STUDY PROTOCOL

Application of **E**conomics & **S**ocial psychology to improve **O**pioid **P**rescribing **S**afety Trial 1 (**AESOPS-T1**):
A cluster randomized trial

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Supported by:

The National Institute on Aging
R33AG057395

Version date: March 18, 2020

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PRÉCIS

Study Title

Application of Economics & Social psychology to improve Opioid Prescribing Safety (AESOPS): A cluster randomized trial

Objectives

There is a lack of evidence that long-term opioid use offers benefit for noncancer pain and an abundance of evidence of harm. The objective of the Application of Economics & Social psychology to improve Opioid Prescribing Safety (AESOPS) trial is to develop and test novel behavioral nudges to encourage adherence to Oregon Pain Guidance and CDC guidelines for opioid prescribing for persons with noncancer pain. We have successfully developed and piloted different nudges in the R21 phase, then we compare these nudge interventions across 374 primary care clinics nationally in a cluster randomized trial.

Design and Outcomes

We will conduct a multi-site cluster randomized trial of 2 behavioral interventions to encourage safer opioid prescribing during ambulatory visits when pain is a symptom. The design is longitudinal with respect to clinician participants and "repeated cross-sectional" with respect to patient observations because the visit observations used for analyses may come from different sets of patients over time. We randomized at the clinic level to avoid intra-clinic contamination of the intervention.

Interventions and Duration. The intervention period will be 18-months in length for all participants, with a 6-month follow-up period to measure persistence of effects after interventions end. The following intervention conditions will be compared: Condition 1: Education, justifications, and precommitments. Guideline education consists of receiving the CDC guidelines and completing a brief online educational module at the start of the study period. This will include educational clinical content related to the CDC guidelines, the Oregon Pain Guidance document, tapering training and other resources tapering training and other resources such as SAMHSA Medication-Assisted Treatment Physician Locator and the Naloxone Provider Guide. When prescribing an opioid, clinicians are prompted to record an explicit justification that appears in the patient electronic health record. Justifications are tailored to first time prescriptions, greater than first time prescriptions, but less than 91 days; and high dose chronic opioid therapy > 90 days of use.

Condition 2: Guideline Education Control. Control group clinicians will receive the CDC guideline and will complete a brief online educational module at the start of the study period. This will include educational clinical content related to the CDC guidelines, the Oregon Pain Guidance document, tapering training and other resources tapering training and other resources

such as SAMHSA Medication-Assisted Treatment Physician Locator and the Naloxone Provider Guide.

Outcome Measures: The primary outcome is clinician aggregate monthly morphine milligram equivalent (MME) dosing. This will be measured for two groups: (i) 50 MME and above, and (ii) below 50 MME daily dose visits. For an observation to qualify for an above 50 MME measure, a clinician has to have treated a patient with at least one visit where $\geq$ 50 MME daily dose triggered high dose decision support. Otherwise, observations are placed in the < 50 MME condition. We will estimate daily milligram morphine equivalent for each clinician by summing the total number of daily morphine equivalents written within a monthly observation period divided by the number of 30 days. For example, suppose a clinician had three qualifying visits over three days in one month and prescribed: Patient #1 is prescribed 200mg ME/day x 30 days, Patient #2 has tapered from 200 mg ME/day to now 100mg ME/day x 30 days and Patient # 3 is on a tapering plan from 60 to 30 mg ME/day and is receiving 50 mg ME/day x 15 days. The clinician's outcome for that month then equals:

[(200 mg/day x 30 days) + 100 mg/day x 30 days) + (50 mg/day x 15 days)] x [1 Month/30 days]

= (300 mg x 1 + 100 mg x 1 + 50 mg x (½)) = 425 mg MED/[Month].

This measures can capture the influence of all relevant CDC guideline prescribing endpoints that aim to reduce reliance on opioids in primary care including: 1) Use of alternatives to opioids (CDC recommendation 1), 2) use of lowest effective starting dose (CDC recommendation 5), 3) lower duration acute pain prescriptions (CDC recommendation 6), 4) Tapering (CDC recommendation 7), 5) avoidance of co-prescribing (CDC recommendation 11) and 6) referral for medication assisted therapy to substitute buprenorphine (CDC recommendation 12). The measures excludes visits below $\geq$ 50mg ME/day as these are low risk for adverse events. Our secondary outcome though captures transitions from low to high dose prescribing. Prescribing data on opioids will be captured using appropriate opioids listed in the Food and Drug Administration's National Drug Code files for scheduled drugs. Oral buprenorphine will be excluded from the calculations as it relates to opioid use disorder treatment. Morphine equivalent dose will be computed by standard means described elsewhere.(Vieweg, Carlyle Lipps, and Fernandez 2005) Qualifying pain visits will be captured by including all ICD10 pain diagnostic codes and excluding active cancer diagnoses.

One of the secondary outcomes is the proportion of dosages that escalated to $\geq$ 50 MME/day over time, which is a computable clinical quality measure from the electronic health record. This is widely used in medicine to evaluate quality improvement and reliability and validity are generally supported.(Persell 2006) Visits are excluded from the denominator when patients have an active cancer or acute pain diagnosis that makes CDC guidelines not apply. Numerator visits are guideline discordant inappropriate actions that occurred at a denominator visit: co-prescription and transition from prior prescription above the 50 mg/day threshold. Daily milligram morphine equivalent for each clinician will be estimated by summing the total number of daily morphine equivalents written within a monthly observation period divided by 30 days. Additional secondary outcomes include the change in opioid prescriptions from any source according to state-level prescription drug monitoring program

(PDMP) data.

STUDY OBJECTIVES

1.1 Primary Objective

Our primary hypothesis is that practices randomized to receive behavioral economic interventions will have lower opioid prescribing rates compared to control practices.

1.2 Secondary Objectives

Secondary outcomes will examine opioid prescribing once interventions stop over 6 months of follow-up to investigate persistence of effects.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Over the last two decades, prescription opioids have grown to become a public health crisis. Today, on average 1 in 5 persons with chronic noncancer pain receives an opioid prescription in the U.S.(Dowell, Haegerich, and Chou 2016) Yet, despite this record level of prescribing, reports of pain in America have not gone down.(Daubresse et al. 2013; Chang et al. 2014) The greater availability of prescription opioids has been accompanied by an alarming rise in the negative consequences related to their use. In 2015, there were over 365,000 emergency department visits for misuse and 20,101 prescription overdose deaths, more than have ever been recorded in U.S. history.("Website" n.d.) The costs of prescription opioids are staggering. Aggregate costs for prescription opioid harms are estimated at over $78.5 billion (in 2013 dollars). One-fourth of the aggregate economic burden is publicly funded (i.e., Medicaid, Medicare, and veterans' programs).("[No Title]" n.d.; Florence et al. 2016)

In 2016, the CDC issued the "CDC Guideline for Prescribing Opioids for Chronic Pain" which gives 12 patient care recommendations: (1) *use alternatives* to opioids, (2) *set realistic goals* for pain and function, (3) *discuss opioid risks* upon therapy initiation, (4) *use immediate release agents* instead of long-acting ones, (5) *use lowest effective starting dose, avoid escalation* above 50 milligram (mg) morphine equivalent (ME) daily dose and abide by a 90 mg ME/day dose prescribing limit, (6) *prescribe lowest dose at lowest quantity needed for acute pain*—usually 3 days with a maximum of 7 days in rare cases (7) *evaluate for and discuss tapering* within 1 - 4 weeks and after 90 days, (8) *prescribe naloxone and evaluate substance use history* with opioid prescription, (9) *review the state prescription drug monitoring program data* (10) *conduct urine drug tests* to provide information about drug use that is not reported by the patient, (11) *avoid co-prescribing* with benzodiazepines, and (12) *refer patients with opioid use disorder to medication-assisted treatment in*

combination with behavioral therapies. Our objective is to increase adherence to the CDC guideline and Oregon Pain Guidance pain management guideline. To evaluate the effects of doing so, we will measure as a primary outcomes clinician aggregate monthly mg ME for patient visits with ≥50 mg ME daily dose. Secondary outcomes include rate of dose escalation to ≥50 mg ME/day.

2.2 **Study Rationale**

Rationale for Accountable Justifications. In the Accountable Justifications intervention, clinicians will be prompted to record an explicit justification for why they are prescribing an opioid that appears in the patient's EHR. Accountable justifications incorporate several behavioral principles. First, they signal an injunctive norm (a norm, often provided by an authoritative source, that strongly indicates how people should behave) indicating that prescribing an opioid is not recommended. This may make the clinician more likely to believe both that not prescribing an opioid is the best medical decision and that prescribing when it is not indicated violates professional standards. Second, it incorporates social accountability. A clinician justification become an explicit, separate part of the medical record, so a clinician's decision to prescribe is subject to the review and judgment of the provider's peers. Third, the justification alert implicitly designates guideline-concordant prescribing as the default action. Defaults are options that are exercised if the decision maker takes no special action to opt in or out of a given choice. Prior to our intervention, choosing to deviate from guidelines did not carry a special requirement to document a clinical rationale in the EHR. Accountable justifications, therefore, reset the default action. Guideline-concordant treatment choices will not require special justification, but a clinician must now "opt-in" to prescribing an opioid by providing a justification for which they are accountable.

Rationale for Precommitments. Precommitment asks the decision-maker to commit to a future expectation. This intervention targets patients with problematic opioid use that do not meet criteria for opioid use disorder. For these patients, taper discussions may be perceived as difficult to initiate at the present time, but perceived as easier in the future because of *present bias.(Loewenstein and Prelec 1992)* Our hypothesis is that the choice to discuss a taper with the patient may benefit from a *precommitment.(Goldstein, Cialdini, and Griskevicius, n.d.; Cialdini et al. 1978)*
In applied work, use of precommitment to a behavior has had notable success. For example, people often state they want to save for retirement but fail to follow through with their intent. The "Save More Tomorrow" retirement savings study elicited a precommitment of future raises to retirement funds; this study increased savings from 3.5 percent to 13.6 percent over the course of 40 months.(Thaler and Benartzi 2004) In our own work in health, we found that physician public precommitment to judicious antibiotic use reduced inappropriate antibiotic prescribing by 19.7 percentage points.(Meeker et al. 2014)

3. STUDY DESIGN

The Application of Economics & Social psychology to improve Opioid Prescribing Safety (AESOPS) trial is a two arm multi-site cluster randomized trial. The primary aim is to test the ability of two interventions based on behavioral economic principles to reduce the reliance on opioids and encourage safe and effective pain management. We will randomize practices in one of 2 conditions: 1) Education, justifications, and precommitments: When prescribing an opioid, clinicians are prompted to record an explicit justification that appears in the patient electronic health record. Justifications are tailored to first time prescriptions, greater than first time prescriptions, but less than 91 days; and high dose chronic opioid therapy > 90 days of use. (2) Guideline Education Control. We will have a sufficient sample size (374 clinics) to detect small effects on the primary outcomes. A null finding will indicate evidence of negligible or no effect. Northwestern includes 55 primary care clinics that contain 289 clinicians with 12,552 patients on chronic opioid therapy for noncancer pain—opioids greater than 3 months. Altamed Medical Group has 30 clinics with 134 clinicians with 17,674 such patients. The primary outcome is milligram morphine equivalents tiered to two levels: (i) above, and (ii) below 50 mg ME daily dose visits. For an observation to qualify for an above 50 mg ME measure, a clinician has to have treated a patient with at least one visit where $\geq$ 50 mg ME daily dose triggered high dose decision support. Otherwise, observations are placed in the < 50 mg ME condition. Secondary, outcomes are benzodiazepine co-prescribing and rate of dose escalation to $\geq$ 50 mg ME/day. We will estimate daily milligram morphine equivalent for each clinician by summing the total number of daily morphine equivalents written within a monthly observation period divided by the number of 30 days. Data from electronic medical records for participating practices are transferred to the Data Coordinating Center on a weekly basis.

4. SELECTION AND ENROLLMENT OF PARTICIPANTS

4.1 Inclusion Criteria

The subjects involved in this trial are clinicians who will be recruited from multiple clinical sites in Illinois and California. The target group of physicians (and the patients that they treat) is fully inclusive and representative. Clinicians will be eligible if they treat adult patients. We will request a waiver of consent for physician participation, but will enroll for any survey assessments.

Each study clinic is required to have an electronic health record (EHR) system in place and have its own physical building (as opposed to multiple clinics sharing the same space, such as the floor of a hospital, where interactions between providers assigned to different intervention groups would be more likely). Clinicians must meet the following inclusion criteria to participate in this study: 1) treat adult patients and 2) practice at one of the study clinics.

An office visit is eligible for inclusion in the outcome denominator if: 1) the patient was 18 years old or older, 2) the provider and practice site were enrolled in the study, and 3) the visit occurred during the 18-month intervention period.

4.2 Exclusion Criteria

Visits will be excluded from the primary analysis when they have active cancer. Cancer exclusions (ICD-10 codes) are listed here.

4.3 Study Enrollment Procedures

We will seek a waiver of consent for intervention, but will enroll for survey assessments. All clinicians with adult patients in participating practices will be contacted by email and in-person meetings. Enrollment and consent will be conducted using an online survey administration application.
The email includes a description of the broad goals of the study, a general description of the intervention, compensation providers would receive for participation, and a link to the electronic consent form and baseline survey.
The baseline survey includes an educational module. After providing consent, providers are asked to complete a 15 to 20 minute online survey and educational module. The educational module contains information about pain management (Oregon Pain Guidance) and safe opioid prescribing for chronic pain (CDC guidelines). The educational module also describes the interventions to which a clinician's site was assigned, including changes they would observe in their electronic health record.

5. STUDY INTERVENTIONS

5.1 Interventions, Administration, and Duration

The intervention period will be 18-months in length for all participants, with a 6-month follow-up period to measure persistence of effects after interventions end. The pre-intervention baseline period will be 6 months in length.

5.2 Handling of Study Interventions

The two conditions to be compared will be referred to as Nudges (Condition 1) and Control (Condition 2). Both groups will receive guideline education. Guideline education consists of receiving the CDC guidelines and completing a brief online educational module at the start of the study period. This will include educational clinical content related to the CDC guidelines, the Oregon Pain Guidance document, tapering training and other resources tapering training and other resources such as SAMHSA Medication-Assisted Treatment Physician Locator and the Naloxone Provider Guide.

Physicians in clinics randomized to the Nudges Condition will be prompted with an EHR nudge if the prescribing history for the patient falls into one of the following three categories: opioid naïve or no recent opioid use, opioid prescription within 90 days, or chronic, high-dose opioids. The criteria for an opioid naïve patient include no recent opioid use or an order for an included opioid and

do not have a start date less than 91 days. The criteria for an opioid prescription within 90 days include: (1) an order for an included opioid with a start date greater than 1 day and less than 91 days and (2) not an opioid prescription with a start date greater than 90 days. The criteria for chronic, high dose opioids are an order for an included opioid that's dose is greater than 50 MME, two or more opioid prescriptions with two different start date both greater than 1 day and less than 91 days, and an opioid prescription with a start date greater than 90 days.

The nudges included in Condition 1 are Accountable Justification (AJ) alerts, Precommitments (PR) to tapering and the PainTracker tool. Accountable Justification alerts pertain to tapering, high dose prescribing, co-prescribing and short duration prescribing for acute pain diagnoses. AJ is an EHR-based intervention that will prompt the clinician to justify, in a free text response, the decision to prescribe an opioid or to not reduce high risk/high dose prescribing. The prompt is designed to inform the clinician that others will see the justification in the patient's medical record as a "High risk prescribing justification" note, and that if no justification is entered, the phrase "no justification given" will appear in the medical record. The behavioral economic principles underlying accountable justification include injunctive norms, social accountability and defaults. These AJ nudges have proven effective in a previous trial set in different prescribing contexts (Madrian and Shea 2001).

Precommitments (PR) is an EHR-based intervention tailored to high dose opioid prescribing that encourages the clinician to commit to a taper discussion with the patient. Precommitments to taper discussions with patients may prompt physicians to initiate these conversations that may seem easier to tackle in the future due to present bias. PainTracker is a pain assessment tool aimed at broadening the understanding of pain and reframing the patient visit around reaching functional goals. It consists of the patient's self-reported pain and prescription opioid dosage over time. AJ, PR and PainTracker are developed within the EPIC electronic health record system.

5.3 **Adherence Assessment**

In order to ensure that the study interventions are being reliably delivered we will create testing scripts that cover logical and coding variation in EHR-based interventions. Study staff will conduct site visits regularly during the intervention to ensure that tests do not fail.

6. STUDY PROCEDURES

6.1 Schedule of Evaluations

Assessment	Screening: Baseline prescribing (Month -17 to Month 0)	Baseline, Enrollment, Randomization: (Day 1)	Intervention start (Month 1)	Continuously Measured or monitored	Intervention end: (Month 18)	Follow-up period: (Month 19 to Month 30)
Clinician-level Assessments						
Informed Consent Form		X				
Demographics		X				
Inclusion/Exclusion Criteria	X	X				
Provider Attitudes Survey		X			X	
Visit-level assessments						
ICD-10 codes	X	X	X	X	X	X
Ordering Data	X	X	X	X	X	X
Adverse Events			X	X	X	

6.2 **Description of Evaluations**

6.2.1 Screening Evaluation

Consenting Procedure

Consenting will only apply for survey assessments. The main study will seek a waiver of consent. With the assistance of each site's medical director, we will send providers at participating sites an introductory email that includes a description of the broad goals of the study, a general description of the intervention, and a link to the electronic consent form and baseline survey. The consent document will indicate that participation is voluntary and that decisions to participate (or not) will have no bearing on any provider's status at his or her clinic. Providers who provide consent to participate will be asked to complete an online survey and will be reimbursed for their time. We will send up to 6 follow up emails to providers who do not respond, and study personnel will contact them in person when feasible.

6.2.2 Enrollment, Baseline, and/or Randomization

Enrollment

We have a waiver of consent for the trial. The intervention will be turned on for all clinics/clinicians randomized to receive the intervention. Start date of the trial will be recorded for each clinic.

Baseline Assessments

- Baseline prescribing monthly morphine equivalents
- Baseline survey to assess provider characteristics and provider attitudes toward practice guidelines, clinical decision support, electronic health records, and practice environment.

Randomization

We will implement a cluster-randomized design at the clinic level to avoid contamination that might occur if individual providers in close proximity are randomized to different interventions. Providers who practice at multiple clinics will be assigned to the intervention of the clinic for which they spend at least 85% of their time. Geographically distinct individual clinics will be the unit of randomization. We will conduct a block randomization of clinics by clinic organization.[15]

7. SAFETY ASSESSMENTS

Data for patients who were noted to have been abruptly stopped of opioid prescriptions, emergency room eligible study visit with a diagnosis that could represent a serious complication of untreated pain will be extracted from study site EHRs and reported to the Data Safety and Monitoring Board. Relative rate of ED visits between study conditions will also be evaluated.

7.1 Specification of Safety Parameters

Data elements from qualifying visits for providers enrolled in the study will be collected from the electronic health record. Clinics will incorporate exclusions (ICD 10 cancer suppressor codes found here) used in the decision to trigger the clinical decision support. Aggregate counts of total visits across sites for which the intervention was triggered, for high dose opioid patients, if abrupt changes to dose (> 20% morphine equivalent daily dose) were made. Such cases will be examined closely to determine if unsafe drops in opioids occurred.

7.2 Methods and Timing for Assessing, Recording, and Analyzing Safety Parameters

Annual reports of our safety measures will be delivered to our Data Safety Monitoring Board.

7.3 Adverse Events

Per CDC guideline clarification, adverse events are defined as an abrupt discontinuation of opioids for persons whose most recent prescription exceeds > 49 morphine equivalent daily dose; or as reported to study staff.(Dowell, Haegerich, and Chou 2019) Emergency department visits will also be evaluated as well as *increases* in prescribing > 20% presumably in response to reports of worsening pain.

7.4 Reporting Procedures

The Principal Investigator will report any unanticipated events to the IRB as well as the Data Safety and Monitoring Board (DSMB) assembled for this study. When notified of an unanticipated event, the DSMB will convene and make a decision as to whether the study should continue. The IRB will also be notified of the DSMB's decision.

7.5 Safety Monitoring

A Data Safety and Monitoring Board (DSMB) will be established by NIH. The following individuals were recommended to NIH with expertise in either opioids, overprescribing or biostatistics/research methods: Joe Frank, Jeanmarie Perrone, and Carl Peiper.

8. INTERVENTION DISCONTINUATION

Following each DSMB meeting, the board will make recommendations to the local IRBs as to whether the study should continue or if changes to the protocol are necessary for continuation.

9. STATISTICAL CONSIDERATIONS

9.1 General Design Issues

Hypotheses

Our primary hypothesis is that practices randomized to receive behavioral economic interventions will have lower opioid prescribing rates compared to control practices. This hypothesis will be evaluated in an intent-to-treat difference-in-differences framework using a mixed-effects regression model on clinician morphine equivalent daily dose. Fixed effects will include the effects of interventions over time (i.e., interactions between randomization assignment and time), using a 6-months prior to the intervention baseline period. Providers and randomization unit (clinic) will be modeled as random effects.

Design

The Application of Economics & Social psychology to improve Opioid Prescribing Safety (AESOPS) trial is a two arm multi-site cluster randomized trial. The primary aim is to test the ability of three interventions based on behavioral economic principles to reduce the reliance on opioids and encourage safe and effective pain management. We will randomize practices in one of two conditions: 1) Education, justifications, and precommitments: When prescribing an opioid, clinicians are prompted to record an explicit justification that appears in the patient electronic health record. Justifications are tailored to first time prescriptions, greater than first time prescriptions, but less than 91 days; and high dose chronic opioid therapy > 90 days of use. (2) Guideline education control. We will have a sufficient sample size (374 clinics) to detect small effects on the primary outcomes.

Outcome Measures

The primary outcomes is clinician aggregate monthly mg morphine equivalent. This will be evaluated for two groups: (i) above, and (ii) below 50 mg ME daily dose visits. For an observation to qualify for an above 50 mg ME measure, a clinician has to have treated a patient with at least one visit where > 50 mg ME daily dose triggered high dose decision support. Otherwise, observations are placed in the < 50 mg ME condition. One of the secondary outcomes is the proportion of dosages that escalated to $\geq$ 50 MME/day over time. Daily milligram morphine equivalent for each clinician will be estimated by summing the total number of daily morphine equivalents written within a monthly observation period divided by 30 days. Additional secondary outcomes include the change in opioid prescriptions from any source according to state-level prescription drug monitoring program (PDMP) data.

9.2 Sample Size and Randomization

Our proposed trial will have a sufficient sample size (374 clinics) to detect small effects on the primary outcomes. A null finding will indicate evidence of negligible or no effect. Northwestern includes 55 primary care clinics that contain 289 clinicians with 12,552 patients on chronic opioid therapy for noncancer pain—opioids greater than 3 months. Sutter includes 273 primary care clinics containing 1,289 clinicians with 53,401 patients with noncancer pain who receive chronic opioid therapy. Altamed Medical Group has 30 clinics with 134 clinicians with 17,674 such patients. .

Assuming an average of 5 clinicians participating per clinic, clinic-level ICC of 0.055 for clinics and 0.03 for clinicians, and Bonferroni multiple-comparison corrections for 3 comparisons (each active treatment arm to control and with each other), we calculate the following number of clinics needed to achieve 0.8 and 0.85 statistical power for a one-tailed tests at the 0.05 level of significance for 3-, 5-, 7- and 12-percentage point reductions in the primary outcome. Based on Weimer et al.,(Weimer et al. 2016) we assume baseline high dose ($\geq$ 50mg ME/day) opioid use is 260 ($\pm$ 35) milligram morphine equivalents daily dose per high-dose patient. With 374 clinics among our participating organizations we will have greater than an 85% chance to detect a 3% change in high-dose opioid use dosage.

Table 1. Number of <u>total</u> number of clinics needed to detect a reduction from 260(+35) MME daily long-term opioid use

	MME Reduction			
Statistical Power	**3%**	**5%**	**7%**	**12%**
0.80	120 clinics	45 clinics	27 clinics	9 clinics
0.85	138 clinics	51 clinics	39 clinics	18 clinics

For our secondary outcome, transition to high dose use from low dose use, assuming conservatively a baseline concordance rate of 70%, we can detect a 3% change with the use of only 260 of our 374 clinics at 80% statistical power. Randomization is described next in Section 9.2.1.

9.2.1 Treatment Assignment Procedures

Randomization of study sites

We have chosen a cluster-randomized design at the clinic level to avoid contamination that might occur if individual providers in close proximity are randomized to different interventions. Providers who practice at multiple clinics are assigned to the intervention of the clinic for which they spend at least 85% of their time.

Geographically distinct individual clinics will be treated as the unit of randomization. These are clinics belonging to one of four larger clinical organizations covering a connected geographic area in either Illinois and California. We will carry out a block randomization of clinics by clinic organization using the statistical computing language R. For each clinic organization, we will construct ordered collections of clinics. We then will employ the sample function in R to return a random permutation of each ordered collection. For each collection of clinic organizations we will draw a sample that represents the largest number of clinics within each clinic organization that was divisible by 2, the number of study arms. We then will use the list function, a function that ties together related data that do not share the same structure, to assign each randomly permuted clinic to a study arm, repeating this process until clinics have filled the two arms of the study in equal measure. Because the number of clinics at each organization is not always divisible by 2, we will treat "remainder" clinics across all organizations differently. These remainder clinics will be randomized to conditions separately. This will be accomplished in a procedure similar to the one described above. Allocation of the sequence will be concealed until after the interventions were assigned.

9.3 Interim analyses and Stopping Rules

No interim analysis will be conducted on primary or secondary outcomes. The Data Safety and Monitoring Board is granted the power to recommend discontinuation of the study to each study IRB, if safety concerns are found. The board will meet biannually throughout the duration of the study to review patient safety and adverse events. Following each meeting, the board will make recommendations to the local IRBs as to whether the study should continue or if changes to the protocol are needed. The Board will compare between study conditions the frequency of emergency department visits, frequency of patients receiving a 20% increase in opioid prescriptions and the proportion abruptly cut-off of opioids (>49 MMED to zero) between visits. We will be extracted from study site EHRs and reported to the Board.

9.4 Outcomes

9.4.1 Primary outcome

The primary outcome is clinician aggregate monthly morphine milligram equivalent (MME) dosing. This will be measured for two groups: (i) 50 MME and above, and (ii) below 50 MME daily dose visits. For an observation to qualify for an above 50 MME measure, a clinician has to have treated a patient with at least one visit where > 50 MME daily dose triggered high dose decision support. Otherwise, observations are placed in the < 50 MME condition.

9.4.2 Secondary outcomes

One of the secondary outcomes is the proportion of dosages that escalated to > 50 MME/day over time. Daily milligram morphine equivalent for each clinician will be estimated by summing the total number of daily morphine equivalents written within a monthly observation period divided by 30 days. Additional secondary outcomes include the change in opioid prescriptions from any source according to state-level prescription drug monitoring program (PDMP) data.

9.5 Data Analyses

We will use means and medians for continuous measures, frequencies for count data, standard deviations and interquartile ranges for variance to describe the sample characteristics. For inferential analysis, our primary hypothesis is that milligram morphine equivalent dose will decrease for persons on high-doses of opioid therapy. We assume a linear mixed effects hierarchical knotted spline regression model which offers a flexible way to accommodate non-linear trends before and after the introduction of the intervention. This model places a knot at the intervention start date allowing slopes before and during treatment to vary for each intervention and control. For our two-group study evaluating the primary outcome, mean milligram morphine daily dose prescribed for intervention and control, we will place a knot at t*, the start of the intervention, and evaluate for each comparison between groups:

$$Y = \beta 1 + \beta 2\text{Time} + \beta 3(\text{Time} - t^*)+ + \beta 4\text{Group} + \beta 5\text{Time x Group} + \beta 6(\text{Time} - t^*)+ \text{ x Group} + \zeta + \eta + \text{error} \quad [1]$$

where (z)+ is a truncated line function that equals z when z is positive and is equal to zero otherwise, ζ is the clinician random effect and η is the clinic random effect.

In addition to the knotted spline regression model, we will also conduct a linear mixed effects hierarchical difference-in-differences regression. This model has fewer interaction terms, and mitigates convergence and collinearity errors:

$$Y = \beta 1 + \beta 2\text{Group} + \beta 3\text{Time} + \beta 4\text{Time x Group} + \zeta + \eta + \text{error} \quad [2]$$

where time is categorical, consisting of: 1) baseline (reference), 2) the intervention period and, 2) the post-intervention period.

The secondary analysis is logistic and replaces Y in Eq.1 with ln[(1 - pi)/pi] where pi is the probability of a guideline concordant decision at visit i.

10. DATA COLLECTION AND QUALITY ASSURANCE

10.1 Data Collection Forms

Two types of data will be collected – data from electronic medical and billing records and data from self-administered online surveys at the beginning and end of the study.

10.2 Data Management

Each of the participating sites will create an extract from their Electronic Medical or Billing Records of the Data Elements. These records will be transferred to the coordinating center on a weekly basis.

The CC has created programs and quality control queries for transforming all of the data into a standard model (Observational Medical Outcomes Partnership Common Data Model, version 5.1).

The data collection forms will be online surveys. The electronic data system, Epic, will have native data capture formats.

10.3 Quality Assurance

10.3.1 *Training*

Staff will be trained on the permissible values present in Electronic Records, frequency of update, and expected volumes of data.

10.3.2 *Quality Control Committee*

The quality control committee will consist of practicing clinicians from each participating clinical organization. They will review automatically refreshing dashboards for potential deviations in coding systems and appropriate values for codes for inclusion in the outcome measures. These dashboards will be reviewed prior to each email distribution.

10.3.3 *Metrics*

Quality control metrics will be based on reports verifying visits were not for cancer exclusions. All drugs prescribed at these visits will be categorized as “opioid” or “non-opioid”. Incorrect categorizations will be corrected and outcome computations recomputed before each email is delivered.

10.3.4 *Protocol Deviations*

Our task tracking system, JIRA will be used to track and document issues. Each issue will include both an assignee and a

reviewer.

10.3.5 *Monitoring*

In addition to data quality reviews, we will also review the integrity of the interventions. On an approximately quarterly basis, staff will visit headquarters of participating sites and verify functionality of decision support tools.

Additionally, practicing clinicians on our study team will have the ability to monitor electronic medical record interventions in their own health systems.

11. PARTICIPANT RIGHTS AND CONFIDENTIALITY

11.1 Institutional Review Board (IRB) Review

The study protocol for all clinic sites will be reviewed and approved by the University of Southern California's Institutional Review Board (IRB). Other sites will rely on the USC IRB through the SMART IRB online reliance system.

11.2 Informed Consent Forms

We will seek a waiver of consent for the main study, but will consent for survey assessments. An electronically signed consent form will be obtained from each participating clinician. The consent form will describe the purpose of the study, the procedures to be followed, the risks and benefits of participation, and compensation for participation.

11.3 Participant Confidentiality

Data will be recorded with SSL protected web sites to a data warehouse and transferred over secure network protocol. Data will be kept in encrypted files on computers in locked offices at USC Schaeffer Center facilities. Only study investigators will have access to a list of study ID codes that will be traceable back to actual subject contact identifiers for clinicians. These codes will be kept in locked offices at USC Schaeffer Center facilities.

11.4 Study Discontinuation

Following each DSMB meeting, the board will make recommendations to the local IRBs as to whether the study should continue or if changes to the protocol are necessary for continuation.

12. COMMITTEES

Data Safety Monitoring Board: Joe Frank, Jeanmarie Perrone, Carl Peiper.

13. PUBLICATION OF RESEARCH FINDINGS

Publication of results from our research will follow the NIH Public Access Policy, which requires that we submit to the National Library of Medicine's PubMed Central an electronic version of final, peer-reviewed manuscripts upon acceptance for publication, to be made publicly available no later than 12 months after the official date of publication.

14. REFERENCES

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15. SUPPLEMENTS/APPENDICES

APPENDIX A. OPIOID PRESCRIBING DIAGNOSES EXCLUSIONS AND MEDICATIONS FOR OUTCOMES ASSESSMENTS

Opioids Trigger List	**Link**	**("Outcome" Tab)**
Opioids Outcome List	**Link**	**("Grouper" Tab)**
Diagnosis of Exclusion	**Link**	
Non-Opioid Dosing for Alternatives	**Link**	

APPENDIX B: STUDY ENTRANCE SURVEY

Online Survey

THE ONLINE SURVEY IS INTENDED TO (1) ELICIT INFORMATION FROM PROVIDERS (2) MONITOR IF "EDUCATION" INFLUENCES RESPONSES TO QUESTIONS ABOUT TREATMENT PREFERENCES. RESPONDENTS WILL HAVE THE OPPORTUNITY TO CHANGE THEIR 'FINAL' ANSWERS AT ANY TIME IN THE SURVEY. WE WILL RECORD ALL ANSWERS AND LOG CLICKS ON INFORMATIONAL LINKS PROVIDED.

Basic information about your clinical background.

1. When did you start working at [*name of clinic*]? (<1 year ago, 1-2 years ago, 3-5 years ago, 5-10 years ago, >10 years ago)

2. When did you finish your clinical training as a physician (i.e., your internship, residency, or fellowship—the one you most recently completed)? (<2 years ago, 2-5 years ago, 5-10 years ago, 10-20 years ago, >20 years ago)

3. What is your clinical specialty? (internal medicine, family practice, general practice, pediatrics, other)

Information about the electronic health record (EHR) used at your clinic.

4. How would you rate your overall level of satisfaction with the electronic health record (EHR) used at your clinic?
   (1= Very unsatisfied , 5=Very satisfied)

5. Thinking about your workflow during an office visit with a patient, how often do you enter at least 1 diagnosis for the visit into the EHR while you are still seeing the patient?

   a. Always
   b. Usually
   c. Sometimes
   d. Rarely
   e. Never
   f. Not applicable: The EHR does not offer a way to enter a diagnosis (or diagnoses) that correspond to the visit.

Quality improvement efforts.

6. Within the past year, have you received any feedback—positive or negative—from your clinic about the quality of care you provide to patients (for any kind of care)?

    a. Yes, positive feedback only
    b. Yes, both positive and negative feedback
    c. Yes, negative feedback only
    d. No, did not receive any feedback at all
    e. Unsure / Can't Remember

7. [If yes to previous] Based on the feedback you received, did you make any changes to the way you deliver medical care?

    a. Yes, made 1 or more changes
    b. No, made no changes
    c. Unsure / Can't Remember

8. In the past year, did you attend any medical educational sessions? *Note: "Medical education sessions" include sessions that yielded credit towards maintenance of certification (e.g., CME) and less formal sessions that did not yield such credit.*

    a. Yes
    b. No
    c. Unsure / Can't Remember

9. [If yes to question 8] Based on the information you received in any of these educational sessions, did you make any changes to the way you deliver medical care?

    a. Yes, made 1 or more changes
    b. No, made no changes
    c. Unsure / Can't Remember

10. [If yes to question 8] Did any of the educational sessions you attended cover opioid prescribing safety?

a. Yes
b. No
c. Unsure / Can't Remember

11. [If yes to question 8] Did any of the educational sessions you attended cover opioid prescribing safety?

a. Yes
b. No
c. Unsure / Can't Remember

12. Based on your general experience as a clinician, please indicate how much you agree or disagree with the following statements:

i. Continuing education is an effective way to improve the quality of care (1 = Strongly agree, 2 = Agree, 3 = Neither Agree nor Disagree, 4 = Disagree, 5 = Strongly Disagree)
ii. Auditing physicians' clinical performance and providing performance feedback is an effective way to improve the quality of care (1 = Strongly agree, 2 = Agree, 3 = Neither Agree nor Disagree, 4 = Disagree, 5 = Strongly Disagree)
iii. Electronic decision support tools (e.g., "pop up" reminders in your EHR) are an effective way to improve the quality of care (1 = Strongly agree, 2 = Agree, 3 = Neither Agree nor Disagree, 4 = Disagree, 5 = Strongly Disagree)
iv. Condition-specific, streamlined electronic order sets are an effective way to improve the quality of care (1 = Strongly agree, 2 = Agree, 3 = Neither Agree nor Disagree, 4 = Disagree, 5 = Strongly Disagree)

Your assessment of clinical guidelines.

13. Please indicate your level of knowledge about the following clinical guidelines.	[Know this guideline in detail / Know this guideline in general, but not every detail / Not familiar with this guideline]
Screening	
Guidelines for colorectal cancer screening (USPSTF guideline: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/colorectal-cancer-screening2)	
Guidelines for breast cancer screening (USPSTF guideline: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/breast-cancer-screening1)	

Guidelines for cervical cancer screening (USPSTF guideline: https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/cervical-cancer-screening2)	
Chronic disease care	
Guidelines for the care of diabetes mellitus (ADA guidelines: https://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.Supplement_1.DC1/DC_42_S1_2019_UPDATED.pdf)	
Guidelines CDC guidelines for opioid prescribing in chronic pain: https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf)	
Acute care	
Guidelines for antibiotic use in non-specific upper respiratory infections (CDC guidelines: https://www.cdc.gov/getsmart/community/materials-references/print-materials/hcp/adult-tract-infection.pdf)	
Guidelines for imaging in acute low back pain (ACP/APS guidelines: https://annals.org/aim/fullarticle/2603228/noninvasive-treatments-acute-subacute-chronic-low-back-pain-clinical-practice?_ga=2.171090592.1829219229.1562111963-458883333.1562111963)	

a. **In the grid below, please estimate the AVERAGE time <u>allocated</u> to you and the amount of time you feel would be <u>needed</u> to provide high quality care for your patients.** *(please check one box)*

Visit type		Time *<u>allocated</u>*	Time *<u>needed</u>*
i.	Complete Physical/Consultation	_____minutes	_____minutes
ii.	Routine Follow-up Visits	_____minutes	_____minutes
iii.	Urgent Care Visits (in general)	_____minutes	_____minutes
iv.	Urgent Care Visits for pain	_____minutes	_____minutes

b. **Which best describes the atmosphere in your office?** *(please check one box)*	Calm, orderly		Busy, but reasonable		Hectic, chaotic
	☐1	☐2	☐3	☐4	☐5

c. **Please indicate how much you agree or disagree with the following statement.** *(please check one box)*	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Overall, I am satisfied with my current job	☐1	☐2	☐3	☐4	☐5

APPENDIX C: POST-STUDY SURVEY

STUDY EXIT SURVEY

1) How would you rate your overall level of satisfaction with the electronic health record (EHR) used at your clinic?
(1= Very unsatisfied, 2=Unsatisfied, 3=Neither satisfied nor satisfied 4=Satisfied 5=Very satisfied)

a) How would you rate your overall satisfaction with the alerts and clinical decision support you received relating to opioid prescribing?
(1= Very unsatisfied, 2=Unsatisfied, 3=Neither satisfied nor satisfied 4=Satisfied 5=Very satisfied, 0= I didn't receive alerts for opioids.

b) How would you rate your overall level of satisfaction with the how these alerts affected visits with your patients?"
(1= Very unsatisfied, 2=Unsatisfied, 3=Neither satisfied nor satisfied 4=Satisfied 5=Very satisfied)

2)

d. **In the grid below, please estimate the AVERAGE time <u>allocated</u> to you and the amount of time you feel would be <u>needed</u> to provide high quality care for your patients.** *(please check one box)*

Visit type	Time *<u>allocated</u>*	Time *<u>needed</u>*
v. Complete Physical/Consultation	_____minutes	_____minutes
vi. Routine Follow-up Visits	_____minutes	_____minutes
vii. Urgent Care Visits (in general)	_____minutes	_____minutes
viii. Urgent Care Visits for pain	_____minutes	_____minutes

e. **Which best describes the atmosphere in your office?** *(please check one box)*	Calm, orderly	Busy, but reasonable	Hectic, chaotic

	☐1	☐2	☐3	☐4	☐5

f. **Please indicate how much you agree or disagree with the following statement.** *(please check one box)*	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
Overall, I am satisfied with my current job	☐1	☐2	☐3	☐4	☐5

4) Please indicate how much you agree or disagree with the following statements.	Strongly Disagree	Disagree	Neither Agree nor Disagree	Agree	Strongly Agree
a. I receive useful information about the quality of care I deliver	☐1	☐2	☐3	☐4	☐5
b. When I receive a new report about the quality of care, it just makes me feel helpless	☐1	☐2	☐3	☐4	☐5
c. My practice evaluates me in a way that is fair	☐1	☐2	☐3	☐4	☐5

i.

13) Are you more frequently engaging patients in opioid discussions since the study started?
Yes ☐
No ☐

14) Please estimate the percentage of your patients in each of these categories:

b. Have complex or numerous medical problems _____%

		c. Have complex or numerous psycho-social problems	_____%
		d. Are generally frustrating to deal with	_____%
a. Suffer from chronic pain	_____%	*e.* Have alcohol or other substance abuse disorders	_____%

15) **Please indicate how much you agree or disagree with the following statements.**	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly Agree
a. Many patients demand potentially unnecessary treatments	☐1	☐2	☐3	☐4	☐5
b. Time pressures keep me from developing good patient relationships	☐1	☐2	☐3	☐4	☐5
c. I am overwhelmed by the needs of my patients	☐1	☐2	☐3	☐4	☐5

17) Opioid prescribing is caused by patients' "demand" for opioids.

Please rate your agreement from 1 (Low) to 10 (High). *

1 2 3 4 5 6 7 8 910

18) Reliance on opioids to treat pain is caused by doctors not having enough time with patients?
Please rate your agreement from 1 (Low) to 10 (High). *
1 2 3 4 5 6 7 8 9 10

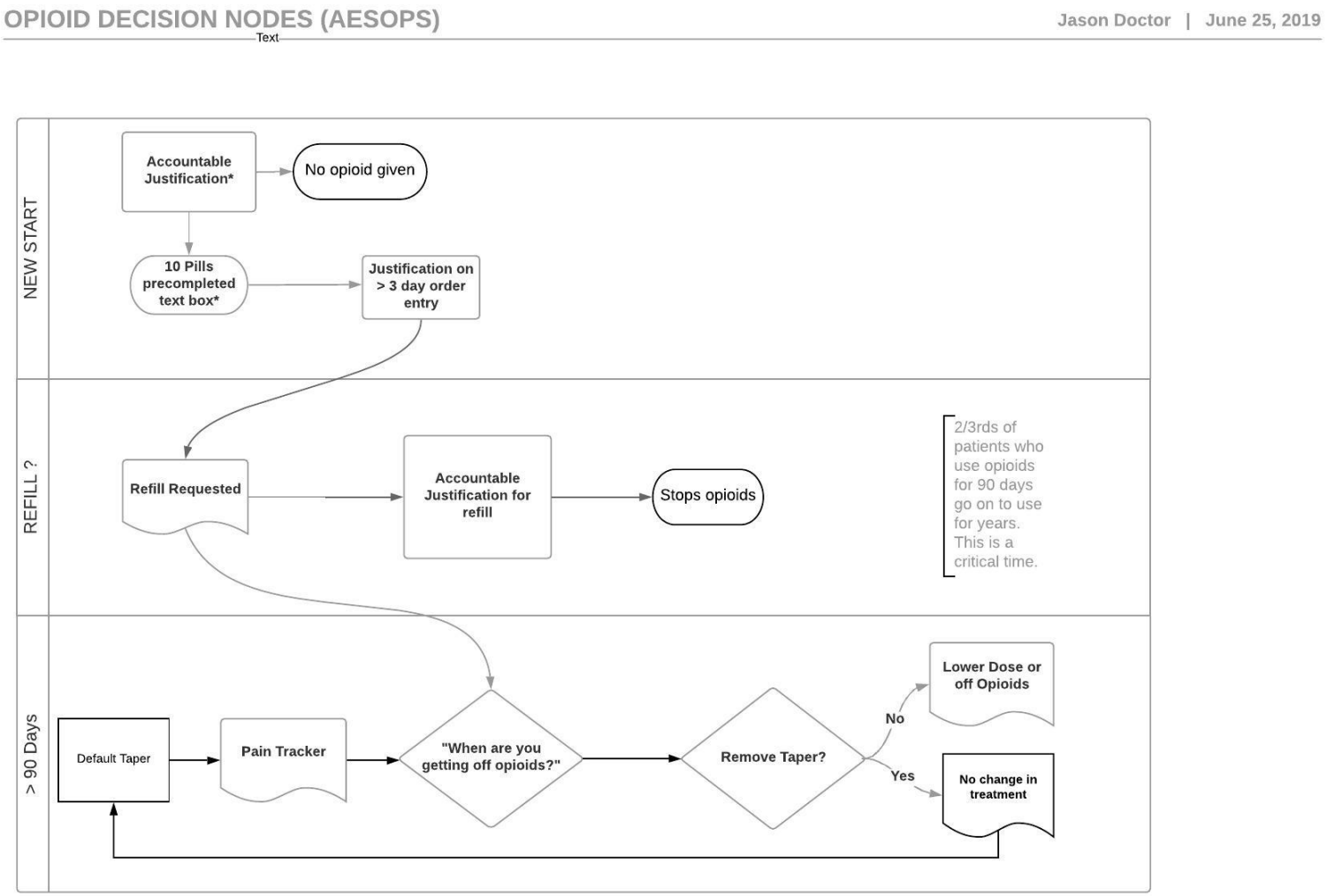
19) Do you generally support performance measurement and quality improvement for

doctors' practices?

Please rate your agreement from 1 (Low) to 10 (High). *

You have completed the exit survey. Thank you very much for your participation!

APPENDIX D: OPIOID DECISION NODES



APPENDIX E: EDUCATION MODULES

All nudges (1A, 1B, and 1C): https://usc.qualtrics.com/jfe/form/SV_74Bay03kAvWkqGx

APPENDIX F: EPIC BUILD TECHNICAL SPECIFICATIONS

AESOPS R21 NU Site
EPIC Build

Lead Site-USC	R21 pilot site-Northwestern
PI: Jason Doctor (jdoctor@usc.edu)	Site PI: Jeff Linder (jlinder@northwestern.edu)
Project Manager-Tara Knight (knight@healthpolicy.usc.edu)	Site project manager: Tiffany Brown (t-brown@northwestern.edu)

1A: Justification alert upon initial opioid order

1B: Justification alert upon 'refill' opioid order

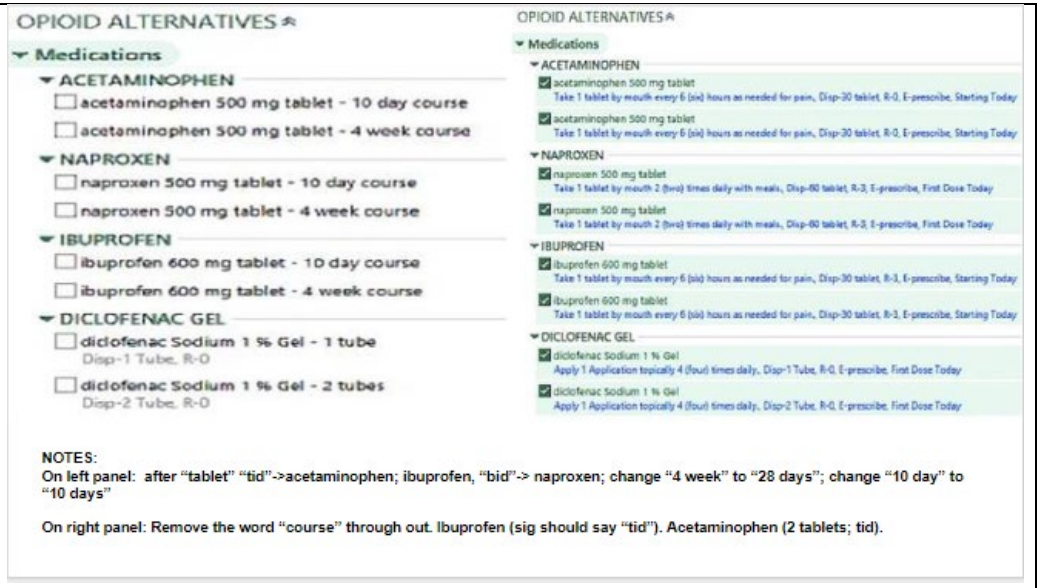
1C: Active Choice (SmartSet) alert for 'refill' >90 days opioid order

2: Integrate new patient assessment 'PainTracker' at point of care when conditions are met

Notes: For all triggers, the triggering medication does not have to have been prescribed by study clinician

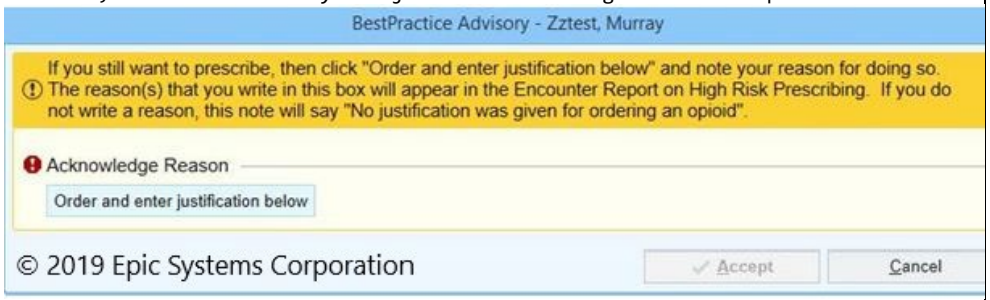
AESOPS Nudge 1A	
Title	Justification alert for initial opioid order
Slides	https://docs.google.com/presentation/d/1R5IQKGGD1kjaifRb7NE8GmbQZrz-8GCH3ZzisPe_33o/edit#slide=id.g4d413a3b8d_0_0
Version	February 15, 2019
Display	Medication order entry display as pop up [Appears when the clinician is going to prescribe]
Trigger Criteria	Visits where order is for an included opioid AND NOT an opioid prescription with a start date < 91 days
BPA Language	Screen 1: DRAFT LANGUAGE: "Your patient, [Name], can become dependent on opioids after being treated for acute pain. Safer alternatives are often just

	as effective. **Please either remove the order or justify the order at signing. This justification will be made part of the patient's record."**  Non-opioid Analgesic Alternatives [ ] Acetaminophen {pull-down dosing} [ ] Naproxen {pull-down dosing} [ ] Ibuprofen {pull-down dosing} [ ] Diclofenac Gel {pull-down dosing} Non-drug Alternative [ ] Physical Therapy (External) [ ] Physical Therapy (NM Internal) [ ] Physical Therapy (Athletico)



Opioid alternatives:
https://docs.google.com/spreadsheets/d/17s6kwLwGLMEK-uTzy6hJdWljzNInBRDXvoYR6Ou6HMM/edit?usp=sharing

[ ] If you still want to prescribe, then click "Order and enter justification below" and note your reason for doing so. The reason(s) that you write in this box will appear in the Encounter Report on High Risk Prescribing. If you do not write a reason, this note will say "No justification was given for an opioid."



DIRECTIONS ON RESPONSE:

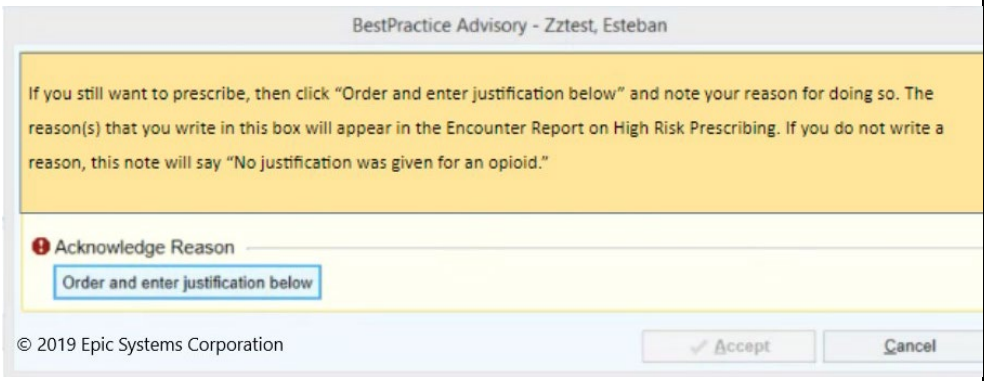
1. free text box-[pre-populated with "no justification given"]
2. Include a button to close out/acknowledge [OK} or [Cancel order]

Button Capture	Buttons: "Remove the following orders?" "Remove" {default} "Justify at Signing" "Accept" Event upon "Accept" "Remove" removes order activates smart set alternative. "Justify at Signing" disposes Screen 2 to fire at signing orders if medication is still in the order list
Intended Audience	MDs, RNs, PAs
Notes:	- Alert should fire during any outpatient encounter type - justification text appears in the encounter report for MyChart, Telephone and Refill encounters - pt- reported medications added to Epic to make pt med list more accurate should NOT fire BPA - will not impact nudge 1A

AESOPS Nudge 1B	
Title	Justification alert for 'refill' opioid order
Version	February 15, 2019
Display	Medication order entry display as pop up [Appears when the clinician is going to prescribe]
Trigger Criteria	Visits where order is for an included opioid AND Opioid prescription with a start date > 1 day and < 91 days AND NOT an opioid prescription with a start date > 90 days

BPA Language	DRAFT LANGUAGE: Screen 1: [Patient name] has an opioid on their medication list within the past 30 days. Opioid refills can lead to long-term opioid use and dependence. This is a critical time to avoid formation of drug dependence by removing the order and choosing an alternative pain management strategy.  Consider alternatives and cancel order: Non-opioid Analgesic Alternatives [ ] Acetaminophen {pull-down dosing} [ ] Naproxen {pull-down dosing} [ ] Ibuprofen {pull-down dosing} [ ] Diclofenac Gel {pull-down dosing} Non-drug Alternative [ ] Physical Therapy (External) [ ] Physical Therapy (NM Internal) [ ] Physical Therapy (Athletico)

Opioid alternatives:
https://docs.google.com/spreadsheets/d/17s6kwLwGLMEK-uTzy6hJdWljzNInBRDXvoYR6Ou6HMM/edit?usp=sharing



DIRECTIONS ON RESPONSE:

3. free text box-[pre-populated with "no justification given"]

	4. Include a button to close out/acknowledge [OK} or [Cancel order]
Button Capture	Buttons: "Remove the following orders?" "Remove" {default} "Justify at Signing" "Accept" Event upon "Accept" "Remove" removes order activates smart set alternative. "Justify at Signing" disposes Screen 2 to fire at signing orders if medication is still in the order list
Intended Audience	MDs, RNs, PAs
Notes:	Alert should fire during any outpatient encounter type

AESOPS Nudge 1C	
Title	Enhanced Active Choice Taper >90 days Opioid Order
Version	February 15, 2019
Display	SmartSet BPA Med Order Entry with Justification* & Patient Question [Appears when the clinician is going to prescribe] * Enhanced Active Choice: Taper vs. Justification/status quo; Taper is 'advantaged' choice.
Trigger Criteria	Total opioid doses is for > 49 MME AND Two or more opioid prescriptions with two different start dates both > 1 day and < 91 days AND Opioid prescription with a start date > 90 days

	Cancer Exclusions: https://docs.google.com/spreadsheets/d/1U203LWNZ5RUY-DemA-HZoy-uUp9GaQuGjXm03sPiosI/edit?usp=sharing
BPA Language	**Taper Activation BPA** [Mr. / Ms.] [Patient Last Name] is at high risk of opioid overdose with total MMED of [total MMED]. To facilitate gradual tapering to a safer dose (< 50 MMED), here are [Mr./Ms.] [Patient Last Name]'s short- and long-acting opioids. 1. **[He/she] is prescribed the following short-acting opioids:** 1. [Short-Acting AESOPS drug #1 generic_name] 2. [Short-Acting AESOPS drug #1 generic_name] 3. [… Short-Acting AESOPS drug #N generic_name] **Taper Suggestion: Discuss 1 pill fewer per day or ≤ 10% MMED reduction in short-acting opioids.** 2. **[He/she] is prescribed the following long-acting opioids:** 1. [Long-Acting AESOPS drug #1 generic_name] 2. [Long-Acting AESOPS drug #1 generic_name] 3. [… Long-Acting AESOPS drug #N generic_name] **Taper Suggestion: If there are no short-acting opioids in #1, discuss moving half MMED to short-acting. This will give the patient more control over dose.** **I will take action toward safer prescribing:** [ ] YES and I oversee [Mr./Ms] [Patient Last Name]'s opioid prescribing [ ] YES and I do not oversee [Mr./Ms] [Patient Last Name]'s opioid prescribing [ ] NO (requires justification at signing for continued high risk prescribing)

Ongoing Taper BPA

[Mr. / Ms.] [Patient Last Name] is at high risk of opioid overdose with total MMED of [total MMED] and is on an ongoing taper to a safer dose (< 50 MMED). To facilitate this ongoing taper, here are [Mr./Ms.] [Patient Last Name]'s short- and long-acting opioids.

1.**[He/she] is prescribed the following short-acting opioids:**

1.[Short-Acting AESOPS drug #1 generic_name]

2.[Short-Acting AESOPS drug #1 generic_name]

3.[… Short-Acting AESOPS drug #N generic_name]

Taper Suggestion: Discuss 1 pill fewer per day or ≤ 10% MMED reduction in short-acting opioids.

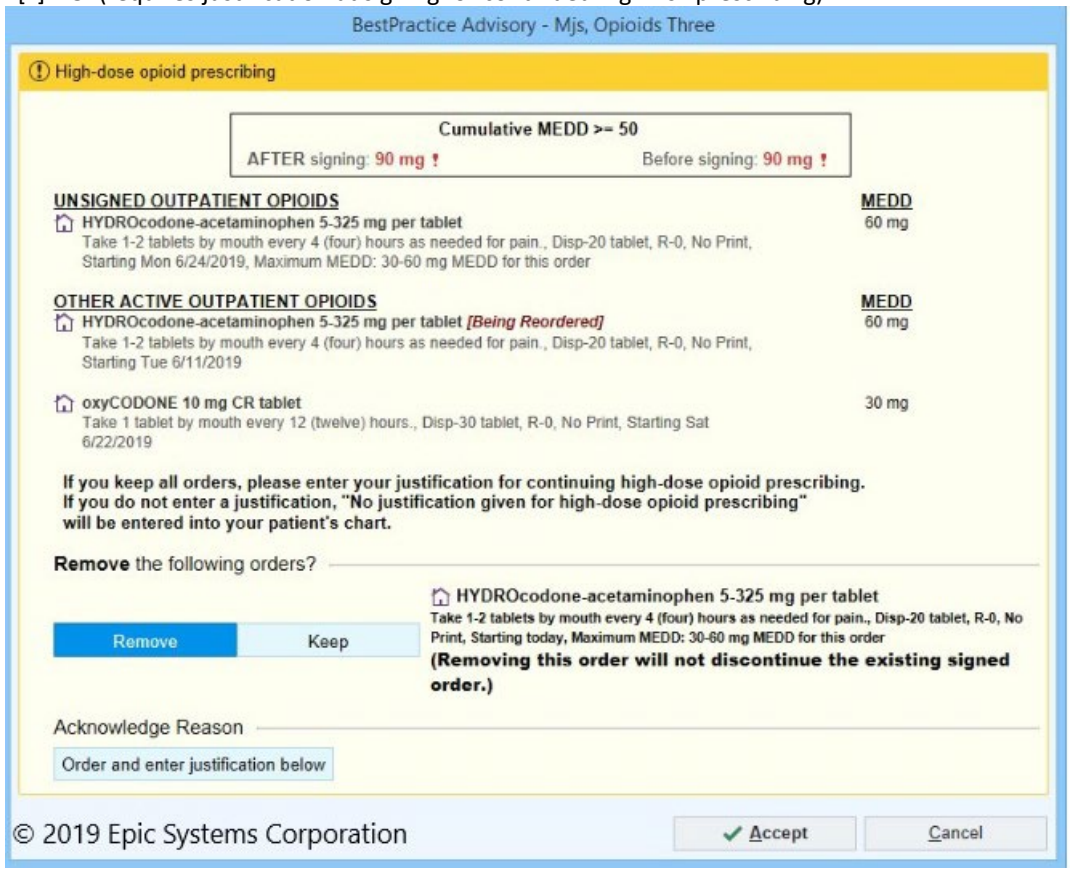
2.**[He/she] is prescribed the following long-acting opioids:**

1.[Long-Acting AESOPS drug #1 generic_name]

2.[Long-Acting AESOPS drug #1 generic_name]

3.[… Long-Acting AESOPS drug #N generic_name]

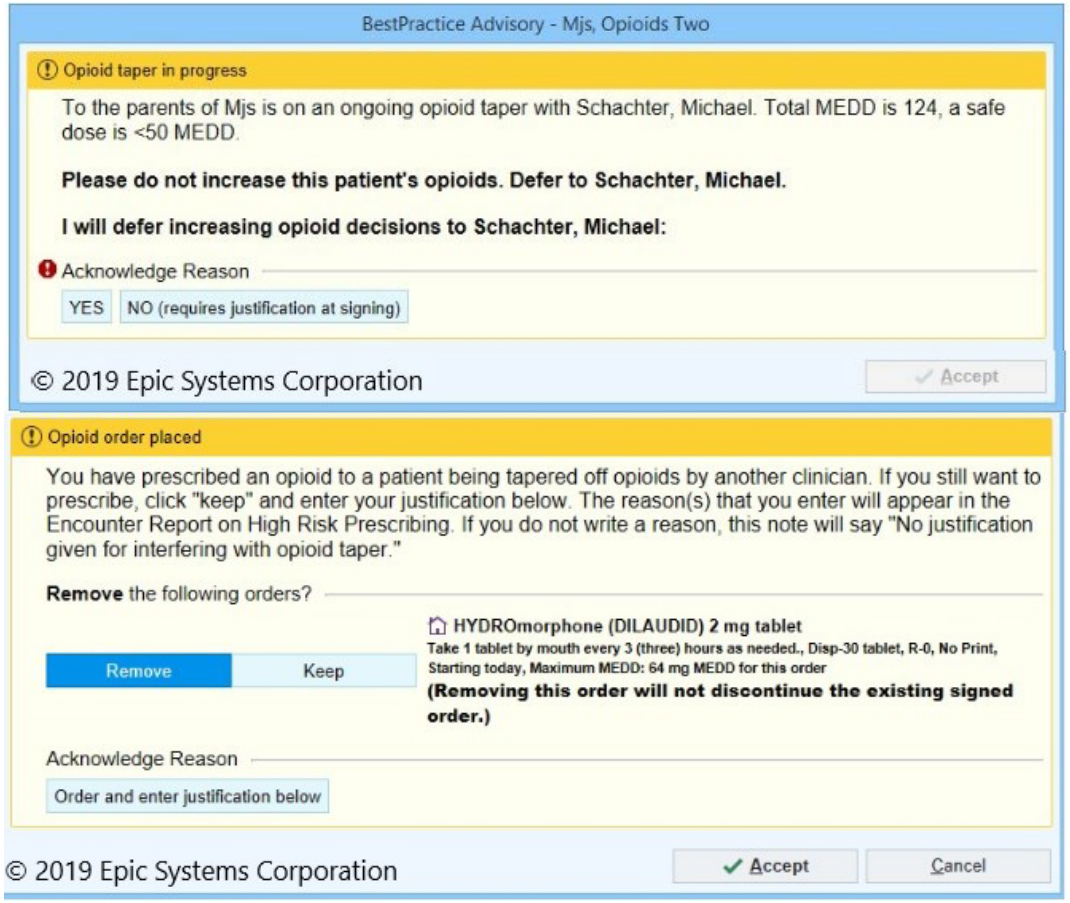
Taper Suggestion: If there are no short-acting opioids in #1, discuss moving half MMED to short-acting. This will give the patient more control over dose.
I will take action toward safer prescribing:
[ ] YES
[ ] NO (requires justification at signing for continued high risk prescribing)



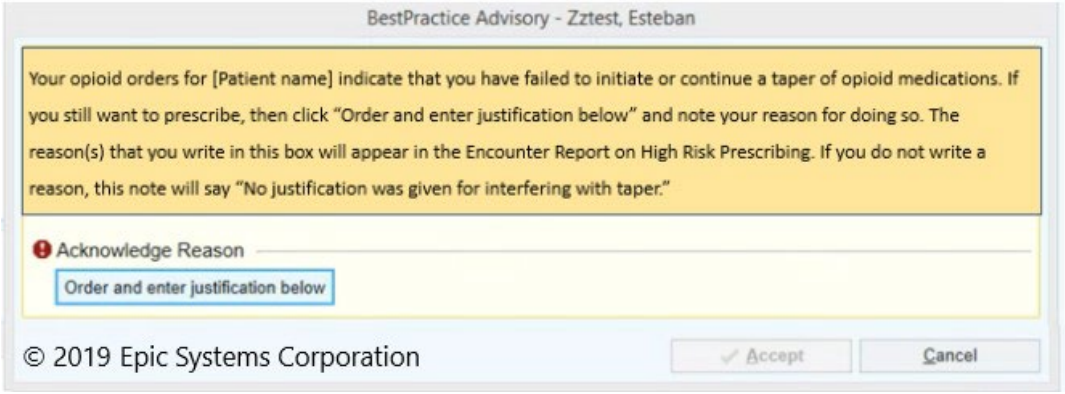
BPA Deferring Opioid Rx

[Mr. / Ms.] [Patient Last Name] is on an ongoing opioid taper with [Tapering Physician Name] (total MMED is [TOTAL|_MMED] a safe dose is < 50 MMED).

Please do not increase this patient's opioids. Defer to [Tapering Physician name].
I will defer increased opioid decisions to Dr. [Tapering Physician name]
[ ] YES
[ ] NO (requires justification at signing for continued high risk prescribing)



Justification at Signing (failure to initiate or continue taper)
Your opioid orders for [Patient name] indicate that you have failed to initiate or continue a taper of opioid medications. If you still want to prescribe, then click "Order and enter justification below" and note your reason for doing so. The reason(s) that you write in

	this box will appear in the Encounter Report on High Risk Prescribing. If you do not write a reason, this note will say “No justification was given for interfering with taper.”  **Justification at Signing (non-deferral)** You have prescribed an opioid to a patient being tapered off opioids by another clinician. If you still want to prescribe, then click “Order and enter justification below” and note your reason for doing so. The reason(s) that you write in this box will appear in the Encounter Report on High Risk Prescribing. If you do not write a reason, this note will say “No justification as given for not proceeding with taper.” 

Button Capture	
Intended Audience	
Notes:	3 BPAs depending on stage of taper; registry data collects if patient is on taper and also tapering clinician ID. Milligram Morphine Equivalent Daily (MMED) is given by EPIC calculator.

AESOPS Nudge 2	
Title	Presentation of patient assessment 'PainTracker' at point of care
Version	February 15, 2019
Display	Either for MA at vitals, during office visit and/or mychart (TBD)
Trigger Criteria	Align with 1C If "Yes" from Nudge 1C, Nudge 2 should fire visits where order is for an included opioid AND Total opioid doses is for > 49 MME AND Two or more opioid prescriptions with two different start dates both > 1 day and < 91 days AND Opioid prescription with a start date > 90 days

	Fires every 30 days at scheduled taper follow-up visit +/- 1 week (If they come in for some other problem within a week of their scheduled appointment). - not more than once every 30 days - tied to ordering prescriber scheduled encounter **Stopping rule:** 2 years (or some fixed date in the future[(e.g., for R21 stop 1/1/2020))
Assessment	See document for all items 'AESOPS NU Pain Tracker build'
BPA Language	assessment opens in separate browser and MA logs out of Epic Pain Tracker Scoring PEG Scoring: To compute the PEG score, add the three responses to the questions above, then divide by three to get a final score out of 10. The final PEG score can mean very different things to different patients. The PEG score, like most other screening instruments, is most useful in tracking changes over time. PHQ Scoring: Total score is determined by adding together the scores of each of the 4 items.Scores are rated as normal (0-2), mild (3-5), moderate (6-8), and severe (9-12). Total score ≥3 for first 2 questions suggests anxiety. Total score ≥3 for last 2 questions suggests depression.
Button Capture	
Intended Audience	
Notes:	Scoring is presented in Epic with graphs showing change over time and shared with patient via portal (mock up attached). Pre-text

	Because you are managing your pain with Dr. XXX, we are asking you to complete a short PainTracker™ survey to help you and your physician understand how pain is affecting your life, including everyday activities, mood and sleep. Your answers can be used to track your progress over time, which will help you set and manage your treatment goals. Please fill out PainTracker™ *1 week or less* before your next visit with Dr. XXX. You may be asked to complete PainTracker™ again for future visits. Thank you for taking the time to complete this survey. *If you need help logging in or are having problems with PainTracker™, please plan to complete PainTracker™ in the clinic at the time of your next visit.*

APPENDIX G. Nudge Trigger Logic for AESOPs, Opioid Nudges

1A: Opioid naïve or no recent opioid use

Order is for an included opioid
AND
NOT an opioid prescription with a start date < 91 days

1B: Opioid prescription within 90 days

Order is for an included opioid
AND
Opioid prescription with a start date > 1 day and < 91 days
AND
NOT an opioid prescription with a start date > 90 days

1C: Chronic, high-dose opioids

Order is for an included opioid
AND
Total opioid doses is for > 49 MME
AND
Two or more opioid prescriptions with two different start dates both > 1 day and < 91 days
AND
Opioid prescription with a start date > 90 days

APPENDIX H. Informed Consent for Provider Survey

Permission to Take Part in a Human Research Study

Title of research study: Application of Economics & Social psychology to improve Opioid Prescribing Safety (AESOPS): baseline survey

Investigator: Dr. Jason Doctor

Why am I being invited to take part in a research study?
We invite you to take part in a research study because you are a clinical provider who treats adult patients in [site name].

Who can I talk to?
If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at 213.821.7943.

This research has been reviewed and approved by the USC Institutional Review Board ("IRB"). You may talk to a IRB staff member at 3720 South Flower Street, Third Floor, Los Angeles, CA 90089, 213.821.1154 or oprs@usc.edu for any of the following:

• Your questions, concerns, or complaints are not being answered by the research team.
• You cannot reach the research team.
• You want to talk to someone besides the research team.
• You have questions about your rights as a research subject.
• You want to get information or provide input about this research.

Why is this research being done?
This research is being done to gauge your current practice and opinions regarding prescribing of opioids for the treatment of noncancer pain.
How long will the research last?
We expect that the survey will take less than 20 minutes to complete.

How many people will be studied?
We expect about XXX physicians will be in this research study at [site name]

What happens if I say yes, I want to be in this research?
If you agree to participate, you may complete the survey electronically. You will be able to provide feedback about your current practices and opinions. Your responses will be coded using your email address and the document linking your randomly assigned code to your email will be kept separate from the data for analysis.

Are there any risks in participating?
No more than minimal risks are anticipated from taking part in this study. If you feel uncomfortable with a question, you can skip that question, or withdraw from the study altogether. If you decide to quit at any time before you have finished the questionnaire, your answers will NOT be recorded.

What happens if I do not want to be in this research?
You may decide not to take part in the research and it will not be held against you.

What happens if I say yes, but I change my mind later?
You can leave the research at any time and it will not be held against you. Since the data are being collected anonymously, once the survey is submitted the research team will not be able to delete your responses if you later decide you do not want your responses included in the study.

Will being in this study help me in any way?
We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include providing new knowledge about how to improve adherence to guidelines for opioid prescribing, which has the potential to help prevent future incidents of opioid use disorder and opioid poisoning death by lowering unnecessary population exposure to these drugs.

What else do I need to know?
This research is being funded by the National Institutes of Health, also called the sponsor. University of Southern California is being paid to conduct this study, but the study doctor and research staff have not received any direct income from the sponsor. There is no charge for you to participate in this study. You will be compensated with a $25 gift card for your participation.

By beginning the survey, you acknowledge that you have read this information and agree to participate in this survey, with the knowledge that you are free to withdraw your participation at any time without penalty.

APPENDIX I. Variable List

List of all elements to be collected:

A.] EDW discrete variables in export

• Patient level

o Age

o Race

o Ethnicity

o Sex

o # of prior visits with clinician who orders opioid during study period

o Medications ordered at encounter with opioid prescription

o Other orders & referrals at encounter with opioid prescription

o Diagnoses associated with opioid order

o Insurance status

o Yes/no to whether the following chronic conditions are on problem list at time of opioid order:

Opioid use disorder

Alzheimer's Disease and related dementia

Arthritis (Osteoarthritis and Rheumatoid)

Asthma

Atrial Fibrillation

Autism Spectrum Disorders

Cancer (Breast, colorectal, lung and prostate)

Chronic kidney disease

Chronic Obstructive Pulmonary Disease

Depression

Diabetes

Heart Failure

Hepatitis (Chronic Viral B 7 C)

Hyperlipidemia (High cholesterol)

Hypertension (high blood pressure)

Ischemic Heart Disease

Osteoporosis

Stroke

• Clinician characteristics:

o Specialty

o Type: Attending/resident/NP/PA

o FTE status

o PCP status (yes/not to patient's PCP)

o Site of care

• Study related clinical decision support:

o Clinician interactions with study BPAs and nudges

• Opioid drug characteristics:

o Order type (e.g., orders only, telephone encounter, in person encounter)

o Drug name

o Dose

o Duration

APPENDIX J. Coded Identifier List

List of all identifiers to be collected or used in this study:

• Medical record number

• Date of birth

• Dates of service: Date of opioid order; Date of encounters associated with opioid order; Date of Emergency Department encounter subsequent to opioid order

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