PATIENT-CENTERED OUTCOMES RESEARCH INSTITUTE

Board of Governors Meeting via Teleconference / Webinar

Tuesday, July 19, 2016

12:00 pm – 2:00 pm ET

Board Members Present:

Grayson Norquist, MD, MSPH, *Chairperson*; Kerry Barnett, JD, *Vice Chairperson;* Debra Barksdale, PhD, RN; Larry Becker; Andy Bindman, MD; Francis Collins, MD, PhD; Allen Douma, MD; Alicia Fernandez, MD; Leah Hole-Marshall, JD; Gail Hunt; Harlan Krumholz, MD, SM; Freda Lewis-Hall, MD; Steve Lipstein, MHA; Barbara McNeil, MD, PhD; Ellen Sigal, PhD; Harlan Weisman, MD Robert Zwolak, MD, PhD

Board Members Absent:

Christine Goertz, DC, PhD; Robert Jesse, MD, PhD; Richard Kuntz, MD, MSc; Sharon Levine, MD

Minutes

Agenda Item	Related Minutes
Call to Order, Roll Call, and Welcome - *Grayson Norquist, MD, MSPH, Chairperson* and *Joe Selby, MD, MPH,* Executive Director	Dr. Norquist chaired and opened the meeting, welcomed all to the meeting of the PCORI Board of Governors and read the Chair Statement on Conflict of Interest.
Consider for Approval: Minutes of the June 21, 2016 Board Meeting - *Grayson Norquist, MD, MSPH*	The following motion was made by Harlan Weisman and seconded by Freda Lewis-Hall **Motion:** Approve the minutes of the June 21, 2016 Board of Governors meeting. *Approved by a majority vote of the voting Board members by voice vote (no opposed; no abstentions)*
Consider for Approval: Proposed Slates for 4 Targeted PFA Awards - *Joe Selby, MD, MPH* - *Evelyn Whitlock, MD, MPH, Chief Science Officer* **Management Strategies for Treatment-Resistant Depression**	Dr. Selby announced that this was the largest number of slates of awards relating to targeted funding announcements and the largest amount of funding commitments brought to the Board of Governors for approval at one time. (*See Attachment A).* He acknowledged the hard work dedicated to these initiatives over the last year. Dr. Zwolak, Chair of the Science Oversight Committee, added his thanks and appreciation to staff, merit reviewers, Committee members and applicants who contributed to the process. Dr. Whitlock began her presentation by giving an overview of the funding pathway and then presented the following four targeted initiatives. The goal of the PFA regarding Management Strategies for Treatment-Resistant Depression (TRD) was to address

	important knowledge gaps regarding the management of treatment-resistant depression. Of the 10 Letters of Intent (LOI) submitted, seven (70%) were invited to submit a full application and all did so. The Selection Committee reviewed the proposed slate, which proposed funding three out of seven (43%) complementary but distinct applications, using a proposed total budget of $39.9 million of the $30M allotted for this PFA, the balance of $9.9M redistributed from other funds allocated to research. The first project is designed to address the research question: What is the comparative effectiveness of electroconvulsive therapy (ECT) vs. ketamine treatment for outpatient treatment-resistant depression (TRD) patients? The mechanism of ketamine is dramatic and can have an immediate response. It is not clear if the effect is due to ketamine or a different metabolite. A question was raised about the trial design's ability to take into account emerging evidence on the mechanism of action. Dr. Whitlock responded that we will inquire with the investigator team if that variable can be worked into the research project. The second project comparing augmentation vs. switching strategies is designed to address the research question: What is the comparative effectiveness, safety, and tolerability of two augmentation strategies with a switching strategy for patients with treatment-resistant depression? And, the third project, Optimizing Outcomes in Treatment-Resistant Depression in Older Adults, considers the comparative benefits and risks of antidepressant switching strategies (adding and switching) in older adults with treatment-resistant depression (TRD). *The following motion was made by Larry Becker and seconded by Ellen Sigal* ***Motion:*** Approve funding for the recommended slate of awards from the Cycle 3 2015 Treatment-Resistant Depression PFA *Approved by a majority vote of the voting Board members by roll call: 13 in favor; 0 opposed; 0 abstentions; 4 recusals: Harlan Krumholz, Steve Lipstein; Barbara McNeil and Gray Norquist*
Clinical Strategies for Managing and Reducing Long-	The priority research questions for the funding initiative on Clinical Strategies for Managing and Reducing Long-Term

Term Opioid Use for Chronic Pain	Opioid Use for Chronic Pain include: • 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? • 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? Of the 28 Letters of Intent submitted, 20 (71%) were invited to submit a full application. Of the 20, 18 applications were submitted (90%). The Selection Committee reviewed the proposed slate, which proposed funding two out of 18 (11%) reviewed applications, using a proposed total budget of $21 million, of the allotted of $40M. Recommended Projects are:: • 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 The Board noted that the Board had allocated up to $40M to this important PFA topic and that with the recommended slate of awards below the allocated amount, funding could still be available under this PFA. It was noted that the Board has also approved the development of another targeted PFA relating to opioid abuse, focusing on prevention of opioid abuse. The Board advised that the Science Oversight Committee should consider whether the uncommitted funds relating to this targeted PFA should be made available for additional studies on this topic, including by re-releasing the PFA. *The following motion was made by Larry Becker and seconded by Kerry Barnett* ***Motion:*** 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 *Approved by a majority vote of the voting Board members by roll call: 15 in favor; 0 opposed; 0 abstentions; 2 recusals:*

New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease	*Harlan Krumholz and Barbara McNeil* The objective of the PFA on New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease was to fund studies that inform decision-making of patients and clinicians as current evidence base lacks high-quality information on the risks and benefits of extending blood thinner treatment beyond three months, and include subgroup analyses looking at older patients and individuals with kidney dysfunction. Of the 12 Letters of Intent submitted, nine (75%) were invited to submit a full application. Of the nine, eight applications were submitted (89% of invited). The Selection Committee reviewed the proposed slate, which proposed funding two out of eight (25%) reviewed applications, using a proposed total budget of $6.5 million, of the allotted $30M. The recommended project, "The Dabigatran, Apixaban, Rivaroxaban, Edoxaban, Warfarin Comparative Effectiveness Research Study (The DARE Warfarin CER Study)", addresses the 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 clots in the legs or lungs (venous thromboembolism or VTE)? The second project, "The Comparative Effectiveness of Warfarin and New Oral Anticoagulants for the Extended Treatment of Venous Thromboembolism", addresses the benefits and harms of different treatment options for the extended treatment of blood clots in the legs and lungs (VTE). *The following motion was made by Gail Hunt and seconded by Debra Barksdale* ***Motion:*** Approve funding for the recommended slate of awards from the Cycle 3 2015 New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease PFA *Approved by a majority vote of the voting Board members by roll call: 12 in favor; 0 opposed; 0 abstentions; 5 recusals: Andy Bindman, Alicia Fernandez, Freda Lewis-Hall, Steve Lipstein and Barbara McNeil.*
Treatment of Multiple Sclerosis	The goal of the Treatment of Multiple Sclerosis PFA was 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). This PFA included an emphasis on treatment of symptoms and rehabilitation in patients with progressive disease. Of the 35 Letters of Intent submitted, 21 (60%) were invited to submit a full application. Of the 21, 13 applications were submitted (62%). The Selection Committee reviewed the proposed slate, which proposed funding four out of 13 (31%) submitted applications, using a proposed total budget of $19.6 million, of the allotted $50M. The Recommended Projects are as follows: • 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 Tele-rehabilitation Intervention for Adults with Multiple Sclerosis (MS) The Board discussed the focus of the recommended awards, the number of LOIs and applications, research funded by other funders in this area, and noted that there is still funding available for this topic under this PFA. The Board discussed efforts underway relating to the Application Enhancement initiative, and advised that the Science Oversight Committee should consider whether the uncommitted funds relating to this targeted PFA should be made available for additional studies on this topic, including by re-releasing the PFA. *The following motion was made by Gail Hunt and seconded by Larry Becker* ***Motion:*** Approve funding for the recommended slate of awards from the Cycle 3 2015 Treatment of Multiple Sclerosis PFA *Approved by a majority vote of the voting Board members by roll call: 15 in favor; 0 opposed; 0 abstentions; ; Alicia*

	Fernandez and Harlan Krumholz were not present for this vote
Consider for Approval: Proposed Slate for Cycle 3 2015 Pragmatic PFA Award - *Evelyn Whitlock, MD, MPH*	Dr. Whitlock summarized the process that led to the recommended slate of awards relating to the PFA for Pragmatic Clinical Studies for 2015 Cycle 3 (*See Attachment B)*. The large pragmatic studies funding announcement funds studies up to $10M in direct costs and up to 5 years duration, with a total available funds of $90M in total costs. Of 47 Letters of Intent submitted, 19 (40%) were invited to submit full applications and all 19 did so (100%). The Scientific Oversight Committee reviewed the proposed slate, which proposed funding one out of 19 (5%) applications, using a proposed budget of $11M, of the allotted $90M. This study, "A Randomized Pragmatic Trial Comparing the Complications and Safety of Blood clot Prevention Medicines Used in Orthopedic Trauma Patients", also complements the slate of awards approved under the NOACs announcement. *The following motion was made by Francis Collins and seconded by Kerry Barnett:* ***Motion:*** Approve funding for the recommended slate of award from the Cycle 3 2015 Large Pragmatic Studies PFA *Approved by a majority vote of the voting Board members by roll call: 15 in favor; 0 opposed; 0 abstentions; 0 recusals; Alicia Fernandez and Harlan Krumholz were not present for this vote*
Consider for Approval: Proposed Slate for Cycle 3 2015 Broad PFA Awards - *Evelyn Whitlock, MD, MPH*	Dr. Whitlock introduced the recommended slate of awards relating to the Cycle 3 2015 Broad PFAs (*See Attachment C)*. She summarized the process that led to the recommended slate of awards. Of the 292 Letters of Intent submitted to the Broad PFAs and 152 (52%) were invited to submit a full application. Of the 152, 128 applications were submitted (84% of invited). The Selection Committee reviewed the proposed slate, which proposed funding 23 out of 128 (18%) applications, using a proposed total budget of $54.4 million. 52% (12) of the applications recommended for funding were resubmissions. Dr. Whitlock briefly explained how the 23 proposed studies contribute to the existing portfolio. These studies are listed in Appendix C. *The following motion was made by Larry Becker and seconded by Gail Hunt*

	Motion: Approve funding for the recommended slate of awards from the Cycle 3 2015 Broad PFA slate *Approved by a majority vote of the voting Board members by roll call: 6 in favor; 1 opposed (Andy Bindman); 0 abstentions; 6 recusals: Debra Barksdale, Steve Lipstein, Barbara McNeil, Gray Norquist, Ellen Sigal and Robert Zwolak; Francis Collins, Allen Douma and Alicia Fernandez were not present for this vote; Harlan Krumholz also announced his intention to recuse prior to the meeting but was not present for this vote.*
Wrap up and Adjournment - *Grayson Norquist, MD, MSPH*	The meeting adjourned at 1:38 pm

Additional Materials: Attachments A, B and C

ATTACHMENT A: Award Slates from Targeted Awards

Approved Slate of Awards: Treatment-Resistant Depression:

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

Approved Slate of Awards: Managing and Reducing Long-Term Opioid Use for Chronic Pain

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 Behavior Therapy for Opioid-Treated Chronic Low Back Pain

Approved Slate of Awards: New Oral Anticoagulants (NOACs) in the Extended Treatment of Venous Thromboembolic Disease

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

Approved Slate of Awards: Treatment of Multiple Sclerosis

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

ATTACHMENT B:

Approved Slate of Award: 2015 Cycle 3 Pragmatic Clinical Studies

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

ATTACHMENT C:

Approved Slate of Awards: 2015 Cycle 3 Broad Award Slates

Addressing Disparities
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

Assessment of Prevention, Diagnosis, and Treatment Options
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 Outcom
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

Communication & Dissemination Research
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

Improving Healthcare Systems
Engaging Patients with Mental Disorders from Emergency Departments into Outpatient Care: A Comparativ 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 Randomize Controlled Trial

Improving Methods for Conducting PCOR
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