



Original Investigation | Health Policy

Integrating Nonpharmacological Options Into Perioperative Pain Care A Cluster Randomized Clinical Trial

Andrea L. Cheville, MD, MSCE; Jeph Herrin, PhD; Sarah Minter, PhD; Veronica Grzegorzczak, MPH; Jon Tilburt, MD; for the Mayo Clinic NOHARM Research Team

Abstract

IMPORTANCE Postoperative pain is commonly treated with opioids, which may contribute to unnecessary opioid-related harms. Scalable approaches to integrate recommended nonpharmacologic pain care could reduce opioid exposure while improving or at least preserving functional recovery outcomes.

OBJECTIVE To evaluate whether an electronic health record (EHR)-embedded intervention promoting nonpharmacologic pain care improves postoperative pain interference and physical function while reducing opioid exposure.

DESIGN, SETTING, AND PARTICIPANTS This cluster randomized clinical trial was conducted from October 16, 2020, through April 30, 2024. Participants included patients undergoing surgery at 22 surgical practices in 6 surgical centers in Minnesota, Wisconsin, Florida, and Arizona.

INTERVENTION A multicomponent EHR-based intervention including a patient-facing *Healing After Surgery* educational guide, clinical decision support, and nonpharmacologic pain care support materials integrated into routine perioperative touchpoints and workflows.

MAIN OUTCOMES AND MEASURES Co-primary outcomes were Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference and Physical Function T scores measured preoperatively and at 1, 2, and 3 months after surgery. Secondary outcomes included opioid prescribing and administration (morphine milligram equivalents [MMEs]), PROMIS Anxiety scores, and health care utilization for 3 months after surgery. Mixed-effects models were used to account for correlation of outcomes within surgery, patient, and cluster, as appropriate for each model.

RESULTS Among 68 141 included surgical procedures (40 892 male patients [60.0%]; mean [SD] age, 59.27 [16.26] years), 43 053 occurred during the intervention period, and 25 088 occurred during the usual care period. The intervention did not change PROMIS pain interference (adjusted mean difference, 0.09; 95% CI, -0.18 to 0.36; $P = .51$) or PROMIS physical function (adjusted mean difference, 0.15; 95% CI, -0.11 to 0.41; $P = .27$) in the intervention compared with control surgical procedures. However, total postoperative opioid exposure was lower during intervention periods (rate ratio, 0.90; 95% CI, 0.82 to 0.99; $P = .03$), corresponding to an approximately 10% relative reduction and an adjusted mean difference of approximately 260 MMEs per patient, with no changes in anxiety, adverse events, or health care utilization. This reduction was driven primarily by lower opioid administration during hospitalization (adjusted rate ratio, 0.94; 95% CI, 0.90 to 0.97; $P = .001$), with an adjusted mean difference of approximately 85 MMEs.

(continued)

Key Points

Question Does an electronic health record (EHR)-based intervention promoting nonpharmacologic pain care improve postoperative patient-centered outcomes and reduce opioid exposure?

Findings In a cluster randomized clinical trial including 68 141 surgical procedures, the intervention did not improve pain interference or physical function but reduced opioid exposure after surgery.

Meaning These findings suggest that system-level EHR strategies may reduce opioid exposure without worsening patient-reported outcomes.

+ Supplemental content

Author affiliations and article information are listed at the end of this article.

Open Access. This is an open access article distributed under the terms of the CC-BY-NC-ND License, which does not permit alteration or commercial use, including those for text and data mining, AI training, and similar technologies.

Abstract (continued)

CONCLUSIONS AND RELEVANCE In this cluster randomized clinical trial of patients undergoing surgery, an EHR-embedded perioperative pain management intervention promoting nonpharmacologic pain care reduced opioid exposure without changes in patient-reported outcomes, suggesting potential for scalable EHR-based strategies to support safer postoperative pain management.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: [NCT04570371](https://clinicaltrials.gov/ct2/show/study/NCT04570371)

JAMA Network Open. 2026;9(9):e2635900. doi:[10.1001/jamanetworkopen.2026.35900](https://doi.org/10.1001/jamanetworkopen.2026.35900)

Introduction

Millions of Americans undergo surgery each year, and recovery is often accompanied by new or worsening pain. Opioids remain a common and often default treatment, sometimes necessary to optimize postoperative recovery.^{1,2} However, a subset of patients prescribed opioids for surgical pain continue to use opioids long after recovery,¹⁻⁵ and some will progress to opioid use disorder or experience opioid-related overdose.⁶⁻⁸ Perioperative opioid use is also associated with impaired surgical recovery, increased postoperative complications and falls, and higher health care utilization and costs.⁹

Clinical guidelines recommend nonpharmacologic pain care (NPPC) modalities including movement-based, behavioral, and physical approaches as part of multimodal postoperative pain management.¹⁰⁻¹⁶ Patients report interest in these approaches,^{17,18} yet barriers to their routine use persist, including clinician unfamiliarity, limited workflow integration, and uncertainty regarding how to incorporate NPPC into time-constrained perioperative care.¹⁹

Electronic health records (EHRs) can standardize and automate guideline-concordant pain management^{20,21} by delivering patient-facing education through portals while also providing point-of-care clinical decision support (CDS) to clinicians. Prior EHR-based pain interventions have primarily targeted clinician prescribing behavior and have not systematically integrated patient education or patient NPPC preferences.²²

As part of a large federal initiative to curb opioid misuse,²³ we conducted the Non-pharmacological Options in Post-Hospital and Rehabilitation Pain Management (NOHARM) pragmatic trial, a study designed to evaluate intervention effectiveness under conditions representative of routine clinical practice. We tested whether a multicomponent, EHR-embedded intervention promoting NPPC could improve postoperative pain interference and physical function and reduce opioid exposure during the first 3 months after surgery, compared with usual care (UC).

Methods

Trial Design and Oversight

The NOHARM trial was a preregistered, population-level, stepped-wedge, cluster randomized pragmatic clinical trial conducted at 6 high-volume surgical centers (3 quaternary referral centers and 3 community hospitals) in Minnesota, Wisconsin, Florida, and Arizona. The protocol has been published previously and is also shown in [Supplement 1](#).²⁴ Twenty-two clusters, defined as panels of surgical procedures distinguished by surgical department or division and site, with minimal overlap in clinicians and postoperative care settings, were randomized to 1 of 5 sequences. After an initial 6-month UC period, clusters crossed over to the intervention at 7-month intervals according to sequence assignment.

This study was approved by the Mayo Clinic institutional review board, which noted that NOHARM proposed testing an enhanced standard of care against UC and, on the basis of advice from

the National Institutes of Health Systems Collaboratory Ethics and Regulatory Committee, granted a waiver of individual patient consent.²⁵ The trial was overseen by an external Data Safety and Monitoring Board appointed by the National Institutes of Aging. This study follows the Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines.

Participants

Enrollment occurred at the level of the surgical procedure, without additional patient-level eligibility criteria (see eAppendix 1, eFigure 1, eAppendix 2, eTable 1, and eTable 2 in Supplement 2). Procedures were grouped by department or division (colorectal, orthopedic, cardiovascular, thoracic, solid organ transplant, gynecologic, and cesarean delivery) to ensure variation in procedural risk, anatomic region, and expected opioid exposure. A validated EHR algorithm identified and enrolled procedures when a surgical case request was placed or 30 days before the scheduled surgery date, whichever occurred later. Emergent surgical procedures were excluded because the intervention required preoperative patient engagement through the patient portal, except for converted cesarean deliveries and cadaveric organ transplantation.

Intervention

Patients scheduled for a qualifying surgery and assigned to an intervention cluster received a multicomponent, EHR-embedded intervention consisting of (1) the *Healing After Surgery* guide delivered through the patient portal before surgery, (2) clinician-directed EHR CDS prompting allied health staff to reinforce patients' NPPC choices, and (3) NPPC education and self-management resources.²⁴ Table 1 illustrates the delivery of intervention components across the perioperative continuum, highlighting how the intervention engaged patients, prompted care teams, and supported NPPC.

Developed with input from the Mayo Clinic Patient Family Advisory Committee, the *Healing After Surgery* guide described opioid risks and harms, encouraged multimodal pain management, and allowed patients to enter their preferred NPPC modalities (yoga, tai chi, walking, guided imagery, music, progressive muscle relaxation, paced breathing, meditation, aromatherapy, transcutaneous electrical nerve stimulation, massage, acupressure, and heat or cold) directly into Epic. These selections were stored in EHR flowsheets and used to drive CDS and portal-based outreach.

Throughout the perioperative period, nurses, therapists, and other allied health staff reinforced patients' selected NPPC strategies, incorporated them into care when feasible, and updated preferences in the EHR. Additional NPPC resources were available through a dedicated website, twice-weekly Zoom sessions, printed, video, and audio materials, and individualized discharge instructions. Further intervention details are provided in eFigures 2 and 3 in Supplement 2. The trial used an encouragement design in which exposure to intervention components was encouraged but not required (Supplement 1).²⁶⁻²⁹

Table 1. Major Components of the NOHARM Intervention Across the Perioperative Care Continuum^a

Intervention component	Preoperative	Hospitalization	Discharge	Postdischarge
Patient engagement	Select preferred NPPC modalities using the HAS guide; learn and practice selected techniques using educational resources	Use preferred NPPC modalities; update preferences as needed	Review pain management plan and recommendations for home NPPC use	Continue preferred NPPC modalities using available educational and community resources
Clinical care	Introduce NPPC; distribute educational materials and workbook; encourage patients to make preoperative selections	Reinforce and facilitate patient-selected NPPC approaches during nursing, physical therapy, and occupational therapy care, when feasible	Review and reinforce individualized pain management plan; support transition to home use	Routine clinical follow-up
EHR support	Deliver HAS guide via patient portal; capture preferred NPPC modalities in Epic flowsheets via HAS	Prompt clinicians through clinical decision support; document and update NPPC preferences	Populate discharge summary with recommendations for home and community use of selected NPPC techniques	Reinforce continued NPPC use through automated portal messaging and targeted outreach

Abbreviations: EHR, electronic health record; HAS, Healing After Surgery; NOHARM, Non-pharmacological Options in Post-Hospital and Rehabilitation Pain Management; NPPC, nonpharmacologic pain care.

^a The NOHARM intervention combined patient engagement, EHR-enabled clinical decision support, and reinforcement by clinical staff across sequential phases of perioperative care.

Usual Care

UC reflected standard perioperative practices and did not include EHR-based patient education or NPPC preference elicitation, or clinician-directed CDS to increase support for NPPC use. UC is further described in [Supplement 1](#).

Randomization and Blinding

The 22 clusters were randomly assigned to 1 of 5 sequences specifying the timing of crossover from UC to the intervention (eFigure 4 in [Supplement 2](#)). Constrained randomization was used to balance postoperative unit clustering, procedural volume, and site.³⁰ EHR-based rule logic assigned individual procedures to clusters. Participants, clinicians, and investigators were not blinded.

Outcomes

Given their validity, responsiveness, and reliability in postoperative populations,³¹⁻³³ Patient-Reported Outcomes Measurement Information System (PROMIS) Pain Interference and Physical Function T scores measured using computerized adaptive tests (CATs) administered primarily through the Epic patient portal ([Supplement 1](#)) were our co-primary outcomes. Assessments were completed preoperatively and at 1, 2, and 3 months after the index surgery. Each patient-reported outcome measure (PROM) was classified according to the intervention status of the cluster at the time of surgery.

To evaluate potential nonresponse bias related to portal nonuse, 6-item printed PROMIS short forms were mailed to patients who did not use the portal and those who did not complete the 1-month assessment. Because these mailed assessments were not prespecified and differed in mode of administration, measurement precision, and item content, they were included in sensitivity analyses rather than the primary analyses.³⁴

Secondary outcomes included PROMIS Anxiety T scores, postoperative opioid exposure, and health care utilization (emergency department visits, hospitalizations, and intensive care unit admissions) ([Supplement 1](#)). Opioid exposure was assessed through 90 days after surgery and censored at subsequent surgery or death in accordance with Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials consensus recommendations.³⁵ In-hospital opioid administration and prescribing were comprehensively captured through the EHR. Because patients received follow-up care outside the health system, postdischarge opioid exposure may have been incompletely ascertained; therefore, patient-reported opioid use and prescriptions were also collected at 3 months. Opioid exposure outcomes included prescribed and administered morphine milligram equivalents (MMEs). Patient-reported NPPC and opioid use, including opioid refills, were assessed at 3 months by self-administered survey.³⁶

Adverse events were passively monitored through EHR-derived *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* codes assigned during trial participation (eTable 3 in [Supplement 2](#)). Opioid-related adverse events included new opioid use disorder and opioid poisoning or toxicity. Adverse events potentially related to NPPC included falls, burns (from heat or transcutaneous electrical nerve stimulation), and muscle sprains, strains, or spasms. Episodes of potential failure to rescue, defined as 3 consecutive severe pain scores (numerical rating scale, 7-10 of 10), were also monitored. Deaths were also abstracted from the EHR.

Patient and Surgery Characteristics

For each surgery, we collected patient age, sex, race, ethnicity, and medical comorbidities. Race and ethnicity were identified using self-reported patient tables and were classified as American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, and other (ie, patients who chose not to disclose, were recorded as unknown, or were unable to provide this information). Data on race and ethnicity are included here to permit assessment of external validity and generalizability. Surgical characteristics included procedure type, duration, laparoscopic

vs open approach, same day vs overnight surgery, hospital length of stay, and colorectal or hip or knee procedure status, as these surgical procedures are often associated with more intense pain.^{37,38}

Sample Size and Statistical Power

Using historical annual volumes for the included clusters, we conducted simulations to estimate detectable clinically meaningful effects with a power of 90%. From a prior study, we calculated the intraclass correlation coefficient for pain interference PROM scores to be $r = 0.037$. For $P = 1, \dots, 5000$ permutations, we randomly assigned the 22 clusters to 5 sequences. For each permutation, we used the closed-form solution of Harrison et al³⁹ for $SE(Q)$, derived from the formula described by Hussey et al,⁴⁰ for true effect Q . For calculations, we used $\sigma^2 = 1$ and $\tau^2 = 0.488$ so that detectable effects would be in SDs of the PROM score, and intraclass correlation coefficient would be 0.037. Over 5000 permutations, the detectable effect ranged between 0.048 SD and 0.055 SD.

Statistical Analysis

All analyses followed the intention-to-treat principle. All methods were appropriate for cluster randomized stepped-wedge trials.⁴⁰ We used mixed-effects models to account for correlation of outcomes within surgery, patient, and cluster, as appropriate for each model. Because cluster randomization may not result in balance across all patient baseline factors, we summarized patient and surgical characteristics for each surgery by intervention status, calculating standardized mean differences (SMDs) for each characteristic; any factors with SMD greater than 0.1 were considered imbalanced and adjusted for in all analyses. Missing baseline characteristics, including baseline PROMIS scores, were imputed using multiple imputation when included in models.

PROMIS Outcomes Analysis

Baseline and follow-up PROMIS scores were summarized by time point and cluster status at index surgery. Differences in anxiety, pain interference, and physical function between intervention and UC periods were evaluated using mixed-effects linear models with follow-up scores as the dependent variable. Models were restricted to surgical procedures with at least 1 postoperative PROM. Models included random effects for surgery nested within patient and cluster (cross-classified to account for patients undergoing procedures in different clusters). Fixed effects included intervention status, study step, survey time (30, 60, or 90 days), baseline PROMIS score, and covariates with imbalance (SMD >0.1). Sensitivity analyses that included CAT and short-form data were identical. We performed 2 sensitivity analyses: first, we replicated the main analysis including CAT and short-form data; second, we replicated the main analyses using only the first surgery for patients with multiple surgical procedures. For the main analysis, we also performed an ad hoc exploratory noninferiority test, using 3 points as the minimally important difference.^{41,42}

Opioid Analysis

To reduce bias from correlated outcomes among patients with multiple procedures and avoid contamination, analyses were restricted to each patient's first qualifying (index) surgery. In contrast, results reported in ClinicalTrials.gov reflect the full cohort, consistent with registry reporting conventions. In-hospital and postdischarge opioid exposure, defined by prescriptions, administrations, or either, was quantified as average daily MMEs, calculated using days hospitalized or days after discharge. Measures were summarized by intervention status, and the proportion of patients with any opioid exposure was calculated for each exposure definition.

Intervention effects were evaluated using mixed-effects models. Any opioid exposure was modeled with a logit link. MME exposure was modeled using generalized linear models with a log link and offset for days of exposure; exponentiated coefficients are presented as rate ratios (RRs). MME distributions were examined and trimmed at the 99th percentile to reduce the influence of extreme outliers. All models included an offset for exposure days (in-hospital or postdischarge) and covariates with imbalance as described above. Results are reported as odds ratios or exponentiated β .

coefficients with 95% CIs and 2-sided *P* values. Models that did not converge were assessed for collinearity and simplified as needed, with modifications noted in the Results.

Utilization Analysis

Utilization events were modeled separately using mixed-effects Poisson models with random effects for cluster and offsets for days at risk. Follow-up was censored at a subsequent qualifying surgery or death. We report crude and adjusted event rates and incidence rate ratios (IRRs) with 95% CIs and 2-sided *P* values.

All analyses were conducted using Stata statistical software version 19 (StataCorp). A 2-sided α level of .05 defined statistical significance. Primary comparisons were based on intervention vs UC periods; for simplicity, these are referred to as intervention and UC periods.

Results

Between October 16, 2020, and April 30, 2024, the NOHARM trial included 68 141 surgical procedures, comprising 62 892 index procedures in unique patients and 5250 subsequent procedures; for additional exclusion information, see eFigure 5 in Supplement 2. The stepped-wedge design included 30 sequence-periods (5 sequences $\times$ 6 periods); surgical volume by sequence-period is shown in the CONSORT flow diagram (Figure). Overall, 43 053 surgical procedures occurred during intervention periods and 25 088 during UC periods.

Postoperative PROM response (≥ 1 completed primary outcome) was 71.7% (30 890 of 43 053 patients) during intervention periods and 68.3% (17 140 of 25 088 patients) during UC periods. Table 2 summarizes patient and surgical characteristics; model-specific analytic samples varied due to differential PROM completion (eAppendix 3 and eTables 4-6 in Supplement 2).

Of the 68 141 surgical procedures, 61 652 (90.5%) occurred in patients identifying as White, 65 364 (95.9%) as non-Hispanic, 2696 (3.9%) as Black or African American, and 40 892 (60.0%) as male; the mean (SD) age was 59.27 (16.26) years. The most common procedures were orthopedic (28 362 procedures [41.6%]), followed by gynecologic (10 636 procedures [15.6%]), colorectal (8293 procedures [12.2%]), and transplant (5268 procedures [7.7%]). Baseline preoperative PROMIS

Figure. Flow Diagram for the Non-pharmacological Options in Post-Hospital and Rehabilitation Pain Management (NOHARM) Trial

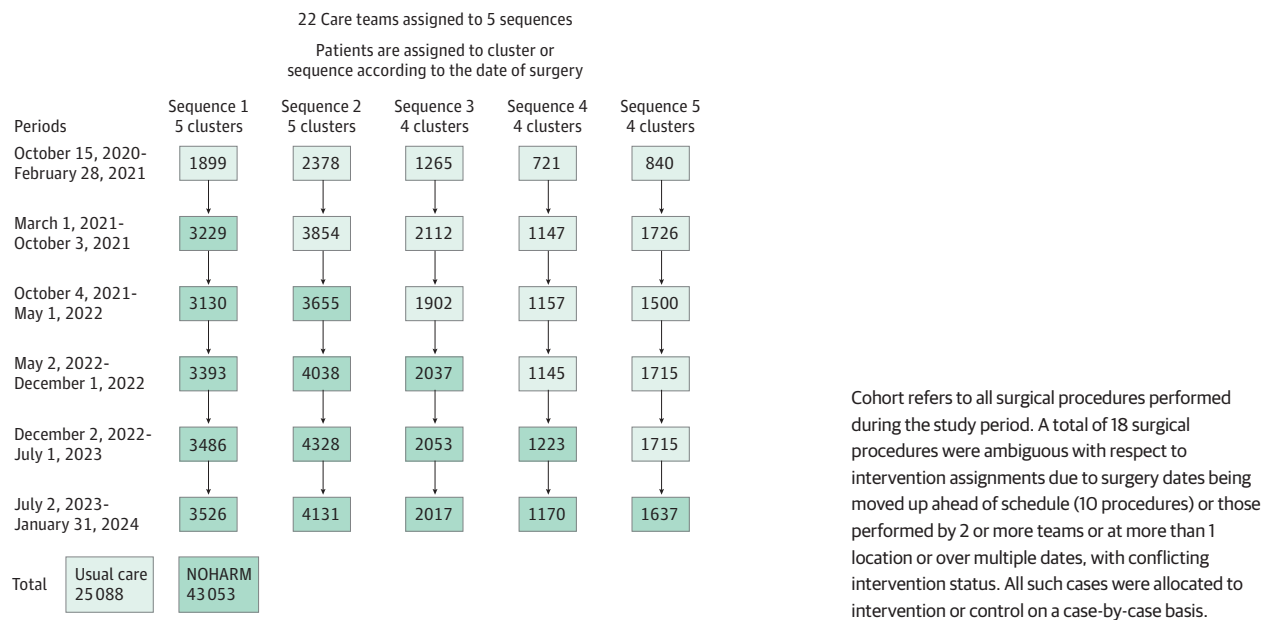


Table 2. Patient and Surgical Characteristics by Intervention Status

Characteristic	Patients, No. (%)	
	Usual care (n = 25 088)	NOHARM (n = 43 053)
Demographics		
Age group, y		
≤40	3681 (14.7)	7695 (17.9)
41-50	2878 (11.5)	4464 (10.4)
51-60	4507 (18.0)	7039 (16.3)
61-70	7236 (28.8)	12 051 (28.0)
71-80	5271 (21.0)	9302 (21.6)
>80	1515 (6.0)	2502 (5.8)
Gender		
Female	10 429 (41.6)	16 818 (39.1)
Male	14 658 (58.4)	26 234 (60.9)
Nonbinary	0	1 (<0.1)
Missing	1 (<0.1)	0
Race ^a		
American Indian or Alaska Native	185 (0.7)	314 (0.7)
Asian	547 (2.2)	1009 (2.3)
Black or African American	1044 (4.2)	1652 (3.8)
Native Hawaiian or Other Pacific Islander	42 (0.2)	71 (0.2)
White	22 682 (90.4)	38 970 (90.5)
Other	588 (2.3)	1037 (2.4)
Ethnicity ^a		
Non-Hispanic	23 316 (92.9)	40 111 (93.2)
All others	458 (1.8)	907 (2.1)
Employment		
Employed	11 229 (44.8)	20 549 (47.7)
Retired	10 310 (41.1)	16 528 (38.4)
Not employed or student or military duty	2341 (9.3)	4294 (10.0)
Disabled	1189 (4.7)	1573 (3.7)
Missing	19 (0.1)	109 (0.3)
Marital status		
Married	17 015 (67.8)	29 672 (68.9)
Single	3772 (15.0)	6449 (15.0)
Divorced	1936 (7.7)	3263 (7.6)
Widowed	1891 (7.5)	2825 (6.6)
Life partnership	245 (1.0)	458 (1.1)
Separated	163 (0.6)	247 (0.6)
Missing	66 (0.3)	139 (0.3)
Education		
Less than high school	4590 (18.3)	7143 (16.6)
High school graduate	737 (2.9)	1230 (2.9)
Some college, vocational, or associate degree	7365 (29.4)	11 660 (27.1)
Bachelor's degree	5786 (23.1)	9175 (21.3)
Master's or doctoral degree	4356 (17.4)	7068 (16.4)
Missing	2254 (9.0)	6777 (15.7)
Rurality (Rural Urban Commuting Area Codes)		
Urban (1-3)	18 150 (72.3)	29 742 (69.1)
Micropolitan (4-6)	2661 (10.6)	5297 (12.3)
Small town (7-9)	2284 (9.1)	4217 (9.8)
Rural (10)	1835 (7.3)	3555 (8.3)
Missing	158 (0.6)	242 (0.6)

(continued)

Table 2. Patient and Surgical Characteristics by Intervention Status (continued)

Characteristic	Patients, No. (%)	
	Usual care (n = 25 088)	NOHARM (n = 43 053)
Site		
Rochester, Minnesota	9812 (39.1)	23874 (55.5)
Scottsdale, Arizona	6551 (26.1)	5358 (12.4)
Jacksonville, Florida	4363 (17.4)	7290 (16.9)
Eau Claire, Wisconsin	799 (3.2)	4301 (10.0)
La Crosse, Wisconsin	1415 (5.6)	1265 (2.9)
Mankato, Minnesota	2148 (8.6)	965 (2.2)
Patient has surgical procedures in both periods	1786 (7.1)	1835 (4.3)
Surgery characteristics		
Surgery: type		
Gynecologic	3799 (15.1)	6837 (15.9)
Cesarean delivery	963 (3.8)	3600 (8.4)
Orthopedic	10 398 (41.4)	17964 (41.7)
Colorectal	4049 (16.1)	4244 (9.9)
Cardiac	1760 (7.0)	6205 (14.4)
Transplant	2982 (11.9)	2286 (5.3)
Pulmonary or thoracic	1137 (4.5)	1917 (4.5)
Surgery: same day	5544 (22.1)	10 971 (25.5)
Discharge disposition		
Home	21 508 (85.7)	37 335 (86.7)
Died	74 (0.3)	170 (0.4)
Other	3506 (14.0)	5548 (12.9)
Surgery: laparoscopic	9139 (36.4)	12 908 (30.0)
Surgery: gastrointestinal or hip or knee replacement	14 285 (56.9)	21 768 (50.6)
Surgery duration, h		
0	2043 (8.1)	5152 (12.0)
1	9852 (39.3)	18 050 (41.9)
2	5862 (23.4)	7622 (17.7)
3	4731 (18.9)	7393 (17.2)
4	2595 (10.3)	4831 (11.2)
Missing	5 (<0.1)	5 (<0.1)
Hospital length of stay, d		
1	5544 (22.1)	10 971 (25.5)
2	6376 (25.4)	10 064 (23.4)
3	3321 (13.2)	4462 (10.4)
3	4222 (16.8)	6942 (16.1)
4-5	3799 (15.1)	7286 (16.9)
6-10	1826 (7.3)	3328 (7.7)
History of cancer	7798 (31.1)	11 947 (27.7)
Baseline scores, mean (SD)		
Baseline pain interference	59.32 (9.92)	59.96 (9.71)
Missing	6110 (36.3)	11 101 (36.6)
Baseline physical function	40.50 (9.04)	39.50 (8.54)
Missing	6091 (36.8)	10780 (36.0)
Baseline anxious	50.73 (9.19)	51.85 (9.16)
Missing	4754 (42.5)	5661 (37.2)

Abbreviation: NOHARM, Non-pharmacological Options in Post-Hospital and Rehabilitation Pain Management.

^a Race and ethnicity were identified using self-reported patient tables and categorized as American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, or other. The other category included patients who chose not to disclose, were recorded as unknown, or were unable to provide this information.

T scores were similar between intervention and UC periods (Table 2). Consistent with the Zelen-type design, 29 278 of 43 053 intervention-period participants (68.0%) reviewed the *Healing After Surgery* guide preoperatively; 88.7% (38 179 of 43 053 participants) selected NPPC options, 50.4%

(21 692 of 43 053 participants) used NPPC during hospitalization, and 52.8% (22 758 of 43 053 participants) reported NPPC use after discharge.²⁹

Co-Primary Outcomes: PROMIS Pain Interference and Physical Function

PROMIS pain interference and physical function scores, our co-primary outcomes, did not differ between intervention periods and UC periods (pain interference adjusted mean difference, 0.09; 95% CI, -0.18 to 0.36; *P* = .51; physical function adjusted mean difference, 0.15; 95% CI, -0.11 to 0.41; *P* = .27) (Table 3). Sensitivity analyses incorporating PROMIS short-form and CAT scores yielded similar results (eTables 7-9 in Supplement 2), whereas sensitivity analyses restricted to the first surgery for each patient were also similar to the main results (eTable 10 in Supplement 2). Noninferiority tests using 3 points as the minimally important difference were all significant indicating equivalence.^{41,42}

Opioid and Other Secondary Outcomes

In prespecified secondary analyses (Table 4), patients receiving the NOHARM intervention experienced lower overall opioid exposure than patients receiving UC (adjusted RR, 0.90; 95% CI, 0.82-0.99; *P* = .03), corresponding to an adjusted mean difference of approximately 260 MMEs per patient. The overall reduction was driven primarily by lower opioid administration during hospitalization (adjusted RR, 0.94; 95% CI, 0.90-0.97; *P* = .001), an adjusted mean difference of approximately 85 MMEs. Opioid prescribing at hospital discharge was likewise lower (adjusted RR, 0.89; 95% CI, 0.84-0.94; *P* < .001), whereas opioid administration (adjusted RR, 0.96; 95% CI, 0.90-1.02; *P* = .15) and prescribing (adjusted RR, 1.05; 95% CI, 0.95-1.17; *P* = .34) after discharge did not differ significantly between groups.

At 3 months, the odds of patients reporting receiving more than 3 opioid prescriptions were lower during intervention periods (3.32% vs 4.52%; odds ratio, 0.72; 95% CI, 0.57-0.92; *P* = .003). In contrast, binary self-reported opioid use (any vs none) did not differ between groups.

Adjusted mean PROMIS anxiety T scores were similar between intervention and UC periods (adjusted mean difference, -0.07; 95% CI, -0.44 to 0.29; *P* = .69) (Table 3). Health services utilization did not differ between intervention and UC periods, including emergency department visits (IRR, 0.98; 95% CI, 0.91 to 1.06; *P* = .67), hospitalizations (IRR, 0.95; 95% CI, 0.87 to 1.04; *P* = .26), or intensive care unit admissions (IRR, 0.81; 95% CI, 0.65 to 1.03; *P* = .08).

Opioid-related adverse events were uncommon and did not differ between groups. New opioid use disorder occurred in 320 participants (0.74%) during intervention periods and 203 participants (0.82%) during UC periods, whereas opioid poisoning or toxic effects occurred in 3 (0.01%) and 4 (0.02%) participants, respectively. Rates of falls, burns, musculoskeletal injuries, episodes meeting

Table 3. Intervention Effects on Patient-Reported Outcomes

Symptom	Adjusted mean difference (intervention vs control), β (95% CI) ^a	P value
Pain interference ^b	0.09 (−0.18 to 0.36)	.51
Physical function ^c	0.15 (−0.11 to 0.41)	.27
Anxiety ^d	−0.07 (−0.44 to 0.29)	.69

^a All models were adjusted for baseline symptom score, study site, study step, age, rural status, and (if imbalanced with standardized mean difference >0.1 for that symptom cohort) laparoscopic status, gastrointestinal or hip surgery, surgery hours, prior prescription, and study step. Models also include random effects for cluster (care team) and patient (to account for multiple surgical procedures).

^b Data are from a sample of Pain Interference Patient-Reported Outcomes Measurement Information System (PROMIS) computerized adaptive test (CAT) responders (intervention, 25 981 participants; usual care, 15 807 participants).

^c Data are from a sample of Physical Function PROMIS CAT responders (intervention, 25 563 participants; usual care, 15 520 participants).

^d Data are from a sample of Anxiety PROMIS CAT responders (intervention, 15 227 participants; usual care, 11 195 participants).

criteria for failure to rescue, and all-cause mortality (559 participants [1.30%] vs 320 participants [1.28%]) were likewise similar between groups.

Discussion

In this large cluster randomized pragmatic trial evaluating a multicomponent, EHR-embedded intervention promoting guideline-concordant perioperative pain care, we found no improvement in the co-primary outcomes of pain interference and physical function. However, the intervention reduced total postoperative opioid exposure (MMEs) by approximately 10% over 3 months without evidence of worsening patient-reported outcomes, opioid-related adverse events, or other monitored safety outcomes. These findings suggest that scalable, EHR-enabled strategies integrating patient education, preference elicitation, and CDS may reduce opioid exposure while preserving patient-centered outcomes

The observation of reduced opioid exposure without measurable improvements in pain interference or physical function warrants consideration. NOHARM intentionally used a pragmatic encouragement design that prioritized scalability over prescriptive changes in clinician behavior (Supplement 1). Patients and clinicians retained substantial discretion regarding whether and how NPPC was incorporated into routine care, likely reducing intervention intensity relative to more tightly controlled efficacy trials.²⁹ Implementation also occurred during the COVID-19 pandemic, when sites experienced fluctuating surgical volumes and workforce shortages that challenged routine clinical operations and limited opportunities for nurses and allied health professionals to reinforce NPPC within already demanding workflows. These findings suggest that pragmatic, low-touch implementation strategies may be better suited to influencing proximal care processes, such as opioid exposure, than more complex patient-centered outcomes.

Design features may also have reduced the ability to detect improvements in pain interference and physical function. Participating departments appropriately sought to include a broad spectrum of procedures, including minimally invasive laparoscopic and thoracoscopic operations from which patients generally recover rapidly but that occasionally result in persistent postoperative pain.^{43,44} Although this enhanced the trial's pragmatic relevance and generalizability, it may have contributed to low average postoperative pain and reduced opportunity to detect clinically meaningful

Table 4. Adjusted Opioid Exposure and Prescribing Outcomes by Intervention Status

Metric	MME (95% CI)				RR (95% CI)	P value
	UC	NOHARM	Adjusted UC ^a	Adjusted NOHARM ^a		
Total opioids MME	398.0 (135.0-1140.0)	400.0 (135.0-1110.0)	2633.8 (1671.9-3595.8)	2373.6 (1521.0-3226.1)	0.90 (0.82-0.99)	.03
Administered opioids						
During index hospitalization ^b	90.0 (0.0-500.0)	60.0 (0.0-503.0)	1305.8 (977.6-1634.0)	1220.6 (914.0-1527.1)	0.94 (0.90-0.97)	.001
During subsequent hospitalization ^{c,d}	0.0	0	160.2 (132.6-187.8)	153.1 (126.9-179.3)	0.96 (0.90-1.02)	.15
Prescribed opioids						
Discharge from index hospitalization ^e	113.0 (60.0-225.0)	113.0 (38.0-250.0)	99.87 (51.9-147.8)	88.9 (46.2-131.5)	0.89 (0.84-0.94)	<.001
Following index hospitalization ^{c,d}	0.0	0.0	148.5 (113.2-183.8)	156.4 (119.4-193.4)	1.05 (0.95-1.17)	.34

Abbreviations: MME, morphine milligram equivalents; NOHARM, Non-pharmacological Options in Post-Hospital and Rehabilitation Pain Management; RR, rate ratio; UC, usual care.

^a Estimates were derived from multivariable mixed-effects generalized linear models with a log link. All models adjusted for study site, laparoscopic status, gastrointestinal or hip surgery, surgery hours, prior prescription, and study step, with random effect for cluster (care team).

^b Opioid medications (oral and parenteral) administered during hospitalization for the index surgery were comprehensively captured as documented in the medication administration record.

^c Opioid medications administered or prescribed by a health system clinician (surgical or nonsurgical) were captured, whereas those administered or prescribed outside the health system were not.

^d Dependent variable (MMEs) was trimmed at the 99th percentile due to extreme outlier values.

^e Administered MMEs represent opioid medications received by patients. Prescribed MMEs represent opioid quantities written on prescriptions and do not indicate whether medications were dispensed or consumed.

JAMA Network Open. 2026;9(9):e2635900. doi:10.1001/jamanetworkopen.2026.35900

September 25, 2026 10/15

Downloaded from jamanetwork.com by Sebastian Mayanz on 10/03/2026

improvements. Because many patients undergoing minimally invasive procedures recover within days to weeks, outcome assessments beginning 1 month after surgery may also have missed the interval during which NPPC exerts its greatest effects. Finally, incomplete outcome ascertainment may have attenuated observed treatment effects if patients experiencing greater symptom burden were less likely to respond.⁴⁵

Although NOHARM did not improve pain interference or physical function, the observed reduction in opioid exposure is clinically meaningful when interpreted within the context of other scalable opioid stewardship interventions. Unlike resource-intensive perioperative pathways, such as Enhanced Recovery After Surgery, or interventions that directly target opioid prescribing,⁴⁶ NOHARM promoted multimodal pain care through routine EHR workflows and existing allied health personnel. Viewed in this context, the approximately 10% reduction in MMEs and 28% reduction in patients receiving more than 3 opioid prescriptions suggest that relatively low-resource health system interventions can produce meaningful population-level reductions in opioid exposure. Although direct comparisons across studies should be interpreted cautiously, these reductions are comparable to those reported for substantially more resource-intensive perioperative opioid stewardship interventions.^{47,48}

Opioid stewardship is likely to require complementary interventions deployed at different stages along the continuum, from initial opioid exposure to opioid-related morbidity. NOHARM's scalable EHR-based approach may complement interventions targeting later stages of opioid-related harm, such as the Healing Communities Study,⁴⁹ by reducing opioid exposure through expansion of NPPC rather than by directly restricting prescribing. More broadly, health care systems have an opportunity to design perioperative care that seeks both to optimize patient recovery and reduce downstream societal harms associated with opioid exposure.

The next challenge is not simply broader deployment of NPPC to reduce opioid exposure, but a more empirical understanding of how these strategies should be implemented. NOHARM paired EHR-based CDS with repeated patient engagement, preference elicitation, allied health reinforcement, and readily accessible NPPC resources across routine perioperative care. This implementation strategy may help explain why NOHARM reduced opioid exposure, whereas some prior EHR-based behavioral nudge interventions did not.^{50,51} Whether earlier intervention or more individualized implementation strategies can extend the benefits of scalable NPPC interventions from proximal care processes to more distal patient-centered outcomes remains an important question for future research.

Limitations

Several considerations should temper interpretation of these findings. The intervention was implemented within a single integrated health system using a common EHR platform, which may limit generalizability to other health systems. Although the cohort reflected the racial and ethnic diversity of the participating health system, representation of some minoritized racial and ethnic groups was limited, precluding robust subgroup analyses. In addition, although the pragmatic design enhanced external validity, it necessarily included diverse surgical populations and care settings, potentially increasing heterogeneity of treatment effects. Furthermore, because NOHARM evaluated a multicomponent intervention, the relative contribution of individual intervention components could not be determined.

Conclusions

In this cluster randomized pragmatic trial of surgical patients, an EHR-based intervention promoting NPPC did not improve pain interference or physical function but was associated with lower postoperative opioid exposure without evidence of harm. Scalable, EHR-embedded, system-level approaches embedded within routine clinical workflows may contribute to safer postoperative pain management.

ARTICLE INFORMATION

Accepted for Publication: July 24, 2026.

Published: September 25, 2026. doi:10.1001/jamanetworkopen.2026.35900

Open Access: This is an open access article distributed under the terms of the [CC-BY-NC-ND License](#), which does not permit alteration or commercial use, including those for text and data mining, AI training, and similar technologies. © 2026 Cheville AL et al. *JAMA Network Open*.

Corresponding Author: Andrea L. Cheville, MD, MSCE, Department of Physical Medicine and Rehabilitation, Mayo Clinic Rochester, 200 First St, Rochester, MN 55905 (cheville.andrea@mayo.edu).

Author Affiliations: Department of Physical Medicine and Rehabilitation, Mayo Clinic Rochester, Rochester, Minnesota (Cheville, Minter); Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut (Herrin); Robert D. and Patricia E. Kern Center for the Science of Health Care Delivery, Mayo Clinic Rochester, Rochester, Minnesota (Grzegorzczuk); Division of General Internal Medicine, Mayo Clinic Scottsdale, Scottsdale, Arizona (Tilburt).

Author Contributions: Drs Cheville and Tilburt had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Cheville, Tilburt.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Cheville, Tilburt.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Cheville, Herrin, Grzegorzczuk.

Obtained funding: Cheville, Herrin, Tilburt.

Administrative, technical, or material support: Cheville.

Supervision: Cheville, Tilburt.

Conflict of Interest Disclosures: Dr Herrin reported receiving grants from Patient-Centered Outcomes Research Institute during the conduct of the study. No other disclosures were reported.

Funding/Support: This work was supported within the National Institutes of Health (NIH) Pragmatic Trials Collaboratory through the NIH HEAL Initiative under award numbers UG3 AG067593 and UH3 AG067593 from the National Institute of Neurological Disorders and Stroke (NINDS) and administered by the National Institute on Aging (NIA). This work also received logistical and technical support from the PRISM Resource Coordinating Center under award number U24 AT010961 from the NIH through the NIH HEAL Initiative, and from the NIH Pragmatic Trials Collaboratory Coordinating Center under award number U24 AT009676 from the National Center for Complementary and Integrative Health (NCCIH), the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Allergy and Infectious Diseases (NIAID), the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute of Minority Health and Health Disparities (NIMHD), NINDS, the National Institute of Nursing Research (NINR), NIA, the NIH Office of Behavioral and Social Sciences Research (OBSSR), and the NIH Office of Disease Prevention (ODP).

Group Information: Mayo Clinic NOHARM Research Team members appear in [Supplement 3](#).

Disclaimer: The content is solely the responsibility of the authors and does not necessarily represent the official views of NCCIH, NCI, NHLBI, NIAID, NIAMS, NIMHD, NINDS, NINR, NIA, OBSSR, or ODP, or the NIH or its HEAL Initiative.

Data Sharing Statement: See [Supplement 4](#).

Additional Contributions: We thank the NIH Pragmatic Trials Collaboratory for providing feedback on study design and implementation.

REFERENCES

1. Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg*. 2017;152(6):e170504. doi:10.1001/jamasurg.2017.0504
2. Gil JA, Gunaseelan V, DeFroda SF, Brummett CM, Bedi A, Waljee JF. Risk of prolonged opioid use among opioid-naïve patients after common shoulder arthroscopy procedures. *Am J Sports Med*. 2019;47(5):1043-1050. doi:10.1177/0363546518819780
3. Wright JD, Huang Y, Melamed A, et al. Use and misuse of opioids after gynecologic surgical procedures. *Obstet Gynecol*. 2019;134(2):250-260. doi:10.1097/AOG.0000000000003358
4. Clarke H, Soneji N, Ko DT, Yun L, Wijesundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ*. 2014;348:g1251. doi:10.1136/bmj.g1251

5. Leroux TS, Saltzman BM, Sumner SA, et al. Elective shoulder surgery in the opioid naïve: rates of and risk factors for long-term postoperative opioid use. *Am J Sports Med*. 2019;47(5):1051-1056. doi:10.1177/0363546519837516
6. Bicket MC, Lin LA, Waljee J. New persistent opioid use after surgery: a risk factor for opioid use disorder? *Ann Surg*. 2022;275(2):e288-e289. doi:10.1097/SLA.0000000000005297
7. Larach DB, Waljee JF, Bicket MC, Brummett CM, Bruehl S. Perioperative opioid prescribing and iatrogenic opioid use disorder and overdose: a state-of-the-art narrative review. *Reg Anesth Pain Med*. 2024;49(8):602-608. doi:10.1136/rapm-2023-104944
8. Wylie JA, Kong L, Barth RJ Jr. Opioid dependence and overdose after surgery: rate, risk factors, and reasons. *Ann Surg*. 2022;276(3):e192-e198. doi:10.1097/SLA.0000000000005546
9. Santosa KB, Priest CR, Oliver JD, et al. Long-term health outcomes of new persistent opioid use after surgery among Medicare beneficiaries. *Ann Surg*. 2023;278(3):e491-e495. doi:10.1097/SLA.0000000000005752
10. Fu VX, Oomens P, Klimek M, Verhofstad MHJ, Jeekel J. The effect of perioperative music on medication requirement and hospital length of stay: a meta-analysis. *Ann Surg*. 2020;272(6):961-972. doi:10.1097/SLA.0000000000003506
11. Wu MS, Chen KH, Chen IF, et al. The efficacy of acupuncture in post-operative pain management: a systematic review and meta-analysis. *PLoS One*. 2016;11(3):e0150367. doi:10.1371/journal.pone.0150367
12. Tick H, Nielsen A, Pelletier KR, et al. Evidence-based nonpharmacologic strategies for comprehensive pain care: the Consortium Pain Task Force white paper. *Explore*. 2018;14(3):177-211. doi:10.1016/j.explore.2018.02.001
13. Bree Collaborative; Washington Agency Medical Directors' Group. Supplemental guidance on prescribing opioids for post-operative pain. July 17, 2018. Accessed August 21, 2026. <https://www.qualityhealth.org/bree/wp-content/uploads/sites/8/2018/04/Supplemental-Bree-AMDG-Postop-pain-18-0423.pdf>
14. OPEN M. Acute care opioid treatment and prescribing recommendations: summary of selected best practices. June 26, 2018. Accessed January 6, 2026. <https://www.michigan.gov/lara/-/media/Project/Websites/lara/bpl/Prescription-Drug-and-Opioid-Commission/Acute-Care-Opioid-Treatment-and-Prescribing-Recommendations---ED.PDF?rev=aa4f2328c13b46309a3ab15289d387ca>
15. Chou R, Gordon DB, de Leon-Casasola OA, et al. Management of postoperative pain: a clinical practice guideline from the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' Committee on Regional Anesthesia, Executive Committee, and Administrative Council. *J Pain*. 2016;17(2):131-157. doi:10.1016/j.jpain.2015.12.008
16. Dowell D, Ragan KR, Jones CM, Baldwin GT, Chou R. CDC clinical practice guideline for prescribing opioids for pain—United States, 2022. *MMWR Recomm Rep*. 2022;71(3):1-95. doi:10.15585/mmwr.rr7103a1
17. Harbell MW, Barendrick LN, Mi L, Quillen J, Millstine DM. Patient attitudes toward acupuncture in the perioperative setting. *J Integr Complement Med*. 2022;28(4):349-354. doi:10.1089/jicm.2021.0311
18. Lane D, Palmer JB, Chen Y. A survey of surgeon, nurse, patient, and family perceptions of music and music therapy in surgical contexts. *Music Ther Perspect*. 2018;37(1):28-36. doi:10.1093/mtp/miy008
19. Giannitrapani KF, Ahluwalia SC, McCaa M, Pisciotta M, Dobscha S, Lorenz KA. Barriers to using nonpharmacologic approaches and reducing opioid use in primary care. *Pain Med*. 2018;19(7):1357-1364. doi:10.1093/pm/pnx220
20. Price-Haywood EG, Burton J, Burstain T, et al. Clinical effectiveness of decision support for prescribing opioids for chronic noncancer pain: a prospective cohort study. *Value Health*. 2020;23(2):157-163. doi:10.1016/j.jval.2019.09.2748
21. Bertsche T, Askoxylakis V, Habl G, et al. Multidisciplinary pain management based on a computerized clinical decision support system in cancer pain patients. *Pain*. 2009;147(1-3):20-28. doi:10.1016/j.pain.2009.07.009
22. Spithoff S, Mathieson S, Sullivan F, et al. Clinical decision support systems for opioid prescribing for chronic non-cancer pain in primary care: a scoping review. *J Am Board Fam Med*. 2020;33(4):529-540. doi:10.3122/jabfm.2020.04.190199
23. Blanco C, Volkow ND. Management of opioid use disorder in the USA: present status and future directions. *Lancet*. 2019;393(10182):1760-1772. doi:10.1016/S0140-6736(18)33078-2
24. Redmond S, Tilburt J, Cheville A; Mayo Clinic NOHARM Research Team. Non-pharmacological Options in Postoperative Hospital-Based and Rehabilitation Pain Management (NOHARM): protocol for a stepped-wedge cluster-randomized pragmatic clinical trial. *Pain Ther*. 2022;11(3):1037-1053. doi:10.1007/s40122-022-00393-x
25. Califf RM, Sugarman J. Exploring the ethical and regulatory issues in pragmatic clinical trials. *Clin Trials*. 2015;12(5):436-441. doi:10.1177/1740774515598334

26. West SG, Duan N, Pequegnat W, et al. Alternatives to the randomized controlled trial. *Am J Public Health*. 2008;98(8):1359-1366. doi:[10.2105/AJPH.2007.124446](https://doi.org/10.2105/AJPH.2007.124446)
27. Schellings R, Kessels AG, ter Riet G, Knottnerus JA, Sturmans F. Randomized consent designs in randomized controlled trials: systematic literature search. *Contemp Clin Trials*. 2006;27(4):320-332. doi:[10.1016/j.cct.2005.11.009](https://doi.org/10.1016/j.cct.2005.11.009)
28. Zelen M. Strategy and alternate randomized designs in cancer clinical trials. *Cancer Treat Rep*. 1982;66(5):1095-1100.
29. Simon GE, Shortreed SM, DeBar LL. Zelen design clinical trials: why, when, and how. *Trials*. 2021;22(1):541. doi:[10.1186/s13063-021-05517-w](https://doi.org/10.1186/s13063-021-05517-w)
30. Li F, Lokhnygina Y, Murray DM, Heagerty PJ, DeLong ER. An evaluation of constrained randomization for the design and analysis of group-randomized trials. *Stat Med*. 2016;35(10):1565-1579. doi:[10.1002/sim.6813](https://doi.org/10.1002/sim.6813)
31. Kagan R, Anderson MB, Christensen JC, Peters CL, Gililand JM, Pelt CE. The recovery curve for the Patient-Reported Outcomes Measurement Information System patient-reported physical function and pain interference computerized adaptive tests after primary total knee arthroplasty. *J Arthroplasty*. 2018;33(8):2471-2474. doi:[10.1016/j.arth.2018.03.020](https://doi.org/10.1016/j.arth.2018.03.020)
32. Pecorelli N, Guarneri G, Vallorani A, et al. Validation of the PROMIS-29 Questionnaire as a measure of recovery after pancreatic surgery. *Ann Surg*. 2023;278(5):732-739. doi:[10.1097/SLA.0000000000006020](https://doi.org/10.1097/SLA.0000000000006020)
33. Khalifeh JM, Dibble CF, Hawasli AH, Ray WZ. Patient-Reported Outcomes Measurement Information System physical function and pain interference in spine surgery. *J Neurosurg Spine*. 2019;31(2):165-174. doi:[10.3171/2019.2.SPINE181237](https://doi.org/10.3171/2019.2.SPINE181237)
34. Segawa E, Schalet B, Cella D. A comparison of computer adaptive tests (CATs) and short forms in terms of accuracy and number of items administered using PROMIS profile. *Qual Life Res*. 2020;29(1):213-221. doi:[10.1007/s11136-019-02312-8](https://doi.org/10.1007/s11136-019-02312-8)
35. Gewandter JS, Smith SM, Dworkin RH, et al. Research approaches for evaluating opioid sparing in clinical trials of acute and chronic pain treatments: Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials recommendations. *Pain*. 2021;162(11):2669-2681. doi:[10.1097/j.pain.0000000000002283](https://doi.org/10.1097/j.pain.0000000000002283)
36. Daoust R, Paquet J, Williamson D, et al. Accuracy of a self-report prescription opioid use diary for patients discharged from the emergency department with acute pain: a multicentre prospective cohort study. *BMJ Open*. 2022;12(10):e062984. doi:[10.1136/bmjopen-2022-062984](https://doi.org/10.1136/bmjopen-2022-062984)
37. Gerbershagen HJ, Aduckathil S, van Wijck AJ, Peelen LM, Kalkman CJ, Meissner W. Pain intensity on the first day after surgery: a prospective cohort study comparing 179 surgical procedures. *Anesthesiology*. 2013;118(4):934-944. doi:[10.1097/ALN.0b013e31828866b3](https://doi.org/10.1097/ALN.0b013e31828866b3)
38. Lindberg M, Franklin O, Svensson J, Franklin KA. Postoperative pain after colorectal surgery. *Int J Colorectal Dis*. 2020;35(7):1265-1272. doi:[10.1007/s00384-020-03580-4](https://doi.org/10.1007/s00384-020-03580-4)
39. Harrison LJ, Chen T, Wang R. Power calculation for cross-sectional stepped wedge cluster randomized trials with variable cluster sizes. *Biometrics*. 2020;76(3):951-962. doi:[10.1111/biom.13164](https://doi.org/10.1111/biom.13164)
40. Hussey MA, Hughes JP. Design and analysis of stepped wedge cluster randomized trials. *Contemp Clin Trials*. 2007;28(2):182-191. doi:[10.1016/j.cct.2006.05.007](https://doi.org/10.1016/j.cct.2006.05.007)
41. Chen CX, Kroenke K, Stump TE, et al. Estimating minimally important differences for the PROMIS pain interference scales: results from 3 randomized clinical trials. *Pain*. 2018;159(4):775-782. doi:[10.1097/j.pain.0000000000001121](https://doi.org/10.1097/j.pain.0000000000001121)
42. Kroenke K, Stump TE, Kean J, Talib TL, Haggstrom DA, Monahan PO. PROMIS 4-item measures and numeric rating scales efficiently assess SPADE symptoms compared with legacy measures. *J Clin Epidemiol*. 2019;115:116-124. doi:[10.1016/j.jclinepi.2019.06.018](https://doi.org/10.1016/j.jclinepi.2019.06.018)
43. Zapf M, Denham W, Barrera E, et al. Patient-centered outcomes after laparoscopic cholecystectomy. *Surg Endosc*. 2013;27(12):4491-4498. doi:[10.1007/s00464-013-3095-0](https://doi.org/10.1007/s00464-013-3095-0)
44. Kikuchi I, Takeuchi H, Shimanuki H, et al. Questionnaire analysis of recovery of activities of daily living after laparoscopic surgery. *J Minim Invasive Gynecol*. 2008;15(1):16-19. doi:[10.1016/j.jmig.2007.08.606](https://doi.org/10.1016/j.jmig.2007.08.606)
45. Zini MLL, Banfi G. A narrative literature review of bias in collecting patient reported outcomes measures (PROMs). *Int J Environ Res Public Health*. 2021;18(23):12445. doi:[10.3390/ijerph182312445](https://doi.org/10.3390/ijerph182312445)
46. Daoust R, Paquet J, Marquis M, et al. Evaluation of interventions to reduce opioid prescribing for patients discharged from the emergency department: a systematic review and meta-analysis. *JAMA Netw Open*. 2022;5(1):e2143425. doi:[10.1001/jamanetworkopen.2021.43425](https://doi.org/10.1001/jamanetworkopen.2021.43425)

47. Sescu D, Dahiya D, Scaramuzzo L, et al. Optimising postoperative spine outcomes: an umbrella review of enhanced recovery after spinal surgery (ERASS) protocols. *Br J Anaesth*. 2025;135(6):1663-1683. doi:10.1016/j.bja.2025.08.037
48. Thiele RH, Sarosiek BM, Modesitt SC, et al. Development and impact of an institutional enhanced recovery program on opioid use, length of stay, and hospital costs within an academic medical center: a cohort analysis of 7774 patients. *Anesth Analg*. 2021;132(2):442-455. doi:10.1213/ANE.0000000000005182
49. Samet JH, El-Bassel N, Winhusen TJ, et al; HEALing Communities Study Consortium. Community-based cluster-randomized trial to reduce opioid overdose deaths. *N Engl J Med*. 2024;391(11):989-1001. doi:10.1056/NEJMoa2401177
50. Altinger G, Sharma S, Maher CG, et al; NUDG-ED Study Group. Behavioural nudges to reduce low-value care for low back pain in the emergency department (NUDG-ED): a 2 × 2 factorial, pragmatic cluster randomized trial. *CMAJ*. 2026;198(13):E486-E499. doi:10.1503/cmaj.251595
51. Dhingra L, Schiller R, Teets R, et al. Pain management in primary care: a randomized controlled trial of a computerized decision support tool. *Am J Med*. 2021;134(12):1546-1554. doi:10.1016/j.amjmed.2021.07.014

SUPPLEMENT 1.

Trial Protocol and Statistical Analysis Plan

SUPPLEMENT 2.

eAppendix 1. Additional methods, results, and discussion

eFigure 1. Identification of surgical procedures for trial inclusion

eFigure 2. NOHARM Intervention Conceptual Diagram

eFigure 3. Prototype of Healing After Surgery menu for NPPC selection.

eFigure 4. NOHARM trial stepped wedge design and implementation timeline across 22 clusters at 6 sites

eFigure 5. Reasons for exclusion and surgeries affected

eAppendix 2. Epic ORP procedure codes

eTable 1. Surgical Categories Included in the NOHARM Trial

eTable 2. NOHARM Trial Qualifying Surgeries

eTable 3. ICD-10 Codes Used to Identify New Occurrences of Opioid Use Disorder and Poisoning

eAppendix 3. Additional analyses conducted to evaluate the robustness of the primary study findings

eTable 4. Patient and surgical characteristics of participants included in Pain Interference Analyses

eTable 5. Patient and surgical characteristics of participants included in Physical Function Analyses

eTable 6. Patient and surgical characteristics of participants included in Anxiety Analyses

eTable 7. Number of PROMs completed via printed PROMIS short forms

eTable 8. Unadjusted mean Physical Function and Pain interference scores with and without printed short forms

eTable 9. Adjusted patient-reported outcome results

eTable 10. Sensitivity Analysis Restricted to Each Patient's First Surgery

eReferences

SUPPLEMENT 3.

Mayo Clinic NOHARM Research Team Members

SUPPLEMENT 4.

Data Sharing Statement