

Promoting the implementation of clinical guidelines for opioid prescribing in primary care using systems consultation

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Table of Contents

90	
91	
92	Abstract
93	1. Introduction/Background
94	2. Objectives
95	3. Selection of Clinics and Subjects
96	4. Registration Procedures
97	5. Treatment Plan
98	6. Measurement of Effect
99	7. Study Parameters
100	8. Statistical Considerations
101	9. Records to be Kept
102	10. References
103	

Abstract

The proposed study uses a sequential, multiple assignment randomized trial (SMART)^{1,2} to test an adaptive version of systems consultation³ consisting of academic detailing, practice facilitation, and physician peer coaching to increase the uptake of safer opioid prescribing practices at three levels of primary care (health system, clinic, prescriber). Academic detailing will be provided to all clinics and prescribers to inform prescribers on the goals of the study, the importance of improving opioid prescribing in primary care, and a review of the latest standards of prescribing guidelines. After three months, clinics will be randomized to receive nothing or receive practice facilitation where clinics will get an in-person or online visit and proceed with monthly teleconferences to improve clinic workflow related to opioid prescribing. Six months later, clinics will receive physician peer coaching that will employ two experienced addiction specialists who will provide guidance to prescribers dealing with tough patient panels. Additionally, this study aims to capture and analyze contextual factors that influence implementation in order to create a simple tool that will guide quality improvement in opioid prescribing. This SMART will deliver these three strategies to 40 primary care clinics from three health systems to compare the effect on average morphine milligram dose of an adaptive systems consultation implementation strategy compared to academic detailing alone over a 21 month time period. To our knowledge, this study would be the first to randomize at two levels to test the efficacy of the implementation of system consultation to improve opioid prescribing in primary care.

1. Background & Significance

Importance of improving prescribing practices in primary care

Opioids are commonly prescribed in primary care to relieve chronic pain. Although potentially effective for this purpose, accompanying burdens have become clear and widespread. In 2017, drug overdose was the leading cause of accidental death in the United States. Although the volume of opioids prescribed in the US declined each year from 2010 to 2015, about 3 times more opioids were prescribed per person in 2015 as in 1999, and prescribing rates still vary greatly, with the highest-prescribing counties prescribing 6 times more opioids per person than the lowest-prescribing counties.⁴ In 2015, 63.1% of drug-overdose deaths involved an opioid,⁵ and approximately half of opioid-related deaths involved prescription opioids.⁶ About half of opioid prescriptions are written in primary care.^{7,8} Clinical guidelines for opioid prescribing in primary care have been advanced, most notably the guidelines issued by the Centers for Disease Control and Prevention in 2016.⁸ Clinical guidelines have established consensus around a few basic ideas: (1) Physicians should discuss the risks and benefits of opioid therapy with patients by reviewing and signing formal treatment agreements before initiating the first opioid dose and throughout treatment.⁸ (2) Clinicians should avoid prescribing opioids in doses higher than 90-100 morphine milligram equivalent (MME) daily; evidence shows that patients with a dose of 100 MME or greater are 11 times more likely to die from overdose than patients taking doses less than 20 MME.⁹⁻¹¹ (3) patients at increased risk for misuse (i.e., those with mental health or substance use disorders) are more likely to receive opioid prescriptions and higher doses; thus, screening for mental health and substance use disorders should be in place.^{9,12-14} (4) Opioid-benzodiazepine co-prescribing in any combination of doses should be avoided to reduce the risk of overdose.¹⁵ (5) Monitoring via urine drug testing should be instituted to ensure appropriate use of opioid medications.¹⁶

Strategies for implementing evidence-based practices

Despite the promotion of evidence-based practices (EBPs) related to opioid prescribing (and many other conditions), the healthcare system is notoriously slow in adopting EBPs.¹⁷ Lau et al. conducted a 2015 review¹⁸ of 91 studies aimed at determining the effectiveness of strategies for implementation of complex interventions in primary care settings. The most commonly used strategies were targeted at individual providers, generally demonstrating small to modest effects, with considerable variability between studies. The authors found little use of implementation strategies targeted at organizations or a wider context (e.g., health systems). Finally, the review found very limited data on the costs and cost-effectiveness of different implementation strategies should be used under what conditions, and that future research should study implementation strategies targeted at levels more broadly defined than individual providers. According to a systematic review focused specifically on the role of external change agents (e.g., coaches, facilitators, academic detailers, etc.) in primary care settings, the more successful implementation strategies tended to be those that offered regular, context-specific follow-up.¹⁹

Systems consultation

Systems consultation is a theoretically and empirically grounded,³ blended implementation strategy^{20,21} consisting of a bundle of 3 discrete strategies: (1) Academic detailing, in which an experienced physician provides recommendations and advice on how to improve clinical practice; (2) Practice facilitation, a team-based advising approach designed to tailor implementation to specific

178 clinical contexts; and (3) Physician peer coaching, in which an experienced physician provides one-
179 on-one clinical advice on managing patient panels to other physicians (who may be less experienced
180 with the selected clinical issue). Several other discrete strategies are also integrated into the systems
181 consultation model, as categorized by Powell et al.'s (2015)²⁰ taxonomy of implementation strategies,
182 including: use of community-academic partnership, where leaders from an academic medical center
183 work with community- based care clinics to improve the health of their communities; audit and
184 feedback , which consists of providing performance feedback to clinics; conducting local assessments
185 to determine the need for implementation; and tailoring implementation strategies to address potential
186 barriers and facilitators.

187 **Adapting implementation strategies to specific contexts**

188 Primary care clinics vary in their opioid prescribing practices and in their capacity to carry out
189 implementation efforts. Clinics and prescribers are influenced by factors such as funding, regulations,
190 geography, and policies. These considerations suggest that strategies for implementing EBPs will
191 work differently in different clinics; moreover, different strategies might work best for different
192 prescribers, depending on the prescriber's patient panel, experience in prescribing opioids, and other
193 influences. Previous implementation research²² suggests that implementation strategies tailored to
194 specific clinics are the most effective, although evidence also suggests that the effect of tailoring
195 varies, and tends to be small to moderate.²³ The literature does not specify the most effective
196 approaches to adaptation or the cost-effectiveness of tailored strategies (compared with non-tailored
197 strategies).^{18,23}

198 **2. Study Objectives**

199 This study aims to understand the optimal sequencing and combination of implementation strategies
200 that specific types of clinics and prescribers need to adopt clinical guidelines for opioid prescribing.
201 The pragmatic goal is to give health systems a tool they can use to predict which clinics and
202 prescribers will benefit most from which sequence and combination of implementation strategies. The
203 bundle of strategies systems consultation consists of include academic detailing, practice facilitation,
204 and physician peer coaching. We propose to recruit 40 clinics and 152 prescribers from 2 health
205 systems for a sequential, multiple assignment randomized trial to receive academic detailing only,
206 academic detailing + practice facilitation, academic detailing + practice facilitation + physician peer
207 coaching, or academic detailing + physician peer coaching. We will use quantitative and qualitative
208 analyses to compare outcomes of sequences and combinations with data collected every 3 months
209 over the 21-month intervention period.

210 **Primary Aim:**

211 Compare the effect of an adaptive systems consultation implementation strategy vs. academic
212 detailing alone on average morphine milligram equivalent dose over 21 months.

213 **Secondary Aims:**

- 214 • Develop an assessment of contextual factors that influence the effectiveness of different
215 implementation strategies.

- Test 4 moderators and assess other factors that affect implementation to use to predict which implementation strategies will be most effective in different settings.
- Estimate the costs of delivering 4 different sequences and combinations of strategies, including the incremental cost effectiveness of adding facilitation and physician peer coaching.

Study Coordination

The UW-Madison Implementation Science and Engineering Lab is the coordinating site for this study. The UW study coordinator will oversee all activities at the 40 clinics which include:

- developing site specific recruitment and data collection processes that meet study objectives;
- training site staff prior to the study on protocol procedures to maintain compliance with the protocol and human subjects regulation;
- communicating with site staff via monthly correspondence to monitor progress, inform of protocol changes/distribute new version of protocol, and address unanticipated issues or challenges;
- and manage all study data.

3. Selection of Subjects

Patients are not the subject of the study. The subjects of study will be the clinic prescribers.

Prescriber panel data will be aggregated to the clinic and prescriber levels. To be included in the aggregated, de-identified prescriber panel data, patients must:

1. have a primary care provider at the clinic;
2. prescriptions for opioid therapy for at least 3 consecutive months;
3. and no cancer diagnosis or reception of hospice care.

Clinics: A total of 40 clinics will be recruited from primary care clinics of the two health systems: UW Health and Bellin Health. This protocol will detail the process at UW Health primary care clinics for which the HS IRB is the IRB of record. Bellin Health will follow similar procedures with oversight from the UW study coordinator.

Clinics will be eligible for the study if they:

1. are a primary care clinic (non-pediatric primary care, internal medicine, or family medicine);
2. have not received the systems consultation intervention; and
3. do not explicitly prohibit initiating opioid therapy.

Change team: Up to 7 team members will be recruited and consented to participate in practice facilitation. Change teams include a change team leader (likely a clinic medical director or other clinician) and supporting clinic staff such as nurse practitioners, physician assistants, registered nurses, lab technicians, and medical assistants.

Prescribers: de-identified patient data will be aggregated at the level of the prescriber and clinic. In this context, prescribers will be known to the study team only by the code number assigned to them by HIP. Data will be obtained only from those clinicians who:

1. are primary care physicians or other providers with prescribing privileges;
2. are not temporary providers who do not manage stable panels or patients;

4. Registration Procedures

Clinic Recruitment

The study team will discuss the study with health system leaders who gave letters of support and identify clinics that may be interested in participating. The study team will present the study to clinicians at an all-provider meeting to build awareness and inform clinics that this study is available to join. Health care leaders will send an email on behalf of the study team to clinic medical directors of the health system. The email will notify medical directors that research is being done at clinics of their health system and instruct them how to opt-out if they wish to decline participation in the study and future contact from the study team. The email will instruct medical directors to direct any questions they have to the study team.

Medical directors who choose not to opt-out of the study will be invited via email to attend the regional academic detailing meetings. Medical directors will be asked to forward the email to any clinic staff who may be interested in participating in the academic detailing meeting. The email will instruct interested medical directors and clinic staff to call the study team if they are interested in attending or have any questions. Clinics will be asked to allow medical directors and interested clinic staff to attend regional academic detailing meetings on clinic time where the study team will explain the study objectives and participation expectations. Medical directors and clinicians will sign consent forms and will be handed information sheets after the study is explained, but before further information about opioid prescribing is presented. Those attending the academic detailing meeting via webinar will be sent the consent form electronically and sign and return the consent form before the meeting. All signed consent forms will be sent via email, fax, or postal service to the study team. Medical directors will be assured that there is no obligation to participate in the study and that their decision is voluntary. The study team will explain to medical directors that the clinic and clinicians can drop out from study participation at any time and that their clinical practice will in no way be affected by their choice to participate or not.

Staff Recruitment

Following the academic detailing meeting an email will be sent out to all clinic staff by the medical director of behalf of the study team. The email will inform clinic staff that research may be conducted at their clinic, what the research activities they may be asked to participate in include, and that they should contact the study team if they have any questions. While clinicians have the opportunity to opt-out of individual-level activities, they still may be involved in the research by virtue of doing their jobs in a clinic where the study is occurring. In a separate email the study team will provide the clinicians who could not make the academic detailing meeting with a link to a webinar. The study team will ask prescribers and clinicians who may participate on the change team who are interested in participating in the study to watch the webinar and sign the consent form. All signed consent forms will be sent via email, fax, or postal service to the study team.

The study team will call medical directors of clinics that have been randomized to receive practice facilitation to schedule the online or in-person clinic visit and ask the medical director to identify individuals who might be interested in participating on a change team. The medical director will

298 identify an appropriate individual who might be interested in being a change team leader, and up to 5
299 additional clinicians to serve as change team members. At the online or in-person clinic visit the study
300 team will provide change team members with a virtual or hard copy information sheet about practice
301 facilitation. The information sheet will inform change team members what is required of them and that
302 their participation is voluntary. The change team will be told that there is no obligation to participate
303 and that their clinical practice will in no way be affected by their choice to participate or not. The study
304 team will assure clinicians that they can take their time to think about their participation and may
305 leave the practice facilitation at any time. While most future meetings are anticipated to be virtual, any
306 face-to-face contacts with clinician subjects will take place at the regional meeting, in the clinician
307 subject's office or in a private room in the clinic at a convenient time for the clinician subject. Virtual
308 meetings will be held securely over WebEx. Online practice facilitation sessions will be recorded to
309 review for notes and accuracy. Notes will be kept securely on Box and recorded sessions will be
310 destroyed.

311 **Consent**

312 A request for a waiver of informed consent will be made for health system leaders and for clinic staff
313 in clinic-level interventions. The study team will ask health system leaders to send out an email on
314 behalf of the study team, informing medical directors about the research and the ability to opt-out of
315 future communication with the study team. Medical directors who do not opt-out by a specified date
316 on the email will be invited to the academic detailing meetings and have the ability to forward the
317 email to other interested clinicians. These subjects will sign consent forms and receive a study
318 information sheet at the academic detailing meeting. Those attending the meeting via webinar will be
319 asked to read, sign, and return consent forms prior to the meeting. Webinar attendees will send the
320 signed consent form to the study team via email, fax, or mail.

321 After the academic detailing meetings, the medical director will send out an email on behalf of the
322 study team to notify clinic employees that research may be done at their clinic and that they have the
323 option to opt-out of the study activities. The study team will consent any prescriber and clinic staff
324 who did not attend the academic detailing meeting, but wish to participate in the study via email.
325 Prescribers will be sent an email with a link to the webinar of the academic detailing meeting and a
326 consent form to read and sign. Prescribers will send the signed consent form to the study team via
327 email, fax, or mail.

328 If participants decide to no longer participate in the study they will contact the PI, Andrew Quanbeck,
329 to rescind their consent. Data that is already collected will be retained for analyses, but no further
330 data of that participant will be provided to the study team.

331 A waiver of signed consent will be requested for qualitative interviews. Participants will be invited over
332 email to participate in interviews. After a week, if the participant does not respond to the email the
333 study team will call the participant to invite them to the study. The study team will call once. If there is
334 no answer a new invite will be sent to a different participant. Participants who agree to be interviewed
335 will be sent information sheets to read. This consent process is supplemental from the consent
336 process participants went through at or before the educational meeting.

337 **Randomization**

338 Randomization will take place at the clinic level at month 3 (practice facilitation) and month 9
339 (physician peer coaching). A research team member will conduct the randomization using the urn
340 randomization program.

341 Randomization of clinics will take place at intervention month 3 on a 1:1 ratio to assign clinics that will
342 receive practice facilitation plus academic detailing or academic detailing only. At intervention month
343 9 all clinics will be randomized on a 1:1 ratio to assign clinics who will receive the current intervention
344 strategy plus physician peer coaching or continue the current intervention strategy for 12 months.
345 Randomizations will be stratified on clinic's 1) health system, 2) number of patients, and 3) average
346 MME being greater or equal to the health system's clinic average.

347 **5. Intervention Plan**

348 While the intervention plan is continuing as intended, due to the COVID-19 pandemic, study
349 intervention activities were put on hold between March 25th and July 15th. Study activities have since
350 resumed as intended.

351 Subjects will receive a combination of the following strategies:

352 **Academic detailing.** Clinicians from participating clinics will be invited to a regionally hosted, in-
353 person training session where they will be provided lunch. The study team will also have a webinar
354 option (such as WebEx) for clinicians who cannot travel to the regional in-person meeting. The
355 session will be designed to both inform and engage clinic staff in the study. The session will be led by
356 Dr. Randall Brown and Jillian Landeck, who are experts in addiction medicine with extensive
357 experience managing the care of long-term opioid patients. Invitees will be medical directors and
358 prescribers (physicians, nurse practitioners, physician assistants), nurses, and staff directly involved
359 in clinic workflows related to opioid prescribing (e.g., medical assistants, lab techs, etc.). We will ask
360 each clinic to designate the clinic medical director to serve as contacts for the research team. The
361 training will cover the goals of the study, the importance of improving opioid prescribing in primary
362 care, a review of the latest standards of guidelines concordant care, how improvements in clinic
363 workflows can affect patient outcomes, clinical topics such as how to address opioid-induced
364 hyperalgesia and balancing patient-reported pain and function during dose reduction, and trainings on
365 how to use electronic medical records to monitor key opioid prescribing outcomes. An assessment
366 will be conducted during the session to elicit contextual characteristic that use the electronic health
367 record to monitor key opioid prescribing outcomes. The assessment will be a survey given at
368 meetings or online (for those joining via webinar)s. If clinicians are watching the academic detailing
369 meeting on their own or via webinar, they can take the survey on REDCap. At the conclusion of the
370 initial meeting, clinicians who attended the meeting will be asked to form change teams at their
371 clinics.

372 A quarterly hour-long academic detailing meeting will be hosted via webinar (such as WebEx) to
373 provide clinics and clinicians further information about the CDC opioid prescribing guidelines.
374 Quarterly webinar meetings will be separate for each study arm.

376 Following the academic detailing meeting, the health systems will create and deliver audit & feedback reports
377 to clinicians. Health systems are already doing this and will customize the reports to fit the study. These reports
378 will let clinicians know about their clinic's opioid prescribing metrics such as average MME, % of patients with
379 urine drug testing, treatment agreements, and mental health screens, and % of patients co-prescribed
380 benzodiazepines. Reports will only be at the clinic level.

381 **Practice facilitation.** Research staff trained in practice facilitation and/or study team members will
382 meet virtually with clinics using WebEx (or visit clinics in-person) and follow up over the course of up
383 to 5 monthly then 4 quarterly videoconferences or teleconferences to help clinics improve processes
384 related to opioid prescribing, such as ensuring that treatment agreements are signed by prescribers
385 and patients at least once a year, and integrating urine drug testing into clinic workflows. Clinic
386 medical directors will create change teams consisting of the clinic medical director and a physician
387 change leader and up to 5 clinic staff. The online or in-person visit will begin with a meeting with the
388 clinic medical director and the change team leader. At the meeting the facilitator will set a plan for the
389 day and answer any questions about the meeting. The facilitator will tour the clinic in-person or
390 virtually over WebEx.²⁴ The facilitator will then meet (in-person or virtually) with the change team for
391 an hour to cover how to make workflow changes such as integrating treatment agreements and urine
392 drug tests into clinic processes. The change team will be educated about the nominal group
393 technique²⁵ and Plan-Do-Study-Act cycles²⁶ (PDSA cycles) to select the area of improvement for the
394 first PDSA cycle. The practice facilitator will assist the change team in filling out the PDSA cycle and
395 the practice facilitator will enter the info into the Change cycle data table for reference for the follow-
396 up conference call. Then the facilitator will debrief with the medical director and change team leader
397 to discuss the next steps for follow-up discussions. Over the next 18 months clinics will be able to call
398 in or meet over WebEx for up to 5 monthly, 60 minute-long meetings, followed by 4 quarterly hour-
399 long follow-up discussions about the workflow changes. Sessions will be recorded using encrypted
400 audio recorders or WebEx's recording feature. Recordings will be used to ensure accurate note
401 taking. Recordings from audio recorders will be stored on the facilitator's password-protected
402 computer or laptop. Once note taking is completed the recordings will be destroyed.

403 **Physician peer coaching.** At UW Health, physician peer coaches will be Drs. Brown and Landeck.
404 At Bellin Health, physicians with relevant experience in opioid prescribing will be nominated by health
405 system leaders to become each systems' physician peer coaches. These coaches will become
406 members of the research team. Drs. Brown and Landeck help their peers manage their patients on
407 opioid therapy. Participating clinics randomized to physician peer coaching will receive up to 4
408 quarterly coaching sessions over 12 months. Physician peer coaches will provide help to prescribers
409 to assist with tough panels through up to four quarterly coaching sessions over 12 months. Coaching
410 consultations will occur in sessions via videoconference (WebEx) or teleconference. Participants
411 attending the physician peer coaching sessions will be asked to take a survey before each session to
412 let the coach know what topics the group needs help with. After each physician peer consulting
413 session, participants will be asked to complete a post-session survey to assess how the session was
414 received and how confident the participant feels about addressing the session topic with patients.
415 After the fourth and last session, participants in the physician peer consultation interventions will be
416 asked to take a final survey to evaluate how the intervention impacted their confidence and
417 experiences treating patients prescribed opioids for chronic pain, and feedback on the intervention
418 itself.

419 **Data collection**

420 *Quantitative data.* Evaluation data extracted from the electronic health records of patients on
421 prescriber panels will be constructed and delivered by the Health Innovation Program (HIP) on behalf
422 of the Wisconsin Collaborative for Healthcare Quality (WCHQ). All members of the collaborative
423 (including UW Health) and other specially invited members (Bellin) submit patient level data extracted
424 from health records to a central data repository (called RBS, or “Repository Based Data
425 Submission”), which HIP is able to access through their Business Associate agreement with WCHQ.
426 The electronic data from the WCHQ is accessed by HIP through a secure File Transfer Protocol
427 (FTP) site that is set up by WCHQ. An FTP is a secure way of moving data from WCHQ to an outside
428 organization such as HIP. Datasets for researchers are constructed from these identifiable datasets
429 that have been transformed into de-identified datasets by HIP Programmers, who are not part of the
430 study team. Patient-level data will be grouped by prescriber and clinic for this project, and prescribers
431 and clinics will be coded so that the Programmers are able to deliver longitudinal data at the
432 prescriber and clinic levels. The study team will not have access to a crosswalk or any other code that
433 would allow re-identification of the de-identified dataset delivered by HIP to the research team.
434 Datasets will be extracted and delivered from the start of the intervention to the end of the 6-month
435 follow-up at intervention month 27. No sensitive information will be included in the analysis dataset.
436 No individual PHI will be collected in the course of this study. Only aggregate statistical output
437 representing groups of subjects will be released.

438
439 *Qualitative data.* The study team will conduct two sets of semi-structured interviews (exact questions
440 will vary based on answers to other questions) using the UW sponsored HIPPA compliant WebEx.
441 Semi-structured interviews will be conducted with two change team leaders or their designees (a total
442 of 8 participants) selected randomly from each intervention group at each participating health system.
443 The interviews will take place at intervention month 18 to better understand what practice facilitation
444 activities were done at clinics, what worked and did not work, and feedback on the intervention. A
445 second set of semi-structured interviews will be conducted with one prescriber (a total of 8
446 participants) selected randomly from each intervention group at each participating health system.
447 These interviews will take place between intervention months 18-21 to better understand what peer
448 support activities were done at clinics, what worked and did not work, what prescribers find
449 problematic, how peer support groups helped prescribers address these issues, and feedback on the
450 intervention. Qualitative interviews will be recorded and transcribed for analysis using WebEx’s
451 recording and transcription feature. All identifying information will be coded and transcripts will be
452 stored securely on a Box folder (no PHI will be uploaded to the Box folder). The recording will be
453 destroyed after it is transcribed.

454 *Assessments.* This study has developed a tailoring assessment based on pilot data to test 4
455 moderators (existence of an opioid prescribing policy at the system level, experience of quality
456 improvement at the clinic level, size of the clinic, and number of high dose patients) and assess other
457 factors that affect implementation through open and closed-ended questions. At 0, 5, 9, and 21
458 months assessments will be administered online (via REDCap) and online or in-person surveys. If in-

459 person visits occur, participants will be asked to complete a hardcopy assessment. In-person
460 assessment data will be entered into ICTR's REDCap.

461 *Detailed contact logs.* Research team members responsible for delivering the implementation
462 strategies will keep detailed logs of contact with clinics and prescribers to estimate measures of
463 adoption and implementation. All identifiable information will be de-identified by a research team
464 member.

465 In the event that subjects (clinic or prescriber) choose to withdraw from the study, data that is already
466 collected will be kept for analyses. No further data will be collected from that subject. If the clinic
467 withdraws, all prescribers at that clinic will not have further data collected.

468 Physician peer consulting surveys

469 The study team will ask participants in the physician peer consulting intervention to take a pre- and
470 post-session survey for each session and a final, post-session survey using UW Madison's version of
471 Qualtrics. Surveys will ask questions about the topics prescribers want to discuss at the upcoming
472 consultation session, how confident they are in addressing the issues discussed at the past session,
473 and their experience with their consultant and the intervention. The surveys will only ask the
474 participant to provide their health system and clinic they practice at so the study team will know which
475 topics to discuss at each clinic's consulting session, understand how the consulting session was
476 receive, and make any adaptations to future consulting sessions. For this reason, health system and
477 clinic information will not be coded or de-identified. However, the research coordinator will code
478 health system and clinic for the analysis.

479 **Privacy and Confidentiality**

480 To mitigate the risk of breaches of confidentiality, all subjects and clinics will be assigned a code
481 number. A list of subject and clinic code numbers will be maintained by a research team member and
482 stored in a password-protected spreadsheet. This data will be kept on a secure, limited access,
483 password-protected file service on ICTR's REDCap and UW's Qualtrics.

484 **Potential Risks:** This research is aimed at improving clinical practice related to opioid prescribing,
485 and falls ultimately under the context of increasing patient safety. As such, the study team believes
486 the risks to clinician subjects and individual patients are minimal, and the intervention will improve
487 patient safety. The potential risks of participation are:

- 488 1. Staff members could feel pressured to participate in the study. Opioid prescribing is a
489 potentially controversial topic.
- 490 2. Prescribers may be uncomfortable discussing their prescribing practices and may resist
491 attempts to change clinical practice. To mitigate any perceived pressure to participate in the
492 study, the research team will make it clear, through written materials and oral instructions, that
493 staff participation in the research is completely voluntary.
- 494 3. There could be a breach of confidentiality that could result in disclosure of research data
495 outside the study team. To prevent this, all subjects will be assigned a code number. The lists
496 will be kept in a locked file at HIP, and will not be shown to staff. Data collected will have the

names removed and the code attached by a research team member. Project staff who have access to data will not have access to subject names.

We have taken the following measures to reduce potential risk to subjects:

1. The primary units of analysis will be the clinic and prescribers; no staff members will ever be identified in presentations or publications.
2. The research team will emphasize the idea that the current implementation study is intended to improve opioid prescribing practices.
3. To address the risk of breach of confidentiality the research team will be provided only de-identified datasets and no individual provider will be able to be ascertained from these datasets nor will any member of the study team attempt to identify providers. Any qualitative data collected will be protected as well. Hard copy data will be kept in a locked cabinet and digital data will be stored on ICTR's REDCap.

UW-ICTR's Data Monitoring Committee.

This study will use UW-ICTR's Data Monitoring Committee. UW-ICTR has established a Data Monitoring Committee (DMC) to provide a key resource for UW-Madison investigators conducting clinical research. This DMC will provide investigators services to ensure appropriate measures are in place to promote subject safety, research integrity and compliance with federal regulations and local policies for individual clinical research protocols in need of DMC review (as determined by the Principal Investigator (PI), the funding agency, the local Scientific Review Committee, or the local IRB, and for which no DMC exists). For these studies, the UW ICTR DMC will be the primary data and safety advisory group for the Principal Investigator.

The DMC is supported in its mission of safety and compliance by experienced ICTR staff to provide administrative assistance, experienced members representing a diversity of backgrounds, skills and knowledge, and the use of the Research Electronic Data Capture (REDCap) tool which provides data management functionality by allowing the development of eCRFs and surveys to support data capture. In providing oversight for the conduct of this study, the ICTR DMC will meet every 12 months during the 5-year study. Additional meetings may be scheduled as determined by the DMC or as requested by the PI. The DMC members will review protocol-specific reports created by statisticians that serve a non-voting member role on the DMC using data pulled from REDCap. These standard reports will include an overview of study objectives, a review of actual and projected accrual rates, an evaluation of patient demographics for balance of randomization, and a summary of the number and seriousness of adverse events. An interim analysis of study results may be performed and source documents may be reviewed to allow the DMC to independently judge whether the overall integrity and conduct of the protocol remain acceptable based on data provided and reported by the Principal Investigator. The DMC will make recommendations to the Principal Investigator that could include actions of continuation, modification, suspension, or termination.

This study may be temporarily suspended or prematurely terminated if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to The National Institute on Drug Abuse. If the study

is prematurely terminated or suspended, the PI will promptly inform the IRB and will provide the reason(s) for the termination or suspension.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to subjects
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination of futility

Study may resume once concerns about safety, protocol compliance, or data quality are addressed and satisfy the applicable federal and institutional regulatory authorities.

6. Measurement of Effect

This proposal uses the Reach, Effectiveness, Adoption, Implementation, and Maintenance (RE-AIM) model as an organizing evaluation framework²⁷ to examine the quality, speed, and impact of implementing the adaptive system consultation strategies. RE-AIM is a comprehensive evaluation framework that assesses implementation in five dimensions. While RE-AIM has been used to evaluate many diseases of fidelity.²⁸ Specific measures for each RE-AIM dimension are presented in Table 1.

7. Study Parameters

Domain	Source	Pertains to aim:	Months* collected
Reach: # and % of patients excluded vs. participating (incl. characteristics)	EHR	PA, SA1	1-21
Effectiveness: Overall rate of opioid prescribing and average MME per clinic and provider	EHR	PA	1-21
# and % of patients completing urine drug testing (past 12 mo.)	EHR	PA	1-21
# and % of patients screened for mental health using PHQ-2 (past 12 mo.)	EHR	PA	1-21
Mental health (PHQ-9) scores for patients screening positive on PHQ-2 (past 12 mo.)	EHR	PA	1-21
Overall rate and dose of opioid-benzodiazepine co-prescribing	EHR	PA	1-21
# and % of patients with treatment agreements (past 12 mo.)	EHR	PA	1-21
# and % of opioid prescriptions above 90 MME	EHR	PA, SA1	1-21
Patient attendance at scheduled clinic visits	EHR	PA, SA2	1-21
# and % of patients prescribed buprenorphine	EHR	PA	1-21
# and % of patients with PEG-3 score (past 12 mo.)	EHR	PA	1-21
PEG-3 scores (past 12 mo.)	EHR	PA	1-21
Adoption (setting): # and % of participating clinics vs. all clinics (incl. characteristics)	HS	SA1	1-21
Adoption (staff): # and % of participating staff vs. all eligible clinic staff (incl. characteristics)	Clinic	SA1	1-21
Clinician attendance at intervention meetings	RT	SA1	1-21
Implementation: Hours of intervention received per clinic & prescriber	RT	SA1	1-21
Adaptations made to protocols during intervention period	RT	SA1	1-21
Assessment of 4 moderators: system-level opioid prescribing policy, clinic-level experience in QI, size of clinic (# patients), # and % of patients on opioid doses > 90 MME	RT; EHR	SA1	0, 5, 9, 21
Qualitative assessment of mechanisms of action & factors influencing implementation	RT	SA1	1-21
Cost of each different implementation sequence & combination	RT	SA2	1-21

Maintenance: 6-mo. Follow-up on all effectiveness outcomes	EHR	All aims	22-27
*Months correspond to intervention months PA: Primary aim; SA1, Secondary aim 1; SA2, Secondary aim 2; RT: Research team; HS: Health system; EHR: Electronic health record			

Clinics will be randomized on a 1:1 ratio to either receive practice facilitation plus academic detailing or academic detailing alone at month 3. At month 9, all clinics will be randomized on a 1:1 ratio to either continue the current intervention or add physician peer coaching to the bundle of strategies. It is anticipated that up to 152 prescribers will be recruited from 40 primary care clinics among 2 healthcare systems. The intervention will last for 21 months followed by a 6 month follow-up period.

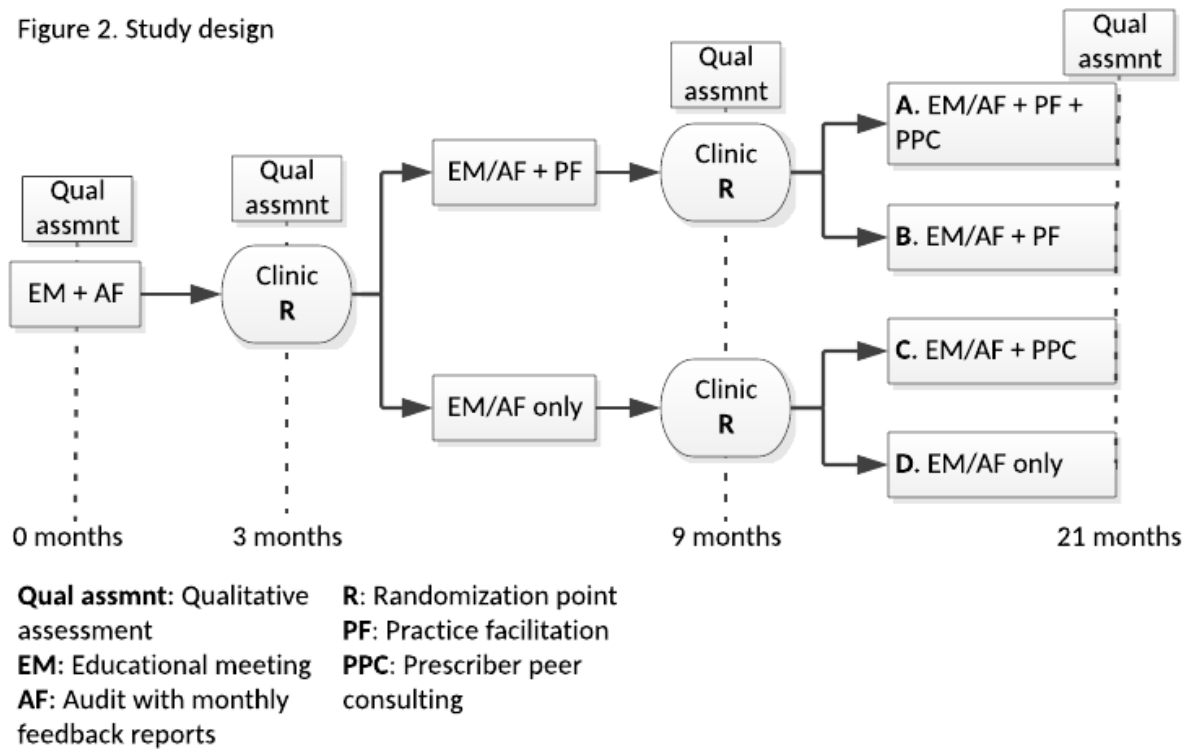
8. Statistical Considerations

Research Design

Analyses will be conducted at two levels, (1) at the clinic level and (2) at the prescriber level. UW Health and Bellin Health primary care clinics will be recruited for participation in the intervention and data collection activities. All clinics and all prescribers within clinics, once randomized, will be included in the intent-to-treat sample. The primary research outcome is morphine milligram equivalent (MME) and will be available for all prescribers within all clinics that consent, regardless of intervention engagement or drop-out.

This study will use a sequential, multiple assignment randomized trial (SMART), which is a factorial design (see Figure 1).^{1,2} This SMART has 4 implementation strategies embedded within it.

Figure 2. Study design



571 **Quantitative data collection and analysis**

572 Data are available for many study measures, allowing for time-series analysis of repeated measures
573 to detect changes in a clinic over time (pre-intervention vs. post-intervention). Clinics and prescribers
574 will be compared to clinics and prescribers receiving only academic detailing by accessing measures
575 through the Wisconsin Collaborative Healthcare Quality system-wide data warehouse at Health
576 Innovation Program (HIP). Programmers and compliance officers at HIP will prepare a de-identified
577 dataset analysis purposes by the study statistician. The dataset will remain on HIP's secure data
578 servers at all times.

579 The quantitative analysis of data from the electronic health record (EHR) will focus primarily on
580 average daily morphine milligram equivalent for chronic pain patients at the clinic and prescriber
581 levels. Changes in outcomes will be assessed through repeated monthly observations assessed
582 retrospectively post-intervention. Data will be collected every three months throughout the 21 month
583 intervention and 6 month follow-up period.

584 The study team will analyze the de-identified dataset delivered by HIP for evaluation purposes. The
585 research team will not have access to any individual patient data or PHI. Prescriber identities will be
586 protected; identifying information (such as staff names) will be replaced with code numbers by the
587 HIP Programmers. The de-identified dataset will be coded by prescriber and clinic and the code key
588 will be kept by HIP Programmers and not provided to the study team.

589 Due to delays in the data delivery from the Wisconsin Collaborative Healthcare Quality the research
590 team will also receive and analyze data that the UW Clinical Research Data Services (CRDS)
591 provides for the clinic feedback reports. The purpose for this is to speed up data analysis. CRDS will
592 act as an honest broker and will not provide the research team with patient-level identifiable data.
593 CRDS will provide data to the research team through ICTR REDCap's file repository feature.

594 **Qualitative data collection and analysis**

595 Interviews over WebEx for practice facilitation and physician peer coaching will be recorded and
596 transcribed. Subjects will be reminded that calls are recorded. The recordings will be transcribed and
597 coded by the study team. Qualitative analyses will be done using Nvivo.

598 Qualitative assessments will be conducted to assess contextual factors of systems consultation.
599 These assessments will be coded to group data at the clinic level for analysis and take place at
600 months 0, 5, 9, and 21 of the intervention.

601 Qualitative data will be collected via REDCap at the prescriber levels will be stored REDCap for
602 analysis purposes. Any publication that results from the study data will not include the names of
603 clinics or staff members where data were collected. All other results will be presented in anonymous
604 aggregated form.

605 **Statistical analysis**

606 Statistical analysis will be conducted by Daniel Almirall at the University of Michigan. Dr. Almirall will
607 be provided a secure, remote login to the password-protected servers at the Health Innovation
608 Program to access the de-identified datasets.

609 The analysis will use a longitudinal (repeated-measures) analysis. Time will be coded such that $t=0$
610 denotes month 3 of the intervention period (the initial randomization); in the following text, data
611 collected prior to $t=0$ is considered baseline data (including the MME prior to month 3). The primary
612 outcome (MME) is a continuous measure and is collected at $t=0$ (at month 3, prior to randomization)
613 and every 3 months up to $t=18$ (intervention month 21) for a total of 7 measurement occasions. (Note
614 that the primary outcome is clustered: repeated measures, within prescribers, within clinics.)
615 Longitudinal regression models, adapted for the analysis of a longitudinal SMART^{29,30} and further
616 extended for use with data arising from a cluster-randomized SMART,³¹ will be used to contrast the 4
617 sequences and combinations of implementation strategies in terms of the average change in MME.

618 A piecewise-linear model with a knot at $t=6$ (MME collected immediately before the second
619 randomization at intervention month 9) will be used to model the temporal trajectories over the course
620 of months 10-21. The model the study plans to use has a linear trend from $t=0$ to $t=3$ for prescribers
621 in academic detailing plus practice facilitation and academic detailing only clinics, and a linear trend
622 from $t=3$ to month $t=18$ for each of the 4 sequences and combinations of implementation strategies.
623 We allow for changes in the mean trajectory (i.e., deflections) at intervention month 9 ($t=6$) since this
624 is the point at which prescribers may begin receiving physician peer coaching.

625 **Cost analysis**

626 This study will estimate the cost of delivering the four different sequences and combinations of
627 strategies, including incremental cost effectiveness of adding practice facilitation and physician peer
628 coaching. Methods and instruments used for cost data collection in the Systems Consultation R34³
629 will be used. Detailed logs of call contacts between members of the research team and the clinic
630 change teams will be kept to estimate the number of hours spent delivering the implementation
631 strategy. The consultants will document the date and duration of each contact they have with clinic
632 staff members, role of the staff member, and a summary of topics discussed. Cost estimates of the
633 intervention will be calculated by multiplying hourly wage rates for physician peer coaches and
634 practice facilitators. Costs for non-personnel may include travel to site visits, the cost of
635 teleconferencing services for follow-up calls, etc.

636 **Power**

637 The estimated sample size for this study is based on the primary aim: a comparison on change in
638 morphine milligram equivalent (MME) between implementation sequences of all three strategies vs.
639 academic detailing only. Based on the pilot data, the inter-clinic correlation coefficient was 0.14.
640 Assuming the average prescribers per clinic is 4, a type-1 error rate of 5%, and an early adoption rate
641 of 50% gives a total of 40 primary care clinics at 80% power to detect an effect size of $d=0.66$
642 between the two implementation sequences on change in MME. In the pilot data we found a standard
643 deviation of 35 MME, which is estimated to detect differences on MME as small as 18 MME.
644

9. Records to be Kept

Data to be collected	Storage	Type of Data
Clinician subject intake	REDCap/ Locked cabinet	Coded
Clinician subject demographics	REDCap/ Locked cabinet	Coded
Qualitative assessment data	REDCap/ Locked cabinet	Coded
Prescriber consent form	REDCap/ Locked cabinet	Coded
Systems consultation coaching log	Box folder/ Locked cabinet	Coded
De-identified patient electronic health record data	HIP	De-identified
Practice facilitation notes	Box folder	Coded
Audio recordings from PF/PPC sessions	Facilitator computer/laptop (audio) or WebEx cloud storage (video)	Recording
Audio recordings from interviews	WebEx secure cloud storage	Recording
Transcriptions of interviews	Box folder	De-identified
Physician peer consulting survey	UW Qualtrics	Coded

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