Planning for Real World Impact
Methods, models, & frameworks for planning pragmatic research.

August 11: 8am - 6pm MDT
August 12: 7:30am - 4:30pm MDT

ACCORDS presents
Colorado Pragmatic Research in Health
2020 VIRTUAL CONFERENCE

Breakfast Session
Early Career Investigator Consultations

COPRH CONFERENCE – CONSULTATION INFORMATION FOR JOSHUA T.B. WILLIAMS, MD

1. <u>Credentials</u>: Joshua T.B. Williams, MD. General pediatrician at Denver Health Medical Center and Assistant Professor of Pediatrics at the University of Colorado Anschutz Medical Campus. E-mail address: joshua.williams@dhha.org
2. <u>Overview of the issue:</u> please see specific aims page below.
3. <u>Draft aims and hypotheses:</u> please see specific aims page below.
4. <u>Any pragmatic study designs or frameworks you are considering:</u> I am considering using the Escoffery scoping review for my SA2 to adapt an existing evidence-based intervention, and I am considering using the RE-AIM framework in my SA3 to assess a pilot pragmatic hybrid type 2 study's outcomes.
5. <u>Target funding agencies:</u> I am submitting this work as a K23 proposal to the NIH's National Institute of Minority Health and Disparities (NIMHD) with a submission deadline of November 12, 2020.
6. <u>Challenges and key questions:</u>
    a. General guidance – does this project align with the scope of pragmatic research and my Career Development Goal of obtaining expertise in pragmatic study design and implementation?
    b. Do I need to have an evidence-based intervention pre-identified for my SA2? Or, should I use my findings from SA1 to inform the type of evidence-based intervention I modify in SA1?
    c. How best should I assess effectiveness, feasibility, and acceptability in SA3? What would it look like to do so through quantitative, qualitative, or CBPR methods?

SPECIFIC AIMS

Every winter, poor and minority American children disproportionately suffer and die from influenza. In a typical US season, ~10 million children get sick, ~50,000 are hospitalized, and 300-500 die.[10] Yet, studies of pandemic 2009 H1N1 and seasonal influenza suggest that Black, poor, and immigrant children are more likely to contract influenza, be hospitalized, and die than white, non-poor, and non-immigrant children.[11–15] Morbidity disparities are associated with disparities in influenza prevention. The seasonal influenza vaccine is recommended for all children ≥6 months,[16] but poor, publicly-insured, and Black children are less likely to be vaccinated than wealthier, privately-insured, and white children.[17–20] Even if vaccinated, poor and minority children are more likely to be vaccinated later in a season after disease activity peaks.[21] **Thus, reducing influenza vaccination disparities is key to reducing disease disparities for poor and minority children.**

Multi-level barriers contribute to vaccination disparities. Among parents, health illiteracy, access to care, and vaccine hesitancy are associated with decreased uptake.[22–26] In my own survey of 255 parents of 2 year-olds at 3 safety-net clinics during the 2019 influenza season, I found 25% of Black parents were vaccine-hesitant; even adjusting for vaccine hesitancy, children of Black parents were significantly underimmunized compared to children of parents of other races/ethnicities. Clinicians may also miss vaccination opportunities or give weak recommendations to parents. In a retrospective study of 322 inpatient children with influenza, I found 42% had a missed opportunity before hospitalization.[27] Vaccine shortages and a lack of reminder-recall programs are system-level barriers. **While multi-level interventions to improve pediatric vaccination rates exist,** [28,29] **none are tailored to the needs and priorities of Black families who receive care in safety-net settings.**

~8,000,000 US children receive care in safety-net centers, of which one quarter are Black.[30] A multi-level influenza vaccination intervention tailored to Black families in safety-net systems could avert hundreds of thousands of pediatric infections every year. *Yet, in the midst of a SARS-CoV-2 pandemic, we lack a current understanding of Black parents' needs and priorities for pediatric influenza vaccination, and prior interventions have not been adequately tailored to Black communities' preferences or tested in pragmatic trials.* It is imperative to address these knowledge gaps to promote vaccination equity and decrease influenza-related morbidity and mortality in Black communities. As a pediatrician in Colorado's largest safety-net system and a fellowship-trained vaccine hesitancy researcher, I am uniquely positioned to address these gaps. **My over-arching career goal is to understand determinants of vaccine hesitancy in minority communities, tailor evidence-based interventions to stakeholders' needs and priorities, and reduce disparities through pragmatic trials.** In this 5-year K23, I will start with pediatric influenza vaccination in Black communities as I:

Aim 1: Explore multi-level needs and priorities for pediatric influenza vaccination in Black communities in Denver, CO. I will conduct focus groups and individual interviews with key stakeholders, including Black parents, Black community leaders, and clinic staff, mapping my insights to the NIHMD research framework.

Aim 2: Adapt an existing multi-level pediatric influenza vaccination intervention to incorporate findings from SA1 through implementation science. I will use the Escoffery et al. framework to adapt an existing, evidence-based multi-level pediatric influenza vaccination intervention to meet stakeholders' highest priorities.

Aim 3: Pilot test the intervention in a hybrid type 2 pragmatic study design at 2 Denver Health Clinics (1 pediatric, 1 family medicine) in historically black neighborhoods. During one influenza season, I will assess outcomes using the RE-AIM framework, as well as feasibility and acceptability of the intervention.

In parallel, I will have coursework and formal mentorship in health disparities, implementation science, and pragmatic trials. Ultimately, this multi-year K23 will prepare me for a multi-center R01 study to reduce pediatric influenza disparities in Black communities, advance the field of health disparities, and provide me with the skills needed to independently explore and address vaccination disparities in minority groups throughout my career.

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2. Project Overview
   a) The majority of weight loss programs produce modest weight loss short term, however most participants regain a significant portion of the weight that they lost. High levels of physical activity (~300 minutes/week of moderate-intensity exercise) is one of the best predictors of long-term weight loss, but the majority of participants are unable to adopt and sustain these levels. The <u>overall objective</u> of this mentored K01 grant is to apply the Multiphase Optimization Strategy (MOST) to develop and pilot test the integration of a novel, Self-Determination Theory (SDT)-based physical activity intervention into a behavioral weight loss program, designed with dissemination and implementation (D&I) in mind from the outset.
   b) Stakeholders for this project include patients (adults seeking weight loss), providers (registered dieticians who deliver weight loss curriculum), and leadership of the University of Colorado Anschutz Health and Wellness Center (AHWC) who make decisions regarding commercial weight loss programs offered at AHWC. The goal would be to initially disseminate to programs offered at AHWC, and then to expand further to offer the intervention on campus and other employers throughout the state of Colorado.

3. Draft specific aims page is provided below.

4. Frameworks I'm considering for my project:
   a) I'm thinking about using a hybrid approach. The Dissemination of Evidence-based Interventions to Prevent Obesity framework (Dreisinger et al. 2012) could be a helpful framework for me as a I develop my intervention, and the Diffusion of Innovation could be used for the dissemination strategy (how I will tell people about the intervention, where they find out about innovations and how to implement them). However, I am still learning about all of the frameworks and I feel very overwhelmed in selecting the framework(s) that is(are) the best fit for my project.

5. Target funding agency: NIH K01 Award

6. Challenges and Key Questions:
   a) A key issue that I would like to discuss with the group and Pragmatic Research Faculty Experts is in answering what types of pragmatic study designs, methods or measures would be best for testing my hypotheses? I would love to incorporate MOST, but I am struggling with the factorial design, given that this activity intervention will be delivered in a group-based setting. I'm considering using a 2^3 full factorial design that randomizes 8 clusters of n=10 participants in order to test 3 different intervention components. However, I am struggling to find examples of cluster randomization using MOST and I'm considering other designs including using a 1:1 setting.
   b) A second issue I would like guidance on is selecting the appropriate pragmatic research planning framework. One of my training aims for my K01 is D&I and currently I'm working on the credits towards the Graduate Certificate in D&I Science at University of Colorado. However, I have only taken one course (Design for Dissemination) and I'm feeling a overwhelmed with all of the frameworks and figuring out how to choose one.

SPECIFIC AIMS

While comprehensive behavioral weight loss programs produce modest (5-10%) weight loss over 3-6 months, approximately 25-50% of lost weight is regained within 1 year (1). Physical activity (PA) is one of the best predictors of sustained weight loss (2, 3) and current guidelines (4) recommend high levels of PA (300 minutes/week of moderate intensity) to prevent weight regain after weight loss. However, long-term adherence to PA is generally poor when adults with obesity enrolled in behavioral weight loss programs are provided an exercise prescription in the range of current guidelines (2, 5). **Thus, novel, effective, and scalable interventions are urgently needed to effectively promote increases in PA needed for weight loss maintenance.** The <u>overall objective</u> of this mentored K01 grant is to apply the Multiphase Optimization Strategy (MOST) (6) to develop and pilot test the integration of a novel, theory-based PA intervention into a behavioral weight loss program, designed with dissemination and implementation (D&I) in mind from the outset.

Motivation for PA is widely considered a significant factor in both initial adoption and long-term maintenance of PA (7) and involves both <u>implicit</u> ("gut reactions") and <u>explicit</u> (conscious thoughts) processes. There is increased evidence that implicit processes are associated with PA behavior (8, 9), however, to date, the integration of both implicit and explicit motivational processes as they relate to PA behavior has not been applied in a weight loss intervention. **In this K01 application, I propose to develop and optimize a theory-based PA intervention targeting implicit and explicit motivation that can be feasibly integrated into behavioral weight loss programs,** thus improving scalability and designing with D&I from the start. My own research, combined with prior evidence, indicates that constructs based on the Self-Determination Theory (SDT) including autonomy support, motivation or self-regulation, and perceived competence may be useful targets for PA interventions among adults with overweight/obesity (10-14). However, the majority of PA interventions targeting SDT-based constructs has employed a traditional research approach, which involves choosing intervention components (e.g. daily logs, individualized support sessions, feedback) based on scientific theory, combining those components into a single package, and testing that package in a randomized controlled trial. Thus, this approach does not tell us which intervention components are effective, at what levels, and in what combination(s) do or do not impact target constructs and maximize increases in PA. MOST is an innovative multi-phase framework adapted from engineering that uses highly efficient factorial experiments to evaluate the individual effect of each intervention component. The present study will use MOST to examine the effect of "active treatment components" on changes in motivation (implicit and explicit) and PA, which vary on cost.

This K01 lays the foundation for my <u>long-term career goal</u> of developing and disseminating theory-based, optimized PA interventions for adults with overweight/obesity that promote sustained behavior change. Along with my mentorship team, I propose to 1) develop a SDT-based PA intervention that targets implicit and explicit motivation and 2) test the feasibility of delivering the PA intervention in adults with overweight/obesity within an existing, guidelines-based behavioral weight loss program. Results will be used to optimize the intervention, <u>in preparation for a subsequent R01 efficacy trial</u>. My specific aims are:

Aim 1: Employ user-centered design methods to develop a SDT-based PA intervention and to select a set of 3 components to test in the pilot. Although I have already identified candidate intervention components, I will engage relevant stakeholders (including adults seeking weight loss, exercise specialists, and experts in the field) during focus groups to determine their perceptions of the intervention components and select 3 components to test in the pilot.

Aim 2: Conduct a cluster randomized pilot trial of the PA intervention that targets implicit and explicit motivation, using a 2^3 full factorial design to pilot test the feasibility and acceptability of the intervention. We will recruit 80 adults with overweight/obesity to receive the group-based, integrated behavioral weight loss intervention over 16 weeks, with a 26-week and 52-week follow-up. Eight cohorts of n=10 participants will be randomly assigned to a combination of the 3 intervention components determined in Aim 1. We will monitor feasibility and acceptability measures including: number of participants screened, proportion of eligible screens who enroll, retention rates for study measures, reasons for dropouts, treatment-specific adherence rates to study protocol, and acceptability ratings.

Aim 3: Explore potential effects of the intervention components on changes in motivation (implicit and explicit), and PA to inform a future R01 efficacy trial. We will measure implicit and explicit motivation for PA, and device-measured PA (activPAL) at 0, 8, and 16 weeks and at the 26-week and 52-week follow-up.

Impact: This K01 award will provide the opportunity to gain the needed proficiency in innovative experimental approaches and D&I research methodology as well as enhance my expertise in behavior change theory and strategy and mixed method research design. These experiences and skills will position me to successfully compete for a R01 to evaluate the efficacy of the optimized PA intervention in generating sustained PA.

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Overview of Health Issue & Statement of Significance

The US remains in the midst of an opioid overdose epidemic, which is most pronounced in rural regions. Excessive opioid prescribing and illegal diversion of these prescriptions have driven the expansion of the crisis rurally. Rural military veterans are prescribed greater than 30% more opioids compared to urban veterans, placing them at greater risk for opioid-related morbidity and mortality. The prevalence of OUD is rising among veterans, with greater than 69,000 having been diagnosed with OUD (Valenstein-Mah et al., 2018). This prevalence rate is more than 4% of all veterans, mirroring the national rate in the nonveteran civilian population.

Medication-assisted treatment (MAT) with buprenorphine, methadone, or naltrexone is the global gold standard treatment for opioid use disorder (OUD). MAT is an evidence-based and cost-effective OUD treatment that reduces morbidity, mortality, the spread of needle born infectious disease, illicit drug use, and crime, all while increasing adherence to medical treatment (Schuckit, 2016; Sigmon, 2014; United States Department of Health and Human Services, 2016). Because of its efficacy, MAT has become widely available in the US Veterans Health Administration (VHA), yet it remains underutilized among veterans with OUD (Valenstein-Mah, Hagedorn, Kay, Christopher, & Gordon, 2018), with only 35% of veterans with OUD initiating MAT (Hagedorn et al., 2018). Therein lies an urgent unmet need to bridge the gap in MAT utilization for rural veterans.

Investigation into why MAT is underutilized within the VHA is limited. To date, research in this field has concentrated primarily on VA providers' perceptions of the barriers and facilitators to expanding MAT availability (Wyse et al., 2018), not its utilization. The factors driving this underutilization in the rural veteran population are undefined, and there is no information about how the perspectives and experiences of rural veterans seeking MAT contribute.

Specific Aims

The central goal of this research is to explore and describe the experiences of rural veterans pursuing MAT for OUD. An enhanced contextual understanding of the perspectives of this group will define the key patient-level barriers to obtaining MAT and will better define the impact of the opioid epidemic on rural veterans, advancing veteran-centered care strategies. To address this central goal, the following Specific Aims will be addressed:

Specific Aim 1: To engage rural veterans with OUD seeking MAT to explore their perspectives related to MAT, and to describe their experiences seeking MAT in the VHA. Qualitative interviews will be conducted, facilitating exploration of patient-level experiences and perspectives as veterans seek MAT in this context. This approach will uncover ways to promote veteran-centered care and identify new treatment alternatives for our Colorado veterans that may also have broader relevance in the VHA nationally.

Specific Aim 2: To engage influential rural veteran service organizations, stakeholders and policymakers in reviewing findings from Aim 1 to identify opportunities and initiate action plans for promoting the inherent recovery capacity of veterans suffering from OUD positive change. A self-advocacy process for veterans will be facilitated through public forums and community-building open discussion to enhance understanding and identify key challenges and strengths.

Pragmatic Study Design

For this pilot project, a descriptive qualitative approach will be used to explore the factors driving MAT underutilization in the rural veteran population. Once we have identified the unique system- and patient-level barriers that exist for military veterans seeking MAT for OUD, a pragmatic study design will be used to test future interventions in real-life care settings.

Target Funding Agencies
I will be conducting this pilot research project in the context of the VA Advanced Fellowship in Health Services Research/COIN fellowship program. In the next 2 years, I hope to submit a VA grant for a Career Development Award.
Key Issue
General guidance – after determining the key patient-level barriers that rural veterans face obtaining MAT, will future interventional work in this area fit in the scope of pragmatic research?
How do I work with the VHA, Veteran Service Organizations (VSOs) and other stakeholders to adapt interventions to their needs and rural context?