Board of Governors Meeting
via Teleconference/Webinar

July 19, 2016

12:00-2:00 p.m. ET

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PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Welcome and Introductions

Grayson Norquist, MD, MSPH
Chairperson, Board of Governors

Joe Selby, MD, MPH
Executive Director

Agenda

Time	Agenda Item
12:00	Call to Order, Roll Call, and Welcome
12:00 – 12:05	**Consider for Approval:** Minutes of the June 21, 2016 Board Meeting
12:05 – 1:05	**Consider for Approval:** Proposed Slates for 4 Targeted PFA Awards
1:05 – 1:15	**Consider for Approval:** Proposed Slate for Cycle 3 2015 Pragmatic PFA Award
1:15 – 1:40	**Consider for Approval:** Proposed Slate for Cycle 3 2015 Broad PFA Awards
1:40	Wrap up and Adjournment

Board Vote

Call for a Motion to:	• **Approve** the minutes of the June 21, 2016 Board meeting
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Voice Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Award Slates from Targeted PFAs

Christine Goertz, DC, PhD
Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH
Chief Science Officer

Cycle 3 2015 Targeted PFAs

- Treatment-Resistant Depression
- Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain
- New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease
- Treatment of Multiple Sclerosis

Pathway to a Funding Announcement

Staff use Tier 1 and Tier 2 review criteria to determine topic eligibility, producing List 1

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Science Oversight Committee (SOC) reviews and endorses topics for topic briefs, producing List 2

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SOC reviews topic briefs and approves them for Advisory Panel review, producing List 3

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Advisory Panel (AP) reviews topic briefs using Tier 3 review criteria, producing List 4

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SOC reviews AP results and staff recommendations; endorses topics for further refinement, producing List 5

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Staff and SOC use Tier 4 review criteria to assess questions; SOC assigns questions to targeted or Pragmatic Clinical Studies PFA, producing Lists 6 and 7

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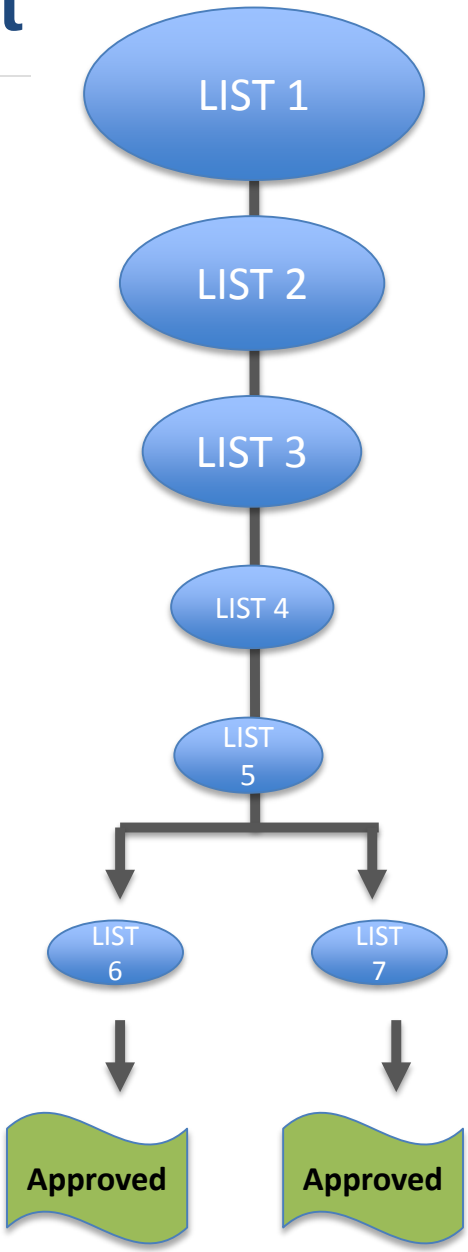
Board reviews and approves questions for targeted PFA

SOC reviews and approves questions for Pragmatic Clinical Studies PFA



Treatment-Resistant Depression

Objective of the PFA

- To address important knowledge gaps regarding the management of treatment-resistant depression

- Priority Research Question:
  - For patients with treatment-resistant depression who have failed two adequate trials of antidepressant medications, what is the comparative effectiveness of augmentation strategies versus switching to other treatments?

- Funds Available: up to $30M

Slate Overview

Process Overview

- 10 Letters of Intent (LOIs) submitted
- 7 LOIs invited to submit a full application (70%)
- 7 applications were received (100% of invited LOIs)
- We are proposing to fund 3 applications* out of 7 received applications (43%)

*Recommended by the Selection Committee

Treatment-Resistant Depression

*3 Recommended Projects**

Project Titles
Electroconvulsive Therapy vs. Ketamine for Severe Resistant Depression
Switching vs. Augmentation in Treatment-Resistant Depression
Optimizing Outcomes in Treatment-Resistant Depression in Older Adults

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Project 1: Electroconvulsive Therapy vs. Ketamine for Severe Resistant Depression

- **Research Question:**
  - What is the comparative effectiveness of electroconvulsive therapy (ECT) vs. ketamine treatment for outpatient treatment-resistant depression (TRD) patients?
- **Population:**
  - Patients aged 18-70 years old with TRD referred for ECT treatment across 4 sites
- **Intervention:** Ketamine infusion treatment
- **Comparator(s):** ECT
- **Outcomes of Interest:**
  - Primary: Treatment response rate
  - Secondary: Depression severity (clinician-rated), changes in self-reported memory impairment and quality of life, psychiatric symptom scores; cognitive and memory assessment
- **Study Design:** Randomized clinical trial, non-inferiority design
  - Sample Size: 400 patients (4 sites)
- **Length of Follow-up:** 6 months

Project 1: Electroconvulsive Therapy vs. Ketamine for Severe Resistant Depression (cont.)

- **Engagement:**
  - Multiple stakeholders were engaged during the planning process (patients, patient advocacy organizations, and third-party payers). These stakeholders will actively participate during study conduct and dissemination
- **Potential Impact:**
  - Evidence from this study supporting the effectiveness of ketamine treatment for treatment-resistant depression could lead to rapid adoption for patients who currently have few treatment options other than electroconvulsive therapy

Project 2: Augmentation vs. Switching Strategies

- **Research Question:** What is the comparative effectiveness, safety, and tolerability of two augmentation strategies with a switching strategy for patients with treatment-resistant depression?
- **Population:** Adults ages 18-80 years old who meet criteria for treatment-resistant depression at specialty clinics across 10 study sites
- **Intervention:** Augmentation or switching in one of 3 treatments arms
- **Comparators:**
  - Arm 1: Augmentation with aripiprazole, an atypical antipsychotic
  - Arm 2: Augmentation with repetitive transcranial magnetic stimulation (rTMS)
  - Arm 3: Switch to venlafaxine, a serotonin-norepinephrine reuptake inhibitor (SNRI)
- **Outcomes of Interest:**
  - Primary: Depression severity (clinician-rated)
  - Secondary: Quality of life; family and social relationships; work productivity, functioning
- **Study Design:** Randomized controlled trial
  - Sample Size: 639 patients
- **Length of Follow-up:** 12 months

Project 2: Augmentation vs. Switching Strategies (cont.)

- **Engagement:**
  - Multiple stakeholders were engaged during the planning process (National Institute of Mental Health (NIMH), U.S. Food and Drug Administration (FDA), hospital administration, pharmaceutical industry, non-researcher clinicians). Advisory board includes patient partners and family members of patients and will be involved in all aspects of study conduct
- **Potential Impact:**
  - Results would provide needed guidance in managing treatment-resistant depression, as no other studies of this size have been done on augmenting and switching strategies for patients who have not responded to two or more antidepressant treatments

Project 3: Optimizing Outcomes in Treatment-Resistant Depression in Older Adults

- **Research Question:** What are the comparative benefits and risks of antidepressant switching strategies (adding and switching) in older adults with treatment-resistant depression (TRD)?
- **Population:** Adults age 60+ years old with TRD at primary care and specialty clinics across 5 sites
- **Intervention:** Add or switch to one of three Step 1 drug pharmacotherapy treatment groups; those who do not improve in Step 1 will continue to Step 2
- **Comparator(s):**
  - Step 1 (N = 1500), 3 arms: adding aripiprazole; adding bupropion; switch to bupropion
  - Step 2 (N = 800), 2 arms: adding lithium; switch to nortriptyline
- **Outcomes of Interest:**
  - Primary: Psychological well-being and remission (depression severity)
  - Secondary: Physical function; social participation; safety (adverse events including falls/fall-related injuries), aging-related variables
- **Study Design:** Randomized controlled trial
  - Sample Size: 1,500 patients
- **Length of Follow-up:** 12 months

Project 3: Optimizing Outcomes in Treatment-Resistant Depression in Older Adults (cont.)

- **Engagement:**
  - Stakeholders will be engaged through the stakeholder advisory board. Patients and health care providers will be engaged through qualitative semi-structured interviews to inform the advisory board and study team
- **Potential Impact:**
  - There is a lack of evidence-based treatment strategies for managing treatment-resistant depression in older adulthood. The current study will provide evidence to address a major public health problem for the country's growing population of older adults

Treatment-Resistant Depression

*3 Recommended Projects**

3 Projects

PFA	Allotted	Proposed Total Budget*
Treatment-Resistant Depression	**$30M**	**$39.9M**

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2015 Treatment-Resistant Depression PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain

Objective of the PFA

- This funding initiative addresses important questions regarding clinical strategies for managing and reducing long-term opioid use of chronic pain

- Priority Research Questions:
  - Among patients with chronic non-cancer pain on moderate/low-dose long-term opioid therapy, what are the comparative effectiveness and harms of strategies used to limit dose escalation?
  - Among patients with chronic non-cancer pain on moderate/high-dose long-term opioid therapy, what is the comparative effectiveness of strategies for reducing/eliminating opioid use while managing pain?

- Funds Available: up to $40 million

Slate Overview

Process Overview

- 28 Letters of Intent (LOIs) submitted
- 20 LOIs invited to submit a full application (71%)
- 18 applications were received (90% of invited LOIs)
- We are proposing to fund 2 applications* out of 18 received applications (11%)

*Recommended by the Selection Committee

Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain

*2 Recommended Projects**

Project Titles
Comparative Effectiveness of Patient-centered Strategies to Improve Pain Management and Opioid Safety for Veterans
A Comparative Effectiveness Randomized Controlled Trial of Mindfulness Meditation versus Cognitive Behavioral Therapy for Opioid-Treated Chronic Low Back Pain

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Project 1: Comparative Effectiveness of Patient-centered Strategies to Improve Pain Management and Opioid Safety for Veterans

- **Research Questions:** What is the comparative effectiveness of two interventions augmenting primary care management of chronic pain patients?
- **Population:** Primary care patients receiving long-term moderate to high-dose opioid therapy for chronic pain at 9 Veterans Affairs (VA) sites
- **Intervention:** Clinical pharmacist-led medication management approach in collaboration with a supervising physician
- **Comparator:** Interdisciplinary pain management team with an emphasis on non-pharmacological pain management approaches
- **Outcomes of Interest:**
  - Primary: Pain severity, opioid daily dose reduction
  - Secondary: Opioid dose escalation, quality of life, adverse effects, fatigue and sleep, mental health, and substance use
- **Study Design:** Randomized controlled trial
  - Sample Size: 1,400
- **Length of Follow-up:** Data collected at baseline, 3, 6, 9, and 12 months

Project 1: Comparative Effectiveness of Patient-centered Strategies to Improve Pain Management and Opioid Safety for Veterans (cont.)

- **Engagement:**
  - Strong engagement by Veterans Affairs (VA) leadership. Veteran and non-VA stakeholder representation on advisory and clinical partner committees
- **Potential Impact:**
  - The study will provide timely evidence on the effectiveness of two different models of integrated, multimodal, interdisciplinary primary care. The sub-study will address the actively debated policy question regarding the role of buprenorphine in management of patients on long-term high-dose opioids for pain

Project 2: A Comparative Effectiveness Randomized Controlled Trial of Mindfulness Meditation versus Cognitive Behavioral Therapy for Opioid-Treated Chronic Low Back Pain

- **Research Question:** What is the comparative effectiveness of mindfulness meditation versus cognitive behavioral therapy on adults with opioid-treated chronic low back pain?
- **Population:** Opioid-treated chronic low back pain patients who are on ≥30 mg/day of morphine-equivalent dose for ≥3 months. Sample will include patients from 7 academic primary care healthcare systems
- **Intervention:** Mindfulness Meditation: 8 weekly, 2 hour group sessions + home practice
- **Comparator(s):** Cognitive Behavioral Therapy: 8 weekly, 2 hour group sessions + home practice
- **Outcomes of Interest:**
  - Primary: Pain severity and physical function
  - Secondary: Quality of life, opioid dose, anxiety, depression, opioid misuse behaviors, pain catastrophizing, pain acceptance, sleep, health care utilization
- **Study Design:** Randomized controlled trial
  - Sample Size: 766
- **Length of Follow-up:** Data collected at baseline, 3, 6, 9, and 12 months

Project 2: A Comparative Effectiveness Randomized Controlled Trial of Mindfulness Meditation versus Cognitive Behavioral Therapy for Opioid-Treated Chronic Low Back Pain (cont.)

- **Engagement:**
  - The patient and family partners have advised on this study since its inception and will continue to be reciprocally engaged as team members throughout the project. Study will include a patient/family advisors group and study advisory committee
- **Potential Impact:**
  - Addresses the critical knowledge gap regarding the effectiveness of non-pharmacologic treatments, specifically the effects of the two treatments among adults with opioid-treated chronic low back pain. This is the first large randomized trial to quantify the impact of a mindfulness meditation intervention on opioid dose

Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain

*2 Recommended Projects**

2 Projects

PFA	Allotted	Proposed Total Budget*
Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain	**$40M**	**$21M**

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2015 Clinical Strategies for Managing and Reducing Long-Term Opioid Use for Chronic Pain PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease

Objective of the PFA

- This initiative addresses important questions comparing alternatives for extended treatment with anti-coagulants (blood thinners) in patients with deep vein thrombosis or pulmonary embolism (types of blood clots) and addresses gaps in high-quality information on the risks and benefits of extending blood thinner treatment beyond three months

- Priority Research Question:
  - How do different strategies for extended anticoagulation (blood thinning) treatment compare for patients who have completed a course of treatment after an initial episode of blood clot in the leg (deep vein thrombosis) or lung (pulmonary embolism)?

- Funds Available: up to $30M

Slate Overview

Process Overview

- 12 Letters of Intent (LOIs) submitted
- 9 LOIs invited to submit a full application (75%)
- 8 applications were received (89% of invited LOIs)
- We are proposing to fund 2 applications* out of 8 received applications (25%)

*Recommended by the Selection Committee

New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease

*2 Recommended Projects**

Project Titles
The Dabigatran, Apixaban, Rivaroxaban, Edoxaban, Warfarin Comparative Effectiveness Research Study (The DARE Warfarin CER Study)
The Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Extended Treatment of Venous Thromboembolism

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Project 1: The Dabigatran, Apixaban, Rivaroxaban, Edoxaban, Warfarin Comparative Effectiveness Research Study (The DARE Warfarin CER Study)

- **Research Question:**
  - How do newer oral blood thinning medications compare to warfarin in terms of safety, effectiveness, and death in the extended treatment of blood clot in the legs or lungs (venous thromboembolism)?
- **Population:**
  - Individuals with an initial episode of blood clot in the deep veins of the leg or lungs and no prior oral blood thinner use who complete 3 months of treatment with an oral anticoagulant and continue on to extended treatment
- **Intervention/Comparators:** Dabigatran, apixaban, rivaroxaban, edoxaban, warfarin
- **Outcomes of Interest:**
  - Primary: Major bleeding, blood clot recurrence
  - Secondary: Death due to any cause
- **Study Design:** Observational cohort study using claims and electronic health record data
  - Sample Size: 416,000
- **Length of Follow-up:** Minimum of 60 days; approximately 2-3 year follow-up (commercial/Medicaid coverage); up to 10-year follow-up (Medicare)

Project 1: The Dabigatran, Apixaban, Rivaroxaban, Edoxaban, Warfarin Comparative Effectiveness Research Study (The DARE Warfarin CER Study) (cont.)

- **Engagement:**
  - Study advisory committee, comprised of national and regional organizations that represent patient interest, including a national multidisciplinary thrombosis organization, were involved in proposal development and will continue to advise the study team throughout the course of the study
- **Potential Impact:**
  - Study will provide insight into the comparative safety and effectiveness of all five oral anticoagulants for the extended treatment of DVT and PE by providing sufficiently powered analyses to understand treatment effect heterogeneity across a number of important subgroups, including age and patients with renal dysfunction

Project 2: The Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Extended Treatment of Venous Thromboembolism

- **Research Question:** What are the benefits and harms of different treatment options for the extended treatment of blood clots in the legs and lungs (venous thromboembolism or VTE)?
- **Population:** Adults with blood clots (VTE) who were treated with blood thinners (anticoagulants) for at least 3 months, enrolled in the participating health systems
- **Intervention/Comparators:**
  - Aim 1: Extended blood thinner treatment versus no extended treatment
  - Aim 2: New oral blood thinners (dabigatran, rivaroxaban, apixaban, or edoxaban) versus warfarin for extended-duration treatment
- **Outcomes of Interest:**
  - Primary: Major bleeding; blood clot recurrence
  - Secondary: Death, quality of life, treatment satisfaction
- **Study Design:** Cohort study (with one-time patient survey)
  - Sample Size: 19,200 patients
- **Length of Follow-up:** Date of initial blood clot through death, loss from the health plan, or end of the study follow-up period; estimated mean follow-up of ~3.8 years

Project 2: The Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Extended Treatment of Venous Thromboembolism (cont.)

- **Engagement:**
  - Proposal developed in conjunction with a national blood clot organization; study advisory committee, consisting of patients, payers, and clinicians will monitor study on quarterly basis
- **Potential Impact:**
  - Information on the relative and absolute effectiveness and safety of different strategies for the extended-duration treatment of VTE will help patients and clinicians to make informed, patient-centered choices

New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease

*2 Recommended Projects**

2 Projects

PFA	Allotted	Proposed Total Budget*
New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease	**$30M**	**$6.5M**

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2015 New Oral Anticoagulants in the Extended Treatment of Venous Thromboembolic Disease PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Treatment of Multiple Sclerosis

Objectives of the PFA

- To fund studies comparing alternative treatments for multiple sclerosis (MS), emphasizing symptoms, quality of life, and functional status outcomes
  - Relapsing, remitting MS is the primary target for disease-modifying therapies (DMTs). PFA included an emphasis on treatment of symptoms and rehabilitation in patients with progressive disease

- Priority Research Questions:
  - What are the comparative benefits and harms of different DMTs or therapeutic strategies in patients with relapsing, remitting MS on symptoms, functioning, quality of life, disease activity, and disease progression?
  - What are the comparative benefits and harms of different approaches, other than DMTs, for ameliorating important symptoms in people with MS?
  - What is the comparative effectiveness of telerehabilitation vs. conventional direct care interventions for improving outcomes in people with MS, such as functional status, fatigue, and quality of life?

- Funds Available: up to $50 million

Slate Overview

Process Overview

- 35 Letters of Intent (LOIs) submitted
- 21 LOIs invited to submit a full application (60%)
- 13 applications were received (62% of invited LOIs)
- We are proposing to fund 4 applications* out of 13 received applications (31%)

*Recommended by the Selection Committee

Treatment of Multiple Sclerosis

*4 Recommended Projects**

Project Titles
A Multi-centric Randomized Pragmatic Trial to Compare the Effectiveness of Fingolimod versus Dimethyl-fumarate on Patient Overall Disease Experience In Relapsing-remitting Multiple Sclerosis: Novel Data to Inform Decision-makers
Rituximab in Multiple Sclerosis -- a Comparative Study on Effectiveness, Safety and Patient-reported Outcomes
Randomized, Double-blind, Crossover, Placebo-controlled Trial of Amantadine, Modafinil, and Methylphenidate for Treatment of Fatigue in Multiple Sclerosis
Comparative Effectiveness Trial Between a Clinic- and Home-Based Complementary and Alternative Medicine Telerehabilitation Intervention for Adults with Multiple Sclerosis

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Project 1: A Multi-centric Randomized Pragmatic Trial to Compare the Effectiveness of Fingolimod vs Dimethyl Fumarate on Patient Experience in Relapsing, Remitting Multiple Sclerosis

- **Research Question:**
  - What is the comparative effectiveness of two oral multiple sclerosis agents on disease activity over 24 months in relapsing, remitting MS (RRMS) patients?
- **Population:** RRMS patients eligible to be treated with either drug with no evidence of disease activity (NEDA) at entry
- **Intervention:** Dimethyl fumarate
- **Comparator:** Fingolimod
- **Outcomes of Interest:**
  - Primary: Improved disease status (time to loss of NEDA status)
  - Secondary: Relapse rate, magnetic resonance imaging (MRI) brain lesions and volume, Expanded Disability Status Scale, self-rated disability, quality of life, cognition, and medication satisfaction
- **Study Design:** Open label randomized controlled trial in 40 centers in U.S. and international locations
  - Sample Size: 1,360 patients
- **Length of Follow-up:** 24 months

Project 1: A Multi-centric Randomized Pragmatic Trial to Compare the Effectiveness of Fingolimod vs Dimethyl Fumarate on Patient Experience in RRMS (cont.)

- **Engagement:**
  - Patients were involved in study concept. Advisory panel will consist of patients, multiple sclerosis advocacy associations, and clinicians
- **Potential Impact:**
  - The study will provide information to assist patients and clinicians in choosing between these two commonly used medications, where there has been no head-to-head trial

Project 2: Rituximab in Multiple Sclerosis: A Comparative Study on Effectiveness, Safety, and Patient Reported Outcomes

- **Research Question:** What is the comparative effectiveness of rituximab compared to other commonly used disease-modifying therapies (DMTs) in terms of long term effectiveness, safety, and patient satisfaction?
- **Population:** Patients with relapsing, remitting multiple sclerosis (RRMS) in health system and international registry
- **Intervention:** Rituximab as escalation or initial therapy
- **Comparators:**
  - Natalizumab and fingolimod in RRMS patients who have switched from other DMTs
  - Interferon beta, glatiramer acetate, and dimethyl fumarate in treatment-naïve multiple sclerosis patients
- **Outcomes of Interest:**
  - Primary: Change in Expanded Disability Status Scale and quality of life over 3 years
  - Secondary: Relapse rate, cognition, disability, treatment satisfaction; brain magnetic resonance imaging (MRI) (subset)
  - Primary safety outcomes: Malignancies, serious infections, and deaths
- **Study Design:** Retrospective/prospective observational cohort
  - Sample Size: 7,501 patients, including 400-1,800 patients on each DMT
- **Length of Follow-up:** at least 3 years

Project 2: Rituximab in Multiple Sclerosis: A Comparative Study on Effectiveness, Safety, and Patient Reported Outcomes (cont.)

- **Engagement:**
  - Includes patients, patient advocates, neurologic organization, national and international multiple sclerosis societies, integrated health system, and Medicare/Medicaid
- **Potential Impact:**
  - Will provide previously unavailable information to help patients and clinicians choose among disease-modifying therapies for relapsing, remitting multiple sclerosis (RRMS)

Project 3: Randomized, Double-Blind, Crossover, Placebo-Controlled Trial of Amantadine, Modafinil, and Methylphenidate for Treatment of Multiple Sclerosis

- **Research Question:**
  - What is the comparative effectiveness of three frequently used treatments for fatigue?
- **Population:**
  - Relapsing, remitting multiple sclerosis (RRMS) or progressive multiple sclerosis patients
- **Intervention/Comparator(s):**
  - Three recommended and commonly used fatigue medications (amantadine, modafinil, and methylphenidate) and placebo
- **Outcomes of Interest:**
  - Primary: Fatigue
  - Secondary: Quality of life
- **Study Design:** Randomized, placebo-controlled trial with crossover
  - Sample Size: 136 (each participant will participate in all 4 arms)
- **Length of Follow-up:** 6 weeks for each medication (plus 2-week wash-out)

Project 3: Randomized, Double-Blind, Crossover, Placebo-Controlled Trial of Amantadine, Modafinil, and Methylphenidate for Treatment of Multiple Sclerosis (cont.)

- **Engagement:**
  - Several patients with multiple sclerosis (MS), MS neurologist, and national MS society will serve on a stakeholder advisory panel
- **Potential Impact:**
  - Provide clearer guidance on relative efficacy and side effects associated with commonly used medications for fatigue

Project 4: Comparative Effectiveness Trial Between a Clinic- and Home-Based Complementary and Alternative Medicine (CAM) Telerehabilitation Intervention for Adults with Multiple Sclerosis

- **Research Question:**
  - What is the comparative effectiveness of a tailored complementary alternative medicine (CAM) neurorehabilitation program delivered in the clinic versus at home by teledelivery for patients with multiple sclerosis?
- **Population:** Patients with multiple sclerosis with a range of impairment
- **Intervention:**
  - Teledelivery to patient's home of evidence-based tailored CAM program, including exercise, yoga, and Pilates
- **Comparator:**
  - On-site delivery of CAM program
- **Outcomes of Interest:**
  - Primary: Quality of life, fatigue, pain, and physical activity
  - Secondary: Physical functioning (endurance, balance, strength, and gait)
- **Study Design:** Cluster randomized controlled trial in 30 sites
  - Sample Size: 820 patients
- **Length of Follow-up:** 12 months

Project 4: Comparative Effectiveness Trial Between a Clinic- and Home-Based Complementary and Alternative Medicine Telerehabilitation Intervention for Adults with Multiple Sclerosis (cont.)

- **Engagement:**
  - Five national multiple sclerosis stakeholder organizations engaged in selection of outcomes and will have ongoing involvement
- **Potential Impact:**
  - Potential to enhance treatment and eliminate barriers to care for patients with multiple sclerosis who have limited physical ability, patients who live in rural areas, and patients who have limited possibilities for transportation to specialty centers

Treatment of Multiple Sclerosis

*4 Recommended Projects**

4 Projects

PFA	Allotted	Proposed Total Budget*
Treatment of Multiple Sclerosis	**$50M**	**$19.6M**

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2015 Treatment of Multiple Sclerosis PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Cycle 3 2015
Pragmatic Clinical Studies PFA Slate

Christine Goertz, DC, PhD
Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH
Chief Science Officer

Pragmatic Clinical Studies Slate Cycle 3 2015

Process Overview

- 47 Letters of Intent (LOIs) submitted
- 19 LOIs invited to submit a full application (40%)
- 19 applications were received (100% of invited LOIs)
- We are proposing to fund 1 application* out of 19 received applications (5%)

*Recommended by the Selection Committee

Pragmatic Clinical Studies – Cycle 3 2015

Proposed Project Title

Project Title
A Randomized Pragmatic Trial Comparing the Complications and Safety of Blood Clot Prevention Medicines Used in Orthopaedic Trauma Patients

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

A Randomized Pragmatic Trial Comparing the Complications and Safety of Blood Clot Prevention Medicines Used in Orthopaedic Trauma Patients

- **Research Question:** Is low molecular weight heparin or aspirin the better medicine to use for preventing death and clinically important blood clots in the lungs of patients who sustain trauma?
- **Population:** Trauma patients ages 18 – 80 years old admitted to hospitals who have sustained a significant orthopedic injury (extremity injuries needing surgery and all pelvis or hip fractures) and requiring blood clot prevention
- **Intervention:** Aspirin
- **Comparator(s):** Low molecular weight heparin
- **Outcomes of Interest:**
  - Primary: Clinically important pulmonary embolism (blood clot in the lungs), surgical complications that require a return to the operating room, and death from other causes
  - Secondary: Patient satisfaction with treatment, out of pocket costs to patients, occurrence of minor blood clots
- **Study Design:** Randomized clinical trial
  - Sample Size: 12,980 (11 Sites)
- **Length of Follow-up:** 3 months

A Randomized Pragmatic Trial Comparing the Complications and Safety of Blood Clot Prevention Medicines Used in Orthopaedic Trauma Patients (cont.)

- **Engagement:**
  - Research team comprised of trauma survivors, blood clot survivors, caregivers, frontline clinicians, professional organizations, payers, and experts in area of blood clots in trauma
- **Potential Impact:**
  - Trauma patients have been historically under-represented in research. Study has potential to improve healthcare and outcomes for these patients by determining which medicine is better at preventing death and reducing complications after trauma

Slate Overview – Cycle 3 2015

Pragmatic Clinical Studies

1 Project

PFA	Allotted	Proposed Total Budget*
Pragmatic Clinical Studies	**$90 Million**	**$11.2M**

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of award from the Cycle 3 2015 Large Pragmatic Studies PFA
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Cycle 3 2015
Broad PFA Slates

Christine Goertz, DC, PhD
Chair, Selection Committee

Evelyn P. Whitlock, MD, MPH
Chief Science Officer

Funding Opportunities

Broad Cycle 3 2015

Broad PFA	Maximum Project Length	Maximum Direct Costs Allowed	Total Available Budget
Addressing Disparities	3 years	$1.5 Million	$8 Million
Assessment of Prevention, Diagnosis and Treatment Options	3 years	$2 Million	$32 Million
Communications and Dissemination Research	3 years	$1.5 Million	$8 Million
Improving Healthcare Systems	3 years	$1.5 Million (small)	$16 Million
	5 years	$5 Million (large)	
Improving Methods for Conducting Patient-Centered Outcomes Research	3 years	$750,000	$12 Million

Broad Cycle 3 2015
Merit Review Criteria

Broad PFAs (except Methods)	Improving Methods for Conducting Patient-Centered Outcomes Research
1. Potential for the study to fill critical gaps and generate actionable evidence 2. Potential for the study findings to be adopted into clinical practice and improve delivery of care 3. Scientific Merit (research design, analysis, and outcomes) 4. Patient-centeredness 5. Patient and stakeholder engagement	***1. Impact on the field of PCOR methods**** ***2. Potential for the study to improve PCOR methods**** 3. Technical merit 4. Patient-centeredness 5. Patient and stakeholder engagement

Slate Overview—Broad Cycle 3 2015

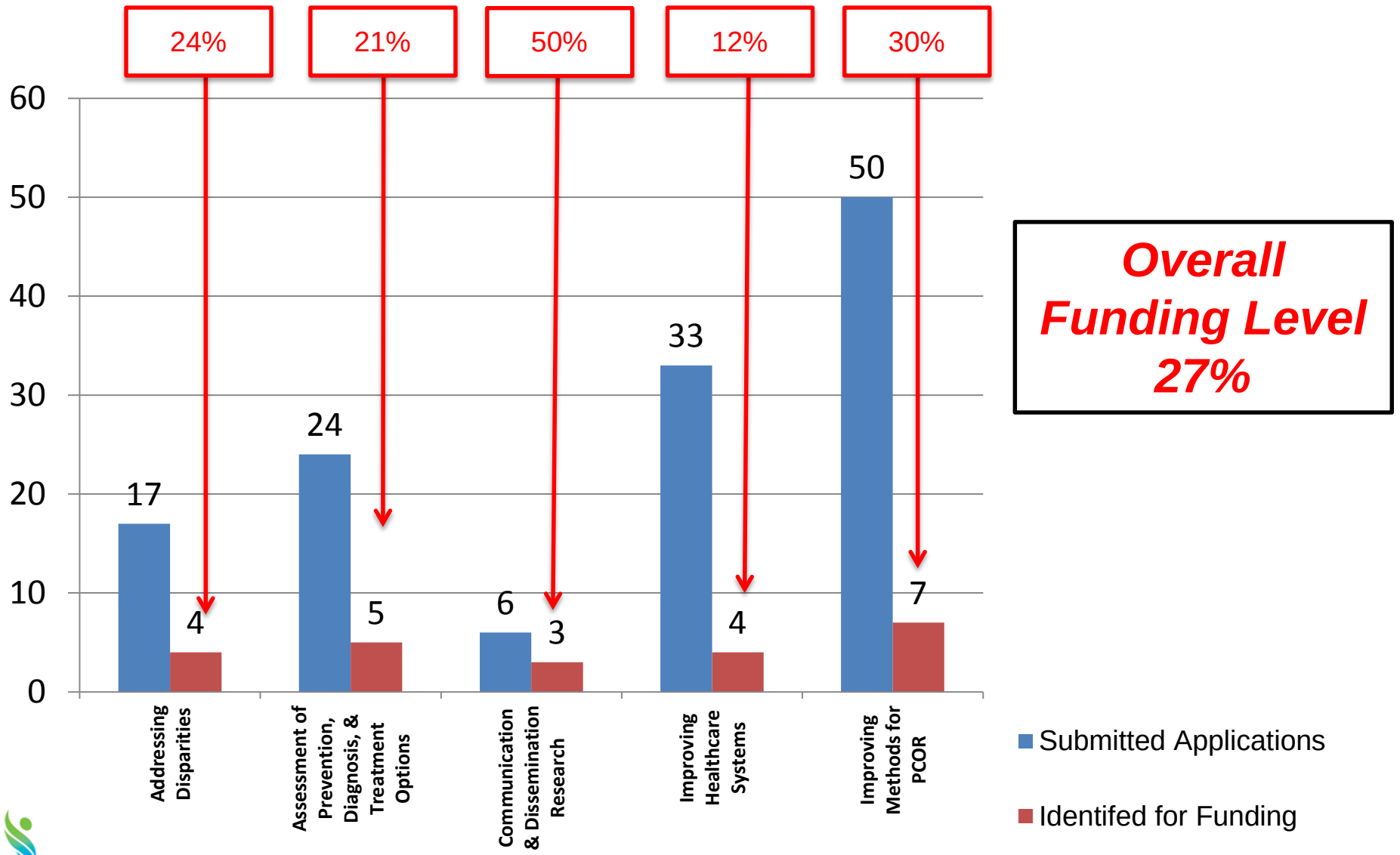
Process Overview

- 292 Letters of Intent (LOIs) submitted
- 152 LOIs invited to submit a full application **(52%)**
- 128 applications were received (84**%** of invited LOIs)
- We are proposing to fund 23 applications* out of 128 received applications (**18%**)
  - **52%** (12) of applications recommended for funding were resubmissions

*Recommended by the Selection Committee

Broad Cycle 3 2015

What Percentage of Applicants are We Proposing to Fund?



Overall Funding Level 27%

Addressing Disparities

*4 Recommended Projects**

Project Title
Home-Based Chronic Kidney Disease (CKD) Care in Native Americans of New Mexico
The HOMBRE Trial: Comparing Two Innovative Approaches to Reduce Chronic Disease Risk among Latino Men
A Stepped-care Intervention to Reduce Disparities in Mental Health Services among Underserved Lung and Head and Neck Cancer Patients and their Caregivers
A Comprehensive Disease Management Program to Improve Quality of Life in Disparity Hispanic Patients Admitted with Exacerbation of Chronic Pulmonary Diseases

Resubmissions in bold.

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Assessment of Prevention, Diagnosis, and Treatment Options

*5 Recommended Projects**

Project Title
A Patient-Centered Framework to Test the Comparative Effectiveness of Culturally and Contextually Appropriate Program Options for Latinos with Diabetes from Low-Income Households
Comparison of Sleep Apnea Assessment Strategies to Maximize TBI Rehabilitation Participation and Outcome
Cognitive-behavioral Therapy vs. Yoga for the Treatment of Worry in Anxious Older Adults: A Randomized Preference Trial
Blood Pressure Checks for Diagnosing Hypertension (BP-CHECK)
Comparative Effectiveness of Treatment Options for Genital Herpes Infection in Pregnant Women to Reduce Adverse Pregnancy Outcomes

Resubmissions in bold.

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Communication and Dissemination Research

*3 Recommended Projects**

Project Title
The Comparative Effectiveness of Probabilistic vs. Patient Narrative Enhanced Risk Communication for Pain Management Following Acute Care
Engaging Patients and Providers in Collaborative Communication on HPV Vaccination (EPPIC-HPV)
Comparative Effectiveness of Encounter Decision Aids for Early Stage Breast Cancer Across Socioeconomic Strata

Resubmissions in bold.

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Improving Healthcare Systems

*4 Recommended Projects**

Project Title
Engaging Patients with Mental Disorders from Emergency Departments into Outpatient Care: A Comparative Effectiveness Workforce Study
Shared Care: Patient-Centered Management after Hematopoietic Cell Transplantation
Benefits of Stroke Treatment Delivered Using a Mobile Stroke Unit Compared to Standard Management by Emergency Medical Services: The BEST-MSU Study
Electronic Patient Reporting of Symptoms During Outpatient Cancer Treatment: A U.S. National Randomized Controlled Trial

Resubmissions in bold.

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Improving Methods for Conducting PCOR

*7 Recommended Projects**

Project Title
Expansion of Methods for Two-Stage Trial Designs for Testing Treatment, Self-Selection and Treatment Preference Effects
Developing and Validating Quantitative Measures to Assess Community Engagement in Research: Addressing the Measurement Challenge
Linking Randomized Clinical Trials and Claims Data for Enhancing Randomized and Non-randomized Patient-centered Outcomes Evidence Generation
Leveraging Visual Analytics for the Identification of Patient Subgroups: Application to Improving the Prediction of Hospital Readmission in the Elderly
Statistical Methods for Phenotype Estimation and Analysis Using Electronic Health Records
Improving Causal Inference Methods via Statistical Leaning with High-dimensional Data
Linking Unique Device Identifiers to Insurance Claims: A Pilot Demonstration

Resubmissions in bold.

*All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Slate Overview – Cycle 3 2015

Broad PFAs

23
Projects

Broads PFA	Allotted	Proposed Total Budget*
Addressing Disparities	$8M	$7.2M
Assessment of Prevention, Diagnosis, and Treatment Options	$32M	$13.7M
Communications and Dissemination Research	$8M	$6.3M
Improving Healthcare Systems	$16M	$20.7M
Improving Methods for Conducting PCOR	$12M	$6.4
TOTAL:	$76M	$54.4M

*Total budget = direct + indirect costs. All proposed projects, including requested budgets and project periods, are approved subject to a programmatic and budget review by PCORI staff and the negotiation of a formal award contract.

Board Vote

Call for a Motion to:	• **Approve** funding for the recommended slate of awards from the Cycle 3 2015 Broad PFAs
Call for the Motion to Be Seconded:	• **Second** the Motion • If further discussion, may propose an **Amendment** to the Motion or an **Alternative** Motion
Roll Call Vote:	• Vote to **Approve** the **Final** Motion • Ask for votes in favor, opposed, and abstentions

Wrap Up and Adjournment

Grayson Norquist, MD, MSPH
Chairperson, Board of Directors