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Electronic health record intervention to increase use of NSAIDs as analgesia for hospitalised patients: a cluster randomised controlled study

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ABSTRACT

Background Prescribing non-opioid pain medications, such as non-steroidal anti-inflammatory (NSAIDs) medications, has been shown to reduce pain and decrease opioid use, but it is unclear how to effectively encourage multimodal pain medication prescribing for hospitalised patients. Therefore, the aim of this study is to evaluate the effect of prechecking non-opioid pain medication orders on clinician prescribing of NSAIDs among hospitalised adults.

Methods This was a cluster randomised controlled trial of adult (≥18 years) hospitalised patients admitted to three hospital sites under one quaternary hospital system in the USA from 2 March 2022 to 3 March 2023. A multimodal pain order panel was embedded in the admission order set, with NSAIDs prechecked in the intervention group. The intervention group could uncheck the NSAID order. The control group had access to the same NSAID order. The primary outcome was an increase in NSAID ordering. Secondary outcomes include NSAID administration, inpatient pain scores and opioid use and prescribing and relevant clinical harms including acute kidney injury, new gastrointestinal bleed and in-hospital death.

Results Overall, 1049 clinicians were randomised. The study included 6239 patients for a total of 9595 encounters. Both NSAID ordering (36 vs 43%, p<0.001) and administering (30 vs 34%, p=0.001) by the end of the first full hospital day were higher in the intervention (prechecked) group. There was no statistically significant difference in opioid outcomes during the hospitalisation and at discharge. There was a statistically but perhaps not clinically significant difference in pain scores during both the first and last full hospital day.

Conclusions This cluster randomised controlled trial showed that prechecking an order for NSAIDs to promote multimodal pain management in the admission order set increased NSAID ordering and administration, although there were no changes to pain scores or opioid use. While prechecking orders is an important way to increase adoption, safety checks should be in place.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Despite the opioid epidemic continuing to cost both money and lives in the USA, adoption of multimodal pain medication in hospitalised patients has been slow. Electronic health record (EHR) interventions have been touted as one way to spur change.

WHAT THIS STUDY ADDS

⇒ This cluster randomised controlled trial of 9595 hospital encounters found that prechecking an order for non-opioid pain medication on a hospital-wide admission order set increased non-steroidal anti-inflammatory (NSAID) prescribing at admission without increasing NSAID-related adverse events.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings indicate that using the EHR to precheck medications during hospital admission can increase NSAID prescribing without a concomitant increase in NSAID-related adverse events and is an easily applicable and relatively inexpensive intervention to turn on.

BACKGROUND

The opioid epidemic continues to lead to death from overdose, now the leading cause of injury-related death in the USA.[1] It has also costs billions of dollars in lost productivity and healthcare costs.[2] The crisis is thought to be related, in part, to overprescribing of opioids. In response to the opioid epidemic, strategies to substitute or add non-opioid pain medication such as acetaminophen or non-steroidal anti-inflammatory (NSAID) to hospital-based pain regimens are being encouraged at hospitals across the country.[3 4] These multimodal pain regimens may help reduce the use of opioids for pain management in the postoperative period and are increasingly being used in multiple settings. However, interventions to improve NSAID use have been disappointing.[5]

Quality improvement projects can be both costly and time consuming to effectively implement. The electronic health record (EHR) provides a mechanism for reaching all clinicians in a health system and has been used to provide clinical decision support for medication use, recognising sepsis and many

other interventions to improve patient care.[6–9] However, clinical decision support can add complexity and workflow tasks that contribute to clinician burn-out, and it needs to be justified in terms of clinical benefit.

In a previous study,[10] we tested whether requiring an active choice for NSAID ordering (a 'hard stop') in the pain management order panel in our standard admission order set changed NSAID prescribing, but we found this approach to be ineffective. Specifically, NSAIDs were ordered in 22% of the intervention arm and 22% of the control arm (p=0.10 accounting for clustering). Similarly, there were no statistical differences in NSAID administration (also accounting for clustering).

As a second phase in this project, we tested whether a prechecked NSAID order was more effective than a 'hard stop' NSAID option. The prechecked NSAID order could be unchecked for any reason by the admitting clinician. The primary objectives of this study were to assess the difference in prescribing and administration of NSAIDs by the first full hospital day. Secondary objectives included average and high pain scores on the first full hospital day the amount of opioids administered the day before discharge and in the discharge prescription, as well as clinical harms between the intervention and control groups.

METHODS

Study design

We conducted a cluster randomised controlled trial designed to assess the effectiveness and safety of an EHR-based intervention to encourage use of NSAIDs for adult inpatients, with the ultimate goal of improving NSAID use without adding ineffective EHR burden for clinicians. Clinicians were the unit of randomisation, and outcomes were compared for patient encounters exposed to a clinician randomised to the intervention or control arm. Clinicians were only randomised if they used the pain panel in the core admission order set. Patients and the public were not involved in the design or conduct of the research.

Site and subjects

Our study was conducted at three hospital sites associated within a single academic hospital system (University of California, San Francisco (UCSF)).

We studied adult patients (≥18 years) during the time period between 3 March 2022 and 3 March 2023. We excluded encounters if the clinician was not exposed to the pain panel of the core admission order set. This included encounters for patients admitted by a small number of services with pre-existing pain treatment pathways with separate pain medication panels, as well as encounters where the patient was expected to have only 'mild pain' assessed by clinicians in the admission order set. In both these cases, the clinician bypassed the admission pain order set and so were not exposed to the intervention. Finally, any clinician associated with the neurosurgery service was not randomised and was not presented with prechecked orders for NSAIDS due to concern for epidural haematoma with NSAID use.

This article followed Consolidated Standards of Reporting Trials reporting guidelines extension for cluster randomised trials (online supplemental eAppendix 1).[11]

Randomisation of clinicians

Clinicians were randomised to the intervention or control group at the moment they first interacted with the pain medication panel of the core admission order set and remained in their randomised group for the remaining period of the trial. Randomisation was blocked and stratified by non-surgical versus surgical services, to ensure balance within each of these groups (figure 1). We included a power calculation to ensure adequate enrolment (online supplemental eAppendix 2).

Description of the intervention

As in our previous study, our institution uses a standard admission order set for most adult hospital admissions. The order set includes essential admission orders including vital sign frequency, lab frequency, intravenous fluid options, tube and drain management, diet choices and venous thromboembolism prophylaxis. Our intervention was embedded in the pain management section.

Clinicians randomised to the intervention arm had NSAIDs prechecked every time they admitted a patient (online supplemental eAppendix 3). They were able to UNcheck NSAIDs if desired. Clinicians randomised to the control arm saw the same NSAID choice and had to either choose an NSAID or click an option to specify that the patient had a contraindication to NSAIDs to admit a patient.

In both intervention and control versions of the pain panel, text immediately below the order panel provided decision support as follows: 'Celecoxib: Do not use in patients with a history of ischaemic heart disease, stroke, recent CABG or heart failure. Ketorolac or ibuprofen: Avoid in patients on therapeutic anticoagulant therapy, acute or chronic kidney disease (estimated glomerular filtration rate (eGFR)<60), gastrointestinal (GI) bleeding in last 6 months, most transplant patients, heart failure' in order to alert clinicians to specific contraindications to NSAID use.

Data sources

We used data from the EHR data warehouse (Clarity), which included billing data in the form of International Classification of Diseases, Tenth Revision (ICD-10) codes, to detect evidence of GI bleeding or acute kidney injury as well as clinician ordering activity, medication administration records and pain score data from nursing flow sheets. We also included hospital discharge prescribing data. We calculated the Charlson Comorbidity Score using previously generated code for administrative databases.[12]

Pain scores at our institution are determined using the Numeric Rating Scale, which is a self-reported scale with 0 being no pain and 10 being the worst possible pain.[13 14] Scores are recorded by nurses in nursing flow sheets.

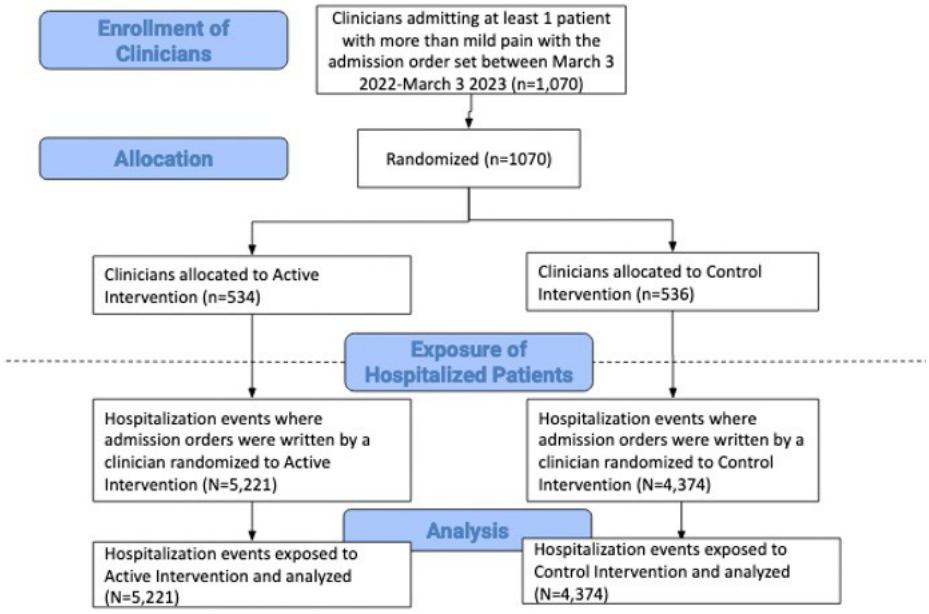

Figure 1 CONSORT diagram (attached separately). CONSORT, Consolidated Standards of Reporting Trials.

Outcomes

Because patient encounters may begin before an admission order (ie, the patient being seen in emergency department or in operating room) and can happen anytime during a calendar day, the available time for a medication to be ordered or administered within a 24-hour time period can vary. For this reason, we elected to focus most of our outcome measures on whether the event had occurred by the end of the first full hospital day, defined as the second midnight of admission. We did this to ensure the capture of a full hospital day, as patients admitted at 11pm would only have 1 hour of time in hospital day 1.

Our primary outcome was the placement of an NSAID order by the end of the first full hospital day. Secondary outcomes included administration of NSAIDs by the end of the first full hospital day, patient pain scores by the end of the first full hospital day including highest and average pain score and total oral morphine equivalents (OMEs) the day before discharge using a common equivalence calculator.[15] OME is a commonly used approximations to compute equianalgesic doses between different types of opioids.[15] We also calculated the opioid equivalence of the discharge prescription using the morphine equivalent daily dose.[15]

We analysed three adverse events as potential clinical harms from NSAID use: in-hospital death, new GI bleed and new acute kidney injury. Clinical harms were defined as a new diagnosis not present on admission. We classified clinical harms by extracting data from Clarity (death) as well as both the patient's inpatient problem list and coded diagnoses that are attached to the hospital account and entered by a medical coder within 2 weeks after the patient is discharged. We used ICD10 codes to define these diagnoses including eGFR[16] (online supplemental eAppendix 4). Finally, we identified patients with preadmission-documented contraindications to an NSAID (chronic kidney disease, organ transplant, allergy, history of GI bleed) using historical coding, billing and patient's problem lists as well as the patient's eGFR on admission. We performed stratified analysis on the group of patients with contraindications to NSAIDs to better understand clinical harms in that specific subset.

Statistical analysis

Baseline characteristics were expressed as numbers and percentages for categorical variables and mean with SD for continuous variables. Differences between control and intervention baseline characteristics were compared by χ^2 or t-test for categorical and continuous variables, respectively. We reran each variable to ensure normality, and for non-normal data reported outcomes as median and IQR.

Because our unit of randomisation was the ordering clinician, but effects were measured at the encounter level, we first tested whether there were differences between clinician groups in terms of observable baseline characteristics, which there were not (online supplemental eAppendix 4). Additionally, we performed a stratified analysis on baseline patient-level data, including only the first patient encounter to see if there were any differences at the patient level.

We then used mixed-effects logistic regression models for each dichotomous outcome, clustering by admitting clinician, to analyse primary and secondary outcomes for each hospital admission exposed to the intervention via their admitting clinician. Data analyses were performed during the month of March 2023. Statistical significance was declared based on $p \leq 0.05$. No multiple testing adjustments were performed. All analyses were performed by using R V.4.0.5.

RESULTS

A total of 1070 clinicians were randomised. Overall, clinicians were 57% female. The clinician type was predominantly residents (49%) with 33% attendings and 15% advanced practice practitioners. The average number of years at UCSF at time of randomisation was 3.5 years. The login department was surgical for 45% of clinicians, medicine for 39% with the remainder being other or missing. There were no statistically significant differences between the randomised groups of clinicians (online supplemental eAppendix 5). We anticipated 80% power to detect an effect size difference of 10% in NSAID ordering between intervention and control groups with 270 encounters in each group. With our much larger sample size of nearly 10 000 encounters in each group, even with the design effect, we were well powered to detect a small difference in NSAID ordering (online supplemental eAppendix 2).

Baseline encounter data

The total cohort included 6239 patients, representing 9595 total encounters. At the encounter level, the median age was 62 years old (IQR 47.0–73.0). Fifty-one per cent were female and the majority (57%) were white. The median Charlson Index Score was 2.0. (IQR 1.0–4.0). Sixty-three per cent of encounters had a surgical procedure during the same hospitalisation. Once we accounted for clinician clustering, there was no significant difference between the baseline data of the two groups except for length of stay which was higher in the intervention group by 1 day (p<0.001) (table 1). The median length of stay for the control group was 2.0 days (IQR 1.0–5.0) and 3.0 days for the intervention group (IQR 1.0–5.0).

NSAID outcomes

Both NSAID ordering and administering by the end of the first full hospital day were higher in the intervention (prechecked) group. NSAIDs were ordered by the end of the first full hospital day in 1586 (36%) encounters in the control group and 2245 (43%) in the intervention group (p<0.001). NSAIDs had been administered by the end of the first full hospital day in the 1317 (30%) patients in the

Table 1 Characteristics of encounters exposed to the intervention, accounting for clustering at the clinician level

Characteristic	Control group N=4374	Intervention group N=5221	P value
Age at admission in years (median (IQR))	62.0 (48.0–73.0)	62.0 (47.0–72.0)	0.22
Charlson Index (median (IQR))	2.0 (1.0–4.0)	2.0 (1.0–4.0)	0.21
Length of stay (median (IQR))	4.30 (7.54)	4.57 (6.54)	0.07
Gender (%)			
Female	2265 (51.8)	2645 (50.7)	0.55*
Male	2103 (48.1)	2567 (49.2)	
All others	2 (0.0)	2 (0.0)	
Race ethnicity (%)			
Native American or Alaska Native	60 (0.6)	26 (0.6)	0.998*
Asian	545 (12.6)	664 (12.9)	
Black or African American	296 (6.8)	370 (7.2)	
Latinx	703 (16.2)	825 (16.0)	
Multirace/ethnicity	105 (2.4)	130 (2.5)	
Native Hawaiian or Other Pacific Islander	21 (0.5)	23 (0.4)	
Other	116 (2.7)	132 (2.6)	
Southwest Asian and North African	45 (1.0)	54 (1.0)	
White or Caucasian	2471 (57.1)	2929 (56.8)	
Language (%)			
Cantonese	100 (2.3)	111 (2.1)	0.50*
Mandarin	30 (0.7)	40 (0.8)	
English	3879 (88.8)	4613 (88.6)	
Russian	24 (0.5)	37 (0.7)	
Spanish	219 (5.0)	291 (5.6)	
All others	114 (2.6)	116 (2.2)	
Surgical procedure during encounter (%)	2604 (59.5)	3398 (65.1)	0.92
Any contraindication to NSAIDs (%)	2742 (26.4)	2610 (27.0)	0.841

P value=clustered by admitting clinician except when denoted by '*'.
NSAID, non-steroidal anti-inflammatory.

Table 2 Outcomes for each included encounter, accounting for clustering at the clinician level

	Control group N=4374	Intervention group N=5221	P value
NSAID outcomes			
NSAID ordered by end of first full hospital day (primary outcome), n (%)	1586 (36.3)	2245 (43.0)	<0.001
NSAID administered by end of first full hospital day, n (%)	1317 (30.1)	1798 (34.4)	0.001
Pain and opioid outcomes			
Highest pain score during first full hospital day (median (IQR))	6.0 (2.0–8.0)	6.0 (3.0–8.0)	<0.001
Average pain score during first full hospital day (median (IQR))	3.1 (0.8–5.1)	3.3 (1.0–5.3)	0.001
Highest pain score during last full hospital day (median (IQR))	5.0 (2.0–8.0)	6.0 (2.0–8.0)	0.001
Average pain score during last full hospital day (median (IQR))	2.8 (0.4–4.9)	3.0 (0.8–5.0)	<0.001
Average daily OME over hospitalisation (median (IQR))	31.3 (7.5–77.1)	32.9 (9.0–80.2)	0.35
Total OME 24 hours day before discharge (median (IQR))	102.0 (20.0–359.4)	112.5 (24–350.0)	0.49
Opioid ordered at discharge, n (%)	2253 (51.5)	2971 (56.9)	0.19
MEDD of discharge prescription, (mean (SD))	60.0 (30.0, 90.0)	60.0 (30.0, 105.0)	0.37
Clinical Harms			
In-hospital death, n (%)	66 (1.5)	77 (1.5)	0.97
New AKI, n (%)	390 (8.9)	498 (9.5)	0.52
New GI bleed, not present on admission, n (%)	45 (1.0)	50 (1.0)	<0.001

P value=clustered by admitting clinician. The mean OME and MEDD only include patients who had an opioid. If there was no opioid administered or prescribed at discharge, that encounter was not included in calculating the mean.
AKI, acute kidney injury; GI, gastrointestinal; MEDD, morphine equivalent daily dose; NSAID, nonsteroidal anti-inflammatory drugs; OME, oral morphine equivalent.

control group and 1798 (34%) patients in the intervention group (p=0.001) (table 2).

When a stratified analysis was performed at the patient level, using only the patient's first encounter, both NSAIDs ordered by the end of first full hospital day (p<0.001, 95% CI 1.24 to 2.06) and NSAIDs administered by the first full hospital day (p=0.02, 95% CI 1.04 to 1.70) remained statistically significant (table 2). These results all account for clustering at the clinician level.

Pain and opioid outcomes

We observed small but statistically significant differences in median average and median highest pain scores both on the first hospital day and last, with the intervention group having slightly higher scores than the control arm at all points of measurement (table 2). None of the opioid outcome differences between the two groups were statistically significant. Average daily OME was 31.3 in the control group and 32.9 in the intervention group (p=0.35). Total OME administered in the 24-hour day before discharge was higher in the intervention group at 101.8 (IQR 20.0–359.5) vs 112.5 (IQR 24–350.0) in the control group (p=0.49), a difference equivalent to 7 mg of oxycodone or 100 mg of tramadol. These results all account for clustering at the clinician level.

Clinical harms

Clinical harms were similar between groups. In-hospital death was 66 (1.5%) in the control group and 77 (1.5%) in the intervention group (p=0.97). New AKI was 390 (8.5%) in the control group and 498 (9.5%) in the intervention group (p=0.52). New GI bleed was 45 (1.0%) in the control group and 50 (1.0%) in the intervention group (p<0.001; a simple χ^2 test without accounting for random effects or clustering by clinician yielded a p=0.81).

When analysed at the patient level, there were no statistically significant differences in any of the clinical harms. When we analysed only encounters for which there was an NSAID contraindication, there were no differences in clinical harms, including new GI bleed. When we performed a subgroup analysis of only patients with contraindications to NSAIDs, we found no statistically significant difference in clinical harms. These results all account for clustering at the clinician level.

NSAID contraindications

In the control group, 1191 (27%) patients had a contraindication to NSAIDs and 1346 (26%) in the intervention group. NSAIDs were ordered despite a contraindication in 214 (4.9%) patients in the control group and 335 (6.4%) patients in the intervention group (p<0.001).

DISCUSSION

Our study found an increase in NSAID ordering and administration with a prechecked NSAID order embedded in a multimodal admission pain order set and no change in OMEs administered. While we observed statistically higher pain scores in the intervention group, the magnitude of the differences was small. Crucially, the prechecked pain panel did not increase the percent of encounters of patients with

evidence of clinical harm from NSAIDs. However, the proportion of encounters of patients with a contraindication to NSAIDs who were nonetheless prescribed an NSAID increased in the prechecked group. Importantly, all analyses accounted for clustering at the clinician level.

EHR clinical decision support has been shown to help reduce undesired utilisation of laboratory tests or imaging,[17 18] but in our study, we attempted to increase utilisation of an opioid-sparing pain medication in order to decrease the use of opioids without adversely affecting pain scores. One study which found that having a preselected or 'defaulted-on' order has been shown to effect change in ordering of common laboratory tests, however, this was in non-medication setting and was not applied to all admitted patients.[19] Most studies focusing on medications focus on medication deprescribing or medication reconciliation, as opposed to encouraging clinicians to add a medication.[7 20–23] Finally, alternative interventions to influence medication prescribing, such as showing cost information or cost savings,[8] have been unsuccessful at changing clinician behaviour. Laboratory test ordering is a straightforward outcome (ordered vs not), whereas medication ordering for analgesia then requires administration as well as better pain management and finally, opioid reduction. Our intervention, prechecking a desired order, was unique in that it showed an increase in prescribing of a specific medication in the intervention group. However, changing behaviour is complex and often requires health system culture change.[24]

Though we saw a difference between the intervention and control groups, the uptake of NSAID use was still low at only 43% in the intervention group. Twenty-six per cent of patients in this group had a known contraindication, leaving one-third of patients in this group who were able to have received an NSAID and may have benefited from the medication. It is possible that the timing of our intervention was not optimal for encouraging NSAID ordering and use. While NSAIDs have not been shown to cause major bleeding for most surgical patients,[25] it may be that surgeons feel more comfortable waiting until after post-operative day 1 to start an NSAID. Our goal to increase NSAID prescribing may have been even more successful if it was targeted to later in the admission such a postoperative day 1 or 2 as opposed to the admission order set, which is completed immediately after surgery. Institution-wide work was ongoing to raise awareness about opioid misuse and the need for multimodal pain control, which may have separately driven ordering behaviour, though we did see a difference between the two groups.

Importantly, despite the statistically significant increase in NSAID prescribing in the intervention group, we did not see a decrease in opioid prescribing. However, pain scores were statistically different, with higher scores in the intervention group. Because of our study's size, we were well powered to detect very small statistical differences, but whether the changes we observed were clinically significant is debatable. Moreover, because we do not have access to functional status information, we cannot tell whether any small increase in pain scores had impact on recovery or return to function. Perhaps the lack of change in opioids may be due to the institution-wide push to decrease opioid prescribing, such that prescribing was more similar across all groups. This may have been because 20% (447/2245) of patients prescribed an NSAID did not actually have an NSAID administered by the end of the first full hospital day. It is unclear if these patients refused, or if it was not offered to them despite the order. More work needs to be done to better understand what groups might most benefit from NSAIDs and use the EHR to target those groups specifically. Given we are now able to harness the EHR to better track potential contraindications and the findings of a very small but statistical difference in GI bleed in this study, we amended our intervention at the conclusion of the study so that NSAIDs are now always unchecked if we can identify a pre-existing contraindication. The order remains available should the clinician want to check it. To ensure patient safety, we added an additional layer of safety to the pain medication panel in which we UNchecked NSAIDs if the patient had a known contraindication to NSAIDs.

LIMITATIONS

Our study had a number of limitations. First, we randomised at the clinician level to avoid contamination of NSAID ordering behaviour for different encounters exposed to a given clinician. However, we clustered by clinician in our analysis, and are certainly well powered to see any differences that might have existed. Additionally, our patient-level data had similar findings to the encounter-level data. Some clinician groups continued to use their own admission order sets, and so these encounters are not included in the study, limiting generalisability. Though across three busy hospital sites, this is a single-centre study also limiting generalisability. There were contraindications for NSAIDs that we were unable to pull from EHR data such as 'monitoring for neutropenic fever' and 'on therapeutic anticoagulation where bleeding risk great than benefit' so may have underestimated the number of patients with a contraindication to NSAIDs. Tracking pain scores is a subjective measure (as opposed to the objective measure of ordered yes/no), a downside of a pragmatic study versus tracking patient-reported outcomes. Many key factors can influence pain scores and OME at discharge, including type of surgery, baseline pain scores (ie, chronic pain) and other factors, which limits our ability to attribute these outcomes solely to our intervention. Finally, our programme occurred simultaneously with efforts at the institutional level to increase the use of non-opioid pain medication and to inform discharge prescribing based on the last 24 hours of pain medication use for all patients. These interventions may have influenced clinicians to order NSAIDs whether they

were in the intervention group or hidden the influence of our intervention on the prescribing of opioids at discharge.

CONCLUSIONS

This cluster randomised controlled trial involving a single EHR intervention that prechecked an NSAID order in the core admission order set, with the goal of increasing uptake of NSAIDs for pain control in adult hospitalised patients. We found an increase in NSAID ordering between the intervention and control groups. The intervention did not affect the quantity of opioids administered the day before discharge, and more work needs to be done to specifically address opioid use and prescribing.

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Competing interests None declared.

Patient consent for publication Not applicable.

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Provenance and peer review Not commissioned; externally peer reviewed.

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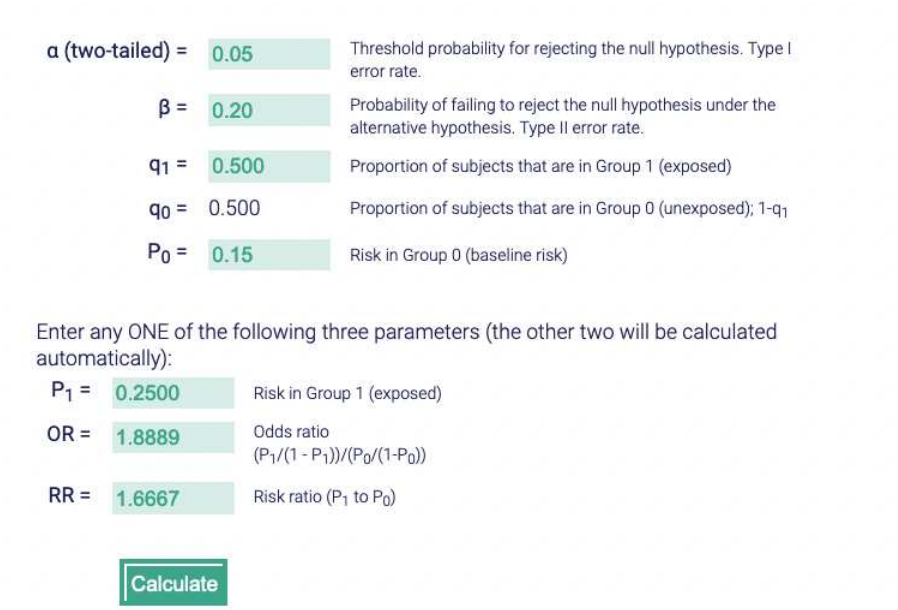
eAppendix 1: CONSORT Checklist
see attached checklist

eAppendix 2: Power calculation:
The power calculation was based on following calculations below:



The standard normal deviate for $\alpha = Z_\alpha = 1.9600$
The standard normal deviate for $\beta = Z_\beta = 0.8416$
Pooled proportion = $P = (q_1*P_1) + (q_0*P_0) = 0.2000$
$A = Z_\alpha\sqrt{P(1-P)(1/q_1 + 1/q_0)} = 1.5680$
$B = Z_\beta\sqrt{P_1(1-P_1)(1/q_1) + P_0(1-P_0)(1/q_0)} = 0.6680$
$C = (P_1-P_0)^2 = 0.0100$
Total group size = $N = (A+B)^2/C = 500$
Continuity correction (added to N for Group 0) = $CC = 1/(q_1 * |P_1-P_0|) = 20$

Sample size (with continuity correction)

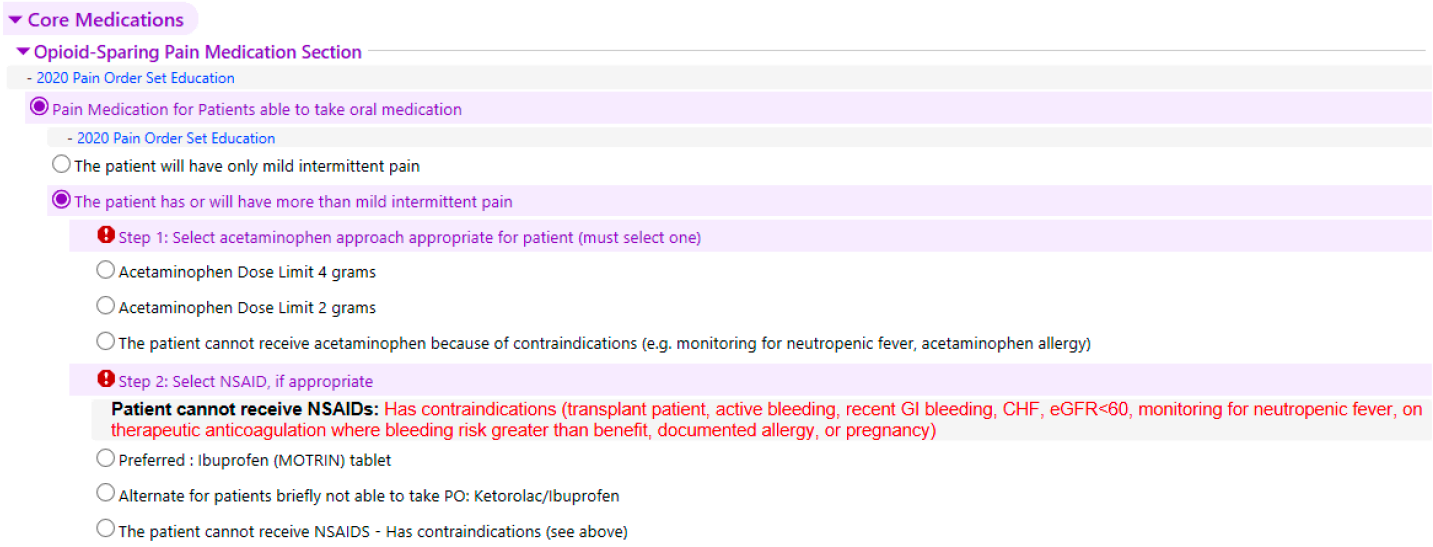
	N	Outcome+	Outcome-
Group 1:	270	68	202
Group 0:	270	41	229
Total:	540	109	431

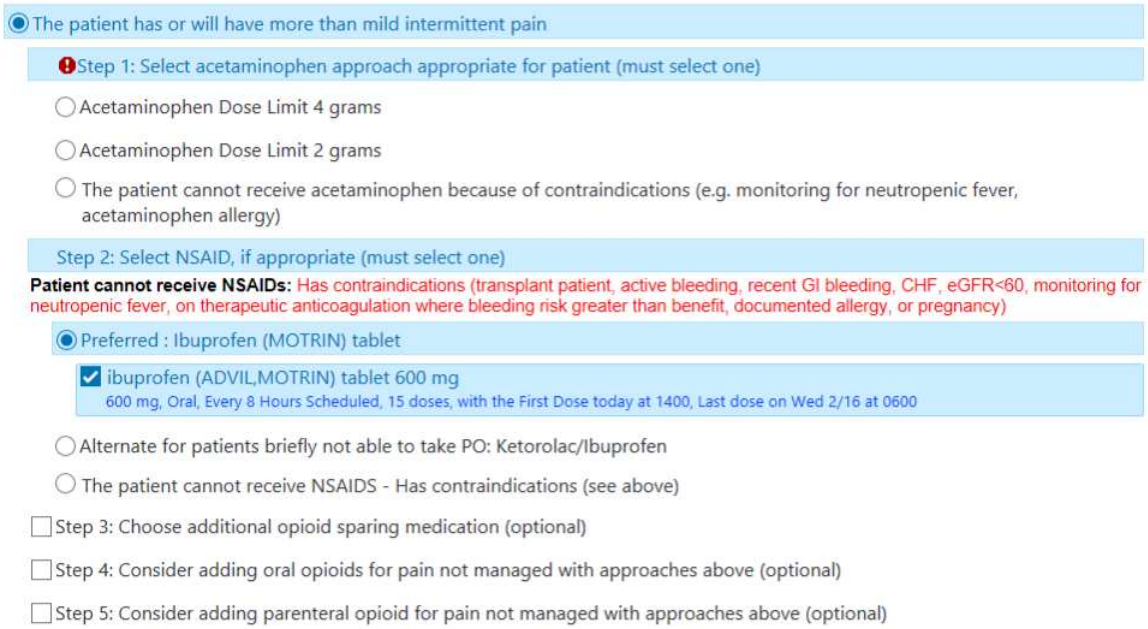
Sample size (without continuity correction)

	N	Outcome+	Outcome-
Group 1:	250	63	187
Group 0:	250	38	212
Total:	500	101	399

Note: This calculator uses the normal distribution (with and without the continuity correction) as an approximation to the binomial distribution.

eAppendix 3: Electronic Health Record Intervention, Hard Stop Versus Prechecked




The patient has or will have more than mild intermittent pain
Step 1: Select acetaminophen approach appropriate for patient (must select one)
Acetaminophen Dose Limit 4 grams
Acetaminophen Dose Limit 2 grams
The patient cannot receive acetaminophen because of contraindications (e.g. monitoring for neutropenic fever, acetaminophen allergy)
Step 2: Select NSAID, if appropriate (must select one)
Patient cannot receive NSAIDs: Has contraindications (transplant patient, active bleeding, recent GI bleeding, CHF, eGFR<60, monitoring for neutropenic fever, on therapeutic anticoagulation where bleeding risk greater than benefit, documented allergy, or pregnancy)
Preferred : Ibuprofen (MOTRIN) tablet
ibuprofen (ADVIL,MOTRIN) tablet 600 mg
600 mg, Oral, Every 8 Hours Scheduled, 15 doses, with the First Dose today at 1400, Last dose on Wed 2/16 at 0600
Alternate for patients briefly not able to take PO: Ketorolac/Ibuprofen
The patient cannot receive NSAIDS - Has contraindications (see above)
Step 3: Choose additional opioid sparing medication (optional)
Step 4: Consider adding oral opioids for pain not managed with approaches above (optional)
Step 5: Consider adding parenteral opioid for pain not managed with approaches above (optional)

eAppendix 4: Defining Clinical Harms

Gastrointestinal Bleed ICD-10 Codes

'I85.01', 'K20.81', 'K20.91', 'K21.01', 'K22.11', 'K25.0', 'K25.2', 'K25.4', 'K25.6', 'K26.0', 'K26.2', 'K26.4', 'K26.6', 'K27.2', 'K27.4', 'K27.6', 'K28.0', 'K28.2', 'K28.6', 'K29.01', 'K29.21', 'K29.31', 'K29.41', 'K29.51', 'K29.61', 'K29.71', 'K29.81', 'K29.91', 'K31.811', 'K50.00', 'K52.81', 'K55.21', 'K92.2', 'K57.01', 'K57.11', 'K57.13', 'K57.21', 'K57.31', 'K57.33', 'K57.41', 'K57.51', 'K57.53', 'K57.81', 'K57.91', 'K57.93', 'K92.2'

Acute Kidney Injury ICD-10 Codes

‘N17.0*’, ‘N17.8*’, ‘N17.9*’, ‘N19*’

eAppendix 5: Baseline characteristics of randomized clinicians admitting at least 1 qualifying patient

Clinician characteristics		Control Group N=536	Intervention Group N=534	p-value
Years at UCSF (mean (SD))		3.5 (3.2)	3.5 (3.1)	0.95
Surgeon (%)		257 (48)	251 (47)	0.80
Gender	Female	301 (57)	296 (58)	1
	Male	224 (43)	219 (43)	
	Non-binary or missing	11 (2)	19 (4)	
Department at Login (%)	Medicine	153 (36)	182 (42)	0.11
	Surgery	206 (49)	179 (42)	
	Other	65 (15)	69 (16)	
	Missing	112 (21)	104 (20)	
Clinician Type (%)	Attending	169 (32)	182 (34)	0.58
	APP	83 (16)	80 (15)	
	Resident	273 (51)	255 (48)	
	Medical Student	10 (2)	14 (3)	
	Other	1 (0.2)	1 (0.2)	

eAppendix1: CONSORT Checklist

Based on the CONSORT guidelines.

		Reporting Item	Page Number
Title and Abstract			
Title	#1a	Identification as a randomized trial in the title.	1
Abstract	#1b	Structured summary of trial design, methods, results, and conclusions	3
Introduction			
Background and objectives	#2a	Scientific background and explanation of rationale	4
Background and objectives	#2b	Specific objectives or hypothesis	4
Methods			
Trial design	#3a	Description of trial design (such as parallel, factorial) including allocation ratio.	4
Trial design	#3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	4
Participants	#4a	Eligibility criteria for participants	5
Participants	#4b	Settings and locations where the data were collected	5
Interventions	#5	The experimental and control interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5

Outcomes	#6a	Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed	6
Outcomes	#6b	Any changes to trial outcomes after the trial commenced, with reasons	5-6
Sample size	#7a	How sample size was determined.	eAppendix
Sample size	#7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomization - Sequence generation	#8a	Method used to generate the random allocation. sequence. 4	
Randomization - Sequence generation	#8b	Type of randomization; details of any restriction (such as blocking and block size) 5	
Randomization - Allocation concealment mechanism	#9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	5
Randomization - Implementation	#10	Who generated the allocation sequence, who enrolled participants, and who assigned participants to interventions	5
Blinding	#11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how.	n/a
Blinding	#11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	#12a	Statistical methods used to compare groups for primary and secondary outcomes	6
Statistical methods	#12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	6

Results			
Participant flow diagram (strongly recommended)	#13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	6
Participant flow	#13b	For each group, losses and exclusions after randomization, together with reason	6
Recruitment	#14a	Dates defining the periods of recruitment and follow-up	4
Recruitment	#14b	Why the trial ended or was stopped	4
Baseline data	#15	A table showing baseline demographic and clinical characteristics for each group	13, eAppendix
Numbers analysed	#16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	6, 13
Outcomes and estimation	#17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	6, 7
Outcomes and estimation	#17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	6, 7
Ancillary analyses	#18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	7, 13
Harms	#19	All important harms or unintended effects in each group (For specific guidance see CONSORT for harms)	7, 14
Discussion			
Limitations	#20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	8

Generalisability	#21	Generalisability (external validity, applicability) of the trial findings	8
Interpretation	#22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	9
Registration	#23	Registration number and name of trial registry	n/a
Other information			
Interpretation	#22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	8, 9
Registration	#23	Registration number and name of trial registry	n/a
Protocol	#24	Where the full trial protocol can be accessed, if available	n/a
Funding	#25	Sources of funding and other support (such as supply of drugs), role of funders	10