

PCORI – is it for you?

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Learning objectives

- Understand how PCORI funding priorities and mechanisms differ from those of NIH and other funding agencies
- Recognize key features of comparative effectiveness and pragmatic research study design
- Become familiar with principles and practices of meaningful stakeholder engagement

Our Mission and Strategic Goals

PCORI helps people make informed healthcare decisions, and improves healthcare delivery and outcomes, by producing and promoting high-integrity, evidence-based information that comes from **research guided by patients, caregivers, and the broader healthcare community.**

Our Strategic Goals:



Increase quantity, quality, and timeliness of useful, trustworthy research information available to support health decisions



Speed the implementation and use of patient-centered outcomes research evidence



Influence research funded by others to be more patient-centered

My PCORI experience

- Stakeholder workshop participant
- Large pragmatic trial PI
- Merit review panel chair

Is PCORI for you?

- Are your research questions *directly* relevant to patients and other decision-makers?
- Are you planning a study using comparative effectiveness and pragmatic methods?
- Do you want to work with patients and other stakeholders throughout the research process?
- Are you willing to work with your PCORI program officer throughout the research process?

PCORI fundamentals

- Patient Centered Outcomes Research Institute
 - Non-governmental nonprofit corporation with legislatively-authorized mission and trust fund
 - Created by 2010 ACA as a new entity to coordinate US comparative effectiveness research (CER) by...
 - Identifying research priorities
 - Establishing research agenda
 - Carrying out research agenda
- Created to fill gaps in research to answer questions of *direct relevance* to decision-makers

Need for research relevant to decision making

“Despite a plethora of diagnostic and treatment options, practical information that can guide health care choices for an individual patient are often elusive... Clinicians and patients need to know not only that a treatment works on average but also which interventions work best for specific types of patients. Comparative patient-centered information is essential to translating new discoveries into better health outcomes, accelerating the application of beneficial innovations, and delivering the right treatment to the right patient at the right time.”

What is CER?

- “CER is the generation and synthesis of evidence that compares the benefits and harms of alternative methods to prevent, diagnose, treat, and monitor a clinical condition or to improve the delivery of care.
- The purpose of CER is to assist consumers, clinicians, purchasers, and policy makers to make informed decisions that will improve health care at both the individual and population levels.”

Institute of Medicine. Initial national priorities for comparative effectiveness research. Washington, DC: Institute of Medicine 2009

IOM vision for national CER program

- Large public-private enterprise
- Infrastructure to support large pragmatic trials, methods development, and workforce expansion
- Involvement of patients, caregivers, and health care providers throughout process
- Public accountability

PCORI does not fund...

- Basic science
- Biological mechanisms
- Pharmacodynamics
- Natural history of disease
- Efficacy of new interventions
- Development of clinical guidelines
- Development of coverage, payment, or policy recommendations
- Cost-effectiveness analysis

PCORI does fund...

- Comparative clinical effectiveness research
 - Randomized controlled trials & observational studies
 - Pragmatic clinical studies
- Studies focused on developing/refining CER methodologies
- Projects focused on building CER capacity
 - PCORnet
 - Engagement

Is PCORI for you?

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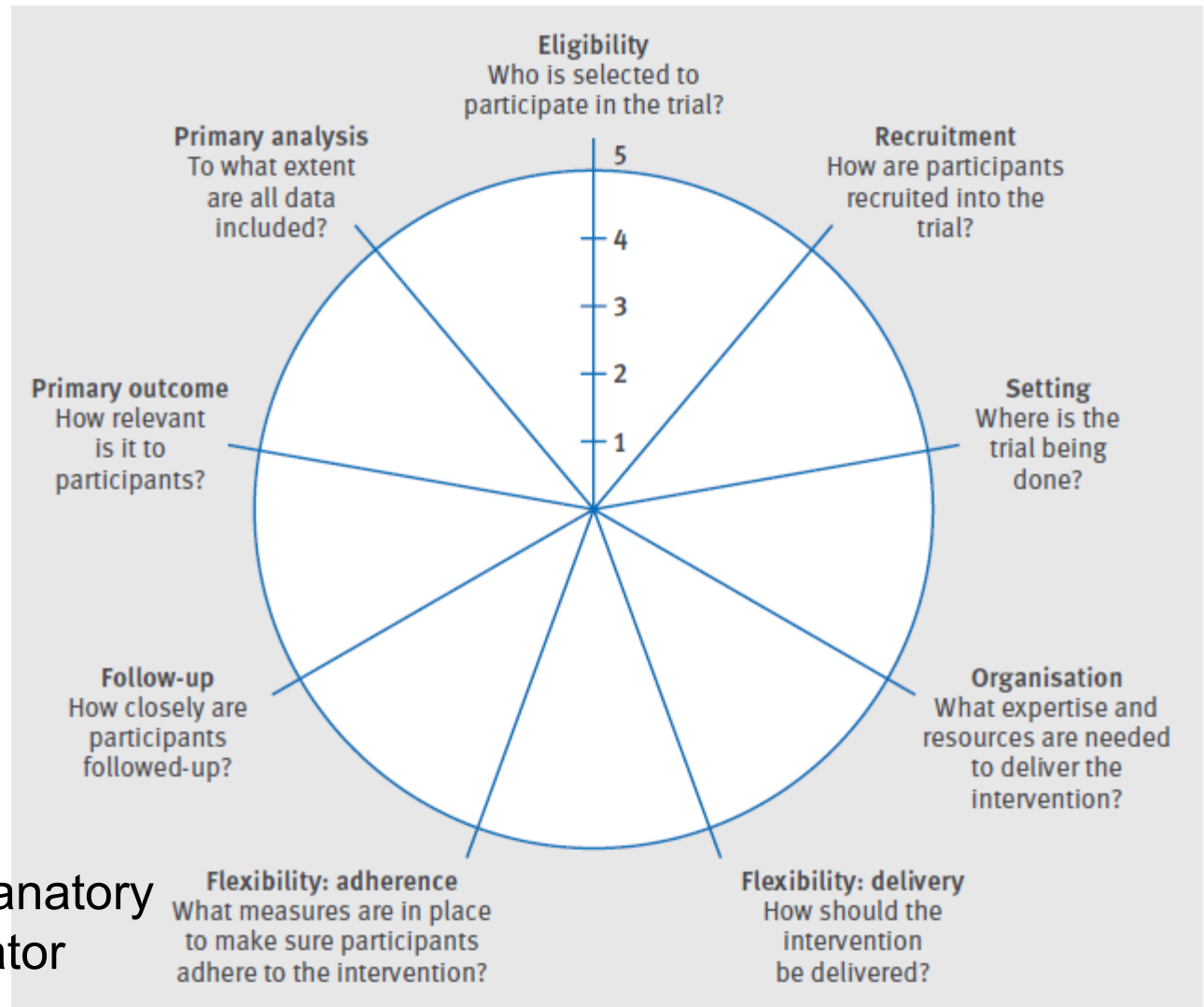
Pragmatic research philosophy

- Studies designed to answer practical questions for decision-makers
 - Patients, clinicians, health care system leaders, policy makers
- Studies designed to maximize applicability of results to “real world” (i.e., external validity), as well as internal validity

Explanatory vs. pragmatic trials

- Efficacy question: Can the intervention cause the outcome of interest?
- Setting: Controlled
- Participants: Selected ideal candidates
- Outcomes: May be short-term or intermediary
- Effectiveness question: Does the intervention work in usual practice?
- Setting: Routine
- Participants: All who might get intervention
- Outcomes: Must be directly relevant to users of the evidence

PRECIS* tool for design



*Pragmatic–Explanatory
Continuum Indicator
Summary

JAMA | Original Investigation

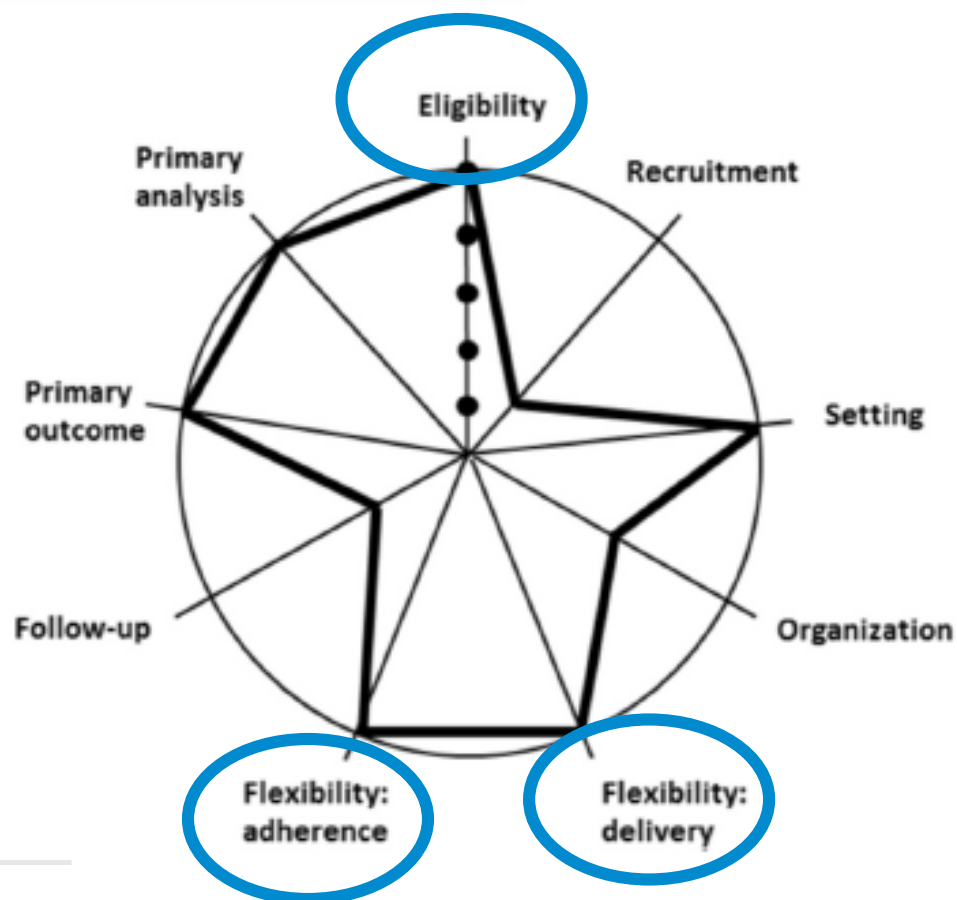
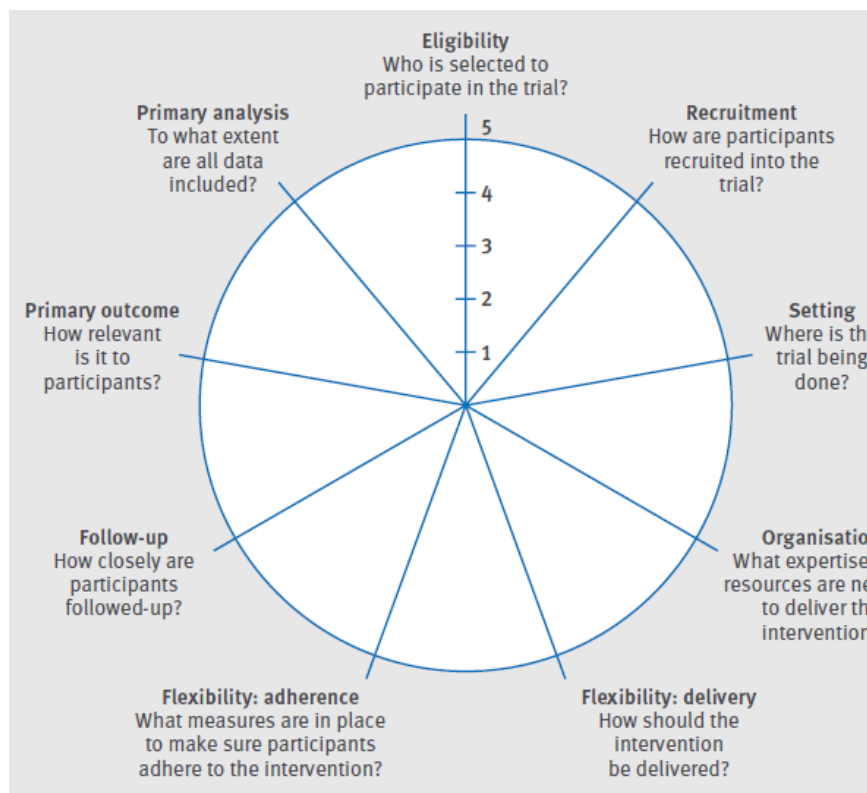
Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain The SPACE Randomized Clinical Trial

Erin E. Krebs, MD, MPH; Amy Gravelly, MA; Sean Nugent, BA; Agnes C. Jensen, MPH; Beth DeRonne, PharmD; Elizabeth S. Goldsmith, MD, MS; Kurt Kroenke, MD; Matthew J. Bair; Siamak Noorbaloochi, PhD

- Opioid therapy was not superior to non-opioid medication therapy for chronic back pain or hip or knee osteoarthritis pain over 12 months

SPACE

Strategies for Prescribing Analgesics Comparative Effectiveness



Background: opioids for chronic pain

- Short-term placebo-controlled efficacy trials: opioids decrease pain more than placebo
 - Chronic back pain: $\Delta \sim 10$ points on 0-100 scale
 - Hip/knee osteoarthritis: $\Delta \sim 7$ points on 0-100 scale
- Evidence gaps
 - Opioids compared to active treatment
 - Opioid treatment > 3 months



The question

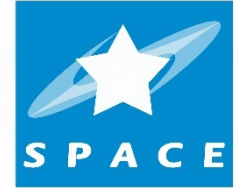


EVIDENCE TABLE

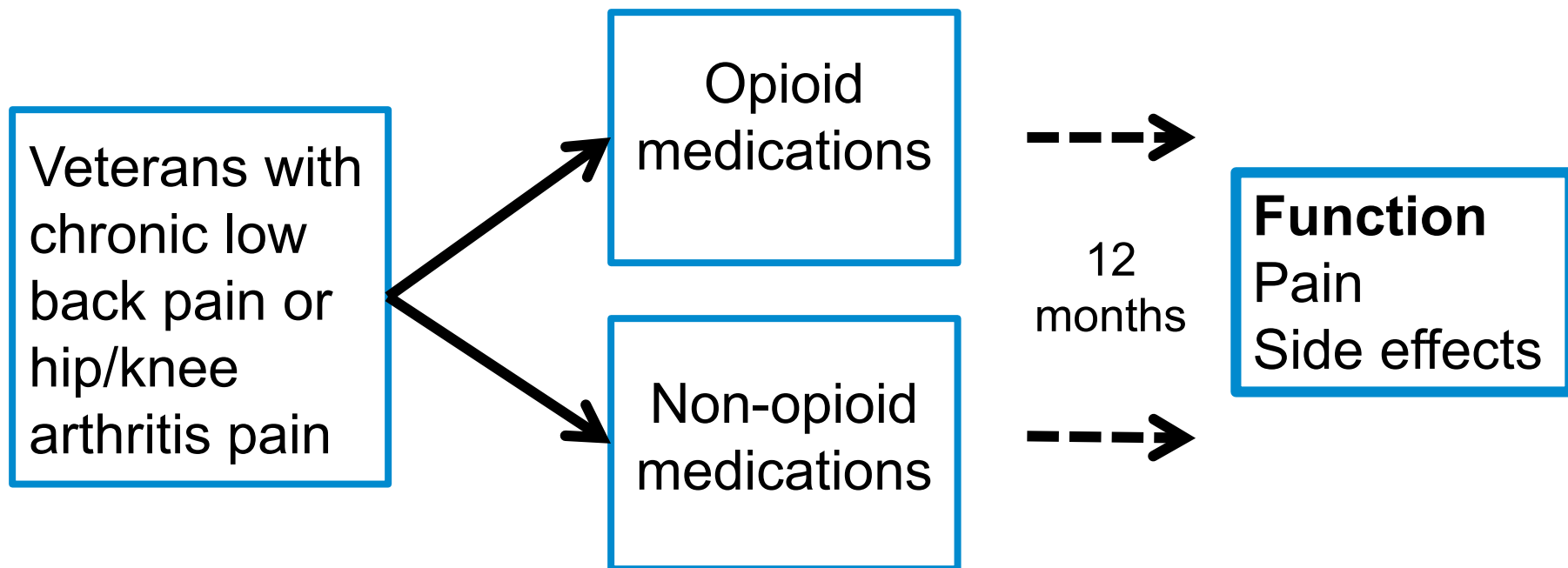
	Recommendations	Sources of Evidence
1	Opioid therapy is indicated for moderate to severe pain that has failed other indicated therapeutic interventions	Breivik, 2001
2	Consider the ethical imperative of benefit-to-harm profile	Joranson et al., 2002 Laval et al., 2002

LE=Level of Evidence; QE = Quality of Evidence; SR = Recommendation (See Appendix A)

Objective



To compare benefits & harms of opioid therapy vs. non-opioid medication therapy over 12 months among patients with moderate-severe chronic back or osteoarthritis pain despite analgesic use



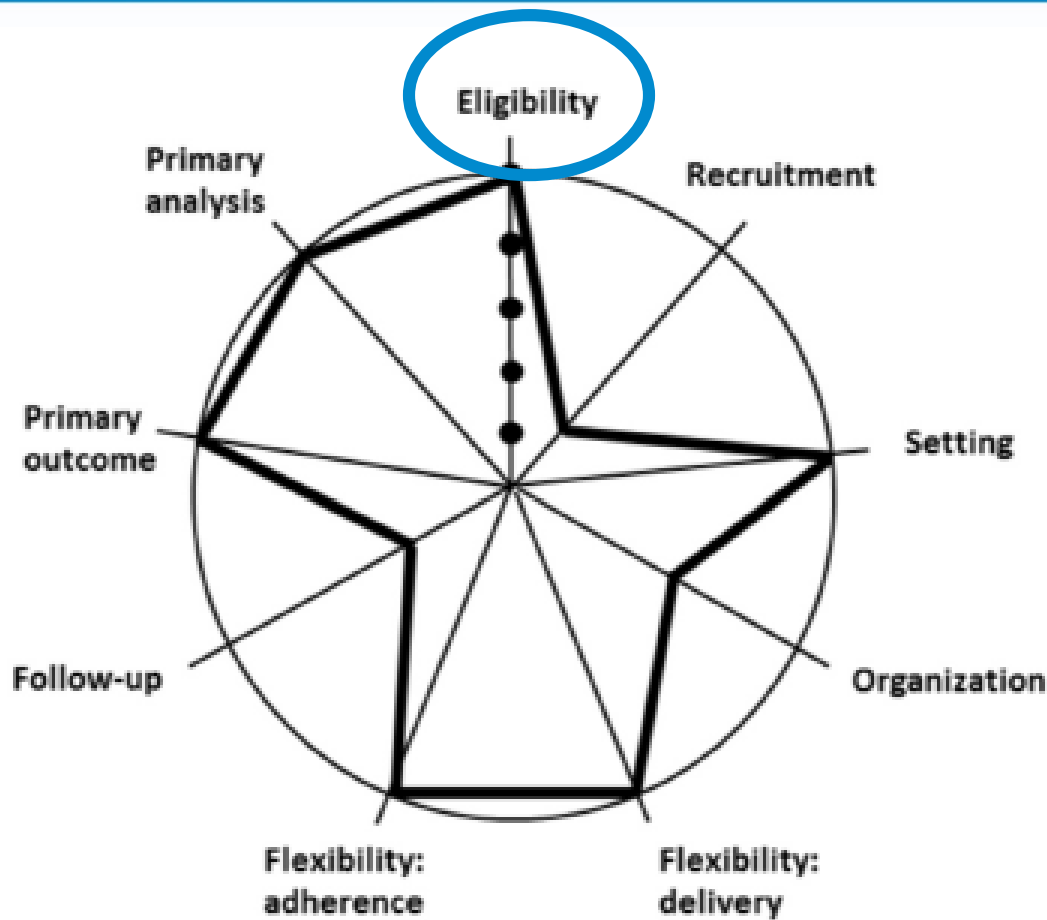
ClinicalTrials.gov: NCT01583985

Funded by VA Health Services Research & Development IIR 11-125

Krebs EE, et al. JAMA. 2018;319(9):872-882

SPACE

Strategies for Prescribing Analgesics Comparative Effectiveness



Eligibility

How similar are patients in the trial to those who would get intervention if it was part of usual care?

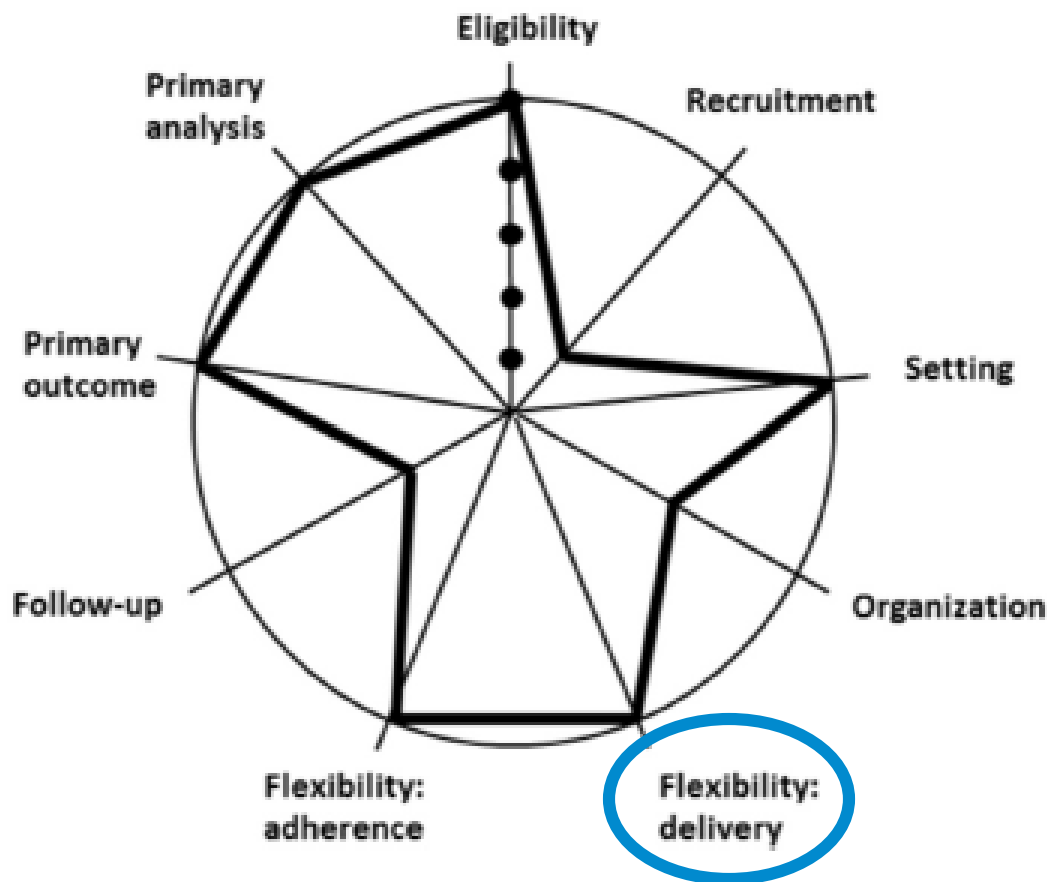
Pragmatic eligibility criteria

- Most pragmatic approach: Include anyone with the condition of interest who is likely to be a candidate for the intervention in usual care
- Examples of non-pragmatic features:
 - Using tests or measures to define eligibility that are not typically used in primary care
 - Excluding people not expected to be highly responsive (good candidates) for the intervention
 - Excluding people with mental/physical/social problems that may make them less likely to follow up or adhere to the intervention

Pragmatic eligibility criteria



- SPACE used highly pragmatic approach
- Inclusion criteria
 - Moderate-severe pain (per 3-item primary care pain measure) despite analgesic use (per patient)
 - Chronic back pain or hip/knee OA pain as “main problem” per patient
- Excluded patients with contraindications to opioids (per guidelines)
 - Did not exclude for severe PTSD/depression, serious medical conditions, or past SUD



Intervention flexibility: delivery
 How different is the flexibility in intervention delivery from the flexibility anticipated in usual care?

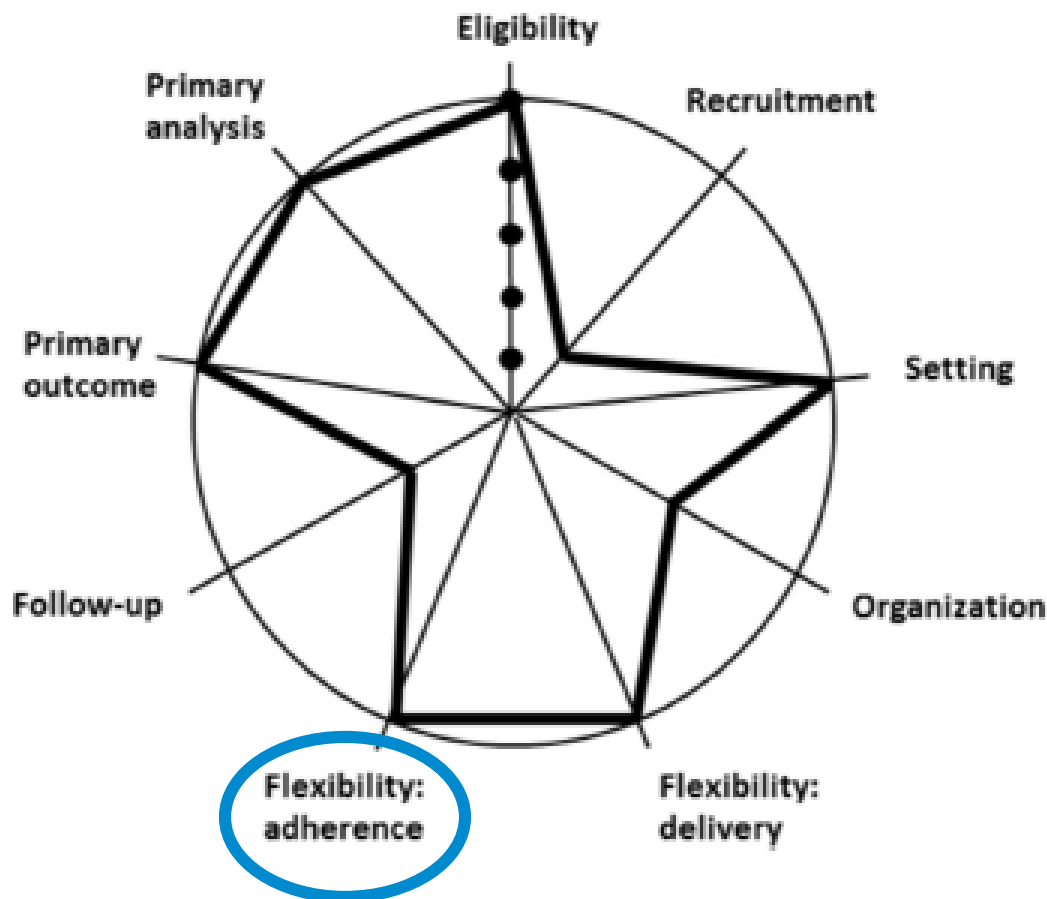
Pragmatic flexibility (delivery)

- Most pragmatic approach: very flexible, with details of intervention implementation left to providers (i.e., how it works in usual practice)
- Examples of non-pragmatic features:
 - Highly specified protocol-driven intervention
 - Monitoring compliance of clinicians delivering intervention
 - Restrictions on co-interventions

SPACE flexibility (delivery)



- SPACE used highly pragmatic approach
- All patients received individualized medication management within assigned treatment group
 - Prescribing strategy included all relevant VA formulary drugs organized into 3 steps (from most common/least expensive to higher risk/higher cost)
 - Starting point determined by past medication use and patient preferences
 - Changes determined by response and preferences
- No restrictions on co-interventions (e.g., nondrug therapies)



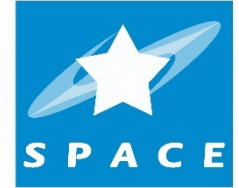
Intervention flexibility: adherence

How different is monitoring and management of patient adherence to the intervention compared with what is done in usual care?

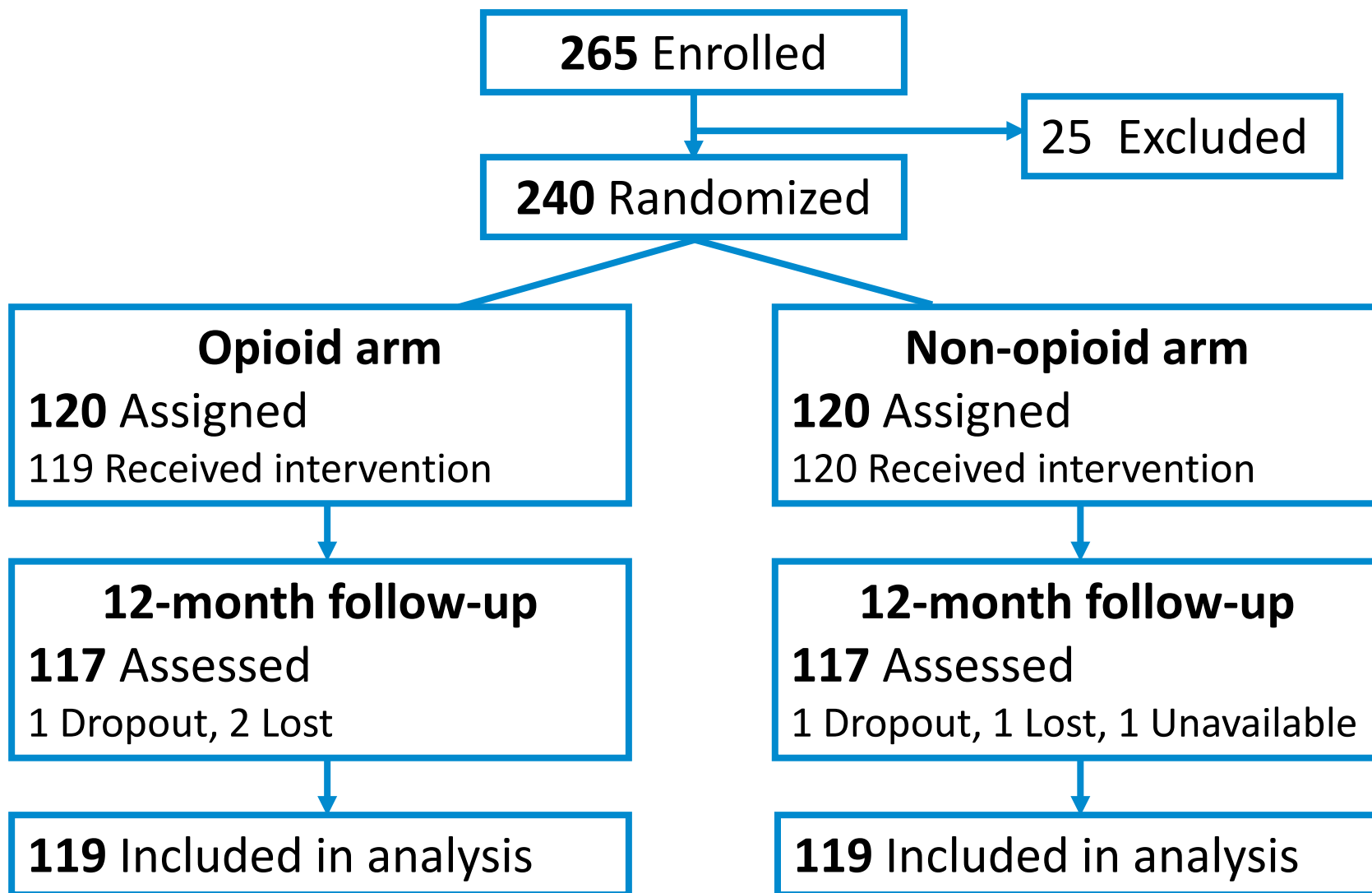
Pragmatic flexibility (adherence)

- Most pragmatic approach: full flexibility in how study patients engage with the intervention
- Examples of non-pragmatic features:
 - Trial pre-screening stage to evaluate adherence
 - Monitoring adherence to intervention and intervening to improve adherence
 - Withdrawing non-adherent patients

SPACE flexibility (adherence)



- SPACE used highly pragmatic approach
- All patients were retained in trial regardless of adherence



Is PCORI for you?

- Do you want to work with patients and other stakeholders throughout the research process?

Stakeholder engagement

- Core aspect of PCORI's mission and approach
- Patients and other stakeholders included as partners in research
 - Share knowledge and perspectives
 - Enhance relevance, usefulness, and uptake of research results

Patient-centeredness vs. engagement

- Patient-centeredness: Study questions, interventions, outcomes, etc. are important to patients
- Engagement defined as “meaningful involvement of patients, caregivers, clinicians, and other healthcare stakeholders throughout the entire research process—from planning the study, to conducting the study, and disseminating study results.”
 - Engagement can help ensure patient-centeredness of study design, conduct, and dissemination



V O I C E

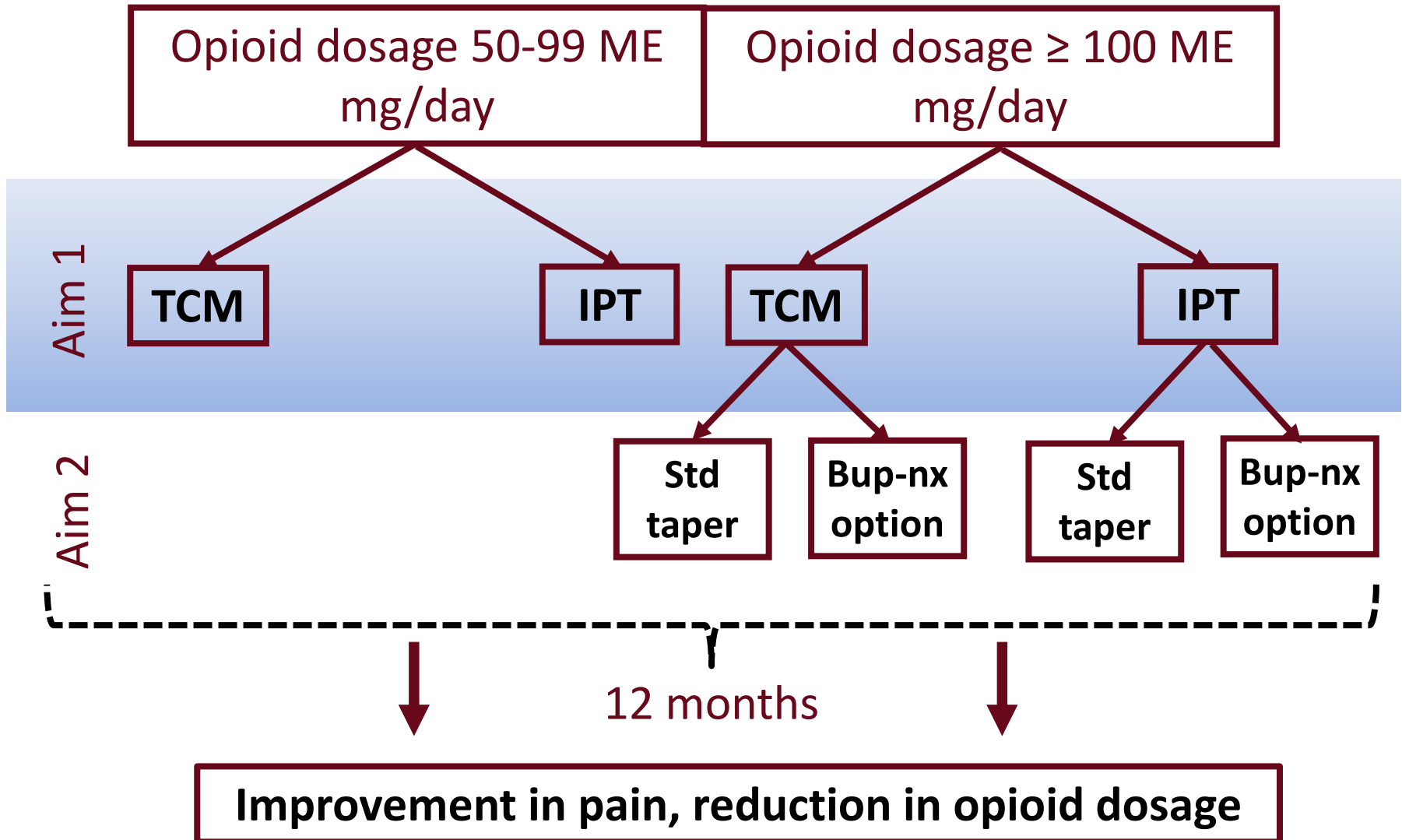
Veterans' Pain Care Organizational Improvement Comparative Effectiveness Study

- Randomized trial of pain care strategies for VA patients with moderate-severe pain despite long-term high-dose opioids
- Aim 1: To compare two pain care models (low intensity vs. higher intensity) for improving pain and reducing opioid use
- Aim 2: To test effect of *offering* rotation to buprenorphine-naloxone (Suboxone)

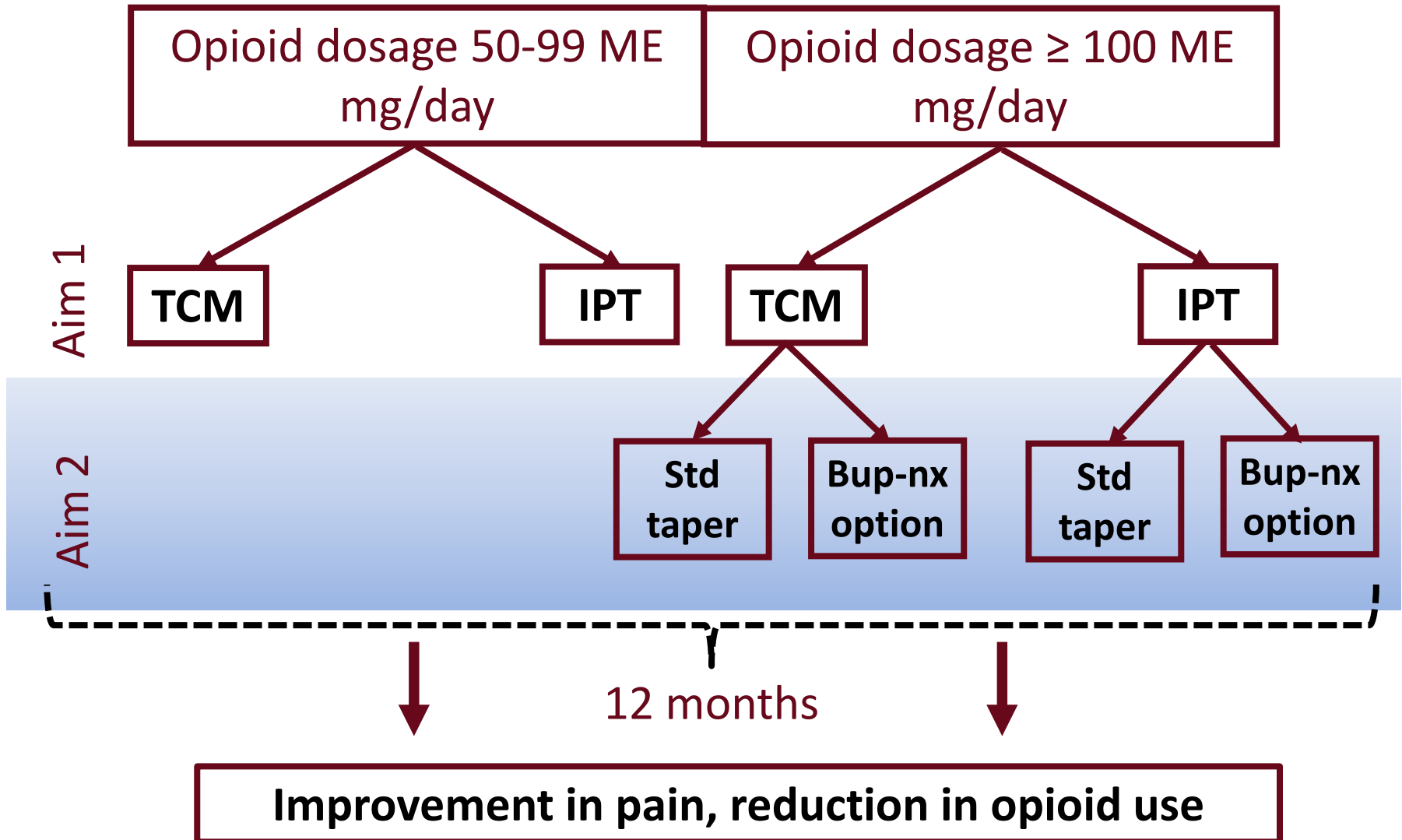


Funded by PCORI OPD-1511-33052 and supported by VA resources and facilities

Veterans with moderate-severe pain despite high-dose opioids



Veterans with moderate-severe pain despite high-dose opioids



Patient-centeredness in VOICE

- Audience for research question = clinical leaders
- Interventions are patient-centered because they employ individualized pain care and patient-centered communication strategies
 - Cited literature, professional experience, and patient partner advice
- Outcomes are patient-centered because they are highly important to patients with chronic pain
 - Cited literature

Importance of patient engagement for VOICE

- Clinicians and patients not necessarily on the same page about appropriateness/safety of pain management options
 - Patients often don't have access to good information about their options
- Opioid reduction is a sensitive topic for many patients

Engagement in VOICE

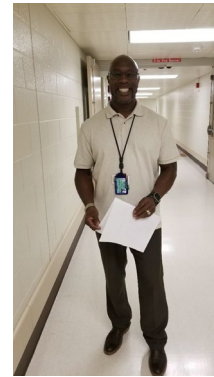
- Proposed development of 3 engagement panels (patient, clinician, and leadership) after funding
- Discussed proposal with 2 existing patient panels to get initial feedback; 2 VA patients from those groups agreed to be named as partners on proposal (and eventually joined VEP)
- Discussed proposal with key VA leaders and obtained high-level letters of support

Veteran Engagement Panel (VEP)

- VEP was formed in start-up phase of study
 - Each study site disseminated information to potentially interested Veterans
 - Sought Veterans with pain experience who wanted to share opinions and collaborate in a team with researchers
 - Candidates completed a short application, followed by a 30-minute phone interview
- VEP members are paid consultants to VOICE
 - 5 year commitment, up to 4 hours/month
 - Professional relationship (not patient-doctor relationship) with research team

VOICE VEP

- 10 Veterans (from 7 of 9 sites)
- 5 women and 5 men
- All have personal experience with pain and VA care
- Selected for diverse personal characteristics, life experiences, and branches/eras of military service



VEP activities

- In-person meeting in Minneapolis (2017)
 - Orientation, introduction, co-learning
- Monthly telephone meetings
 - Structured agenda, reports, interaction
- Review of patient-facing study documents
- Participation in local site visits
- Participation in workshops and research presentations (UMN engagement presentation; PCORI national meeting)
- Collaboration on informational materials

How to Taper an Opioid Medication

Insights for Veterans on when and how to slowly stop taking pain medication with the help of your medical team

Special Approaches to Tapering: Buprenorphine

A series of painful back injuries landed Navy veteran Jamie Cochrane, 66, into a local emergency room in October 2014, and prompted doctors to prescribe high-dose Oxycontin for pain relief.

After three months, his team of physicians at the VA in West Haven, Conn., urged him that it was time to dial back the amount he was taking. But because of their



Is PCORI for you?

- Are you willing to work with your PCORI program officer throughout the research process?

PCORI funds contracts, not grants

- PCORI actively manages contracts and holds PIs accountable to milestones and deliverables
- Protocol and personnel changes require prior approval

Yes, PCORI is for me!

- To develop a competitive proposal, all the usual advice applies
- In addition...
 - Demonstrate patient-centeredness
 - Develop a strong engagement plan
- Unique aspects of PCORI merit review
 - Patient-centeredness and engagement are criteria
 - Patient and stakeholder reviewers are included on review panels

Unique Review Criteria and Patient and Stakeholder Reviewers: Analysis of PCORI's Approach to Research Funding



Laura P. Forsythe, PhD, MPH^{1,*}, Lori B. Frank, PhD¹, A. Tsahai Tafari, PhD¹, Sarah S. Cohen, PhD, MS², Michael Lauer, MD³, Steven Clauser, PhD¹, Christine Goertz, D.C., PhD⁴, Suzanne Schrandt, JD^{1,5}

- Study of PCORI merit review outcomes
 - How do scientist, stakeholder, and patient reviewers influence scores/funding?
 - How do technical merit vs. other criteria influence scores/funding?
- Included 1312 applications from 5 funding cycles
 - Predictors: pre-discussion scores by reviewer type
 - Outcomes: final scores, funding

Unique Review Criteria and Patient and Stakeholder Reviewers: Analysis of PCORI's Approach to Research Funding



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- Overall, 51% were discussed, 9% funded
- The strongest predictor of final scores for all reviewer types was pre-discussion scientist rating of technical merit
- Predictors of funding
 - Scientist ratings of potential to improve health care, technical merit, patient-centeredness
 - Patient ratings of potential to improve health care
 - Stakeholder ratings of potential to improve health care

PCORI proposal pearls

- Put patient-centeredness up front and weave throughout proposal
 - Major component of the rationale (significance)
 - Address patient-centeredness throughout methods
- Focus on the science
 - Strong comparative effectiveness design
 - Strong statistical plan (e.g., power)
 - Strong evidence of feasibility
- Start work on engagement plan early
 - For most proposals, quality of plan is more important than pre-established engagement relationships

Thank you! Questions?

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