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Evaluating the effectiveness of email-based nudges to reduce post-operative opioid prescribing: study protocol of a randomized controlled trial

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ABSTRACT

Introduction

Surgical patients are commonly prescribed more opioids at discharge than needed to manage their post-operative pain. These excess opioids increase the risks of new persistent opioid use, opioid-induced ventilatory impairment, and opioid diversion. This study tests the effectiveness of two behavioral nudges, one based on peer behavior and one based on best practice guidelines, in reducing excessive post-operative opioid prescriptions.

Methods and analysis

The study will be conducted at 19 hospitals within a large health care delivery system in northern California. Three surgical specialties (general surgery, orthopedic surgery, and obstetric/gynecological surgery) at each hospital will be randomized either to a control group or to one of two active intervention arms. One intervention is grounded in the theory of injunctive norms, and provides feedback to surgeons on their post-operative opioid prescribing relative to prescribing guidelines endorsed by their institution. The other intervention draws from the theory of descriptive norms, and provides feedback similar to the first intervention but using peers' behavior rather than guidelines as the benchmark for the surgeon's prescribing behavior. The interventions will be delivered by a monthly email. Both interventions will be active for twelve months. The effects of each intervention relative to the control group and to each other will be tested using a four-level hierarchical model adjusted for multiple hypothesis testing.

Ethics and dissemination

Using behavioral nudges rather than rigid policy changes allows us to target excessive prescribing without preventing clinicians from using their clinical judgment to address patient pain. All study activities have been approved by the RAND Human Subjects Protection Committee (ID 2018-0988). Findings will be disseminated through conference presentations, peer-reviewed publications, and social media accounts.

Trial registration number

NCT05070338

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study includes multiple surgical specialties (general, orthopedic, obstetric/gynecologic) and a large sample size (19 hospitals) across diverse settings, allowing for broad generalizability.
- Randomized controlled trial design allows us to account for secular decline in opioid prescribing.
- Intervention is informed by behavioral theory, with careful attention to details that affect behavioral response.
- Incomplete prescribing data at the study site compromises some analyses.

INTRODUCTION

Background

Despite high awareness of the opioid epidemic, clinicians still overprescribe opioids after surgery.[1-7] This post-operative overprescribing puts both patients and communities at risk, increasing the patient's likelihood of developing chronic opioid use[8-14] or opioid-induced ventilatory impairment[11] and adding to the reservoir of unused opioids available for misuse and diversion.[11, 15]

The discrepancy between clinicians' awareness of the opioid epidemic and the degree of overprescribing—over half of opioid pills prescribed after surgery go unused[7]—suggests that prescribing practices are not based on purely rational decisions. Indeed, behavioral research has shown that judgment and decision making of both laypeople and experts in a variety of disciplines falls short of rational standards in systematic and predictable ways.[16-19] Even well-informed clinicians make cognitive errors when estimating the benefits and harms of treatment, and these errors are especially likely where there is uncertainty about risks and benefits (as with opioid prescribing decisions for individual patients).[20]

In recent years, behavioral economists and experimental psychologists have successfully leveraged behavioral insights to design "choice architecture" that "nudges" individuals to make better decisions without infringing on their freedom of choice.[21, 22] Such behavioral nudges are promising strategies for changing clinician prescribing behavior because they are often more cost-effective than traditional interventions,[23] can be integrated into existing clinical workflows, and are rapidly scalable once built.

One powerful type of behavioral nudge relies on the strong motivation that most people have to conform with their peers' behavior.[24, 25] Abundant research has found that people (including clinicians) are strongly motivated to adhere to prevailing social norms,[24, 25] and that nudges based on describing social norms can be used to influence prescribing decisions.[26]

Another type of behavioral nudge relies on motivation to follow injunctive norms—to do what is considered the "right thing to do." For example, clinicians may be motivated to follow best practice guidelines published by a well-respected organization. Previous studies suggest that such guidelines are in reality often ignored and thus ineffective in changing behavior,[27, 28] but there is insufficient evidence to determine whether they are more or less effective than nudges that describe peer behavior.

Both of these types of nudges—nudges based on descriptive norms and nudges based on injunctive norms—have been applied to the issue of excessive post-operative opioid prescribing.[29-38] The results have been promising, but because most of these studies have used a pre-post design, it is possible that the observed decreases in prescribing can be explained by a secular trend. Furthermore, all of these studies have bundled and tested different interventions together (eg, grand rounds presentations or patient education in addition to nudges), making the effectiveness of the nudges alone unclear. Accordingly, the evidence base for the effectiveness of behavioral nudges in influencing post-operative opioid prescribing is limited. In this paper we describe the protocol for a study that addresses these knowledge gaps, using a

randomized controlled trial (RCT) design and testing nudges in the absence of other interventions. This study will also make a novel contribution to the literature by directly testing which type of nudge —descriptive or injunctive—is more effective.

Specifically, in this RCT we will investigate the extent to which descriptive and injunctive norms, conveyed through nudges delivered monthly by email, can each change post-operative opioid prescribing behavior. Across 19 hospitals in a large health system in northern California, surgeons within three surgical specialties (general, orthopedic, and obstetric/gynecological surgery) will be randomized to receive either nudges based on peer prescribing behavior (descriptive norm), nudges based on prescribing guidelines (injunctive norm), or no nudges (status quo).[1]

Research questions

1. How does an email-based nudge that alerts surgeons when they prescribe opioid quantities above guidelines (injunctive norm nudge) affect post-operative opioid prescribing at discharge compared to the status quo?
2. How does an email-based nudge that alerts surgeons that they are prescribing opioid quantities that are higher than what peers prescribe (descriptive norm nudge) affect post-operative opioid prescribing at discharge compared to the status quo?
3. What is the comparative effectiveness of an injunctive norm nudge versus a descriptive norm nudge in reducing post-operative opioid prescribing?
4. If surgeons do change their post-operative opioid prescribing behavior in response to nudges, does this change persist one year after the nudges have stopped?

Significance

Our study will provide evidence regarding the comparative effectiveness of two low-cost behavioral nudges based on peer norms and guidelines, the interactions between clinician characteristics and the type of nudge, and the persistence of behavior change after nudges are turned off. Results from this study may inform a scalable, low-cost intervention that can reduce patient harm by changing clinician behavior in real-world practice.

METHODS AND ANALYSIS

Overview of design

We will conduct a 3-arm cluster randomized controlled trial of two behavioral nudges compared to usual post-surgical care. One nudge will provide feedback on the surgeon's prescribing behavior relative to institutional prescribing guidelines (an injunctive norm); the other will provide feedback on their prescribing behavior relative to their peers (a descriptive norm). Three surgical specialties (general surgery, orthopedic surgery, and obstetric/gynecological surgery)

[1] There will be a total of 23 physical hospitals participating. One set of three physical hospitals and another set of two physical hospitals are located together, each set functioning as a hospital campus. A third set of two hospitals essentially share the same surgical staff. We treat each of these three sets as a single hospital for the purposes of this study, both to capture the organization structure and to minimize the potential for spillover effects, resulting in 19 hospital units. For brevity and clarity, we refer to these 19 hospital units simply as "hospitals" throughout.

within 19 hospitals will be randomized such that all surgeons within a given specialty at a given hospital will receive one of 3 conditions: control, guideline-based nudge, or peer-based nudge.

Setting

This study will take place across 19 hospitals within Sutter Health, a large not-for-profit healthcare system in California. Importantly for the generalizability of this study, these hospitals are geographically diverse and vary widely in size and the populations served (Table 1).

Table 1. Characteristics of study site hospitals

	Number of hospitals
Number of beds	
0–99	10
100–499	5
500+	4
Urbanicity	
Large central metro	5
Large fringe metro	5
Medium metro	6
Small metro	–
Micropolitan	2
Non-core	1
Proportion of patients on Medicaid*	
Less than 25%	13
25–50%	5
50–75%	1
75% or more	–
Proportion of patients who identify as non-Hispanic White*	
Less than 25%	1
25–50%	5
50–75%	8
75% or more	5

* Proportions calculated from electronic health record data among patients eligible for our study between June 2020 and May 2021

Like many other healthcare organizations in the United States, this health system accepts multiple commercial preferred provider organization (PPO) and health management organization (HMO) plans, Medicare, and Medicaid. Because of this payer mix, there is no single, fixed drug formulary and clinicians can prescribe as they choose, per patients' individual plans or preferences.

Sample size and characteristics

Our study intervention targets 778 surgeons (Table 2). Though discharge medication orders are sometimes written by a clinician other than the surgeon, such as a hospitalist or nurse practitioner, we posit that the surgeon is still ultimately responsible for all medication orders written for their patients. If surgeons cannot influence medication orders written by other clinicians for their patients, the effect of the intervention will be attenuated.

Table 2. Characteristics of eligible study site surgeons

	Percent of surgeons			
	Total (n = 778)	General surgery (n = 187)	Orthopedic surgery (n = 244)	Obstetric/ gynecological surgery (n = 347)
Year of medical degree				
1960–1969	0.7	–	0.4	1.3
1970–1979	7.3	7.9	7.4	7.0
1980–1989	21.3	20.8	23.4	20.0
1990–1999	28.5	30.3	23.4	31.1
2000–2009	26.2	28.7	31.6	21.0
2010–2019	16.0	12.4	13.9	19.7
Sex				
Female	39.9	28.2	5.0	71.7
Male	60.1	71.8	95.0	28.3

Randomization scheme

The study design has four levels: patients, surgeons, surgical specialties, and hospitals. Randomization will take place at the level of the surgical specialty, using a blocked scheme to ensure that each arm has a balance of large and small hospitals and a sample size of surgeons similar to the other two arms.

Intervention

Surgeons randomized to our study intervention will receive one of two types of behavioral nudges delivered as monthly emails. The two nudges will be active for twelve months (October 2021–October 2022).

To ensure that the nudges target only *inappropriate* opioid prescribing, surgeons will receive nudges only when they write opioid prescriptions that exceed post-operative opioid prescribing guidelines developed by multidisciplinary teams at the Mayo Clinic.[32, 39, 40](and personal communication with Professor Elizabeth Habermann, Ph.D., MPH, on opioid prescribing guidelines for caesarean section, March 12, 2021; unreferenced) These guidelines recommend ranges of 5mg oxycodone tablet quantities specific to the procedure performed and are partly based on patient surveys of actual post-operative opioid use.

In both nudge conditions, eligibility for receiving a monthly nudge is contingent upon at least two of the surgeon's patients being discharged with a post-operative opioid prescription exceeding the quantities specified by the Mayo Clinic guidelines. Though it may seem counterintuitive for the descriptive norm nudge to be based implicitly on prescribing guidelines, this choice ensures patient safety and avoids confounding the content of the nudge with the threshold for receiving a nudge.

Intervention arm 1: nudge based on descriptive norms

Surgeons randomized to this condition will receive an email with the following content at the end of each month in which at least two of their patients are discharged with a post-operative opioid prescription that exceeds the prescribing guideline for the procedure performed.

[Subject line: Your peers vs. your opioid prescribing safety record]

Dear Dr. [Name],

In an effort to reduce opioid use among our surgical patients, Sutter Health is reviewing opioid prescriptions and prescribing patterns for surgeons and will be communicating the findings.

In [month], at least XX of your patients were discharged with opioid prescriptions exceeding the amount prescribed by YY% of your peers for these procedures.

YY% of [specialty] surgeons at Sutter Health prescribe within the ranges below.

We will continue to send you opioid prescribing safety reports.

Sincerely,
[Signature(s) of chief medical executive, chief of staff, and/or surgical department chair at the surgeon's hopsital]

Procedure	**Amount prescribed by your peers (5mg oxycodone tablets)***
[Procedure name]	0–XX
[Procedure name]	0–XX
[Procedure name]	0–XX

*5-mg oxycodone = 7.5-mg hydrocodone = 75-mg tramadol

The ranges of 5mg oxycodone tablets displayed in the email will be the same as the ranges stipulated by the prescribing guidelines, but this nudge will not include any language about guidelines.

Intervention arm 2: nudge based on injunctive norms
This condition will be identical to the first condition, except the content of the monthly emails will refer to safety guidelines rather than the surgeon's peers.

[Subject line: Best practice guidelines vs. your opioid prescribing safety record]

Dear Dr. [Name],

In an effort to reduce opioid use among our surgical patients, Sutter Health is reviewing opioid prescriptions and prescribing patterns for surgeons and will be communicating the findings.

In [month], at least XX of your patients were discharged with opioid prescriptions exceeding the amounts recommended by safety guidelines for these procedures.

For patient safety, Sutter Health recommends prescribing within the ranges below for these procedures. Doing so will also meet best practice safety guidelines for post-operative opioid prescribing.

We will continue to send you opioid prescribing safety reports.

Sincerely,
[Signature(s) of chief medical executive, chief of staff, and/or surgical department chair at the surgeon's hopsital]

Procedure	**Amount recommended by Sutter Health (5mg oxycodone tablets)***
[Procedure name]	0–XX
[Procedure name]	0–XX
[Procedure name]	0–XX

*5-mg oxycodone = 7.5-mg hydrocodone = 75-mg tramadol

Control arm
Surgeons randomized to the control arm will not receive any nudges and will not be informed of the study.

Eligibility criteria
The nudges that a surgeon in either intervention arm will receive are based on that surgeon's eligible discharge opioid prescriptions in the previous month. Eligible prescriptions meet all of the following criteria:

- the patient is at least 18 years old at the date of surgery
- the patient is discharged to their home
- the surgical procedure has an applicable post-operative opioid prescribing guideline
- the surgical procedure is the only surgical procedure performed during the patient's hospital stay
- the prescription is for an opioid taken orally (tablets, capsules, or liquid solution)

To avoid contamination between the intervention arms, surgeons who operate across multiple surgical specialties (defined as surgeons who performed less than 90% of their total procedures in one specialty between June 2020 and May 2021) will not be eligible.

Patient and public involvement
Since the study intervention only targets clinicians, we have not chosen to involve patients directly in the development of this study. However, the prescribing guidelines upon which our intervention is based were created with input from patients via stakeholder groups and post-discharge surveys.[32, 39]

Data collection
Prescribing data, clinician characteristics (eg, sex, type of medical degree, year of medical degree), patient characteristics (eg, age, sex, body mass index, comorbidities), and case characteristics (eg, procedure type, length of operating time) will be obtained by querying the electronic health record database.

Hospital characteristics (eg, number of beds, urbanicity) will be obtained from California's Office of Statewide Health Planning and Development (OSHPD) datasets.

Data analyses

Primary Outcomes

Our primary outcome is the share of discharge prescriptions that were above the guideline for the respective procedure (see above for how guidelines were identified). Prescribing above guidelines is the outcome to which both nudges are linked (even though the descriptive norm nudge does not explicitly refer to guidelines) and thus a key measure of whether clinician behavior responds to the nudges. We define a prescription as being above guidelines if the morphine milligram equivalent (MME) quantity of opioids prescribed is above the ceiling for the procedure-specific guideline (guidelines range from zero to a ceiling). If no opioid is prescribed at discharge, we will code this as within guideline.

Secondary Outcomes

We will also analyze the following secondary outcomes to further understand the effects of the intervention.

- MMEs prescribed at discharge
- Days' supply of opioids prescribed at discharge
- Share of discharges where any opioid was prescribed
- Share of patients on opioids for greater than three months post-discharge
- Number of 30-day all-cause emergency department visits
- Number of 30-day all-cause hospitalizations
- Share of discharge opioid prescriptions above prescribing guidelines in the 12 months after the nudges end

Data analysis

We will analyze outcomes at the level of the discharge using a four-level hierarchical linear model (HLM),[41] thus capturing the clustering inherent in the study design and data generating process. We will analyze outcomes at the patient level, and patients are nested within surgeons, who are nested within specialty, which are nested within hospitals. Both primary and secondary outcomes will follow this modeling structure. To improve the precision of our estimates, we will also include a set of observable patient covariates (X), surgeon covariates (Z), specialty covariates (U), and hospital covariates (W). For patient i, treated by surgeon p, in specialty s, at hospital h, we consider the following HLM formulation for continuous outcomes Y_{ipsh}:

$$Y_{ipsh} = \beta_0 + \beta_1 ARM1_{sh} + \beta_2 ARM2_{sh} + \gamma_{1h} ARM1_{sh} + \gamma_{2h} ARM2_{sh} + \omega_1 X_{ipsh} + \omega_2 Z_{psh} + \omega_3 U_{sh} + \omega_4 W_h + \gamma_h + \eta_{sh} + \varphi_{psh} + \varepsilon_{ipsh} \#(1)$$

$ARM1_{sh}$ and $ARM2_{sh}$ are indicator variables for whether specialty s, at hospital h were assigned to treatment arm one or two respectively. The key terms in the equation are $\beta_1$and β_2, the covariate-adjusted treatment effects of arms 1 and 2 relative to the control arm; β_1 answers research question 1 and β_2 answers research question 2. We will use an F-test to compare coefficients β_1 and β_2 to answer research question 3. The model allows for the possibility that the treatment effect varies across hospitals, as captured by the random effects (γ_{1h},γ_{2h}).

Unexplained variation in each of the levels is captured by the random effects ε_{ipsh}, φ_{psh}, η_{sh}, and γ_h. We will initially model these six random effects as independent but will also investigate whether including a covariance structure across these components is appropriate. The coefficients ω_1, ω_2, and ω_3, capture the influence of the covariates at the patient, surgeon, and specialty respectively, and covariates will be mean centered as appropriate to aid in model interpretation. Covariates may include but are not limited to the following: Level 1: patient age, patient sex, patient comorbidities, procedure type, length of operating time; Level 2: surgeon sex, year of surgeon's medical degree; Level 3: total volume of procedures within the specialty: Level 4: number of beds, urbanicity, proportion of patients on Medicaid. Given that the covariates will not change the estimate of the treatment effect (in expectation), only reduce unexplained variance, we will choose a final pool of covariates that we find to be predictive the primary outcome. Model estimates of the treatment effects will adjust standard errors for clustering due to the due to clustered assignment of the interventions.

For binary outcomes, we implement a hierarchical generalized linear model by including a logit link for Equation (1). Note that the Level 1 error term ε_{ipsh} is also eliminated. The concatenated model for all four levels with a binary outcome then reduces to:

$$logit(Y_{ipsh}) = \beta_0 + \beta_1 ARM1_{sh} + \beta_2 ARM2_{sh} + \gamma_{1h} ARM1_{sh} + \gamma_{2h} ARM2_{sh} + \omega_1 X_{ipsh} + \omega_2 Z_{psh} + \omega_3 U_{sh} + \omega_4 W_h + \gamma_h + \eta_{sh} + \varphi_{psh} \#(2)$$

In the binary outcome version, the parameters $\beta_1$and β_2 again identify the treatment effects of arms 1 and 2 relative to the control arm, with interpretation of these parameters adjusted relative to the link function implemented.

Heterogeneity analysis

We will test for heterogeneity in the treatment effect along several domains. Specifically, we will add terms interacting characteristics of the surgeon with each treatment arm and conduct an F-test of the interaction terms for each nudge.

1. Specialty: We will also conduct analyses to test whether the response to each nudge varies by surgeons' specialty.
2. Volume of surgeries: We will test for heterogeneity by number of surgeries performed over the 12 month study period. We will only include surgeries for which we have guidelines in this count.
3. Baseline opioid prescribing: We will categorize surgeons based on the portion of their surgeries in the 12 months prior to the start of the intervention that were above guidelines. We expect that the intervention will have a larger effect for surgeon with a higher share of prescription above guidelines.

Longitudinal analysis

In addition to assessing the treatment effect averaged over the entire 12-month period, we will also analyze treatment effects by month to assess how the treatment effect evolves over time. For this analysis, we will interact study month indicators with the treatment assignment indicators.

Persistence analysis

We will conduct a secondary analysis to examine whether nudge effects persist once the nudges are discontinued. The data will include the RCT data analyzed in the model above, but also data collected for one year post-intervention (the "persistence period"). The analysis model above

will be modified by adding an indicator for the RCT period versus persistence period plus interaction terms for period and each nudge to the model. The statistical significance of these interaction terms will be used to assess whether the treatment effect significantly differs post-RCT.

Adjustment for multiple hypothesis testing

Two varieties of multiple testing concerns are present. For any instance of Equations (1) or (2), we simultaneously test for a treatment effect in either study arm and difference in treatment effect between arms. Across secondary outcomes within the same domain, we also consider a series of tests for each arm. As appropriate, we will employ family-wise error rate and false discovery rate corrections[42, 43] to account for simultaneously tested hypotheses.

ETHICS AND DISSEMINATION

Throughout the development of this study, we paid careful attention to the possibility that reducing post-operative opioid prescriptions might result in greater post-surgical pain. We believe that the risk presented by our nudge interventions is negligible, both because the nudges do not prevent the clinicians from using their own clinical judgment and because previous studies have found that reducing the amount of opioids prescribed after surgical operations did not affect patient satisfaction,[44, 45] pain scores,[44-46] or refill rates.[47-49] Given this negligible level of risk, the RAND Human Subjects Protection Committee approved a waiver of informed consent for participating clinicians and their patients.

Data indicative of adverse events (opioid refills and emergency department visits within 30 days of hospital discharge) will be monitored throughout the intervention period by an independent data safety and monitoring board (DSMB) comprising four experts in surgery, interventional pain management, statistical methodology and risk assessment, and research ethics. The DSMB may recommend modifying or terminating the trial based on its interim analyses.

Once results are obtained for primary and secondary outcomes, we will submit these results to ClinicalTrials.gov. Findings will also be disseminated through conference presentations, peer-reviewed publications, and social media accounts.

Author contributions: AK and ZW wrote significant portions of the manuscript. ZW and LM developed the quantitative analysis plan. All authors contributed to conceptualizing the study and developing the methodology, and read and approved the final manuscript.

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Competing interests: None

Ethics approval: All study activities have been approved by the RAND Human Subjects Protection Committee (ID 2018-0988).

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SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on Page No
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 12
	5b	Name and contact information for the trial sponsor	12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	documented in IRB materials; available upon request
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3–4
	6b	Explanation for choice of comparators	3
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4–5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6–8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8–9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	6
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	NA
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	NA
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	8–9
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	NA
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9–10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	10–11
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	11
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	documented in IRB materials; available upon request
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NA
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	NA

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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Evaluating the effectiveness of email-based nudges to reduce post-operative opioid prescribing: study protocol of a randomized controlled trial

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Evaluating the effectiveness of email-based nudges to reduce post-operative opioid prescribing: study protocol of a randomized controlled trial

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ABSTRACT

Introduction

Surgical patients are commonly prescribed more opioids at discharge than needed to manage their post-operative pain. These excess opioids increase the risks of new persistent opioid use, opioid-induced ventilatory impairment, and opioid diversion. This study tests the effectiveness of two behavioral nudges, one based on peer behavior and one based on best practice guidelines, in reducing excessive post-operative opioid prescriptions.

Methods and analysis

The study will be conducted at 19 hospitals within a large health care delivery system in northern California. Three surgical specialties (general surgery, orthopedic surgery, and obstetric/gynecological surgery) at each hospital will be randomized either to a control group or to one of two active intervention arms. One intervention is grounded in the theory of injunctive norms, and provides feedback to surgeons on their post-operative opioid prescribing relative to prescribing guidelines endorsed by their institution. The other intervention draws from the theory of descriptive norms, and provides feedback similar to the first intervention but using peers' behavior rather than guidelines as the benchmark for the surgeon's prescribing behavior. The interventions will be delivered by a monthly email. Both interventions will be active for twelve months. The effects of each intervention relative to the control group and to each other will be tested using a four-level hierarchical model adjusted for multiple hypothesis testing.

Ethics and dissemination

Using behavioral nudges rather than rigid policy changes allows us to target excessive prescribing without preventing clinicians from using their clinical judgment to address patient pain. All study activities have been approved by the RAND Human Subjects Protection Committee (ID 2018-0988). Findings will be disseminated through conference presentations, peer-reviewed publications, and social media accounts.

Trial registration number

NCT05070338

STRENGTHS AND LIMITATIONS OF THIS STUDY

- The study includes multiple surgical specialties (general, orthopedic, obstetric/gynecologic) and a large sample size (19 hospitals) across diverse settings, allowing for broad generalizability.
- Randomized controlled trial design allows us to account for secular decline in opioid prescribing.
- Intervention is informed by behavioral theory, with careful attention to details that affect behavioral response.
- Incomplete prescribing data at the study site compromises some analyses.

INTRODUCTION

Background

Despite high awareness of the opioid epidemic, clinicians still overprescribe opioids after surgery.[1-7] This post-operative overprescribing puts both patients and communities at risk, increasing the patient's likelihood of developing chronic opioid use[8-14] or opioid-induced ventilatory impairment[11] and adding to the reservoir of unused opioids available for misuse and diversion.[11, 15]

The discrepancy between clinicians' awareness of the opioid epidemic and the degree of overprescribing—over half of opioid pills prescribed after surgery go unused[7]—suggests that prescribing practices are not based on purely rational decisions. Indeed, behavioral research has shown that judgment and decision making of both laypeople and experts in a variety of disciplines falls short of rational standards in systematic and predictable ways.[16-19] Even well-informed clinicians make cognitive errors when estimating the benefits and harms of treatment, and these errors are especially likely where there is uncertainty about risks and benefits (as with opioid prescribing decisions for individual patients).[20]

In recent years, behavioral economists and experimental psychologists have successfully leveraged behavioral insights to design "choice architecture" that "nudges" individuals to make better decisions without infringing on their freedom of choice.[21, 22] Such behavioral nudges are promising strategies for changing clinician prescribing behavior because they are often more cost-effective than traditional interventions,[23] can be integrated into existing clinical workflows, and are rapidly scalable once built.

One powerful type of behavioral nudge relies on the strong motivation that most people have to conform with their peers' behavior.[24, 25] Abundant research has found that people (including clinicians) are strongly motivated to adhere to prevailing social norms,[24, 25] and that nudges based on describing social norms can be used to influence prescribing decisions.[26]

Another type of behavioral nudge relies on motivation to follow injunctive norms—to do what is considered the "right thing to do." For example, clinicians may be motivated to follow best practice guidelines published by a well-respected organization. Previous studies suggest that such guidelines are in reality often ignored and thus ineffective in changing behavior,[27, 28] but there is insufficient evidence to determine whether they are more or less effective than nudges that describe peer behavior.

Both of these types of nudges—nudges based on descriptive norms and nudges based on injunctive norms—have been applied to the issue of excessive post-operative opioid prescribing.[29-38] The results have been promising, but because most of these studies have used a pre-post design, it is possible that the observed decreases in prescribing can be explained by a secular trend. Furthermore, all of these studies have bundled and tested different interventions together (eg, grand rounds presentations or patient education in addition to nudges), making the effectiveness of the nudges alone unclear. Accordingly, the evidence base for the effectiveness of behavioral nudges in influencing post-operative opioid prescribing is limited. In this paper we describe the protocol for a study that addresses these knowledge gaps, using a

randomized controlled trial (RCT) design and testing nudges in the absence of other interventions. This study will also make a novel contribution to the literature by directly testing which type of nudge —descriptive or injunctive—is more effective.

Specifically, in this RCT we will investigate the extent to which descriptive and injunctive norms, conveyed through nudges delivered monthly by email, can each change post-operative opioid prescribing behavior. Across 19 hospitals in a large health system in northern California, surgeons within three surgical specialties (general, orthopedic, and obstetric/gynecological surgery) will be randomized to receive either nudges based on peer prescribing behavior (descriptive norm), nudges based on prescribing guidelines (injunctive norm), or no nudges (status quo).

Research questions

1. How does an email-based nudge that alerts surgeons when they prescribe opioid quantities above guidelines (injunctive norm nudge) affect post-operative opioid prescribing at discharge compared to the status quo?
2. How does an email-based nudge that alerts surgeons that they are prescribing opioid quantities that are higher than what peers prescribe (descriptive norm nudge) affect post-operative opioid prescribing at discharge compared to the status quo?
3. What is the comparative effectiveness of an injunctive norm nudge versus a descriptive norm nudge in reducing post-operative opioid prescribing?
4. If surgeons do change their post-operative opioid prescribing behavior in response to nudges, does this change persist one year after the nudges have stopped?

The null hypothesis is that surgeons who receive nudges will prescribe the same quantities of post-operative opioids as surgeons who do not; our alternative hypotheses are that surgeons who receive either type of nudge will prescribe fewer post-operative opioids than those who receive no nudges, surgeons who receive the descriptive norm nudge will prescribe fewer post-operative opioids than those who receive the injunctive norm nudge,[26] and these differences will persist one year after the nudges have stopped.

Significance

Our study will provide evidence regarding the comparative effectiveness of two low-cost behavioral nudges based on peer norms and guidelines, the interactions between clinician characteristics and the type of nudge, and the persistence of behavior change after nudges are turned off. Results from this study may inform a scalable, low-cost intervention that can reduce patient harm by changing clinician behavior in real-world practice.

METHODS AND ANALYSIS

Overview of design

We will conduct a three-arm cluster randomized controlled trial of two behavioral nudges compared to usual post-surgical care. One nudge will provide feedback on the surgeon's prescribing behavior relative to institutional prescribing guidelines (an injunctive norm); the other will provide feedback on their prescribing behavior relative to their peers (a descriptive norm). Three surgical specialties (general surgery, orthopedic surgery, and

obstetric/gynecological surgery) within 19 hospitals will be randomized such that all surgeons within a given specialty at a given hospital will receive one of three conditions: control, guideline-based nudge, or peer-based nudge.

Setting

This study will take place across 19 hospitals within Sutter Health, a large not-for-profit healthcare system in California. Importantly for the generalizability of this study, these hospitals are geographically diverse and vary widely in size and the populations served (Table 1).

Table 1. Characteristics of study site hospitals

	Number of hospitals
Number of beds	
0–99	10
100–499	5
500+	4
Urbanicity	
Large central metro	5
Large fringe metro	5
Medium metro	6
Small metro	–
Micropolitan	2
Non-core	1
Proportion of patients on Medicaid*	
Less than 25%	13
25–50%	5
50–75%	1
75% or more	–
Proportion of patients who identify as non-Hispanic White*	
Less than 25%	1
25–50%	5
50–75%	8
75% or more	5

* Proportions calculated from electronic health record data among patients eligible for our study between June 2020 and May 2021

Like many other healthcare organizations in the United States, this health system accepts multiple commercial preferred provider organization (PPO) and health management organization (HMO) plans, Medicare, and Medicaid. Because of this payer mix, there is no single, fixed drug formulary and clinicians can prescribe as they choose, per patients' individual plans or preferences.

Sample size and characteristics

Our study intervention targets 778 surgeons (Table 2). Though discharge medication orders are sometimes written by a clinician other than the surgeon, such as a hospitalist or nurse practitioner, we posit that the surgeon is still ultimately responsible for all medication orders written for their patients. If surgeons cannot influence medication orders written by other clinicians for their patients, the effect of the intervention will be attenuated.

Table 2. Characteristics of eligible study site surgeons

	Percent of surgeons			
	Total (n = 778)	General surgery (n = 187)	Orthopedic surgery (n = 244)	Obstetric/ gynecological surgery (n = 347)
Year of medical degree				
1960–1969	0.7	–	0.4	1.3
1970–1979	7.3	7.9	7.4	7.0
1980–1989	21.3	20.8	23.4	20.0
1990–1999	28.5	30.3	23.4	31.1
2000–2009	26.2	28.7	31.6	21.0
2010–2019	16.0	12.4	13.9	19.7
Sex				
Female	39.9	28.2	5.0	71.7
Male	60.1	71.8	95.0	28.3

The 778 surgeons targeted by our study intervention operate at a total of 23 physical hospitals. One set of three physical hospitals and another set of two physical hospitals are located together, each set functioning as a hospital campus. A third set of two hospitals essentially share the same surgical staff. We treat each of these three sets as a single hospital for the purposes of this study, both to capture the organization structure and to minimize the potential for spillover effects, resulting in 19 hospital units. For brevity and clarity, we refer to these 19 hospital units simply as "hospitals" throughout.

Power considerations

Statistical power to identify effects of the nudges was examined using recent past data from the participating hospitals. We estimated design parameters required by the PowerUpR package in R software,[39] which provides the capability to estimate statistical power for randomized block clustered designs. Examining medication dose, input parameters for the calculation included unconditional intracluster correlations (ICC) for the hospital (ICC=0.005), service line (ICC=0.039), and provider (ICC=0.337) levels; the number of service line groups (up to three per hospital); the number of providers by service line expected to participate in the study; and number of patients per service line. The ICCs were empirically determined from our preliminary data. We assumed that covariates informative of the dosage would explain between 25 percent and 50 percent of the dosage variation at each of the patient, provider, and service line levels (i.e., R^2 between 0.25 and 0.50). We derived statistical power, assuming one third of the service line groups within hospital will be randomly assigned to each study arm (two treatment and one control). We computed power for pairwise comparison of each of the two nudge arms versus the no nudge arm and adjusted our alpha level to account for multiple comparisons (alpha=0.05/2). We will have 80% power to detect significant differences between the intervention conditions of at least a minimum detectable effect size (MDES) = 0.347 standard deviations (SDs) when R^2=0.25, while R^2=0.5 would yield a MDES of 0.305.

Randomization scheme

The study design has four levels: patients, surgeons, surgical specialties, and hospitals. Randomization will take place at the level of the surgical specialty, using a blocked scheme to ensure that each arm has a balance of large and small hospitals and a sample size of surgeons similar to the other two arms.

Intervention

Surgeons randomized to our study intervention will receive one of two types of behavioral nudges delivered as monthly emails. The two nudges will be active for twelve months (October 2021–October 2022).

To ensure that the nudges target only *inappropriate* opioid prescribing, surgeons will receive nudges only when they write opioid prescriptions that exceed post-operative opioid prescribing guidelines developed by multidisciplinary teams at the Mayo Clinic.[32, 40, 41](and personal communication with Professor Elizabeth Habermann, Ph.D., MPH, on opioid prescribing guidelines for caesarean section, March 12, 2021; unreferenced) These guidelines recommend ranges of 5mg oxycodone tablet quantities specific to the procedure performed and are partly based on patient surveys of actual post-operative opioid use. While some patients may require higher quantities (eg, patients with particularly high opioid tolerance, body mass index, or pain levels), these guidelines are appropriate for the vast majority of patients.

In both nudge conditions, eligibility for receiving a monthly nudge is contingent upon at least two of the surgeon's patients being discharged with a post-operative opioid prescription exceeding the quantities specified by the Mayo Clinic guidelines. Though it may seem counterintuitive for the descriptive norm nudge to be based implicitly on prescribing guidelines, this choice ensures patient safety and avoids confounding the content of the nudge with the threshold for receiving a nudge.

Intervention arm 1: nudge based on descriptive norms

Surgeons randomized to this condition will receive an email with the following content at the end of each month in which at least two of their patients are discharged with a post-operative opioid prescription that exceeds the prescribing guideline for the procedure performed.

> [Subject line: Your peers vs. your opioid prescribing safety record]
>
> Dear Dr. [Name],
>
> In an effort to reduce opioid use among our surgical patients, Sutter Health is reviewing opioid prescriptions and prescribing patterns for surgeons and will be communicating the findings.
>
> In [month], at least XX of your patients were discharged with opioid prescriptions exceeding the amount prescribed by YY% of your peers for these procedures.
>
> YY% of [specialty] surgeons at Sutter Health prescribe within the ranges below.
>
> We will continue to send you opioid prescribing safety reports.

Sincerely,
[Signature(s) of chief medical executive, chief of staff, and/or surgical department chair at the surgeon's hospital]

[Table including each procedure type performed by this surgeon in the reference month and the corresponding "Amount prescribed by your peers (5mg oxycodone tablets)", with a footnote stating the conversion factors for hydrocodone and tramadol]

The ranges of 5mg oxycodone tablets displayed in the email will be the same as the ranges stipulated by the prescribing guidelines, but this nudge will not include any language about guidelines.

Intervention arm 2: nudge based on injunctive norms
This condition will be identical to the first condition, except the content of the monthly emails will refer to safety guidelines rather than the surgeon's peers.

[Subject line: Best practice guidelines vs. your opioid prescribing safety record]

Dear Dr. [Name],

In an effort to reduce opioid use among our surgical patients, Sutter Health is reviewing opioid prescriptions and prescribing patterns for surgeons and will be communicating the findings.

In [month], at least XX of your patients were discharged with opioid prescriptions exceeding the amounts recommended by safety guidelines for these procedures.

For patient safety, Sutter Health recommends prescribing within the ranges below for these procedures. Doing so will also meet best practice safety guidelines for post-operative opioid prescribing.

We will continue to send you opioid prescribing safety reports.

Sincerely,
[Signature(s) of chief medical executive, chief of staff, and/or surgical department chair at the surgeon's hospital]

[Table including each procedure type performed by this surgeon in the reference month and the corresponding "Amount recommended by Sutter Health (5mg oxycodone tablets)", with a footnote stating the conversion factors for hydrocodone and tramadol]

Control arm
Surgeons randomized to the control arm will not receive any nudges and will not be informed of the study. By not informing them of the study, we will prevent a Hawthorne effect and obtain an

accurate representation of status quo prescribing behavior against which to test the effects of the nudges.

Eligibility criteria
The nudges that a surgeon in either intervention arm will receive are based on that surgeon's eligible discharge opioid prescriptions in the previous month. Eligible prescriptions meet all of the following criteria:

- the patient is at least 18 years old at the date of surgery
- the patient is discharged to their home
- the surgical procedure has an applicable post-operative opioid prescribing guideline
- the surgical procedure is the only surgical procedure performed during the patient's hospital stay
- the prescription is for an opioid taken orally (tablets, capsules, or liquid solution)

To avoid contamination between the intervention arms, surgeons who operate across multiple surgical specialties (defined as surgeons who performed less than 90% of their total procedures in one specialty between June 2020 and May 2021) will not be eligible.

Patient and public involvement
Since the study intervention only targets clinicians, we have not chosen to involve patients directly in the development of this study. However, the prescribing guidelines upon which our intervention is based were created with input from patients via stakeholder groups and post-discharge surveys.[32, 40]

Data collection
Prescribing data, clinician characteristics (eg, sex, type of medical degree, year of medical degree), patient characteristics (eg, age, sex, body mass index, comorbidities), and case characteristics (eg, procedure type, length of operating time) will be obtained by querying the electronic health record database.

Hospital characteristics (eg, number of beds, urbanicity) will be obtained from California's Office of Statewide Health Planning and Development (OSHPD) datasets.

Data analyses
Primary outcomes
Our primary outcome is the share of discharge prescriptions that were above the guideline for the respective procedure (see above for how guidelines were identified). Prescribing above guidelines is the outcome to which both nudges are linked (even though the descriptive norm nudge does not explicitly refer to guidelines) and thus a key measure of whether clinician behavior responds to the nudges. We define a prescription as being above guidelines if the morphine milligram equivalent (MME) quantity of opioids prescribed is above the ceiling for the procedure-specific guideline (guidelines range from zero to a ceiling). If no opioid is prescribed at discharge, we will code this as within guideline.

Secondary outcomes

We will also analyze the following secondary outcomes to further understand the effects of the intervention.

- MMEs prescribed at discharge
- Days' supply of opioids prescribed at discharge
- Share of discharges where any opioid was prescribed
- Share of patients on opioids for greater than three months post-discharge
- Number of 30-day all-cause emergency department visits
- Number of 30-day all-cause hospitalizations
- Share of discharge opioid prescriptions above prescribing guidelines in the 12 months after the nudges end

Primary analysis

We will analyze outcomes at the level of the discharge using a four-level hierarchical linear model (HLM),[42] thus capturing the clustering inherent in the study design and data generating process. We will analyze outcomes at the patient level, and patients are nested within surgeons, who are nested within specialties, which are nested within hospitals. Both primary and secondary outcomes will follow this modeling structure. To improve the precision of our estimates, we will also include a set of observable patient covariates (X), surgeon covariates (Z), specialty covariates (U), and hospital covariates (W). For patient i, treated by surgeon p, in specialty s, at hospital h, we consider the following HLM formulation for continuous outcomes Y_{ipsh}:

$$Y_{ipsh} = \beta_0 + \beta_1 ARM1_{sh} + \beta_2 ARM2_{sh} + \gamma_{1h} ARM1_{sh} + \gamma_{2h} ARM2_{sh} + \omega_1 X_{ipsh} + \omega_2 Z_{psh} + \omega_3 U_{sh} + \omega_4 W_h + \gamma_h + \eta_{sh} + \varphi_{psh} + \varepsilon_{ipsh} \#(1)$$

$ARM1_{sh}$ and $ARM2_{sh}$ are indicator variables for whether specialty s, at hospital h were assigned to treatment arm one or two respectively.

The key terms in the equation are $\beta_1$and β_2, the covariate-adjusted treatment effects of arms 1 and 2 relative to the control arm; β_1 answers research question 1 and β_2 answers research question 2. We will use an F-test to compare coefficients β_1 and β_2 to answer research question 3. Thus, the effect of each nudge is estimated relative to receiving no nudges and to the other nudge.

The model allows for the possibility that the treatment effect varies across hospitals, as captured by the random effects (γ_{1h},γ_{2h}). Unexplained variation in each of the levels is captured by the random effects ε_{ipsh}, φ_{psh}, η_{sh}, and γ_h. We will initially model these six random effects as independent but will also investigate whether including a covariance structure across these components is appropriate. The coefficients ω_1, ω_2, and ω_3, capture the influence of the covariates at the patient, surgeon, and specialty respectively, and covariates will be mean centered as appropriate to aid in model interpretation. Covariates may include but are not limited to the following: Level 1: patient age, patient sex, patient comorbidities, procedure type, length of operating time; Level 2: surgeon sex, year of surgeon's medical degree; Level 3: total volume of procedures within the specialty: Level 4: number of beds, urbanicity, proportion of patients on Medicaid. Given that the covariates will not change the estimate of the treatment effect (in expectation), only reduce unexplained variance, we will choose a final pool of covariates that we

find to be predictive the primary outcome. Model estimates of the treatment effects will adjust standard errors for clustering due to the due to clustered assignment of the interventions.

For binary outcomes, we implement a hierarchical generalized linear model by including a logit link for Equation (1). Note that the Level 1 error term ε_{ipsh} is also eliminated. The concatenated model for all four levels with a binary outcome then reduces to:

$$logit(Y_{ipsh}) = \beta_0 + \beta_1 ARM1_{sh} + \beta_2 ARM2_{sh} + \gamma_{1h} ARM1_{sh} + \gamma_{2h} ARM2_{sh} + \omega_1 X_{ipsh} + \omega_2 Z_{psh} + \omega_3 U_{sh} + \omega_4 W_h + \gamma_h + \eta_{sh} + \varphi_{psh} \#(2)$$

In the binary outcome version, the parameters $\beta_1$and β_2 again identify the treatment effects of arms 1 and 2 relative to the control arm, with interpretation of these parameters adjusted relative to the link function implemented.

These analyses will be conducted after the intervention ends. Any interim analyses conducted during the intervention period will be solely for the purposes of safety monitoring or planning related studies; the intervention will not be altered unless recommended by the study's data safety and monitoring board.

Heterogeneity analysis

We will test for heterogeneity in the treatment effect along several domains. Specifically, we will add terms interacting characteristics of the surgeon with each treatment arm and conduct an F-test of the interaction terms for each nudge.

1. Specialty: We will also conduct analyses to test whether the response to each nudge varies by surgeons' specialty.
2. Volume of surgeries: We will test for heterogeneity by number of surgeries performed over the 12 month study period. We will only include surgeries for which we have guidelines in this count.
3. Baseline opioid prescribing: We will categorize surgeons based on the portion of their surgeries in the 12 months prior to the start of the intervention that were above guidelines. We expect that the intervention will have a larger effect for surgeon with a higher share of prescription above guidelines.

Longitudinal analysis

In addition to assessing the treatment effect averaged over the entire 12-month period, we will also analyze treatment effects by month to assess how the treatment effect evolves over time. For this analysis, we will interact study month indicators with the treatment assignment indicators.

Persistence analysis

We will conduct a secondary analysis to examine whether nudge effects persist once the nudges are discontinued. The data will include the RCT data analyzed in the model above, but also data collected for one year post-intervention (the "persistence period"). The analysis model above will be modified by adding an indicator for the RCT period versus persistence period plus interaction terms for period and each nudge to the model. The statistical significance of these interaction terms will be used to assess whether the treatment effect significantly differs post-RCT.

Adjustment for multiple hypothesis testing

Two varieties of multiple testing concerns are present. For any instance of Equations (1) or (2), we simultaneously test for a treatment effect in either study arm and difference in treatment effect between arms. Across secondary outcomes within the same domain, we also consider a series of tests for each arm. As appropriate, we will employ family-wise error rate and false discovery rate corrections[43, 44] to account for simultaneously tested hypotheses.

ETHICS AND DISSEMINATION

All study activities have been approved by the RAND Human Subjects Protection Committee (ID 2018-0988).

Throughout the development of this study, we paid careful attention to the possibility that reducing post-operative opioid prescriptions might result in greater post-surgical pain. We believe that the risk presented by our nudge interventions is negligible, both because the nudges do not prevent the clinicians from using their own clinical judgment and because previous studies have found that reducing the amount of opioids prescribed after surgical operations did not affect patient satisfaction,[45, 46] pain scores,[45-47] or refill rates.[48-50] Given this negligible level of risk, the RAND Human Subjects Protection Committee approved a waiver of informed consent for participating clinicians and their patients.

Data indicative of adverse events (opioid refills and emergency department visits within 30 days of hospital discharge) will be monitored throughout the intervention period by an independent data safety and monitoring board (DSMB) comprising four experts in surgery, interventional pain management, statistical methodology and risk assessment, and research ethics. The DSMB may recommend modifying or terminating the trial based on its interim analyses.

Once results are obtained for primary and secondary outcomes, we will submit these results to ClinicalTrials.gov. Findings will also be disseminated through conference presentations, peer-reviewed publications, and social media accounts. Deidentified data will be made available upon reasonable request.

Author contributions: AK and ZW wrote significant portions of the manuscript. ZW and LM developed the quantitative analysis plan. AK, ZW, LM, MM, XY, RR, and KW contributed to conceptualizing the study and developing the methodology, and read and approved the final manuscript.

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Competing interests: None

Ethics approval: All study activities have been approved by the RAND Human Subjects Protection Committee (ID 2018-0988).

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on Page No
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	2
	2b	All items from the World Health Organization Trial Registration Data Set	NA
Protocol version	3	Date and version identifier	NA
Funding	4	Sources and types of financial, material, and other support	12
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 12
	5b	Name and contact information for the trial sponsor	12
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	NA
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	documented in IRB materials; available upon request
Introduction			

Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	3–4
	6b	Explanation for choice of comparators	3
Objectives	7	Specific objectives or hypotheses	4
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	4
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	4–5
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	8
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	6–8
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	11
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	NA
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA

Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	8–9
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	6
Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	5
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	NA
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	6
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	NA
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	NA
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	NA

	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	8–9
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	NA
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	9–10
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	10–11
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	NA
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	11

	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	11
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	11
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	12
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	documented in IRB materials; available upon request
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	NA
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	12
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	NA

Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	11
	31b	Authorship eligibility guidelines and any intended use of professional writers	NA
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	NA
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.