepped-wedge QI project. The QI intervention was initiated immediately after the health system's routine policy rollout in February 2016. It was delivered over 4-6 months at each clinic and implemented in three waves (March-July 2016; September-December 2016; January-June 2017), with 3 clinics per wave; the QI wave assignment was non-random, based on each clinic's preference. Participants The intervention subjects were volunteer clinical staff (prescribers, nurses and others) at each intervention clinic. The evaluation subjects (target patient population) were identified by the search of EHR-based data from the problem list, encounter, and billing records,using the health system-developedcriteria: age ≥ 18 years old; active-patient status (seen at the clinic in the past 3 years); primary care provider within the health system; no diagnosis of malignant neoplasm (except non-melanoma skin cancer) or palliative or hospice care status; and meeting at least one of the two criteria: 1) ≥1 opioid prescription issued in the prior 45 days and ≥3 opioid prescriptions issued in the prior 4 months; or 2) ≥1 opioid prescription issued in the prior 45 days, and presence of a chronic pain diagnosis and a controlled substance agreement. For the analyses, buprenorphine was excluded from the "eligible opioid" list due to its primary utility locally as a treatment for opioid use disorder. QI Intervention The intervention was developed by the project's multidisciplinary team with input from the health system leadership and clinicians to ensure alignment with opioid prescribing guidelines and the health system's policies, procedures and resources, as detailed elsewhere.19 Briefly, the QI intervention at each clinic consisted of: a) one 1-hour academic detailing session, delivered by the project physicians, outlining the project, the national guidelines, and the health system's opioid policy recommendations; b) two 20-21 question online educational modules: one on shared decision-making in the context of opioid therapy for chronic pain, and another on the guideline and health system policy

recommendations for opioid therapy management; and c) six 1-hour practice facilitation (PF) sessions delivered at each clinic over 4-6 months by the project's trained facilitators. The PF sessions focused on optimizing clinical workflows to promote clinician adherence to the guideline and health system policy recommendations with measurable outcomes ("QI targets"). The selection of QI targets for the PF sessions was driven by each clinic team's preference.19 Participating clinical staff were eligible for up to 23 AMA PRA Category 1™ Credits for completing the intervention. Measures De-identified outcome measures were extracted monthly from the EHR (Epic Systems Corporation) from baseline (January 2016) through project end (December 2017). Data were analyzed at the clinic level. Outcome measures were selected based on the opioid prescribing guideline15-17 and policy recommendations, and availability of EHR data entered as a part of health system's routine care.19 The percentage of target patients with a "current" (signed within the past 12 months) treatment agreement was chosen as the primary outcome based on the health system's opioid policy, which recommended its routine completion, followed by annual updates.19 Secondary outcome measures were: a) "current" (past 12 months) urine drug testing (UDT) and b) depression screen with a two- or nine-item Patient Health Questionnaire (PHQ)21,22 (a positive screen using a two-item questionnaire automatically triggered completion of a nine-item questionnaire); c) prescription drug monitoring program (PDMP) database check; d) completion of the opioid misuse risk screen with the Diagnosis, Intractability, Risk, Efficacy (D.I.R.E.) tool;23 and e) the rate of opioid-benzodiazepine co-prescribing in at least one of the prior 3 months. Secondary outcomes a-d were based on the UWH policy. The co-prescribing measure was not a part of the health system's policy, but was included based on guideline recommendations advising against co-prescribing.15-17 Additional measures of interest commonly used to assess opioid interventions15-18 included: a) percentage of target patients relative to the total adult clinic panel; b) daily opioid dose, calculated per target patient as an average morphine-equivalent dose (MED; milligrams/day) by adding up the doses of all opioids (except buprenorphine) prescribed for outpatient treatment in the prior 90 days and dividing the sum by 90; and c) percentage of target patients prescribed MED ≥90 mg/day (past 90 days). Opioid and benzodiazepine prescription data were extracted from the medication list. Statistical analysis Nine clinics were predicted to provide 80% power to detect a clinically meaningful (20%) increase in the use of a treatment agreement (see Additional File 1 for a detailed sample size discussion). Primary and secondary outcomes were defined a priori. SAS Version 9.4 was used for statistical analyses. Baseline (January 2016) and project end (December 2017) data were collected using clinic-level averages, weighted by target patient panel size per clinic. Descriptive statistics were used to describe these data. Single and two-sample means tests evaluated outcome changes between baseline and exit data within and between the intervention and comparison clinics, respectively. For the PDMP outcome measure, the end date was changed from December to March 2017 due to changes in state law and health system requirements, which led to approximately 100% PDMP check documentation across the clinics starting in April 2017. The primary evaluation of intervention impact was conducted using a mixed-effects regression analysis model. The model leveraged the monthly EHR data and accounted for the timing of intervention delivery in the intervention clinics by contrasting clinic-level pre-intervention data, with data collected during and then after the intervention (stepped-wedge analysis). The stepped-wedge analysis was further augmented by adding comparison clinics' monthly data during the same assessment period. Linear curves were fitted to the monthly outcomes as fixed effects, with baseline values and slopes of change separately estimated for intervention and comparison clinics. Additional fixed effects were included to allow the slopes of fitted curves for intervention clinic outcomes to change in relation to the intervention and post-intervention periods. Random effects were included at the levels of both the primary care provider (PCP) within each clinic and the clinic as a whole to account for correlation among monthly observations from the same PCP or the same clinic. Observations were also weighted by the number of target patients within each PCP's monthly panel. Estimates of the differential slopes (pre-intervention, intervention and post-intervention) for the intervention clinics and a single, study-long slope for the comparison clinics were used to

assess the impact of the intervention on the intervention clinics' outcomes. Baseline differences between intervention and comparison clinic characteristics, and between clinic and PCPs within each study group, were accounted for in differential baseline intercepts and slopes, and with random intercept and slope effects, respectively. See Additional File 2 for details of the mixed effect model and result interpretation. A subgroup analysis was conducted among target patients treated with MED ≥90 mg/day, because of their increased risk for opioid-related harm.18 The significance and magnitude of changes were assessed with p values (significance level: two-tailed $p<0.05$), 95% Confidence Intervals (CIs), and/or Cohen's d (ES, 0.2-0.4: small; 0.5-0.7: medium; ≥0.8: large effect size).

Results

Participating clinic staff (intervention subjects) A total of 215 unique health care providers, including 73 prescribers and 142 other clinic staff from the enrolled *4 family medicine and 5 internal medicine* clinics completed at least one component of the QI intervention (intervention subjects; Table 1). Among the intervention subjects, 48.4% completed half or more of the intervention components; 44.7% completed at least 4 of the 6 practice facilitation sessions (Table 1). The intervention participation was voluntary, and not all clinic health care providers participated; although data on the total clinic staff were not collected, it was estimated that less than 50% of the clinical staff received the intervention.

Baseline characteristics of the target patient population Across the 26 evaluated primary care clinics, 3,148 target patients (58.1% women, mean age 53.3 ±13.8 years) were identified, with 1,431 in the intervention and 1,717 in the comparison clinics. These patients comprised 1.9% of the intervention and 2.0% of the comparison clinics' adult patient panels. A comparison of weighted, clinic-level baseline characteristics showed that the target patients in the intervention and comparison clinics (Table 2) did not differ in a statistically significant way in relatively high daily MED doses and the rates of opioid-benzodiazepine co-prescribing. They also did not differ in their overall low rates of "current" treatment agreements, urine drug testing, completed opioid risk assessment, and documented PDMP check. However, the intervention clinics, relative to the comparison clinics, had higher rates of completed depression screening (8.1%±10.4 vs. 1.1%±1.3, p=0.019) and of patients prescribed MED ≥90 mg/day (23.0%±8.8 vs 15.5%±7.3, p=0.038). No statistically significant differences in baseline characteristics were noted in a subgroup of target patients treated with MED ≥90 mg/day in the intervention (N=359) and comparison (N=283) clinics.

Primary Outcome Analysis: Mixed-Effects Regression Analysis Regression analysis of monthly outcomes by clinic and prescriber recognized variations in the timing of the intervention from clinic to clinic within the intervention group. This analysis did not reveal statistically significant changes in outcomes in the stepped-wedge pre-post analyses, which contrasted the pre-intervention with the combined intervention and post-intervention periods. Augmentation with data from the comparison clinics did not impact these findings. See Additional File 3 for detailed results.

However, when the evaluation specifically focused on the intervention period, separating it from the post-intervention period, several statistically significant changes were noted in the intervention clinics, after accounting for the trends in the comparison clinics (see Additional File 3). The completion rate of new treatment agreements (incidence rate) increased by 9.4% in the intervention clinics during the intervention months in both the overall target population (p=0.023; 95%CI=[0.028,0.159]) and 15.9% in the subgroup of patients treated with MED ≥90 mg/day (p=0.044, 95%CI=[0.029,0.289]); these differences were not sustained post-intervention in either group. In addition, in the intervention clinics, among the overall target population and in the high-dose subgroup, MED

decreased post-intervention (by -2.75 and -6.50 mg/day, respectively), but not during the intervention period (0.80 and 12.43 mg/day, respectively).

Secondary outcomes: means tests Both the intervention and comparison clinics improved on all outcomes among the target population (Table 3), except the prevalence of opioid-benzodiazepine co-prescribing, which improved in the comparison clinics only (p=0.006). When comparing the change in outcomes between the intervention and comparison clinics, no statistically significant differences were noted. However, Cohen *d* effect sizes favored the intervention clinics, except for opioid-benzodiazepine co-prescribing (a small ES in the intervention and a moderate ES in the comparison clinics).

Among the subgroup of target patients prescribed MED ≥90 mg/day (Table 4), all outcomes tended to improve in both the intervention and comparison clinics. Comparing the change in outcomes, prevalence of urine drug screening increased twice as much in the intervention clinics (38.8%±4.4 vs. 19.1%±7, p = 0.020). While there were no other statistically significant differences between the intervention and comparison clinics, Cohen's *d* effect sizes again favored the intervention clinics.

Discussion

Strengths of this study include its large sample size, breadth of application, and pragmatic approach to testing under actual clinical conditions. The outcome analysis was conservative; it was conducted on the global clinic level, without accounting for how many clinic staff members participated in the QI efforts, the clinic-selected improvement targets, the clinic's participation efforts or its leadership's support. Those strengths, however, also led to the primary limitation of this QI project. Not all prescribers received the intervention; yet, because all target patients within a clinic were evaluated as an aggregate EHR data set, we are unable to separate the specific outcomes of patients whose prescribers and other health care providers received the intervention from patients whose clinicians did not receive it. However, this limitation makes all the more remarkable the statistically significant difference in urine drug screening among higher-risk patients (treated with high-dose opioids) and the universal favoring of intervention by Cohen's d effect sizes.

Another limitation was the absence of randomization in clinic assignment to intervention versus comparison groups. Randomization would have avoided potential selection bias. However, because clinic participation was voluntary, a convenience sample approach was necessary. Although we excluded clinics actively engaged in other opioid-related QI initiatives, clinics we approached who declined to participate may have done so because they had more fully embraced the concept of implementing the system-wide policy changes, such that their addition to the comparison group artificially elevated that cohorts' average changes. In addition, each intervention clinic selected their own targets for focused improvements, potentially further diluting the intervention effects on any one of the measures.

State-wide legislative changes during our QI project represented a potential substantial confounder. In April 2017, a state law went into effect requiring clinicians to check a patient's PDMP record before prescribing any controlled substances, including opioids. As a result, many health systems across the state, including the evaluated health system, implemented a system-wide requirement of PDMP check documentation prior to issuing prescriptions for controlled substances. This led to an essentially 100% adherence to this practice starting in April 2017. In addition, in 2017, the State Medical Examining Board introduced a new requirement that all prescribers complete 2 hours of approved Continuing Medical Education (CME) on opioid prescribing guidelines for chronic pain. While we

ameliorated the impact on our PDMP metric by changing that measure's end date to March 2017, there is little question that these two external factors and the general increase in public discourse relating to opioid-related harms during the QI period likely contributed to a dilution of our intervention effects. Our baseline and exit data demonstrated that there was substantial room for improvement in the monitoring of patients treated with long-term opioids. The legal and licensing changes and the PDMP check requirements can lead to a decrease in the number of prescriptions for opioids and prescribed opioid doses.[24] However, these changes do not necessarily translate into reduction in overdose admission rates, which have recently increased in the state.[25] This suggests that developing methods to increase clinician adherence to guidelines through education on opioid addiction care and non-opioid therapies for chronic pain remains an important area of research to improve patient outcomes.

This QI project did not show statistically significant impact of our intervention on the primary or secondary outcomes in a non-randomized stepped-wedge analysis. However, the intervention did yield a marked, statistically significant increase in urine drug screening for higher-risk patients treated with high-dose opioids. It also yielded a transient increase in the incidence of new treatment agreements during the intervention period. Further, the magnitude of change in outcomes for all target patients, as assessed by Cohen's d effect size values, suggests that the intervention may help reduce high-dose opioid prescribing in primary care patients treated with long-term opioids for chronic pain. For these reasons, our results offer the chance of conclusive success through a similar intervention under more rigorous conditions. This hypothesis can be tested by applying a similar intervention to prescribers of moderate-dose and high-dose opioid-treated patients, and comparing the results not of the entire clinic population, but only those patients whose prescriber(s) received the intervention.

Conclusions

Augmenting a routine opioid-policy rollout with a QI intervention targeting implementation of chronic pain-related opioid prescribing guidelines did not add a substantial benefit in terms of guideline-concordant care metrics or opioid prescribing in primary care. However, improvements during the intervention period and in a subgroup of patients treated with higher-dose opioids suggest that the favorable effect sizes noted in the intervention clinics may yield statistically significant results under more rigorous implementation conditions.

Declarations

Ethics approval and consent – The University Institutional Review Board determined that this project was a QI initiative, not constituting human subjects research as defined under 45 CFR 46.102(d).

Consent for publication – Not Applicable

Availability of data and materials – The datasets generated and/or analyzed during the current study are not publicly available due to institutional policy on patient data sets, but may be available from the corresponding author on reasonable request.

Competing interests – The funding for this study came from a competitive peer-reviewed researcher-initiated unrestricted grant from Pfizer, awarded to the Interstate Postgraduate Medical Association in partnership with the University of Wisconsin; Pfizer was not involved in the design and conduct of this project or the manuscript write-up. Some of the authors (AEZ, JMR, PDS, DB, WJT, RMV, DLH) were employed during the project by the University of Wisconsin (UW); the UW Health primary care clinics were the target for the described QI intervention. In addition,

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Authors' contributions - All authors substantially contributed to this work in accordance with editorial guidelines. AEZ contributed to project conception, design, and conduct, and drafted the manuscript. RMV, PS, MWA, KN, DB, WJT, and DLH contributed to project conception, design and execution, and edited the manuscript. RPL contributed to the manuscript preparation and write-up. All authors read and approved the final version and agree to responsibility for their contributions.

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Abbreviations

AMA PRA: American Medical Association Physician's Recognition Award; CI: confidence interval; EHR: Electronic Health Record; LB, UB: lower bound, upper bound; CME: continuing medical education; MED: morphine equivalent dose; MEDD: morphine-equivalent daily dose; PC: primary care; PCP: primary care provider; PDMP: prescription drug monitoring program; PF: practice facilitation; QI: Quality Improvement; SAS: statistical analysis system; UDT: urine drug testing

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Tables

Table 1. Completion of the intervention components among the intervention clinics' staff.

sition	Completed ≥1 intervention component	Completed ≥50% of the intervention components*	Completed Academic Detailing	Completed Online Opioid Module	Completed Online Shared Decision Making Module	Completed ≥1 Practice Facilitation Session	Completed ≥4 Practice Facilitation Sessions
Wave 1 Intervention Clinics							
Clinic 1: Internal Medicine (urban, residency clinic)							
), DO	7	5	6	4	3	6	2
, PA	3	0	1	1	0	3	1
, MA, IA, N	17	9	1	10	4	16	10
ıer ff	7	1	0	1	0	1	1
Total	34	15	8	16	7	26	14
Clinic 2: Internal Medicine (urban, non-residency clinic)							
D, DO	8	5	7	5	4	1	1
P, PA	0	0	0	0	0	0	0
, MA, MA, LPN	24	14	23	11	9	6	6
ther taff	8	2	4	2	2	2	2
Total	40	21	34	18	15	9	9
Clinic 3: Family Medicine (rural; residency clinic)							
D, DO	8	3	6	3	3	5	2
NP, PA	1	1	1	1	1	1	1
, MA, CMA, LPN	9	8	8	2	2	8	8
Other staff	4	1	3	0	0	5	2
Total	22	13	18	6	6	19	13
Wave 2 Intervention Clinics							
Clinic 4: Family Medicine (urban; residency clinic)							
), DO	4	3	3	2	1	4	3
, PA	1	0	0	0	0	1	0
, MA, IA, N	6	3	3	4	4	5	5
ıer ff	3	2	3	1	1	3	2
Total	14	9	9	7	6	13	10
Clinic 5: Family Medicine (urban; residency clinic)							
), DO	11	5	9	4	2	4	4
, PA	4	1	3	0	0	2	1
, MA, IA, N	11	3	10	3	3	3	2
ıer ff	8	0	0	0	0	5	4

Total	34	9	22	7	5	14	11
Clinic 6: Internal Medicine (urban; residency clinic)							
), DO	7	1	7	0	0	6	2
, PA	3	1	3	1	0	3	1
, MA, IA, N	14	5	12	2	1	14	5
ner ff	3	0	0	0	0	2	0
Total	27	7	22	3	1	25	8
Wave 3 Intervention Clinics							
Clinic 7: Family Medicine (suburban; non-residency clinic)							
), DO	3	3	2	1	1	3	3
, PA	1	1	1	1	1	1	0
, MA, IA, N	7	5	6	2	2	6	5
ner ff	2	0	0	0	0	2	1
Total	13	9	9	4	4	12	9
Clinic 8: Internal Medicine (urban; residency clinic)							
), DO	4	1	3	1	1	2	1
, PA	2	2	2	1	1	1	1
, MA, IA, N	6	4	5	0	0	6	4
ner ff	3	3	2	1	0	3	3
Total	15	10	12	3	2	12	9
Clinic 9: Internal Medicine (urban; residency clinic)							
), DO	4	4	4	2	1	4	3
, PA	22	1	2	0	1	1	0
, MA, IA, N	10	7	9	1	2	8	7
ner ff	0	0	0	0	0	0	0
Total	16	12	15	3	4	13	10
All Intervention Clinics							
), DO	56	30	47	22	16	34	22
, PA	17	7	13	5	4	12	6
, MA, IA, N	104	58	77	35	27	68	53
ner ff	38	9	12	5	3	23	15
Total	**215**	**104**	**149**	**67**	**50**	**137**	**96**

* 50% completion applies to individuals who completed two of the four intervention components: Academic Detailing, Online Opioid Module, Online Shared Decision Making Module, Practice

Facilitation (4 of 6 sessions)

Table 2: Baseline characteristics of the target patient population.

Characteristics	Intervention clinics at baseline (N=1,431)	Comparison clinics at baseline (N=1,717)	p value*
Women, % (SD)	57.7 (7.1)	60.7 (8.9)	0.400
Mean age, years (SD)	53.6 (3.2)	53.8 (3.5)	0.864
Completed treatment agreement (past 12 months), % (SD)	24.8 (13.8)	29.2 (18.3)	0.531
Completed urine drug testing (past 12 months), % (SD)	24.7 (11.8)	31.3 (16.2)	0.285
Completed depression screening (past 12 months), % (SD)	8.1 (10.4)	1.1 (1.3)	**0.019**
Completed opioid misuse risk assessment, % (SD)	0.2 (0.4)	0.7 (1.8)	0.478
Documented PDMP Check (past 12 months), % (SD)	0.0 (0.1)	0.3 (1.2)	0.503
Co-prescribed benzodiazepines in at least 1 out of 3 past months, % (SD)	19.9 (4.3)	24.7 (7.4)	0.089
Percentage of the adult clinic population, % (SD)	2.0 (0.9)	2.1 (0.6)	0.906
MED (past 90 days), mg/day, mean (SD)	75.7 (29.7)	55.9 (19.4)	0.063
MED ≥ 90 mg/day (past 90 days), % (SD)	23.0 (8.8)	15.5 (7.3)	**0.038**

Legend

Population of adult patients with opioid-treated chronic non-cancer pain in the 9 intervention and 17 comparison primary care clinics: characteristics at baseline (January 2016) based on the equally-weighted clinic averages.

MED: Morphine-equivalent Dose; PDMP: Prescription Drug Monitoring Program; SD: standard deviation

* p value was determined using the two-sample means test comparing clinic-level values for intervention versus comparison clinic groups

Table 3. Target Patient Population: Change in Outcomes.

	Change in Intervention clinics (N=1,255 at exit)			Change in Comparison clinics (N=1,632 at exit)			Change in Intervention versus Comparison clinics		
teristics	Change from baseline	p value†	Cohen's *d*	Change from baseline	p value†	Cohen's *d*	Difference	p value‡	Cohen's *d*
eted ent nent (past nths), % I (LB,UB)	32.0 (6.7) (18.8, 45.2)	<0.001	2.1	29.2 (6.7) (16.1, 42.4)	<0.001	1.5	2.8 (9.6) (-16.1, 21.6)	0.816	0.1
eted urine esting 2 s), % I (LB,UB)	33.4 (7.0) (19.8, 47.1)	<0.001	2.6	25.7 (5.3) (15.3, 36.1)	<0.001	1.7	7.7 (8.7) (-9.3, 24.7)	0.277	0.4
eted sion ing (past nths), % I (LB,UB)	49.2 (6.1) (37.2, 61.1)	<0.001	3.4	55.4 (6.9) (41.8, 69.0)	<0.001	3.3	6.2 (9.6) (-25.1, 12.6)	0.526	0.3
eted misuse sessment, , I (LB,UB)	5.4 (3.0) (-0.5, 11.3)	0.070	0.9	10.1 (5.8) (-1.4, 21.5)	0.050	0.7	-4.7 (7.4) (-19.2, 9.9)	0.417	0.3
ented Check 2 s), % I (LB,UB)	50.7 (6.3) (38.3, 63.1)	<0.001	3.8	39.9 (7.8) (24.6, 55.2)	<0.001	2.0	10.8 (10.8) (-10.4, 32.0)	0.301	0.4

scribed liazepines ast 1 out st s, % (SE), I (LB,UB)	-1.2 (1.6) (-4.3, 1.9)	0.461	0.3	-5.4 (1.8) (-9.0, -1.8)	0.006	0.7	4.3 (2.7) (-0.9, 9.5)	0.143	0.7
tage of ult clinic tion, % I (LB,UB)	-0.3 (0.2) (-0.6, 0.0)	0.042	0.4	-0.4 (0.1) (-0.6, -0.1)	0.056	0.5	0.0 (0.2) (-0.3, 0.4)	0.547	0.1
past 90 mg/day, SE), I (LB,UB)	-11.6 (2.4) (-16.4, -6.9)	<0.001	0.4	-9.9 (3.0) (-15.8, -4.1)	0.0001	0.6	-1.7 (4.0) (-9.6, 6.2)	0.937	0.2
: 90 y (past 90 % (SE), I (LB,UB)	-3.5 (1.1) (-5.8, -1.3)	0.002	0.4	-1.6 (0.7) (-3.0, -0.1)	0.004	0.2	-2.0 (1.3) (-4.5, 0.6)	0.270	0.7

Legend

Population of adult patients with opioid-treated chronic non-cancer pain in the 9 intervention and 17 comparison primary care clinics; characteristics at exit (December 2017) and their patient-weighted change from baseline.

CI (LB,UB): Confidence Interval (Lower Bound, Upper Bound); MED: Morphine-equivalent Dose; PDMP: Prescription Drug Monitoring Program; SE: standard error

* Exit data for the PDMP outcome was collected in March 2017; starting in April 2017, the PDMP check documentation rose to approximately 100% across all clinics due to the changes in documentation requirements.

† p value was determined using the single sample mean test comparing clinic-level changes in outcomes from baseline to exit

‡ p value was determined using the two-sample means test comparing clinic-level changes in outcomes from baseline to exit for intervention versus comparison clinic groups

Table 4. Target Patient Population Treated with ≥ 90 mg/day of Morphine-equivalent Opioid Dose: Change in Outcomes.

	Change in Intervention clinics (N=271 at exit)			Change in Comparison clinics (N=248 at exit)			Change in Intervention versus Comparison clinics		
ıcteristics	Change from baseline	p value†	Cohen's *d*	Change from baseline	p value†	Cohen's *d*	Difference	p value‡	Cohen's *d*
ıleted ıent ment 12 ıs), % CI (LB,UB)	41.1 (9.3) (23.0, 59.3)	<0.001	1.9	40.9 (8.2) (24.9, 56.9)	<0.001	2.0	0.2 (12.2) (-23.7, 24.1)	0.783	0.0
ıleted drug g (past 12 ıs), % CI (LB,UB)	38.8 (4.4) (30.2, 47.4)	<0.001	2.3	19.1 (7.0) (5.4, 32.8)	0.036	1.0	19.8 (10.4) (-0.7, 40.2)	**0.020**	0.8
ıleted ssion ning (past ɔnths), % CI (LB,UB)	54.2 (7.6) (39.4, 69.0)	<0.001	2.6	60.6 (9.7) (41.5, 79.7)	<0.001	2.6	-6.3 (13.1) (-32.1, 19.4)	0.528	0.2
ıleted l misuse sment, % CI (LB,UB)	7.2 (3.8) (-0.3, 14.7)	0.060	0.9	10.3 (6.6) (-2.7, 23.3)	0.074	0.6	-3.1 (8.5) (-19.7, 13.6)	0.582	0.2
ımented	56.5	<0.001	3.8	45.2	<0.001	2.3	11.3	0.263	0.4

² Check 12 ıs)*, % CI (LB,UB)	(6.9) (43.0, 70.0)			(8.0) (29.6, 60.8)			(11.3) (-10.8, 33.4)		
escribed diazepines east 1 out ast ıs, % (SE), CI (LB,UB)	-5.8 (3.5) (-12.6, 0.9)	0.091	0.5	-6.0 (5.1) (-16.0, 4.0)	0.039	0.4	0.1 (6.7) (-13.0, 13.3)	0.486	0.0
ntage of lult clinic ation, % CI (LB,UB)	-0.2 (0.1) (-0.3, 0.0)	0.030	0.4	-0.1 (0.0) (-0.1, 0.0)	0.031	0.3	-0.1 (0.1) (-0.2, 0.1)	0.224	0.5
(past 90 , mg/day, (SE), CI B)	-26.9 (10.0) (-46.5, -7.3)	0.007	0.5	-33.8 (16.5) (-66.2, -1.4)	0.005	0.6	6.9 (21.6) (-35.3, 49.2)	0.356	0.1

Legend

Population of adult patients with chronic non-cancer pain treated with opioid dose ≥ 90 morphine-equivalent mg/day in the 9 intervention and 17 comparison primary care clinics; characteristics at exit (December 2017) and their patient-weighted change from baseline.*

CI (LB,UB): Confidence Interval (Lower Bound, Upper Bound); MED: Morphine-equivalent Dose; PDMP: Prescription Drug Monitoring Program; SE: standard error

* Exit data for the PDMP outcome was collected in March 2017; starting in April 2017, the PDMP check documentation rose to approximately 100% across all clinics due to the changes in documentation requirements.

† p value was determined using the single-sample mean test comparing clinic-level changes in outcomes from baseline to exit

‡ p value was determined using the two-sample means test comparing clinic-level changes in outcomes from baseline to exit for intervention versus comparison clinic groups

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- AdditionalFile2.Mixedeffectmodelandsampleresults.docx
- AdditionalFile3.Summaryofmixedeffectsmodelresults.docx
- AdditionalFile1.SampleSizeEstimation.docx