Pain/Opioid CORE: Works in Progress

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Pain/Opioid CORE Investigators and Partners

Principal Investigators

- **Alicia Heapy, PhD**; Pain Research, Informatics, Multimorbidities, and Education (PRIME) Center of Innovation, VA Connecticut
- **William Becker, MD**; Pain Research, Informatics, Multimorbidities, and Education (PRIME) Center of Innovation, VA Connecticut
- **Erin Krebs, MD, MPH**; Center for Care Delivery and Outcomes Research (CCDOR), VA Minneapolis

Partners

- **Dr. Friedhelm Sandbrink**, National Director, Pain Management, Opioid Safety, Prescription Drug Monitoring
- **Dr. Benjamin Kligler**, National Director, Integrative Health Coordinating Center
- **Dr. Joseph Liberto**, National Mental Health Program Director, Substance Use Disorders
- **Dr. Francesca Cunningham**, Director of VAMedSAFE, Pharmacy Benefits Management
- **Dr. Robert Kerns,** Partner Group Chair, Yale University

What is a CORE?

HSR&D has funded four COREs: 1) Suicide Prevention, 2) Pain/Opioid, 3) Access, and 4) Virtual Care

The goal of each Consortium for Research (CORE) is to support and accelerate collaborative research that will lead to measurable improvements in the care delivered to Veterans in each of these areas by developing:

a prioritized set of research goals informed by a review of current research, gaps in existing research, and the needs of the Veterans Health Administration, and

a collaborative network of researchers to achieve those goals.

CORE Do Not

- Determine VA's research or operational funding priorities (though HSR&D or Partners may choose to be informed by CORE recommendations)
- Act as gatekeepers to HSR&D or operational funding, or to program offices
- Write letters of support for IIRs/CDAs/grants
- Serve as consultants tasked with doing evaluation work for operational Partners (though CORE may help facilitate the formation of partnerships with operations to complete this work)

Pain/Opioid CORE Mission and Goals

Foster high-quality, high-impact and Veteran-centered research focused on improving pain care and reducing opioid harms by building a network of researchers and promoting multidisciplinary, cross-institutional research collaborations.

- Develop research network and cultivate partnerships
- Identify priority research areas
- Develop mentoring structures for early career investigators
- Disseminate pain and opioid relevant findings to patients, Partners and researchers

Areas of Focus

- Interventions for pain
- Pain care delivery models
- Pain and opioid-related practice and policy initiatives
- Management of opioid dependence and opioid use disorder

Strategic Plan: Main Activities

Identify priority research areas

Portfolio review of VA, NIH, PCORI funded studies

Delphi consensus study

VA Evidence Synthesis Program (ESP)

Developing and further cultivating partnerships

Partner and Internal Leadership Committees

CORE Veteran Engagement Panel (VEP)

Building a research network

Strategic priority area work groups

Rapid pilot projects

Identify tools and interventions ready for wider implementation

Mentorship resources for early career researchers

Disseminating impacts

Infographics for high impact research

CORE Work Groups

Domain-based work groups to promote scientific study in priority areas.

- Medication for Opioid Use Disorder (MOUD) Implementation (Chair: Adam Gordon, MD)
- MOUD Use in Perioperative Care (Co-Chairs: Thomas Hickey, MD and Will Becker, MD)
- Mentorship of Junior Researchers Studying Pain and/or Opioids (Chair: Mathew Bair, MD)
- Heterogeneity of Treatment Effects in Pain- and Opioid-Related Research (Chair: Kelli Allen, PhD)
- OUD in Long-Term Opioid Therapy Diagnostic Challenges (Co-Chairs: Sara Edmond, PhD, William Becker, MD).

- For more information or to get involved in a Work Group, contact Brian Coleman, DC at brian.coleman2@va.gov

Rapid Start Funding Program

- Support research in our pain/opioid priority areas defined by Partners and recent HSR&D State of the Art Conferences on non-pharmacologic pain treatment and opioid safety
  - Becker, W.C., Krebs, E.E., Edmond, S.N. *et al.* A Research Agenda for Advancing Strategies to Improve Opioid Safety: Findings from a VHA State of the Art Conference. *J Gen Intern Med.* **35,** 978–982 (2020). https://doi.org/10.1007/s11606-020-06260-9
  - Becker, W.C., DeBar, L.L., Heapy, A.A. *et al.* A Research Agenda for Advancing Non-pharmacological Management of Chronic Musculoskeletal Pain: Findings from a VHA State-of-the-art Conference. *J Gen Intern Med.* **33,** 11–15 (2018). https://doi.org/10.1007/s11606-018-4345-6
- Fund projects of up to one year that are likely to meaningfully inform future applications for funding as a VA study or answer priority questions
- Preference for early career investigators and investigators not located at HSR&D Centers of Innovation (COINs)

Rapid Start 2020 Awardees

- Feasibility, Pain and Functional Outcomes of a Novel Mixed Reality Based System to Manage Phantom Pain for Patients with Lower Limb Amputation **PI: Thiru Annaswamy, MD; North Texas VA**
- A Modified Hub and Spoke Model to Improve Access to MOUD **PI: Gregory Beehler, PhD; VA Western New York Center for Integrated Healthcare**
- Development of a Virtual Reality Toolbox for Chronic Pain Self-Management Among Veterans **PI: Christopher Fowler, PhD; James A. Haley Veterans' Hospital, Tampa**
- VHA Clinician Attitudes and Practice Regarding Buprenorphine Treatment and Impact on Patient Outcomes in Veterans with Opioid Use Disorder **PI: Allison Lin, MD; VA Ann Arbor**
- Understanding Primary Care Experience for Homeless-Experienced Veterans with Cooccurring Pain and Addiction **PI: Allyson Varley, PhD; Birmingham VA**

Rapid Start 2021

- We are interested in:
  - Applications that support HSR&D career development applications or other submissions that focus on Veteran populations
  - Applications that promote collaborations with clinical and/or operational partners on topics that are a high priority for them
  - Secondary analysis of previously collected data
- Principal investigators must have a minimum 5/8ths VA appointment
- If the applicant is a fellow, there must be a mentor with a 5/8ths VA appointment
- Project budgets range from $10,000-$30,000
- Projects should be completed within 1 year
- FY2021 Rapid Start: Submission deadline March 15, 2021
- RFA to be released February 3, 2021

For more information or to receive the RFA, contact Brian Coleman, DC at brian.coleman2@va.gov

Delphi Study Examining Challenges of Applying DSM-5 Opioid Use Disorder Criteria among Patients on Long-term Opioid Therapy for Pain

Effective Management of Pain and Addiction:
Strategies to Improve Opioid Safety
A VA Health Services Research & Development Service
State of the Art Conference

Background

- CDC and VA/DoD Guidelines: If benefits do not outweigh harms of continued opioid therapy, optimize other therapies and work with patients to taper to lower dosages or discontinue opioids.
- Many patients on long-term opioid therapy (LTOT) for whom benefit no longer outweighs harm do not neatly fit the Diagnostic and Statistical Manual – 5 (DSM-5) Opioid Use Disorder (OUD) criteria
- These challenges well-described in the literature: P Compton, S. Savage, J. Ballantyne, M. Sullivan, A. Manhapra, W. Becker among others

DSM-5 OUD Criteria

1. Opioids are often taken in larger amounts or over a longer period than was intended.
2. There is a persistent desire or unsuccessful efforts to cut down or control opioid use.
3. A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.
4. Craving, or a strong desire or urge to use opioids.
5. Recurrent opioid use resulting in a failure to fulfill major role obligations at work, school, or home.
6. Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.
7. Important social, occupational, or recreational activities are given up or reduced because of opioid use.
8. Recurrent opioid use in situations in which it is physically hazardous.
9. Continued opioid use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance.
10. Exhibits tolerance*
11. Exhibits withdrawal*

Background

- Some experts believe creating a new diagnostic entity may:
  - Improve understanding of epidemiology
  - Facilitate clinical research
  - Improve clinical management and outcomes
  - Decrease overuse of/misapplication of OUD diagnosis
  - Increase focus on sub-optimal pain care
- Other experts believe a separate diagnostic entity is not needed and may in fact be harmful
- During SOTA XV (Sept. 2019):
  - Especially in era of long-term opioid therapy de-implementation, challenges may be intensifying
  - Definitional problems complicating clinical, research, policy matters
  - Delphi Study proposed

Delphi Methodology

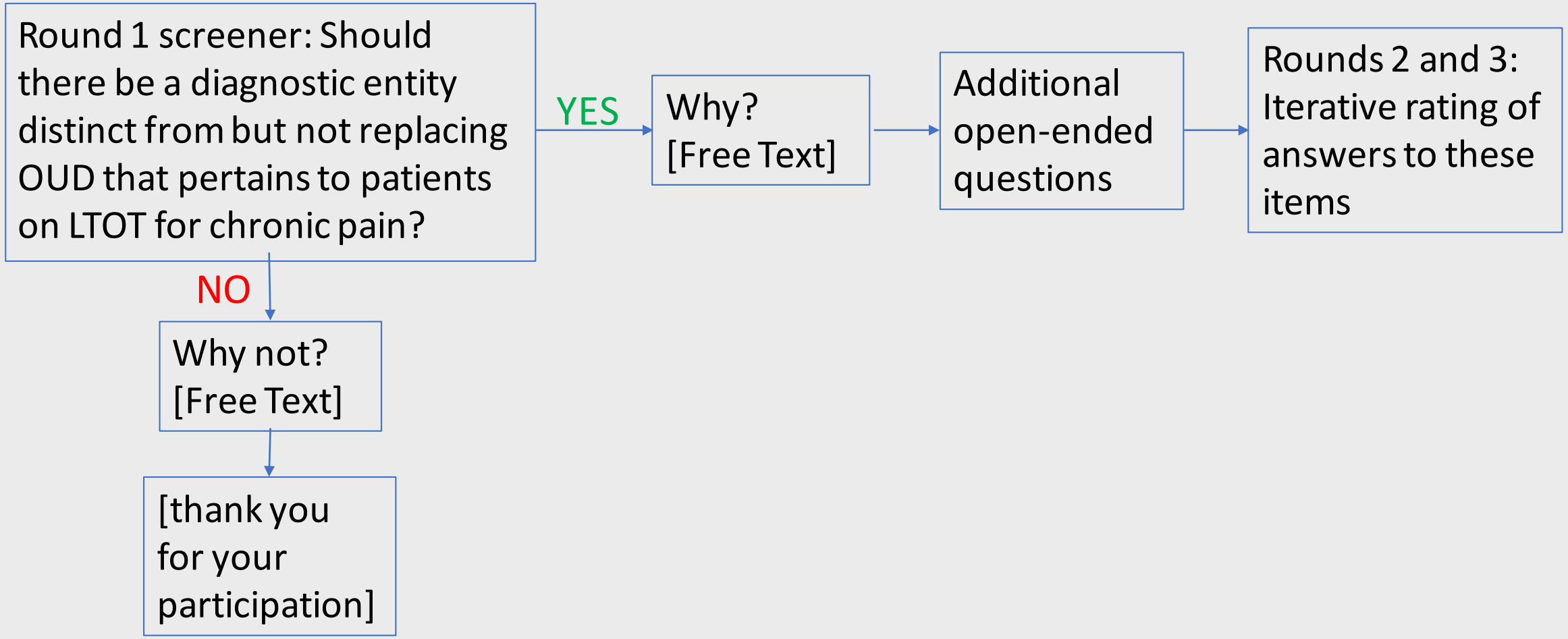
- Developed by RAND
- Exploration and generation of consensus
- Convening subject matter experts
- Anonymous input, iterative rounds
- Sharing of input, voting, molding consensus when possible

Methods

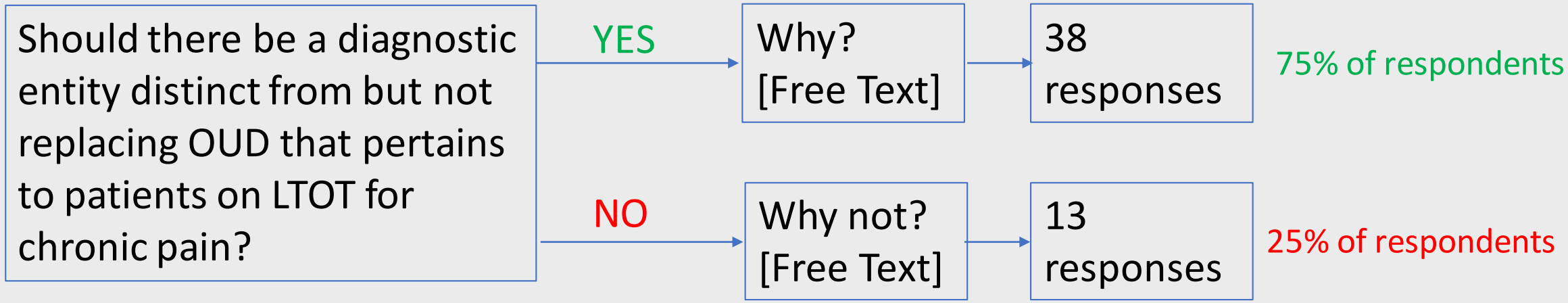
- Designed 3-round online survey with multidisciplinary input

- Delphi Panel formation/survey roll-out:
  - Invited *invitees* to SOTA XV: 60 multidisciplinary experts in ≥3: Pain, LTOT, OUD, MOUD, Research
  - 51 accepted (and partially completed Round 1)→44 completed all of round 1→31 "Screened in" to Round 2→23 completed round 2→21 completed round 3

Survey rounds



Round 1 Screener



- Used rapid qualitative analysis to summarize data and compile a thematic codebook.
- Performed thematic coding and analyses to distill findings and identify representative quotes
- Analysis still in progress.

Round 1 Screener : Qualitative Results

“Pro” Themes

- A new entity would facilitate research and access to treatment
- Patients with Condition X present differently from patients with OUD:
  - The behavioral and social consequences of opioid use for this population are distinct from the consequences described in DSM-5
  - It is difficult to determine if problems are caused by pain or by opioids

Round 1 Screener: Qualitative Results

"Pro" Quotes

- *"[LTOT patients] are not good fits for traditional evidence-based addiction treatment because they don't fit the profile of patients with OUD who have been studied. We need a new category so we can better understand these patients and create, evaluate, and disseminate better treatments for them."*

- *"The current OUD diagnosis does not adequately capture the range of presentations that are encountered in clinical practice. While some may clearly meet the current criteria, others fall into more of a 'gray' zone that is nuanced, where no current label fits well or is helpful in conducting optimal patient care."*

Round 1 Screener: Qualitative Results

"Con" Themes

- OUD and "Condition X" are biologically indistinguishable
- A new entity would worsen stigma for patients with OUD
- There are better ways to address the issues with LTOT and OUD
  - Modify DSM-5 criteria
  - Address stigma directly
  - Conduct more research to see if these symptoms are truly distinct from OUD

Round 1 Screener: Qualitative Results

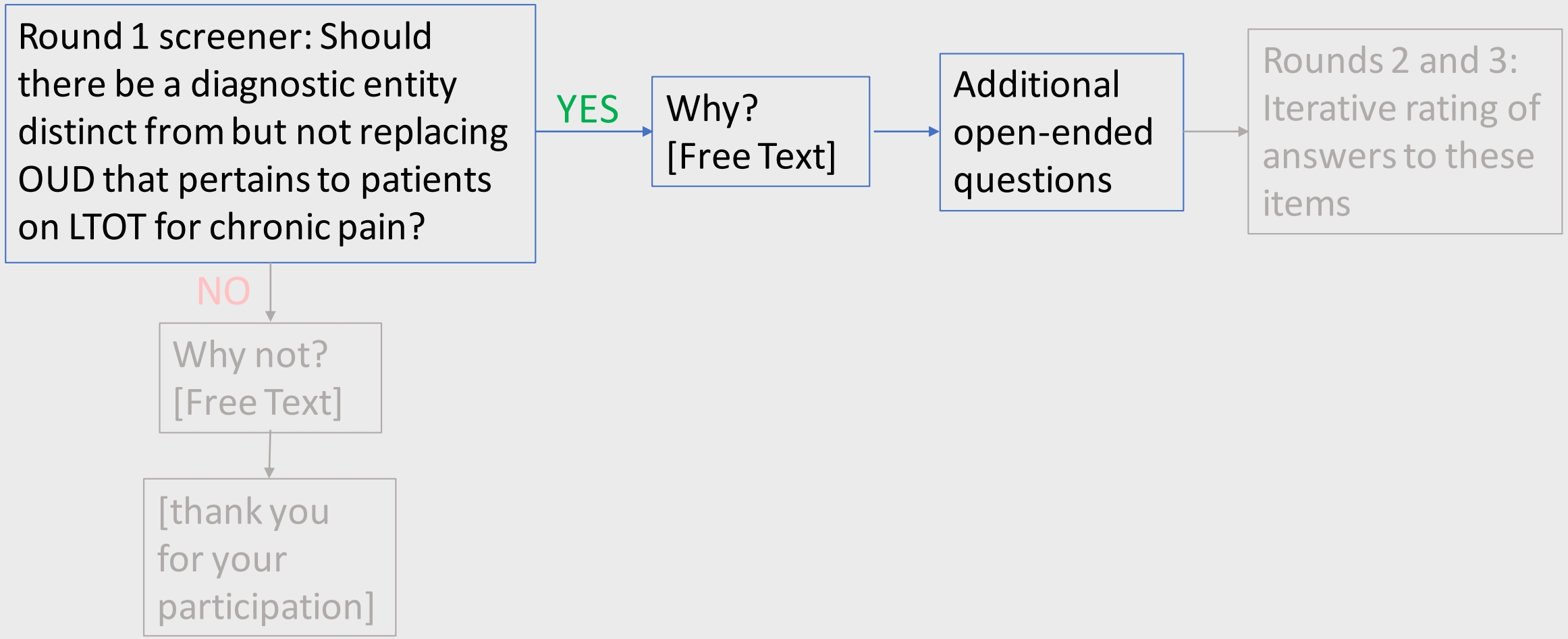
“Con” Quotes

"From a brain perspective, it shouldn't make a difference whether opioids are prescribed or illicit, if a use disorder develops there is something going on that requires a diagnosis and treatment.”

“Rather then coming up with new diagnostic labels, I feel providers need to take the time to honestly explain to their patients the iatrogenic effects of long-term opioids...”

“Perhaps we could draft different 'Consequences' for people with complex dependence and remove the exclusion of tolerance and withdrawal.”

Round 1 Methods



Round 1 Methods

Open-ended questions included:

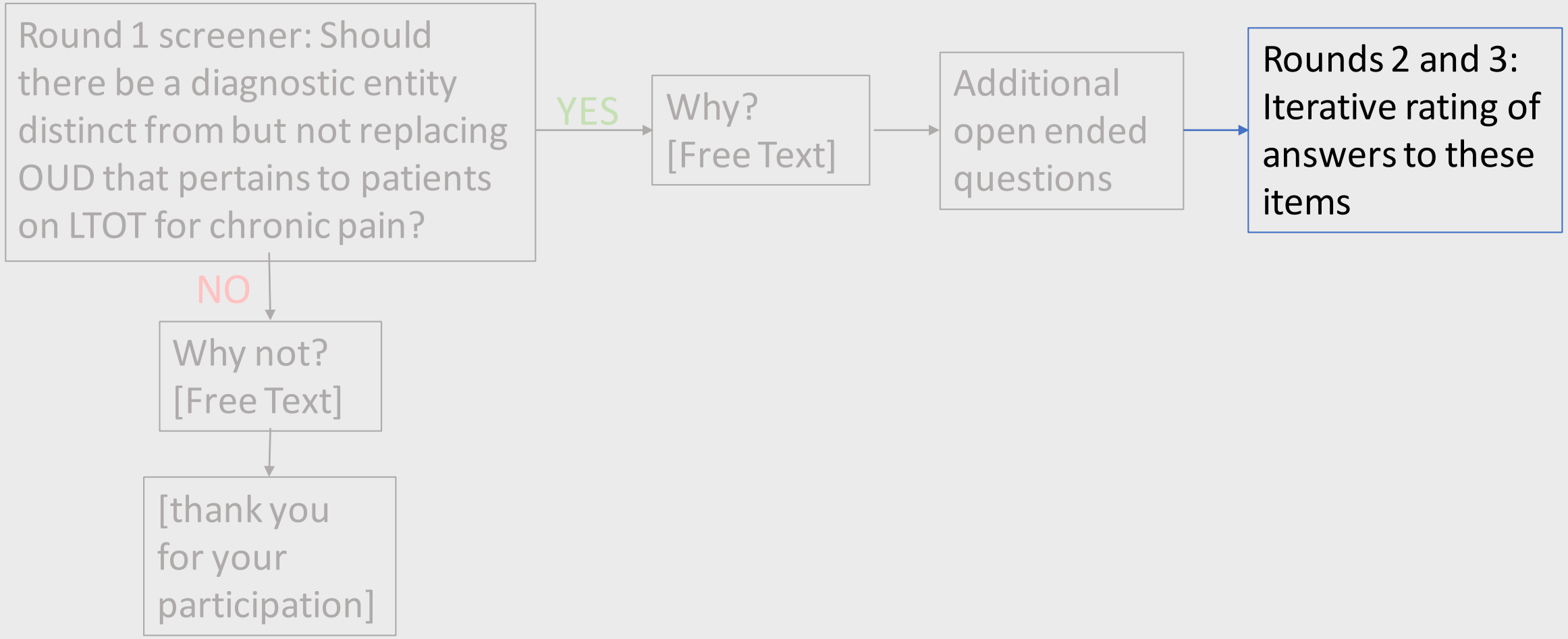
- Please describe a person who would be diagnosed with Condition X (How did he or she present? What were they prescribed? How did the treatment course go? What behaviors manifest themselves over time? How is this person different from a person with OUD)?
- How would you differentiate Condition X from OUD?
- Please complete the sentence “Condition X is defined as ____”
- Please list the diagnostic criteria for condition X:
- Additional questions about gradations of severity, relationship between Condition X and OUD, treatment options, and potential names

Round 1 Results → Round 2 Survey

Used Rapid Qualitative Analysis to summarize free text, open-ended answers and identify distinct concepts; performed a content analysis to assess concept concentration and generate potential diagnostic criteria. We generated 31 potential criteria; the most common potential criteria included:

- Chronic pain, prescribed LTOT
- Poor functioning and/or LTOT is not working well
- Difficult tapering (patient is resistant, patient deteriorates when a taper is attempted, inability to taper)
- Patient beliefs contribute to the maintenance of LTOT (belief that nothing else works, desire to continue taking opioid despite lack of benefit and/or identified harms)
- Tolerance, withdrawal

Survey rounds



Round 2 Methods

To what extent do you agree that each of the following features/criteria should be included as a criterion/feature of Condition X?”

1	2	3	4	5	6	7
Strongly Disagree	Disagree	Somewhat disagree	Neither agree nor disagree	Somewhat agree	Agree	Strongly Agree

- LTOT is ineffective (e.g., pain or functioning is not improving or is worsening)
- Benefits of LTOT no longer outweigh harms (CDC language)

Even if your scores already reflect it, if you prefer one of the above items, please indicate it here:

If you agree the concept should be captured but prefer a different wording, please provide your preferred wording here:

Other comments on these features:

Round 2 Results

Most highly endorsed criteria included:

- Benefits of LTOT no longer outweigh harms
- Difficulty tapering: when a taper is attempted, patient exhibits psychological or physical symptoms (e.g., withdrawal, pain flare, depression)
- Does not meet criteria for OUD per DSM-5, i.e., does not have at least 2 DSM-5 criteria not including tolerance and withdrawal caused by opioid use
- Exhibits opioid tolerance (e.g., may ask for a higher dose, with motivation seeming to be a desire for pain control, or dose was escalated over time by a provider and then maintained at a high dose)

Round 2 Results

Participants were split 50/50 on the question: “Do you believe Condition X and OUD can co-occur?”

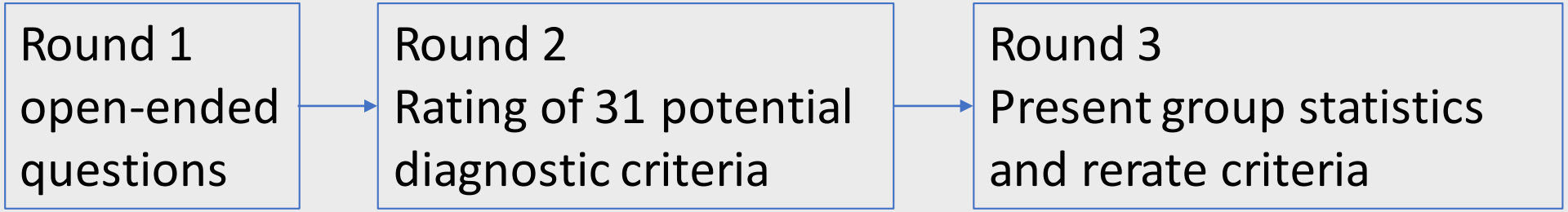
Well-liked names included:

- Iatrogenic Opioid Dependence
- Prescription Opioid Dependence
- Complex Persistent Opioid Dependence

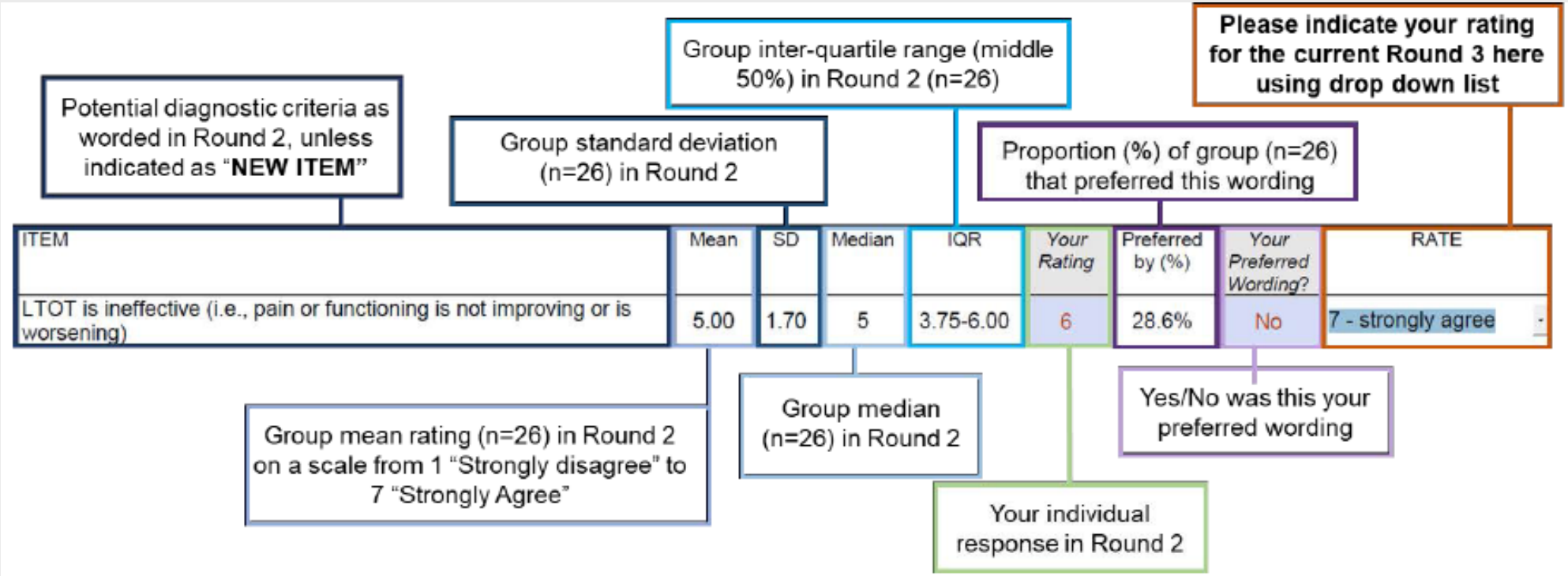
…but participants had feedback on the pros and cons to many name choices.

Round 3 Methods

- Added 3 items based on qualitative feedback in Round 2
- Presented group statistics (Mean, SD, Median, IQR) along with individual response from Round 2
- Asked participants to re-rate responses
- *Analysis still in progress!*



Round 3 Methods



ITEM	Mean	SD	Median	IQR	*Your Rating*	Preferred by (%)	*Your Preferred Wording?*	RATE
LTOT is ineffective (i.e., pain or functioning is not improving or is worsening)	5.00	1.70	5	3.75-6.00	6	28.6%	No	
Benefits of LTOT no longer outweigh harms	5.63	1.53	6	5.00-7.00	7	71.4%	Yes	

Planned products/next steps

- Delphi protocol paper
- Pro/Con paired essays re: round 1 screening question
- Qualitative analysis of Why/Why Not free text answers to Round 1 screening question
- Main Delphi results (Rounds 1, 2, and 3)

- Smaller workgroup to enumerate research priorities and clinical recommendations regarding “Condition X,” including stakeholders such as patients

Questions/Comments?

Veteran Engagement Panel (VEP)

VEP recruitment

- Goal: diverse, national panel of Veterans who have personal experience with at least one focus area:
  - Chronic or persistent pain
  - Opioid pain medications
  - Opioid addiction or suboxone
- Application process
  - Written statement of interest
  - Telephone interview with CORE engagement staff

Paid Opportunity to Improve Research on Pain & Opioids

Benefits to Veteran Community:

- Share your opinions about research ideas and studies in progress
- Ensure research studies consider Veterans' input and opinions
- Have a meaningful influence on how research is done and shared

Who Can Participate?

- Veterans who have personal experience with chronic pain, opioid pain medication and/or opioid addiction and have used VA healthcare
- We are particularly interested in hearing from women and are seeking racial and ethnic diversity

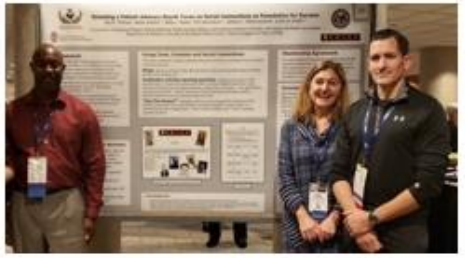
What will you do?

Attend monthly meetings by phone

Attend 2 meetings in person at the Minneapolis VA (travel costs will be paid)

Duration: 4 years

You will be paid for your time: $50/per hour



You will be a part of a panel and your opinion will contribute critical direction for developing research studies. Veterans will work alongside researchers **not as a research subject**, but **as a team member** to build innovative research and improve VA healthcare and help your fellow Veterans.

If you are interested in learning more, please

VEP members

- 12 members selected by CORE leadership consensus
- Reside in 9 states
- Experience with 2-3 focus areas
- Varied professional, work, & volunteer experiences

Characteristic	Number (%)
Men	7 (58%)
White	6 (50%)
Age group	
<40	2 (17%)
41-55	5 (42%)
>55	5 (42%)
Experiences	
VA health care use	10 (83%)
Chronic pain	11 (92%)
Opioid use	11 (92%)
OUD	5 (42%)

Panel development process

- COVID-19 delay → 5 hours of virtual orientation in summer/fall 2020
- Orientation content
  - Introductions
  - Technology review, completion of membership agreements
  - Overview of VA research, CORE goals, and CORE stakeholders
  - Discussion of medical research regulation/constraints
  - Development of group norms and privacy/confidentiality expectations
  - Practice effective feedback/communication approaches
  - Evaluation and reflection

Process for working with VEP

Initial planning

- Researcher & CORE staff meet & work together to develop key questions for VEP

VEP session prep

- CORE staff writes facilitation guide
- Researcher & CORE staff do dry run, finalize materials

VEP meeting

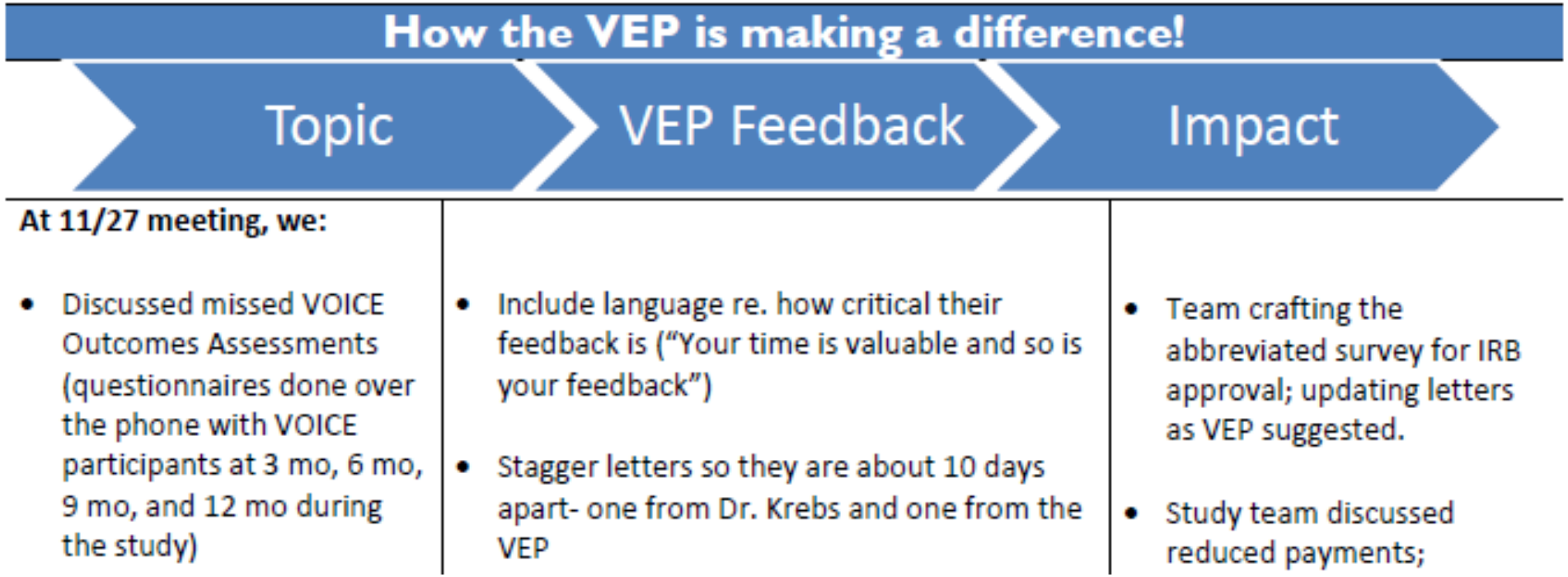
- CORE staff facilitates and researcher attends
- CORE staff provides notes/executive summary to PI

Pre-VEP planning questions

- What kind of feedback do you want?
  - Overall research plan or idea?
  - Plan for how to recruit people for your study?
  - Recruitment materials (flyers, brochures, etc.)?
  - Survey, focus group or interview questions?
  - Review of consent form?
  - Review of health education information?
  - Feasibility/acceptability of methods, from a patient's perspective?
  - Dissemination of research findings?
- Why are you PERSONALLY interested in this area of research? What makes you passionate about this project?
- Who do you want to enroll in your study?
- What will you ask people in your study to do? (limit to 4 key points)
- Why might people want to join your study?

Post-VEP feedback loop

EXAMPLE



Adapted with permission from materials developed by the Wisconsin Network for Research Support, https://winrs.nursing.wisc.edu/

Completed VEP project reviews

- Recruitment phone script (Will Becker, Connecticut VA)
- Decision aid for pain options (Marianne Matthias, Indy VA)
- Recruitment materials (Erin Reilly, Bedford VA)
- ANNIE text messaging (Una Makris, Dallas VA)

Next steps for Pain/Opioid CORE VEP

- Continue consultation on individual investigator projects and VACO pain management initiatives
  - Encourage participation of CORE rapid start project investigators
- Collaborate on website content (featuring VEP bios)
- Support CORE translation/dissemination efforts

Questions? Comments? Ideas for VEP review?