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Adapting to Disruption of Pragmatic Clinical Trials Studying
Nonpharmacological Approaches to Pain Management
during the COVID-19 Pandemic: Lessons Learned from the
NIH-DOD-VA Pain Management Collaboratory

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VA Connecticut Healthcare System & Yale University

VA HSR&D Spotlight on Pain Management

November 3, 2020

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For more information: www.painmanagementcollaboratory.org

TBM

BRIEF REPORT

Adapting to disruption of research during the COVID-19 pandemic while testing nonpharmacological approaches to pain management

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Outline

- Changes in the Management of Pain
- Introduction to the NIH-DOD-VA Pain Management Collaboratory (PMC)
- Pain Management Collaboratory Coordinating Center Response to the COVID-19 Pandemic
- Effects of COVID-19 Pandemic on PMC Pragmatic Clinical Trials
- Lessons Learned and Moving Forward

Gap between Evidence and Practice

- Growing evidence to support integrated, coordinated, multimodal and interdisciplinary models of pain care that support patient activation and pain self-management



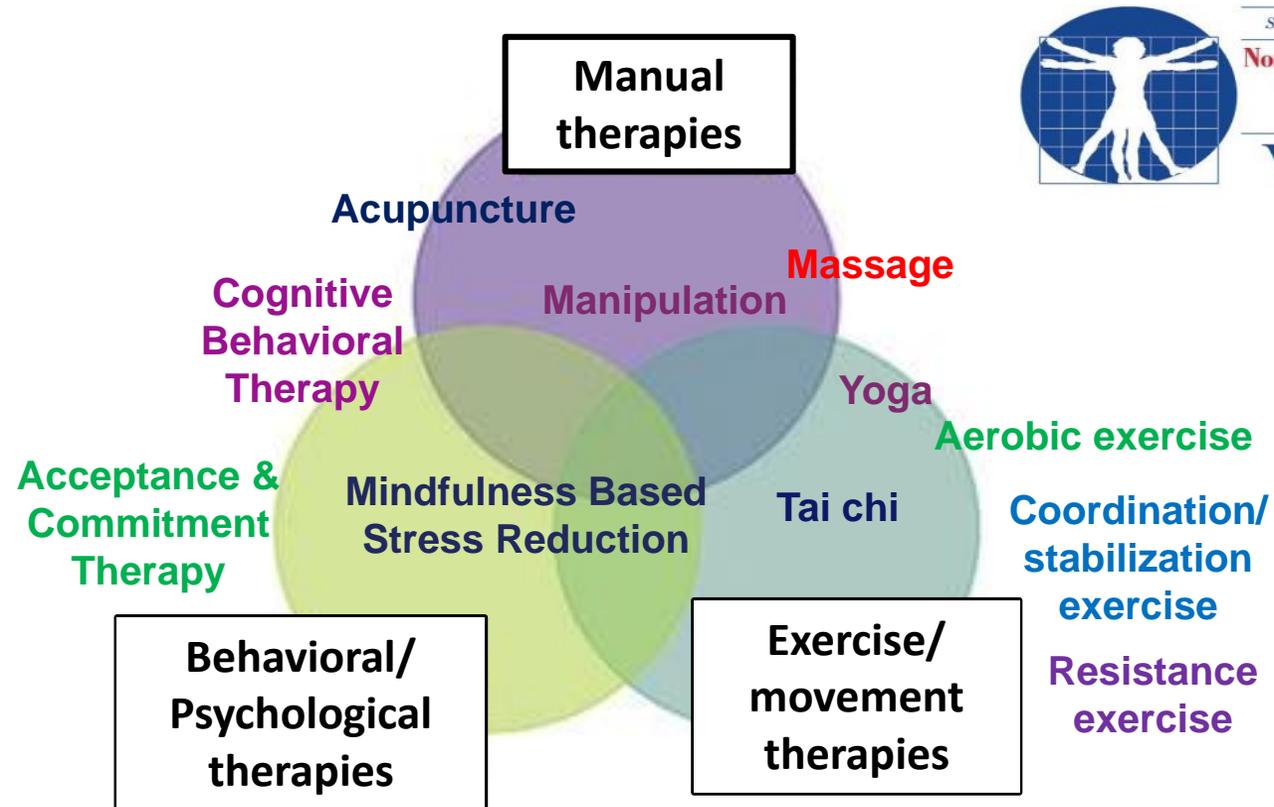
- Significant organizational/systems, provider and patient-level barriers to timely and equitable access to these approaches



- Veteran and Military health systems are ideally positioned to address this gap as learning health systems

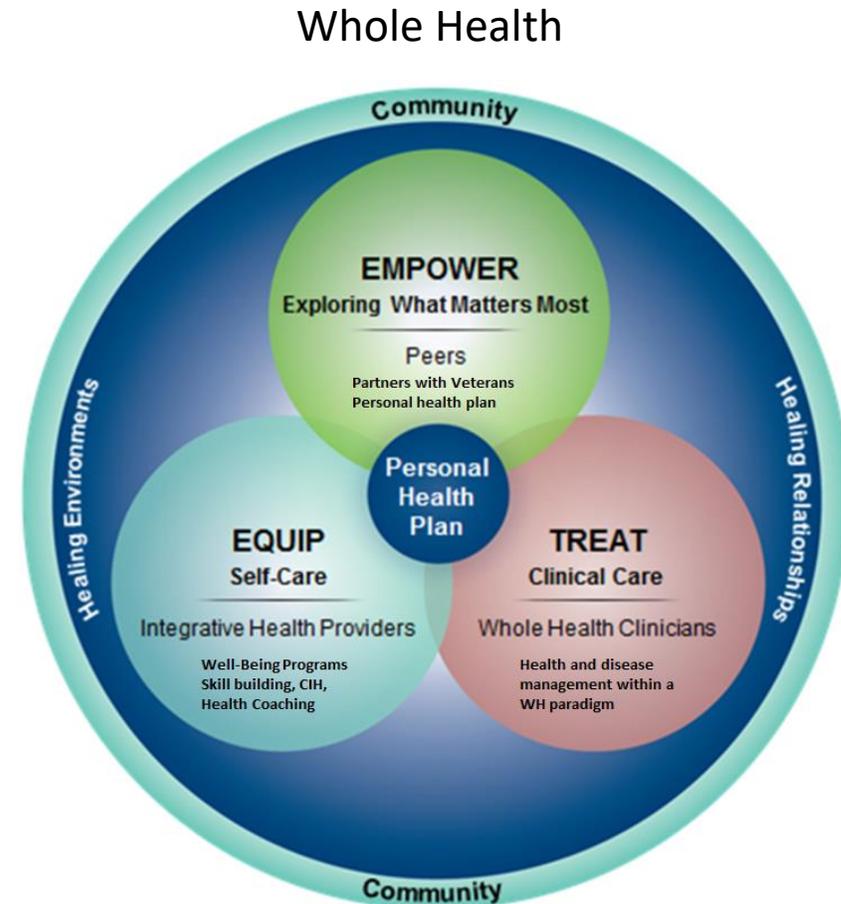
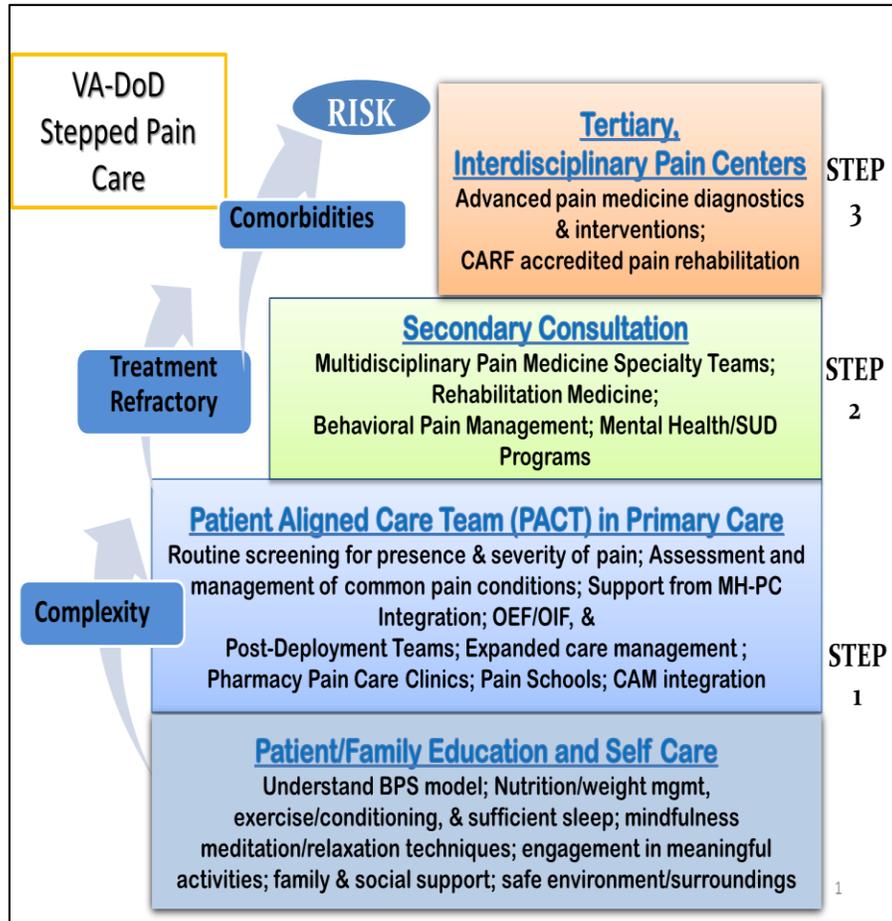
A Shift in Pain Management

- Primary use of evidence-based, nonpharmacological approaches



STATE OF THE ART CONFERENCE
Non-pharmacological Approaches
to Chronic Musculoskeletal
Pain Management
VA HSR&D

Models of Integrated Pain Care (VA & DOD)



Pain Management Collaboratory (PMC)



- Investment of \$81 million over 6 years from collaborative sponsorship efforts from:
 - National Institutes of Health
 - National Center for Complementary and Integrative Health, National Institute for Neurological Disorders and Stroke, National Institute of Drug Abuse, National Institute of Alcohol Abuse and Alcoholism, National Institute of Child Health and Human Development, National Institute of Nursing Research, Office of Behavioral and Social Sciences Research, Office of Research on Women's Health
 - Department of Defense
 - Clinical Rehabilitative Medicine Research Program, Military Operational Medicine Research Program
 - Department of Veterans Affairs
 - Health Services Research & Development Service, Office of Research and Development

Pain Management Collaboratory (PMC)



- Key Objective
 - Conduct pragmatic clinical trials to evaluate whether nonpharmacological approaches for management of pain and innovative care models are effective when delivered in the Veterans Health Administration (VHA) and/or the Defense Health Agency (DHA)
- General Structure
 - 11 phased (UH3 planning + UG3 implementation) pragmatic clinical trials
 - Support from a centralized Coordinating Center (PMC³)
 - Work closely with a Steering Committee, External Board, and Patient Resource Group

PMC Pragmatic Clinical Trials

C. Goertz/C. Long: Chiropractic Care for Veterans: A Pragmatic Randomized Trial Addressing Dose Effects for cLBP (NIH)

S. Taylor/S. Zeliadt: Complementary and Integrative Health for Pain in the VA: A National Demonstration Project (VA)

D. Burgess: Testing Two, Scalable, Veteran-Centric Mindfulness Based Interventions for Chronic Musculoskeletal Pain: A Pragmatic, Multisite Trial (DOD)

A. Heapy: Cooperative Pain Education and Self-management: Expanding Treatment for Real-world Access (COPEX ExTRA) (NIH)

S. Farrokhi/C. Dearth/E. Russell Esposito: Resolving the Burden of Low Back Pain in Military Service Members and Veterans (RESOLVE Trial) (DOD)

B. Ilfeld: Ultrasound-Guided Percutaneous Peripheral Nerve Stimulation: A Non-Pharmacological Alternative for the Treatment of Postoperative Pain (DOD)

M. Rosen/S. Martino: Engaging Veterans Seeking Service-Connection Payments in Pain Treatment (NIH)

J. Fritz/D. Rhon: SMART Stepped Care Management for Low Back Pain in Military Health System (NIH)

K. Seal/W. Becker: Implementation of a Pragmatic Trial of Whole Health Team vs. Primary Care Group Education to Promote Non-Pharmacological Strategies to Improve Pain, Functioning, and Quality of Life in Veterans (NIH)

S. George/S.N. Hastings: Improving Veteran Access To Integrated Management of Chronic Back Pain (AIM Back) (NIH)

D. McGeary/J. Goodie: Targeting Chronic Pain in Primary Care Settings Using Internal Behavioral Health Consultants (DOD)

Pain Management Collaboratory Coordinating Center (PMC³)



- Purpose

- Provide national leadership and strategic direction for the PMC program for internal and external stakeholders
- Support and enable the PCTs to conduct efficient, large-scale trials
- Development and refinement of innovative tools, best practices, and other resources in the conduct of high impact pragmatic clinical trials



Leadership and Operations Core

PMC³ Steering
Committee

Project
Managers

Military Treatment
Facility Engagement
Committee (MTFEC)

NIH-VA-DOD
Sponsors

Work Groups

Stakeholder
Engagement

Biostatistics &
Study Design

Electronic Health
Record

Phenotypes &
Outcomes

Implementation
Science

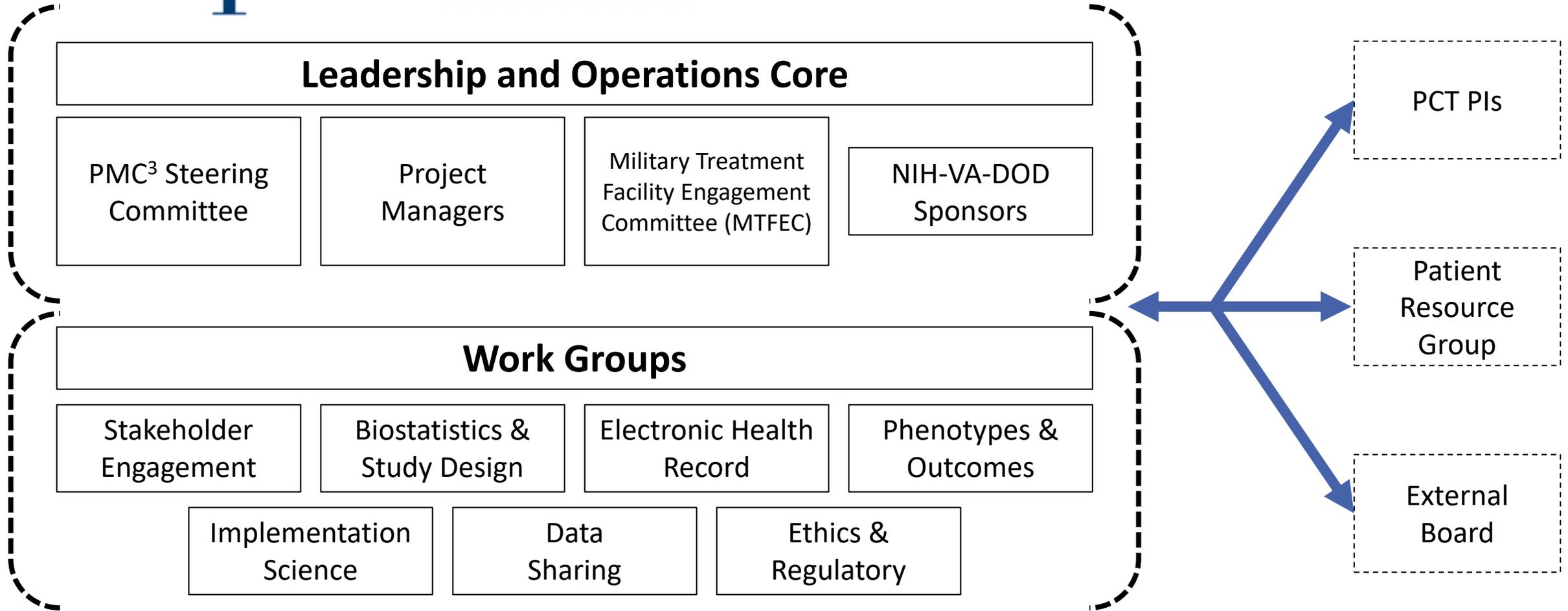
Data
Sharing

Ethics &
Regulatory

PCT PIs

Patient
Resource
Group

External
Board

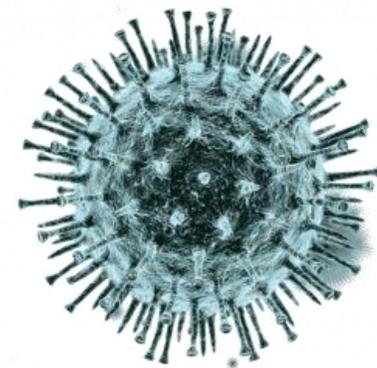
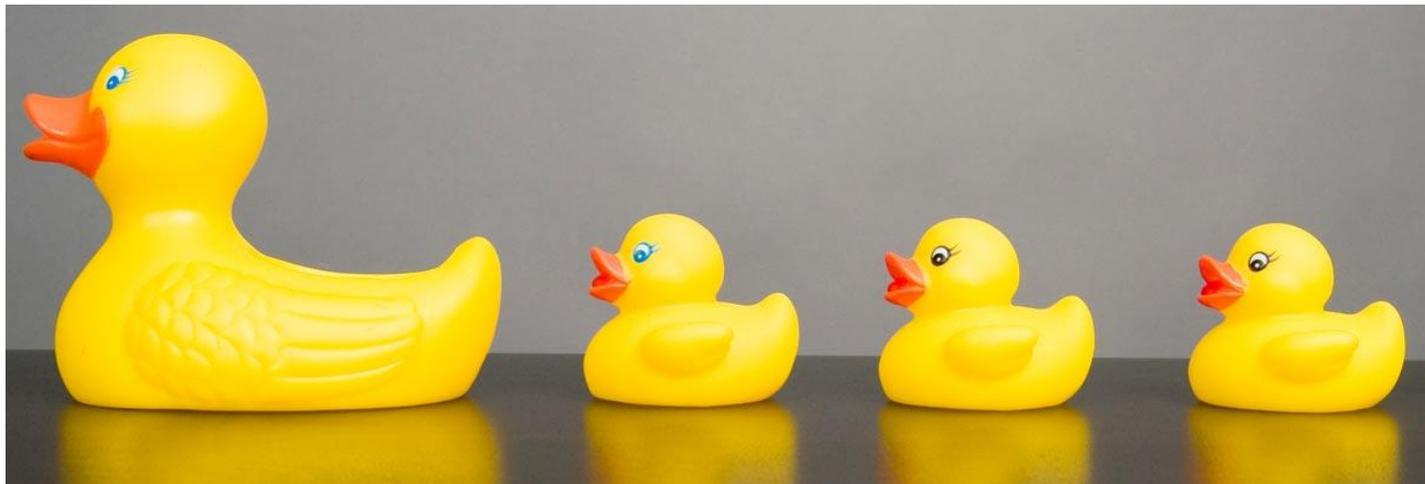


PMC Trials – Pragmatic Design

- What is a pragmatic trial?
 - Trials designed to show the real-world effectiveness of the intervention in broad patient groups embedded in clinical practice setting
- Why pragmatic studies?
 - Emphasize generalizability of results and protect rigor
 - Results may inform VHA, DHA, and other health care systems about nonpharmacological treatments for pain management

Pre-February, 2020 – “Business as Usual”

- Most trials transitioning between planning and implementation phases
 - Few already beginning recruitment for implementation phase
 - Few wrapping up planning pilot studies
- Many trials working with study teams and PMC³ resources to finalize plans with study sites for full-scale, implementation trial



March, 2020 – COVID-19

- PMC³ and PMC recognizes the potential challenge of the COVID-19 Pandemic to ongoing PCTs
 - Aggressive development and enactment of a plan-of-action to address key issues
 - Need for response and plan-of-action by PCTs to adapt appropriately
 - Open dialogue between PCT PIs and PMC³ Directors, representatives from sponsoring agencies
 - Need for tracking of impacts and responses to identify opportunities for reflection and for sharing with scientific community



PMC³ Response to COVID-19

- PMC Work Groups
- COVID-19 Challenges Tracking Tool
- COVID-19 Impact on Pain Outcomes

A Vehicle of Communication - The PMC Work Groups



- Although the PMC is a large, mainly decentralized effort, our culture emphasizes
 - Good communication
 - Collaborative, congenial relationships
 - Cross-collaboratory standards
- PMC work groups at the heart of this culture
 - Common link between PCTs and PMC³
- Recognized the need for a mechanism of rapidly and efficiently communicating and documenting changes in SOP due to COVID-19
 - Use the domain-focused work groups

PMC COVID-19 Challenges Tracking Tool



- Spreadsheet used to track multiple domains and characterize impact of COVID-19 on PCT operations
 - Project Managers → PMC³ Leadership
 - Frequent review with stakeholders across the PMC
- Organized into specific domains:
 - Intervention delivery
 - Data collection
 - Trial integrity
 - Clinical outcomes
 - Regulatory approval
 - Study recruitment
 - Statistical analyses
- Tasks assigned to other work groups or members of PMC³ as appropriate

PMC COVID-19 Challenges Tracking Tool



PMC COVID-19 Issues Tracking

*Please add the most recent items at the bottom

Num	Identification Date	WG	Domain	Issue	Follow-up	Action Item (Yes/No)	Action Assigned To	Notes
1	2020.03.26	Ethics & Reg	Intervention Delivery	1) What platforms are approved for use for virtual groups or delivery of remote interventions? 2) There is a need for real-time sharing of this information. We want to not only find solutions for our current situation, but we also want to be able to add to the literature for delivering interventions remotely.	2020.4.23 update: UniversityMN Zoom has been approved by VA CIRB for use with DP#19. VA is potentially allowing Cisco web-ex and Microsoft Teams. DoD is potentially allowing Adobe Connect. VA sites have been successful with VA Video Connect (VVC) in research.	Yes	EHR	MIKE R: The VA has approved and supports cloud-based conferencing tools. Cisco Webex, Microsoft Teams and Skype for Business.
2	2020.03.26	Ethics & Reg	Trial Integrity	1) Changes to Protocol. It's hard to know what to do. We don't want to put big changes into place only to have it change back. 2) 18 Months from now – realistically what will visits in a hospital look like? Will there be any?	1) It is important for you to communicate with your Funding PO, IRB, and DSMB regarding any potential changes to your protocols. 2) Be mindful of flow of communication within teams – make sure WG info is getting back to entire team.	Yes	Ethics & Reg Biostats	Some are exploring Virtual Consent. Discussed at the August 27 2020 Ethics & Reg WG meeting. Amy has a tracking tool that outlines remote/virtual consent procedures and plans for all studies. Bob suggested possibly involving the PRG for help in thinking through the virtual consent process, reviewing the instructions and process for clarity, and to possibly consider using PRG group as pilot subjects to go through the process of remote consent.
3	2020.03.26	Ethics & Reg	Intervention Delivery	Pause to enrollment and/or changes to the way care was delivered – can we still make outcomes generalizable at the end?	The delivery of care might change for some (virtual during this time). How much is telehealth going to influence the outcomes?	No	BioStats	CINDY COMMENT 4-30-20: With regards to sharing documents I would use either MS OneNote or MS Forms.
4	2020.03.26	Ethics & Reg	Data Collection	1) All Research staff is working from home. 1a) There is inability to obtain enough VA laptops and VA cell phones. Restrictions still in place that don't allow research staff to call subjects from personal cell phones. 1b) Snail-mail has also been affected – there is no one in the office to print and send mailings.	1) Can voice over IP or Skype be used? 2) Can encrypted email be used? Can VA research activities use My HealthVet for email?	Yes	Data Sharing	MIKE R: VA has purchased 50k in laptops have the user check with IT and get put on a list when they become available. Skype is authorized for use in the VA as well as MS Teams and Cisco Webex.
5	2020.03.26	Ethics & Reg	Trial Integrity	Social isolation and anxiety may influence pain outcomes more than the regular intervention.	We don't know how pain, in general, will be effected by the social isolation and anxiety caused by this pandemic.	No		
6	2020.04.03	Phen & Outcomes	Data Collection	It was determined that COVID-19 will <u>not</u> have a major impact on the data collection plan for <u>outcome data</u> . Everyone on the call was collecting outcomes data via remote data collection methods such as phone or online assessments. [Please note DP20 and DP21. not in attendance.]	Investigators have in-person baseline visits or interventions that will be impacted. Address in Biostats or Implementation Science	Yes	BioStats	
7	2020.04.03	Phen & Outcomes	Outcomes	Self-report: Phenotype COVID testing and status.	Develop questions to phenotype this domain	Yes	Phen & Outcomes	

COVID-19 Impact on Pain Outcomes

- Pain is a complex, multidimensional, personal and social experience
 - Important to consider potential impacts of changes in socially relevant phenotyping variables
 - Pain Outcomes \leftrightarrow pandemic stressors, heightened anxiety, depression, isolation
- Phenotypes and Outcomes WG created a concise, PMC-harmonized COVID-19 outcome measure
 - Structured to be applicable to pain, but not directly attributable
 - Widespread adoption across trials

COVID-19 Outcome Assessment Instrument

7-item Self-report Instrument

Purpose: Measure impact of COVID-19 on covariates related to pain related outcomes

Domains

- Access to Health Care
- Social Support
- Finances
- Ability to meet Basic Needs
- Mental/Emotional Health
- Sick with COVID-19
 - Self
 - Others

Effects on PMC PCTs

- PMC PCT Status
- Pain Care Delivery
- Pain Care Outcomes
- Regulatory Approvals and Ethical Issues
- Participant Recruitment
- Sample Size and Analyses
- Benefit of Pragmatic Research

PMC PCT Status as of May, 2020

- 3 trials with continued implementation phase trial recruitment (with study protocol revision)
- 1 trial with temporary suspension of implementation phase trial recruitment
 - Continued follow up for previously enrolled participants
- 4 trials with temporary delay in start of implementation trial recruitment (with or without study protocol revision)
- 2 trials with temporary suspension of pilot study recruitment/completion
 - With continued follow up for previously enrolled participants
- 1 trial with temporary delay in start of pilot study recruitment

Effect on Pain Care Delivery

- Suspension of non-urgent/non-emergent face-to-face healthcare based on national, state, and facility-level directives
- Shift towards increased use of telehealth services across all of healthcare
 - Maintained access to some form of care during period of disruption for Veterans and Military Servicemembers
 - In one PCT assessing technology-assisted care delivery, the digitalization of “usual care” resulted in fewer differences between the treatment and control arms

Effect on Pain Care Outcomes

- Reduction in clinical encounters due to suspension of face-to-face care → potential for missing data that were planned for use in phenotyping and outcome analyses
- Some trial designs included multiple intervention components that were affected in varying ways, which we anticipate will yield potential alterations in the strength of treatment effects based on changes in delivery media
 - From patient perspective, these shifts might be positive or negative

Effect on Regulatory/Ethical Issues

- National research stoppages in both Veterans Health Administration and Defense Health Agency
- PMC PCTs reminded of responsibility to remain in timely and open communication with their institutional review boards and sponsoring agencies
 - Particularly in context of necessitated study protocol modifications, in accordance with regulations for human subjects research

Effect on Regulatory/Ethical Issues

- Informed Consent
 - Changes in consent processes involving the use of sophisticated virtual processes (e.g., receiving/sending encrypted email and smartphone screen capture of informed consent documents)
 - Changes in delivery media from internally hosted applications to third-party software applications
 - These modifications may make it difficult for some study participants to fully comprehend informed consent materials

Effect on Participant Recruitment

- Range of effects very likely
 - Decreased frequency of clinical encounters → decreased presence of EHR data used to identify eligible participants and recruit them as participants
 - Some individuals may be more inclined to participate in PCTs as a function of limited availability of other pain interventions during pandemic period
- Increased stakeholder engagement through streamlined communication channels and interest in maintaining continuity of care

Effect on Sample Size and Analyses

- Downstream effects of changes in delivery interventions
 - Change in intervention → Affect on treatment fidelity → Reconsider study design
 - Moderating and mediating effects of COVID-19 and its impact on the fidelity of interventions, particularly usual care
- No simple solutions, no existing frameworks for study design and statistical analyses → A need for innovation and new approaches

Benefit of Pragmatic Research

- Main benefit of a pragmatic trial approach is the ability to “learn” within actual health environments through a bidirectional model of research and practice
- Minimizing the burden on research participants, investigators, and clinical care teams
 - Similar actions in the case of future disruptions to research activities
- Pragmatic nature affords the ability to respond quickly and adapt as the healthcare system adapts to disruption

What did we learn...

- A quick response, including detailed annotation of impacts and modifications, has been beneficial to track and communicate impacts of COVID-19 with important PMC stakeholders
- COVID-19 causes adaptation of clinical research in many unplanned ways
 - As intensity of pandemic ebbs and flows across the US, we can continue to expect varying levels of impact on multi-site PCTs

What did we learn...

- Pragmatic research is well suited to adapt to challenges that may arise that disrupt usual health care delivery
 - Some trials already examining methods well suited to transition to remote/telehealth methods
- Some challenged in reverse, where control arm begins to look like intervention arm
- All must consider treatment fidelity in modified study protocols and analyses of treatment effects

... and what's still to learn

- Detailed challenges from PCTs
 - Implementation Science work group conducting serial questionnaire for qualitative analysis of impacts on PCTs over time
- PCTs are somewhat well positioned to respond to disruption – but how much disruption is too much? And how applicable are their findings if healthcare returns to its “pre-disruption” form?

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- Our PCT Study Participants
- Today's Attendees



Questions?



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