State of Michigan
Department of Licensing and Regulatory Affairs
Marijuana Regulatory Agency

VETERAN MARIJUANA RESEARCH (VMR) GRANT PROGRAM

2021

REQUEST FOR PROPOSALS

VETERAN MARIJUANA RESEARCH (VMR) GRANT

RESPONSE DOCUMENT

ESTIMATED TIMELINE	
Issue Date	June 1, 2021
Inquiries Due	June 11, 2021
Inquiries Response Posted	June 18, 2021
Proposals Due	July 16, 2021
Anticipated Start Date	July 30, 2021

PART V: INFORMATION REQUIRED FROM APPLICANT(S)

Applicant(s) must submit one proposal. Electronically submitted proposals must have a scanned signature or e-signature and cannot exceed 15 MB.

Applicant(s) must provide responses to each section below. Be as descriptive as possible and answer each question in its entirety; some questions have multiple components. In your responses, provide a straight-forward, concise description of the applicant(s)'s ability to meet the requirements of the RFP. Questions that do not apply should be answered "N/A."

V-A Identification of Organization

State the full name and address of the organization, the organization's federal identification number, the organization's telephone and fax numbers, and what percentage of the organization is located in Michigan.

BEGIN APPLICANT RESPONSE

Regents of the University of Michigan
3003 S. State Street, SPC 1274
Ann Arbor, MI 48109
P: 734-936-1361
F: 734-764-8510
EIN: 38-6006309

The organization is located 100.0% in Michigan

END APPLICANT RESPONSE

V-B Authorized Negotiator

State the name of one (1) contact person and his/her telephone number, fax number, and electronic mail address. The contact person must be authorized to be the negotiator for the proposed Grant Agreement with the State.

BEGIN APPLICANT RESPONSE

Kellie Buss
Sr. Project Representative, ORSP
P: 764-936-1361
F: 734-764-8510
E: klbuss@umich.edu

END APPLICANT RESPONSE

V-C Method for Addressing the Problem

State in succinct terms the applicant(s)'s proposed method for addressing the problem presented in Section III-B, Problem Statement. Describe any significant obstacles the applicant(s) has had coordinating and managing clinical trial research.

Background and Rationale

In 2018, the voters of the state of Michigan passed the Michigan Regulation and Taxation of Marihuana Act. A provision of this law provides funding for research on the effectiveness of marijuana (hereafter, cannabis) to treat "*the medical conditions of United States Armed Services Veterans and preventing Veteran suicide*". This application proposes a set of three concurrent randomized clinical trials (RCTs) that test the effectiveness of various cannabis constituents in treating common medical symptoms - chronic pain, anxiety, and insomnia - that increase the risk of suicide, especially in Veterans.[1-5] For example, our prior studies of Veterans have found that male Veterans with anxiety disorders have twice the risk of dying by suicide as those without; for women risk is increased 3.5-fold.[5] Of pain conditions, diagnoses of back pain, migraine, and psychogenic pain are associated with dying by suicide among Veterans, and more generally, Veterans are susceptible to the risk of suicide and overdose stemming from their high prevalence of chronic pain[6] and use of opioids.[7] Lastly, insomnia is associated with 1.5 times higher odds of suicide attempt among Veterans, even after adjustment for factors associated with suicide risk, including substance use disorder, anxiety, bipolar disorder, and depression.[8] By proposing studies aimed at these common symptoms that are "upstream" of suicide, our approach will lead to a reduction in suicide attempts through mitigating symptoms that worsen suicide risk.

It is widely acknowledged that the Drug Enforcement Agency scheduling of cannabis obstructs therapeutic cannabis research, yet our group successfully conducts NIH-funded cannabis and cannabinoid research that has overcome this barrier. For example, we recently received large NIH grants to conduct or design RCTs that elucidate the analgesic and sleep impacts of cannabidiol (CBD) and Δ-9-tetrahydrocannabinol (THC) in knee osteoarthritis and multiple sclerosis (MS), as well as the opioid-sparing potential of CBD following surgery. These grants required FDA approval but are utilizing FDA-approved forms of THC (dronabinol) and CBD (Epidiolex) to ease the regulatory burden and increase study efficiency through bypassing the 6-9 months necessary for approval of a Schedule I license.

For the proposed RCTs, we will employ an even more pragmatic design, using conditions that represent "real world" cannabis use, wherein we will randomize eligible study participants to receive evidence-based and tailored guidance on how to appropriately use the products they obtain from state-licensed dispensaries, or usual practices (i.e., no guidance). We will only enroll participants who report that they are already using cannabis medicinally, and we will not be prescribing, dispensing, or recommending cannabis, avoiding designs that would require the highest levels of regulatory control. However, these are Randomized (the randomization is to education vs. no education), Controlled (i.e., the group that receives no instructions is the control group) Trials that address the health of veterans, and are aimed at helping better control three symptoms known to increase the risk of suicide.

The tailored educational guidance will draw from the scientific literature and clinical expertise of scientists and physicians who work directly with medical cannabis patients to develop best practices for use based on: 1) individual symptoms (e.g., pain vs. anxiety vs. insomnia); 2) recommended cannabinoid content (THC vs. CBD); 3) therapeutic levels of cannabis or cannabinoids according to the scientific literature, and; 4) route of administration (e.g., smoking, edibles, tinctures, etc…).[9-11] These studies will yield particularly useful information for Veterans and beyond since Michigan and many of states and countries have legalized or decriminalized cannabis, but not given patients nor providers appropriate guidance regarding use patterns that will maximize the potential benefits of cannabis products while simultaneously minimizing harm. Thus, if our educational programs are found to be effective, they could be rapidly implemented throughout the state and beyond to help individuals get relief of these symptoms, hopefully reducing downstream risk of suicide or other mental health consequences. We will measure these aspects of actual consumption using a customized smartphone app in which participants will enter data on these use parameters each time they use cannabis. We will also employ state-of-the-art analysis methods that account for differences between the treatment recommendation and actual use, maintaining the integrity of the clinical trial design. In addition, we will objectively measure sleep and activity data using wearable sensors (e.g., Fitbits), allowing a detailed and comprehensive picture of how these products affect Veteran health.

This approach is both innovative and useful since we will conduct our studies in real-world settings where Veterans currently use cannabis products for symptom self-management. We will obtain University of Michigan Institutional Review Board (IRB) approval for our proposed studies as well as other appropriate regulatory approvals (e.g., FDA). This design is essential to meeting the timeline specified in the announcement. Further, we will recruit and retain thousands of participants that will enable three, rather than a single, clinical trial. As participants may be using variable quantities of cannabis, our trials and observational study will also allow us to investigate differential outcomes based on cannabis use patterns (e.g., those who recently initiated use vs. those who have used cannabis for many years). Our proposed study protocols provide considerable scientific structure to these already-occurring personal experiments, such that we can more definitively assess whether cannabis products can improve the health of Veterans and ultimately reduce their risk of suicide.

Statute Description	Our Application
To provide $20 million annually to one or more clinical trials that are approved by the United States food and drug administration	We will conduct *three* randomized, controlled trials that will obtain rigorous and appropriate regulatory approval through the appropriate agencies (e.g., University of Michigan IRB, the FDA, etc…).
Sponsored by a non-profit organization or researcher within an academic institution	These trials will be conducted by researchers at the University of Michigan.
Researching the efficacy of marijuana in treating the medical conditions of United States armed services veterans	Our three clinical trials will investigate the effects of a tailored educational intervention designed to help participants effectively use marijuana for treating some of the most common symptoms afflicting Veterans (chronic pain, anxiety, and insomnia) – all of which are risk factors for veteran suicide. By alleviating these symptoms, our approach would reduce suicide attempts by mitigating symptoms that worsen suicide risk.
And preventing veteran suicide	We acknowledge that our study is unable to directly assess the efficacy of marijuana in preventing veteran suicide. To design a study of that nature would require tens or hundreds of thousands of participants. Given the ethical issues surrounding suicide as a treatment outcome, we also believe that such a study would be better suited to an epidemiological design rather than a randomized controlled trial.

Research team. The structure and role of our team is described more fully later in this application. In brief, our team is led by co-Principal Investigators (co-PIs) Drs. Amy Bohnert, Kevin Boehnke, and Daniel Clauw, all three of whom are faculty members at the University of Michigan. These investigators have extensive combined experience in clinical trials, Veteran health and medical conditions, cannabis, and leading large projects from federal, industry, and state funding agencies. In addition, numerous co-investigators and staff with complementary expertise will aid with content development, intervention design and manualization, software design, recruitment, stakeholder engagement, RCT implementation, data management, statistical analysis, and publication to ensure speedy dissemination of our results.

Overview of proposed studies. We will perform the proposed studies using an innovative design wherein three randomized controlled trials are superimposed upon a much larger observational study. In so doing, we will not only be able to test the effectiveness of our intervention but also recruit one of the largest and best characterized cohorts ever assembled of Veterans using medical cannabis, enabling many additional and impactful scientific contributions that will support Veteran health.

For the **observational study**, we will recruit 3000 Veterans from across Michigan that want to participate in a study investigating whether naturalistic cannabis product use can improve pain, anxiety, or insomnia.

Participants must be currently using cannabis products for pain, anxiety, or insomnia symptom management at the initiation of the study period. To enhance recruitment and reduce participant burden, all study visits will be conducted via video conference or phone call. Participants will be recruited through: 1) Dr. Bohnert's existing research and community outreach infrastructure, which is geographically distributed throughout the state; 2) Building partnerships with non-profit Veteran organizations, and; 3) leveraging our existing relationships with Veteran Affairs medical centers (VA) in Michigan, as three members of our investigative team have salaried appointments in the VA and have conducted studies recruiting Veterans in Michigan. Our team will collect and analyze health and symptom patterns in connection to cannabis use in the larger cohort of 3000 individuals using state-of-the-art methods that strengthen causal analysis within non-randomized clinical studies.

Once Veterans are enrolled in the observational study, they will begin using a smartphone app called MyDataHelps, which can also be used on any internet-enabled device if an individual does not have a smartphone. MyDataHelps was developed by a Michigan-based firm and enables new types of pragmatic digital trials such as the ones we propose. This app is currently used in several large well-known studies, including the NIH All of Us study and the eFramingham study.[12-15] This app will ask participants a series of validated self-report Patient Reported Outcomes (PROs) that will track each participant's individual symptoms, including the primary outcomes of interest: pain, anxiety, and insomnia. Our prior studies using the MyDataHelps app with Michigan residents to deploy these surveys has resulted in survey completion rates >90%. Daytime activity data and sleep characteristics will be continuously and unobtrusively collected with wrist-worn actigraphy (e.g., FitBit). Use of these technology-enabled data collection methods offer a number of benefits. They are accessible to participants, who can complete PROs when and where they choose and provide activity data simply by wearing the activity monitor. Automated data collection, scoring, and storage of MyDataHelps is uniquely scalable for large studies. Additionally, real-time data collection shows superior sensitivity to change relative to traditional "recall" surveys that are biased by memory heuristics that favor recent and extreme experiences. Therefore, our choice of assessment methodology has both pragmatic and scientific advantages.

Veterans enrolled in the observational study **who indicate that they wish to receive education about cannabis use** for pain, anxiety, or insomnia symptoms will also be allowed to enroll in the **pragmatic RCTs** (12 weeks in duration). We will recruit n=200 "tailored guidance" participants and n=200 controls for each symptom, resulting in **3 RCTs** of **n=400 each**. In these trials, individuals who declare their wish to receive education focused on managing these respective symptoms with cannabis will be randomized to receive either "usual practices" or "tailored guidance". For usual practices, participants will use cannabis products of their own choosing and will be asked about what products they use, how they make decisions about them, and what they've discovered about the effectiveness of these products. For tailored guidance, participants will still be responsible for purchasing their own products and ultimately deciding how to use them, but in addition will receive evidence-based education about cannabis use for their symptoms (described more fully below). Once the participant has completed the pragmatic trial phase for any of the three symptoms, they will then re-enter the observational study. Regardless of enrollment in the pragmatic RCTs, we will follow all participants for at least one year after enrollment, collecting a wide battery of validated patient-reported outcomes every three months, weekly measures of side effects as well as pain, anxiety, and insomnia symptoms, and daily measures of cannabis use.

Our primary objective in these three pragmatic RCTs is to determine whether this educational intervention improves symptom management (i.e., is cannabis effective in treating pain, insomnia and anxiety). Our secondary objectives will encompass: 1) how well participants tolerate cannabis, i.e., whether this educational intervention effects cannabis's side effect profile and cannabis use disorder symptoms, and 2) to study the effect of cannabis use on health outcomes within the entire sample by using advanced causal inference techniques to compare Veterans with varying cannabis use patterns (e.g., how daily vs. monthly use may affect sleep patterns, measured via sensors).

These studies will complement the placebo-controlled randomized controlled trial proposed by the Multidisciplinary Association for Psychedelic Studies (MAPS), which tests whether controlled cannabis administration for five weeks reduces post-traumatic stress disorder (PTSD) symptoms. Our team has a working relationship with the coordinating investigator of that study, Dr. Sue Sisley MD, evidenced by our previous work together that resulted in several published articles investigating outcomes of cannabis use among people with chronic pain.[16-18] As such, we anticipate working together collaboratively to support both studies - especially with regards to Veteran engagement and recruitment. For example, participants from the MAPS study who wish to do so could seamlessly enroll in the observational study after that clinical trial is complete, and we will advertise both studies to all potential participants.

Tailored Guidance Educational Intervention

The tailored guidance cannabis coaching intervention will be developed based on the latest scientific literature as well as the extensive clinical experience of Dr. Evan Litinas, who has worked with medical cannabis patients for nearly a decade. Dr. Litinas and other investigators will train cannabis coaches and manualize the intervention. Participants randomized to receive "tailored guidance" will be assigned to four manualized educational sessions (via video conference or teleconference) with a trained cannabis coach who has expertise and training on appropriate medical cannabis use for these conditions. Sessions will occur at trial initiation, 2 weeks, 5 weeks, and 9 weeks after initiation; a total of up to 4 hours total over the course of the intervention. Participants randomized to receive "usual practices" will also meet with a cannabis coach on the same schedule of study visits, but instead of receiving educational guidance they will be asked a set of questions about how they currently use cannabis such that we will be able to better understand the naturalistic use environment. This information will be used to complement and enhance future versions of the education intervention.

In tailored guidance sessions, the cannabis coach will assess the primary symptom of interest (pain, anxiety, or insomnia) and current use patterns. They will then educate participants on routes of administration, cannabinoid content, and appropriate therapeutic levels of cannabis or cannabinoids according to the scientific literature for managing symptoms of pain, anxiety, and insomnia. Educational content will also include known side effects of cannabis (e.g., common effects like dizziness or sedation, rare side effects like hallucinations or vomiting[19]) as well as specific risks associated with administration routes, such as respiratory harm from smoking[19] or unregulated vaporized concentrate products,[20] and the delayed onset of edible products.[21] The first session will largely focus on educating about the differential effects of THC and CBD, the effect onset and duration of effects of each administration route (i.e., smoking, vaporizing, eating, topicals, tinctures), how to methodically approach quantity used, and effectively tracking symptoms when using cannabis. The following sessions will focus on suggestions of how participants might consider adjusting their use patterns to minimize negative side effects while maximizing benefit, referring to standardized decision trees for each condition that take into account clinical changes, cannabis side effects, and harm reduction. As educational sessions will be conducted via video conference or phone, they will be recorded so that we can ascertain whether the educational sessions elicit behavior change and enhance the effectiveness of using cannabis to manage pain, anxiety, and insomnia symptoms. Investigators will also review 10% of these sessions to monitor that the intervention is faithfully delivered according to the manual. If this intervention is found to improve outcomes, the coaching model and training materials will facilitate speedy dissemination.

Example: A participant has trouble falling asleep and staying asleep, and smokes high-THC joints several times per day to aid with sleep. Given these symptoms and use pattern, the cannabis coach would provide education regarding synchronizing use with when symptoms occur (i.e., at night) as well about alternative products and timing of use, such as a 1:1 CBD:THC tincture 30 minutes before trying to fall asleep as well as a THC-dominant capsule right at bedtime. Cannabis coaching will be offered as suggestions rather than prescribed as medical advice. Coaches will not provide access to specific cannabis products.

Rationale: THC and THC analogs have known positive effects on insomnia, especially in the context of chronic pain or PTSD (which many participants will have).[22-28] CBD can reduce anxiety and intoxication associated with THC,[29] so co-administration may be useful to help with falling asleep. Tinctures typically take effect

within 15-45 minutes to help with falling asleep, capsules typically take 1-3 hours to take effect and will last 6-8 hours, which may help the participant stay asleep.[9] If the participant does not wish to take a tincture instead of smoking, the coach may offer education about alternative inhalation routes such as vaporization, as vaporization results in less exposure to combusted material and carcinogens. If the participant is uninterested in any option except smoking, this education may still result in harm reduction if the participant chooses to smoke one joint at bedtime rather than several throughout the day, reducing total smoke exposure.

Incentives

Participants in the **observational study** will receive $50 for completing each visit (baseline, 3 months, 6 months, 9 months, and 12 months), as well as $10/month for 70% or greater completion of daily measures ($370 in total).

Participants in the **pragmatic RCT**s will receive an additional $50 for completing the baseline visit for trial initiation, $25 for each intervening study visit, and $50 for completing the 12-week visit at the end of the trial (an additional $175). In addition to the "tailored guidance" or "usual practices" sessions, symptom and use assessments will occur at each study visit.

Outcome Measures

All self-reported outcomes (PROs) will be collected via the digital data collection platform MyDataHelps (via a smart phone or other internet-connected device).

Our *primary outcome* for the three trials will be measured via a Patient Global Impression of Change patient-reported outcome measures specific to each symptom domain (pain, insomnia, and anxiety).[30,31]

Our *primary outcome* for the observational study will be the PROMIS Scale Global health v1.2, a 10-item measure used to assess overall/general health and functioning.[32]

Secondary outcomes – clinical trials

For all RCTs, we will collect data on side effects of cannabis products based on the known side effects of THC and CBD from FDA-approved dronabinol and Epidiolex.[33,34] We will also assess symptoms of cannabis use disorder using the Cannabis Use Disorder Identification Test - Revised (CUDIT-R) version in all participants.[35] The CUDIT-R is an 8-item measure that assesses cannabis use frequency and cannabis-associated problems (e.g., inability to stop using cannabis, memory issues). This measure is scored from 0-32, with scores of 8-11 indicating possibly hazardous use and 12 or higher indicating possible cannabis use disorder. Changes in CUDIT-R scores will be compared from baseline (prior to treatment) to the end of treatment (week 12). Lastly, we will use the Positive and Negative Suicide Ideation (PANSI) scale to assess changes in suicidal ideation from baseline through the end of the RCT.

1) For the chronic pain RCT, we will measure average daily pain intensity using a 0-10 Numeric Rating Scale assessed each day in the week prior to treatment (baseline) vs. the same daily measurement of pain for seven days at the end of treatment (weeks 11-12).[30,31] Average scores over the 7-days pre- and post-treatment will provide the most reliable and sensitive assay of chronic pain.[36] Participant scores will be compared from baseline to the end of treatment.
2) For the insomnia RCT, we will use the Insomnia Severity Index, which is a 7-item measure that grades severity of insomnia from not clinically meaningful through clinically meaningful (range 0-28).[37] Items assess difficulty falling and staying asleep, problems with waking up too early, sleep satisfaction, current level of distress around sleep problems, and how much sleep problems interfere with daily functioning. Additionally, we will administer items of the Consensus Sleep Diary each day for seven days pre- and post-treatment to characterize broader aspects of sleep quality.[38] We will also assess total sleep minutes and sleep efficiency collected from wearable sensors. Participant scores will be compared from baseline to the end of treatment.

3) For the anxiety RCT, we will use the 4-item measure from the PROMIS 29+2 to assesses daily anxiety[39] for seven days pre- and post-treatment. Items assess the frequency of the following problems over the past 7 days: uneasiness, difficulty focusing, worried, and fear. This measure is scored from 0-20, with higher scores indicating more severe anxiety. Scores will be summed for each day and averaged across the week to produce a reliable assay of anxiety for each participant. Participant scores will be compared from baseline to the end of treatment.

Note: We acknowledge that it is common for Veterans to have co-morbid pain, anxiety, and/or insomnia. Participants will enroll in whichever RCT focuses on their primary symptom of concern, but we will also plan on tracking other symptoms throughout. I.e., if a participant is using cannabis primarily for pain but has co-morbid anxiety and insomnia, they would enroll in the pain RCT and would report all three symptoms over the course of the study to see how they change over time.

Secondary outcomes – Observational study
For the observational study, we will collect data on side effects of cannabis products based on the known side effects of THC and CBD. We will also investigate trajectories in CUDIT-R score over the course of the study. We will use the Positive and Negative Suicide Ideation (PANSI) scale to assess suicidality in all study participants over the course of the study, allowing us to investigate novel trajectories of cannabis use/symptom clusters that may be associated with increased or decreased risk of suicidal ideation. Lastly, we will also collect data on ED visits and other healthcare utilization throughout the study – including following the RCTs. This will allow us to investigate the longer-term health effects of the intervention, comparing against those in the observational study who did not go through the pragmatic RCT.

Exploratory outcomes – All studies
We will collect data on numerous exploratory and explanatory measures, including:
1) Cannabis use frequency and cannabinoid content through ecological momentary assessment;
2) Effects of cannabis on cognition (measured via a cognitive task module in MyDataHelps);
3) Pain phenotype: e.g., whether pain is associated with inflammation vs. nerve damage vs. central nervous system dysfunction;[40-42]
4) Demographic and social factors associated with cannabis use and symptoms of pain, anxiety, and insomnia, as well as military history (years of service, deployments, combat, etc.)
5) Post-traumatic stress disorder symptoms;
6) Symptoms known to be associated with these conditions such as depression, fatigue, ability to participate in social roles, and cognitive function;[43]
7) Use of other prescription medications and healthcare utilization, and;
8) Passively-collected health data through electronic devices including physical activity, heart rate, and sleep patterns.

Analysis plan
Randomized Clinical Trial Outcomes
Prior to testing the effect of group assignment, we will undertake several analyses to ensure that valid measures and models are used. This will include checks on the balance of randomization so that any imbalances can be adjusted for in the models. We will quantify the missing data and determine if missingness is related to participant characteristics. When data are not missing at random, we will either adjust for these variables or develop weights. When data are missing at random, we will use multiple imputations and conduct sensitivity analysis to examine the impact of the imputation compared to leaving the data as missing.

All statistical hypothesis tests will use $\alpha = 0.05$ for significance testing. Contingency tables and t-tests will be used to examine bivariate associations. We will assess treatment effects by using Generalized Estimating Equations to examine changes in the dependent measures over the study period. GEEs have the advantage of: 1) adjusting for correlations between data points (e.g. repeated measurements on individuals); 2) retaining participants with incomplete data; and, 3) allowing time-varying independent variables. If a visual inspection

of the distributions of the outcome variables indicates the effect of group may vary over time, we will examine the impact on the model fit of including categorical variables for assessment time and an interaction of intervention by assessment time. As we will collect detailed cannabis use data among those in the tailored guidance vs. usual practices groups, we will be able to adjust for individuals in the usual practices who may already be using products in a way that is consistent with the best practices from the educational intervention.

Cohort Analysis

The study will support secondary analyses of the relationship between many types of cannabis use patterns and many health outcomes, greatly enhancing the value of the project. This includes testing types of cannabis exposure that would be infeasible to assign via randomization. However, because these cannabis exposures are not randomized, the analyses will need to address potential confounding, i.e., factors that are causes of both cannabis use choices and health outcomes. We will follow the approach of "emulated trials" for these analyses.[44,45] This is a process by which the research team, with input from stakeholders, specifies an ideal randomized controlled trial (the "target trial") and then designs an observational study that matches the trial in features such as inclusion/exclusion criteria and measurement strategies. This approach has been recently used to study the effectiveness of the mRNA COVID vaccine under "real world" conditions[46] and is well-suited to rich survey data collected from a large cohort, as in the proposed study. Analyses will generally follow the same approach as in primary analyses, but the statistical methods will switch to modeling designed to account for confounding over time, such as marginal structural models[47] and related methods.[48]

Sample Size

We have selected our sample size for the three Randomized Clinical Trials to ensure we are sufficiently powered (i.e., 80%) to detect an effect size that is relatively small, or specifically, a Cohen's d effect of 0.30. Assuming a two-sided $\alpha = 0.05$ and 90% retention over follow-up, this translates to our selected sample size of 400 per trial.

Feasibility of proposed approach

Our research team has considerable experience and an established record in: 1) studying naturalistic trends in medicinal and recreational cannabis use for pain[16-18,49-57], 2) studying pain, insomnia and anxiety,[1,4-7,16-18,40,41,43,49,50,52-54,57-141] 3) studying risks of suicide among Veterans and in the broad population,[1,3-7,131,142-160] 4) performing research with Veterans, both in the Veteran's Administration healthcare system and in the community,[1,3,5-7,106-115,117-133,135,142-144,146-148,150-191] and 5) collecting rich patient-reported symptoms and passively-collected health data.[1,3,5-7,13,106-115,117-133,135,142-144,146-148,150-191] This experience influences our belief that it is practical and important to study cannabis effects on pain, anxiety, and insomnia as these common conditions that increase suicide risk among veterans, and that suicide outcomes such as attempts and death are relatively rare (albeit important) outcomes. Thus, it is very difficult to ensure sufficient sample size or a generalizable population in clinical trials with these outcomes. We have also had significant success conducting both classic clinical trials and pragmatic designs and publishing our results in high impact journals.[5,6,65,66,100,106,114,115,121,130,176,180,182,188,192-199] As such, we are confident of our ability to perform the proposed studies.

Impact and potential benefits

Cannabis policies have advanced more rapidly than cannabis science, with 37 states having legalized cannabis for medical purposes. The clinical trial literature on cannabis-based medicines for suicide-related outcomes and underlying risks due to symptoms such as chronic pain, anxiety, and insomnia remains woefully inadequate due to the barriers to using existing products, the proliferation of easily available dispensary products, and stringency of inclusion/exclusion for such trials which make it unlikely that such results would be generalizable to most consumers. Through this proposal, we will empirically test high-quality cannabis use guidance for conditions that are known to be strong risk factors for Veteran suicide, which are also some of the most common conditions that people use cannabis products. Our pragmatic, randomized clinical trial design will overcome many of the limitations of existing clinical trial research, including small sample size, use of products that are not available to consumers, and short follow up. Further, our focus on harm reduction and evidence-

based guidance removes barriers to participation and lowers the risks to study participants, who will not be receiving a novel drug but instead will be receiving education. Lastly, unlike the study drug interventions in other clinical trials, our educational intervention is easily scalable - not only to Veterans in Michigan but also to people with chronic pain, anxiety and sleep issues in Michigan and the many other states and countries which have passed medical or adult use cannabis legislation. Doing so will catalyze the critical work of minimizing harm and maximizing benefit from these widely available products, which may also ultimate lower incidence of Veteran Suicide.

END APPLICANT RESPONSE

V-D Management Summary

(1) Describe management procedures that will be used by the organization to complete the proposed project.

(2) Describe the organization's quality control measures, including measures for ensuring compliance as well as eligibility determination. In your description, include information regarding separation of duties.

(3) Selected applicant(s) must provide fiscal control and financial accounting procedures that will assure that grant funds will be accounted for and properly dispersed in a way that will allow the Issuing Office to clearly review and verify all grant related expenditures. Describe the organization's internal control policy:

- Identify the type of accounting system/software the organization will use to account for grant funds,
- Identify how duties will be separated,
- Describe how the organization will account for grant funds, i.e., will grant funds be placed in a separate bank account, will the grant funds be assigned a unique code(s) within the organization's overall accounting system. Ensure funds are maintained in a non-interest-bearing account.
- Indicate whether internal and external audits of the organization's operations are performed on an annual basis. Selected applicant(s) must provide a copy of the organization's most recent audited financial statement as well as a copy of the organization's most recent single audit as required by OMB Circular 200.36

(4) Describe your agency's data security plan.

BEGIN APPLICANT RESPONSE

(1) Management procedures

Established in 1817, the University of Michigan (U-M) is one of the world's largest public universities, and it has long been considered one of the major research institutions in the United States. It is an internationally recognized research university with a broad spectrum of expertise in biomedical research. Research is conducted within the nineteen academic schools and colleges, as well as within several large-scale research institutes, which emphasize interdisciplinary work. Teaching and research often cross traditional Departmental and School boundaries, especially because of the University's impressive set of interdisciplinary research centers and institutes. U-M's dedicated departmental and institutional staff ensure appropriate disbursement and management of funds, regulatory issues, and

research conduct, with a long history of successfully managing large grants and awards from the Michigan state government, foundations, industry, and government agencies.

The management procedures will: 1) aligns the program with goals of the research and program partners; 2) ensure that project tasks and deliverables are achieved; 3) monitors project performance; and 4) closes out the project. The most efficient and cost-effective way to manage a program of this size is to work within a foundation of robust project management practices. The Leadership Team and Program Manager will develop the master project management plan and track progress. Other core directors are responsible for developing functional project plans in support of the overall master plan. Regular meetings will be held to review progress and the status of deliverables.

Administration will be supported by a cadre of highly capable faculty and staff that already successfully administer several large center and other grants and state contracts. Overarching programmatic administration will be coordinated by a lead project manager, Laura Thomas, who will work with Amy Harms, our grants administrator in Anesthesiology. Ms. Harms will be principally responsible for the fiscal administration of the projects and working with both institutional and sponsor organizations to establish necessary contracts, managing budgets, procurement, and coordinating any intellectual property or materials transfer matters that may arise over the course of the program period.

Key Management Protocols

Formulation of a monitoring and reporting plan that documents the necessary information required to effectively manage the data from study start-up to delivery of study outcome analysis is required. Here we describe how the Leadership Team will oversee monitoring and reporting.

Leadership Meetings. The Leadership Team, Team Leads, and key staff will have a weekly conference call to discuss progress of the project, including recruitment, retention, and any other challenges.

Document and Record Control. Documents and records will be reviewed by the leads according to role function. Any changes to Standard Operating Procedures (SOPs) due to modifications for this project will require a formal approval by the Co-PIs. Records will be retained for all protocol data, quarterly reviews, and approvals. Study data will be entered in the secure research site portal.

Tracking. In our prior studies, we developed participant recruitment electronic "dashboards" that contain tracking information for each individual's progress through recruitment and study protocols. The dashboard generates automated weekly reports of the participant recruitment activities, randomization, and survey completion.

Hiring and Supervision of Staff. We will engage Michigan Medicine Human Resources to post and fill positions on the research team. Staff will have annual performance appraisals and be encouraged to develop performance goals using the SMART (Specific, Measurable, Achievable, Relevant, Time bound) process. Policies are described in detail here: https://hr.medicine.umich.edu/pay-benefits/employment-policies

Training Program. All key personnel will be required to complete a training program at the start of the study to align the team to the overall goal and task deliverables. Tests may include their proficiency to follow internal documented procedures. Also, we will ensure that all personnel involved in handling research subjects are trained according to University of Michigan human subjects research standard practices. Training will be documented, verified for its effectiveness, and reviewed annually. If needed, we will provide repeat and continued education training. Training specific to the cannabis coaching will be overseen by the directors of the Cannabis Coaching and Manualization Core.

Quality Control Inspection. Monitoring and quality control will be overseen by the director of the Data Collection, Management, and Privacy Core. These inspection requirements and check-points will be tailored to the methods by which the data will be handled, processed, stored and transferred. The inspection process includes confirmation of data accuracy and completeness.

(2) Quality Control Measures, compliance, and eligibility determination

The following protocols will be undertaken to ensure high quality control procedures are used throughout the conduct of the study.

Hiring

We will follow all University of Michigan policies to ensure that well-qualified candidates are selected, using a fair and rigorous process.

Training

Staff and investigators associated with the project will undergo appropriate annual training for project-specific procedures (see details below). In addition, all staff and investigators have received appropriate training per institutional guidelines, including training on Humans Subjects research, HIPAA, and Good Clinical Practices.

Training procedures

1. Study coordinator or study investigators will review the Data Safeguards with all study staff. The Data Safeguards is a guideline administered by the University of Michigan Medical School Data Office for Clinical and Translational Research. It outlines the "do's and don'ts" of data usage for research. The guidelines explain what personal health information includes and how to properly protect and store data.
2. All study staff will be trained by the study coordinator or investigators to properly enroll participants per protocols, guidelines, and recruitment scripts. A staff member will need to be observed successfully recruiting a participant independently five times before training will be considered complete.
3. All study staff will be trained by the study coordinator and investigators to properly conduct a risk assessment.
4. All study staff will be trained by study coordinator or investigators to follow the Participant Non-Compliance Plan.
5. All cannabis coaches will be trained by investigators to administer the manualized intervention for chronic pain, anxiety, and insomnia.

Adverse Events

Cannabis-related side effects will be monitored and identified via two mechanisms:

- Telephone and/or email follow-up conducted by Co-PIs, Co-I, or Study Coordinator/Research Assistants.
- Self-reporting in survey responses by subject via MyDataHelps app.

All adverse event reporting will be done in accordance with institutional guidelines per IRBMED.

Data Monitoring Plan

Interim monitoring will be conducted monthly by the study coordinator and/or investigators

1. Observe enrollment calls and assess staff adherence to study protocol and scripts
2. Random "spot checks" of participants' data within the study participant tracking database and the MyDataHelps data collection application to ensure data completion and accuracy. Monitor data quality through routine review of submitted data to identify and follow-up on missing data.
    a. Consent form completion
    b. Survey responses
    c. Fitbit Data: heart rate, physical activity, geospatial location, sleep
3. Review risk assessments, AEs, and subject withdrawals to verify proper reporting and measures were completed.
4. Review protocol deviations to verify completion of corrective action and to verify proper recording and reporting.
5. Submission and tracking of protocol amendments. Documentation of IRB approvals.
6. Study team will review in team meetings the weekly "participant retention and activity engagement" reports generated from the study dashboard

Compliance

IRB and ethics

The study will be reviewed and approved by the Institutional Review Board (IRBMED, University of Michigan, Ann Arbor, MI). Before implementing this study, the protocol, the proposed informed consent form and other information to be provided to subjects, will be reviewed by a properly constituted Institutional Review Board (IRB). Any amendments to the protocol must be reviewed and approved by IRBMED. This study will be carried out in compliance with the protocol and the principles of Good Clinical Practice, as described below:

1. ICH Harmonized Tripartite Guidelines for Good Clinical Practice 1996. Directive 91/507/EEC, The Rules Governing Medicinal Products in the European Community.

2. US 21 Code of Federal Regulations dealing with clinical studies (including parts 50 and 56 concerning informed consent and IRB regulations).

3. Declaration of Helsinki and amendments, concerning medical research in humans (Recommendations Guiding Physicians in Biomedical Research Involving Human Subjects)

Eligibility determination:

Inclusion Criteria for all participants:

- Ability to read and speak English sufficiently to allow for written informed consent and patient-reported outcomes measures;
- Currently using cannabis products for treatment of pain, insomnia, and/or anxiety symptoms;
- Adult (aged 21 years or older);
- Armed Services Veteran;
- Willingness to attend all virtual study visits;
- Willingness to wear Fitbit or other similar sensor for passive-data collection;
- Willingness to fill out daily diary via smartphone to assess symptom status and cannabis use (Note: The study team has budgeted appropriately to procure smartphones and data plans for study participants).

Inclusion criteria for clinical trials:

Note: We acknowledge that it is common for Veterans to have co-morbid pain, anxiety, and/or insomnia. Participants will enroll in whichever RCT focuses on their primary symptom of concern.

Additional Inclusion Criteria (chronic pain trial)

- Wish to receive education on cannabis use for treating chronic pain (primary symptom);
- Willingness to attend cannabis coaching sessions to receive education on effective cannabis use.

Additional Inclusion Criteria (insomnia trial)

- Wish to receive education on cannabis use for treating insomnia (primary symptom);
- Willingness to attend cannabis coaching sessions to receive education on effective cannabis use.

Additional Inclusion Criteria (anxiety trial)

- Wish to receive education on cannabis use for treating anxiety (primary symptom);
- Willingness to attend cannabis coaching sessions to receive education on effective cannabis use.

Exclusion Criteria

- Inability to provide informed consent (e.g., cognitive impairment, unable to sufficiently communicate in English);
- If participant volunteers that they are pregnant;

- Unable to attend study visits or planning to move out of the state of Michigan during course of study;
- Risk for eminent harm - Suicidal ideation or wish to die as assessed with the PANSI (Positive and Negative Suicide Ideation) questionnaire and further risk assessment by study team members. This will only apply to (anticipated to be rare) instances were ensuring participant immediate safety supersedes all other treatment needs, as determined by the study psychiatrist.

Quality Control of Eligibility Determination: The majority of eligibility determination will be based on participant self-report on surveys in the MyDataHelps app, which will be programmed to determine whether a participant meets criteria. The program manager will review responses to confirm that this process functioning correctly. A few criteria may require judgment from research staff during conversations for recruitment (e.g., mentioning pregnancy status). All staff will be trained to conduct these conversations consistently. Study-specific decision aids will be used to ensure consistent determinations. The program manager will review all discretionary decisions, with support from the PIs.

(3) Fiscal Control:

The University of Michigan Office of Research (UMOR) financial management and oversight activities align with the requirements laid out in the University of Michigan Statement on Stewardship and the Fiscal Responsibilities Standard Practice Guide (SPG) 500.1. Within UMOR, financial management and oversight is viewed as a shared responsibility between the Office of the Vice President of Research and its reporting departments, programs, and initiatives, which comprise the entirety of UMOR.

- University of Michigan uses Oracle's PeopleSoft (M-Pathways) which integrates financials and physical resources, human resource management and student administration.
- Sponsored Programs manages the financial post-award activities of the University of Michigan's research enterprise and other sponsored activities to ensure compliance with applicable federal, state, and local laws as well as sponsor regulations.
- Sponsored funds (grants) are accounted for individually and assigned their own chartfields, the building blocks of the University of Michigan financial reporting structure, whose elements provide a common framework for internal and external financial reporting and analysis.
- An external audit of the consolidated financial statements is conducted annually. The current independent auditing firm is PriceWaterhouseCoopers. University of Michigan Audit Services conducts an annual risk assessment and develops an audit plan for the fiscal year based on Input from more than 150 university leaders, across all areas of the university, during annual risk assessment meetings; benchmarking with peer institutions to understand their significant and emerging risks; and alignment with the university's enterprise strategic risks. Copies of the FY2020 Audited Financial Statement and FY20 Report on Federal Awards in Accordance with the Uniform Guidance are included under separate cover, as specified in Section V-F.

(4) **Data security plan**:

All data collected on study participants will be obtained and managed specifically for research purposes and will follow best practices in data collection and protections. The types of data to be collected in aggregate across projects include medical status and history; self-report questionnaires that assess physical and psychological symptoms and life functioning; data from electronic monitors. The data file containing the linkage of subject identity to study ID number and any group assignments will be maintained using a limited access, password-protected database on a password-protected desktop maintained by Michigan Medicine's Health Information Technology and Services (HITS), a unit of the University of Michigan. All other data will be contained in datasets without identifying information.

Study personnel and appropriate oversight organizations (e.g., IRBMED) will have access to the study databases when necessary. All assessment forms will be collected either via a web-enabled Electronic Data Capture System (EDC). The EDC website will be available via secure access and security will be implemented using firewalls, unique user IDs and passwords, secure socket level (SSL) encryption, trusted third party certificates, and standard operating system maintenance, backups and patches. Any paper forms will be kept in a secure, locked filing cabinet located at the University of Michigan's Chronic Pain and Fatigue Research Center (CPFRC) in Ann Arbor, MI, USA. The Michigan EDC system for this study will be a protected, industry-leading survey system, MyDataHelps, which follow all regulatory requirements regarding subject confidentiality and human subject safety and backs up all data every 24 hours. All MyDataHelps data is stored on secure, protected servers, and a copy is sent via a secure file transfer mechanism across the UM firewall to be stored on HITS servers at UM. A study team member will serve as the database manager and, along with the PIs will be responsible for the development of electronic case report forms, data entry modules, the study websites, data quality control, and beta testing of all forms before placing the study into production.

END APPLICANT RESPONSE

V-E Work Plan

Provide clear and concise work plans for meeting the following components, with detailed explanation:

1) Provide for the coordination and overseeing of clinical trial(s) to determine the efficacy of marijuana in treating the medical conditions of U.S. armed services veterans and preventing veteran suicide.
2) Recruit and evaluate researchers to accomplish the goals of this grant.
3) Demonstrate the ability to work with researchers who can garner the United States Food and Drug Administration approval for the clinical trials.
4) Ensure the maximum amount of grant dollars are used to coordinate and oversee clinical trials with a minimal amount of grant dollars used for administrative costs.
5) Work with organizations closely tied to veterans and veterans' programs.
6) Provide the Grant Administrator with a grant budget to which monitoring and reporting will be tied. Please see attachment A for the budget template to be used.
7) Establish research goals, approve projects, exercise financial and management oversight, and document and review results.
8) Publish the results of the clinical trials.

BEGIN APPLICANT RESPONSE

1) Provide for the coordination and overseeing of clinical trial(s) to determine the efficacy of marijuana in treating the medical conditions of U.S. armed services veterans and preventing veteran suicide.

This study will be led by the Co-PIs, who have extensive experience in clinical trial and observational research, including Dr. Bohnert's program, funded by contracts from the state of Michigan, on expanding treatment access for opioid use disorders. This experience is demonstrated by their proven ability to successfully conduct and publish the findings of meaningful and impactful clinical trials with pharmacological and non-pharmacological interventions, including education-based interventions.[112,115,116,130,144,180,188,200-202] We will

obtain approval from the University of Michigan IRB, and any other IRBs as needed, to ensure the scientific quality and ethical oversight of the study, and obtain any additional regulatory approvals as necessary (e.g., FDA, DEA). We will also appoint a Data Safety and Monitoring Board to oversee participant and data safety in this trial.

2) Recruit and evaluate researchers to accomplish the goals of this grant.

Principal Investigators

Our team of co-Principal Investigators (co-PIs) has complementary expertise to ensure that all aspects of the study can be carried out. They are Drs. Amy Bohnert, Kevin Boehnke, and Daniel Clauw, all three of whom are faculty members at the University of Michigan. Both Drs. Bohnert and Clauw have successfully managed very large grants and contracts, with Dr. Clauw alone having been responsible for over $100M in federal grant funding.

Dr. Bohnert is a Professor of Anesthesiology, Psychiatry, and Epidemiology at the University of Michigan (UM). She is an internationally renowned epidemiologist whose research team has been very involved in studying Veterans, mental health and the risk of suicide.[3,5-7,106,108-115,117-129,131-133,135,143-163,165-177,179-191,203] Her research, funded by NIH, CDC, and the VA, has been foundational in understanding the balance of benefits and harms of opioid analgesic use, and she has content expertise in pain and substance use disorders. She currently uses the MyDataHelps and Fitbits to collect data from individuals on wait lists for outpatient psychiatry care and has experience with all of the programs and risk management protocols necessary to study suicide risk. She also has led the Michigan Opioid Collaborative since 2017, which is supported by contract from the Michigan Department of Health and Human Services (described more below).

Dr. Boehnke is a Research Investigator in the Department of Anesthesiology at UM and a nationally renowned cannabis expert. He is currently involved in several NIH-funded clinical trials investigating effects of cannabinoids on pain and sleep. He has led numerous studies showing that people with chronic pain substitute cannabis for opioids and other pain medications, mostly without clinician oversight.[16-18,49,50,52-57] Dr. Boehnke has provided guidance on CBD for the Arthritis Foundation,[204] and is currently a Technical Expert Panel member for two national committees on cannabinoid use for pain, including a collaboration between the office of Veterans Affairs and Oregon Science and Health University.

Daniel J. Clauw, MD is a Professor of Anesthesiology, Rheumatology, and Psychiatry at UM. He serves as the Director of the Chronic Pain and Fatigue Research Center (CPFRC), which is one of the world's leading pain research groups. Dr. Clauw is an internationally renowned pain researcher and expert on centralized pain syndromes, and currently leads or has previously led numerous federally funded projects related to chronic pain including the NIH-funded UM Fibromyalgia Center for Research Translation, the Back Pain Consortium Research Program, and the Multidisciplinary Approach to the Study of Chronic Pelvic Pain network. He has extensive experience in clinical trial design, conduct, and interpretation, as well as considerable expertise in cannabinoids.[16,17,49-51,103,140,199,205-235]

Co-Investigators

We have assembled a team of co-Investigators (co-Is) with vast experience in the following: clinical expertise in veteran health; clinical and research expertise insomnia/sleep disturbances, chronic pain, and anxiety; health assessments (patient-reported and ambulatory measures); social determinants of health; data management; statistical methods/analyses, and cannabis (medical and problematic use). These co-investigators, their expertise, and contributions are listed in section V-G under Personnel.

3) Demonstrate the ability to work with researchers who can garner the United States Food and Drug Administration approval for the clinical trials.

We will work with the UM Michigan Investigator Assistance Program (MIAP), which is a sponsored UM program that assists with FDA submissions for IND/IDE applications. MIAP provides comprehensive

regulatory support, guidance, and education services to investigators involved in Food and Drug Administration (FDA) regulated clinical research. MIAP's primary focus is providing regulatory assistance to sponsor-investigators of drugs, biologics, and medical devices. This includes Investigational New Drug (IND) services such as: regulatory needs assessments; exemption rationale development; assistance with FDA meeting preparation; assistance with IND application submissions, including protocol and informed consent development; assistance with regulatory compliance, document preparation, and FDA contact and correspondence; sponsor investigator training; and ongoing study assistance, including safety reporting, FDA annual report preparation, protocol amendments, and IND closeout. We have used this service in the past, obtaining IND approval through FDA for clinical trials using compounds including dronabinol (synthetic THC), Epidiolex (CBD), milnacipran, and duloxetine.

4) Ensure the maximum amount of grant dollars are used to coordinate and oversee clinical trials with a minimal amount of grant dollars used for administrative costs.

Our group has extensive experience in managing large contracts through both the State of Michigan (Dr. Bohnert) and the National Institutes of Health (Dr. Clauw) which have resulted in high-quality, impactful science that has shaped both policy and clinical care. Our budget has dedicated **$8,968,532** amount to covering salary for project leads, personnel involved in analytical support, partnerships with Veteran organizations, and research staff, with only **$989,036 (9.932506% of the total budget requested)** going towards administrative and indirect costs.

5) Work with organizations closely tied to veterans and veterans' programs.

Three members of our investigative team (Drs. Bohnert, Hosanagar, and Silveira) have concurrent appointments at the Department of Veterans Affairs in Ann Arbor, which will be leveraged for Veteran involvement. This includes access to the VA Ann Arbor and Central VA IRBs and Research and Development Committees, and partnerships with ongoing, large scale research recruitment efforts (e.g., the Million Veterans Project). They will lead efforts to obtain stakeholder input on proposed research programs from the Veteran Engagement Research Council at the Ann Arbor VA.

In addition, we will partner with several non-profit organizations that advocate for Veteran issues, such as: The Veterans Action Council, Weed for Warriors, the Veterans Cannabis Project, the American Legion, Disabled American Veterans, Vietnam Veterans of America, and Veterans of Foreign Wars. To facilitate these connections, we will also coordinate with the MAPS research team or the research teams of other funded VMR studies to give joint presentations to these groups to build stronger partnerships with these organizations as well as enhance recruitment for both of our studies.

6) Provide the Grant Administrator with a grant budget to which monitoring and reporting will be tied. Please see attachment A for the budget template to be used.

Please see the attached budget provided by the grant administrator for our department.

7) Establish research goals, approve projects, exercise financial and management oversight, and document and review results.

Proposed timeline:

We have outlined above the proposed goals of our research activities. In the first stage of the project, we will refine these goals based on feedback from stakeholders and partners and from regulatory reviews (e.g., IRB). We will seek all necessary regulatory approval as part of this process. The final, approved protocol will be implemented as soon as possible.

We will use established University of Michigan protocols for financial oversight of the project, as detailed elsewhere. The PIs have continuous access to financial reporting and all charges to the project through the M-Reports software. The University Human Subjects Incentive Program (HSIP) ensures fair, timely, and accurate accounting for payments to participants throughout the state and avoiding the potential for waste or fraud.

We will specify clinical trial analyses via clinicaltrials.gov once all protocols have been approved through the appropriate regulatory bodies. The data core will develop code for analyzing results before data are fully collected, and then analyze results, which will be reviewed by the study team and the Data Safety and Monitoring Board for the study.

Table 1. PROJECT TIMELINE	**Project quarter**							
	8/21 - 10/21	**11/21 - 01/22**	**2/22 - 4/22**	**5/22 - 7/22**	**8/22 - 10/22**	**11/22 - 1/23**	**2/23 - 4/23**	**5/23 - 7/23**
Hire/train staff; Develop study materials; Design study database	X	X						
Develop and manualize intervention	X	X						
Build community partnerships and awareness	X	X	X	X	X	X		
Regulatory requirements fulfilled (IRB)	X	X						
Data collection (observational study and RCTs)		X	X	X	X	X	X	X
Data entry and cleaning		X	X	X	X	X	X	X
Dissemination: publications and presentations		X	X	X	X	X	X	X

8) Publish the results of the clinical trials.

Our team has an impressive publication record in this space, demonstrated by our many research articles related to clinical trials, veteran health issues (e.g., chronic pain), and cannabinoid science that have been published in high impact journals, including the Journal of the American Medical Association, the New England Journal of Medicine, and JAMA Psychiatry.[5,6,65,66,100,106,114,115,121,130,138,176,180,182,188,192-199]

END APPLICANT RESPONSE

V-F Current and Prior Experience and Funding Disclosure

Current and prior experience in administering clinical trials is important to the selection process. Each applicant(s) must provide a copy of the organization's most recent audited financial statement and single audit (if applicable). The audited financial statement and single audit must be sent under separate cover.

Proposals submitted by applicant(s) should include:

(1) A description of the organization's experience in conducting the type of work proposed. Include current activities and activities for the previous ten years. Include project results.

Our team has relevant expertise in clinical trials, health effects of cannabis, and recruiting veterans and studying veteran-specific health concerns, indicated primarily by published work in each of these areas by our co-PIs below. These studies have utilized a variety of study designs for delivering useful educational interventions as well as using cutting-edge techniques for measuring symptom burden

and drug use, including patient-reported outcomes, neuroimaging, virtual and in-person therapy, educational interventions, and FDA-approved drug studies.

Clinical Trials. The principal investigators of this proposal have extensive experience in leading and managing clinical trials, including with veterans.[65,98,99,104,114,115,180,188,193,194,199,201-203,209,218,234,236-251] Of relevance to the current project, we have shown that: 1) educational interventions show clinical and statistically significant effects on chronic pain symptoms, 2) brief virtual visits with health counselors can reduce risk of drug overdose and non-medical drug use; 3) we have the proven ability to design and complete complex interventional studies with FDA approval.

Health Effects of Cannabis. The principal investigators of this proposal have extensive experience in performing cannabis research - both examining potential benefits as well as harms of cannabis products.[16-18,49-53,55,56,191,208,252] Of relevance to the current project, we have shown that naturalistic cannabis product use is associated with positive clinical impacts, including improved symptom management and substitution of cannabis for medications with greater risk profiles (e.g., opioids). However, this use is typically not overseen by medical providers, leaving many patients without clear guidance on how to appropriately use these products for their health conditions, potentially leading to harmful or suboptimal outcomes.

Recruiting Veterans and Studying Veteran-specific Health Concerns. Our study team has extensive experience in recruiting and studying veterans as well as conducting impactful research aimed at understanding and improving Veteran health.[1,3,5,7,106-115,119,120,143-152,158,161-177,179] In particular, we have elucidated many risk factors associated with Veteran suicide (including pain of various etiologies, anxiety, benzodiazepine, and opioid use) and conducted clinical trials to develop innovative ways of improving Veteran healthcare.

(2) If applicant(s) received a similar grant award from the State of Michigan in prior years for the type of project proposed, provide a summary of project accomplishments. Include a plan for addressing and resolving past problems.

The applicants are the recipient of several prior contracts from the State of Michigan during 2017-present. Specifically, Dr. Bohnert leads the Michigan Opioid Collaborative, which is supported by contract from the Michigan Department of Health and Human Services, with funds originating from SAMHSA under the State Targeted Response and State Opioid Response federal initiatives. Blue Cross Blue Shield of Michigan became an additional sponsor and partner in 2020.

The Michigan Opioid Collaborative provides support to clinicians with the goal of expanding access to medications for opioid use disorders. Behavioral Health Consultants located in each region of the state conduct outreach to clinicians in their area to assess interest in medications for OUD, provide information about training opportunities, and address myths about addiction and OUD medications. They participate in community organizations (e.g. county Opioid Task Forces), and address other barriers in each community, (e.g., identifying pharmacies willing to carry buprenorphine). For interested clinicians, the program offers same-day consultation on patient issues from addiction-boarded physicians located at the University of Michigan and Michigan State University. Program team members also provide technical assistance to clinics determining care processes and staff training gaps. In 2020, services expanded to include consultation of Hepatitis C Virus pharmacotherapy, stigma training led by a peer support specialist, and expanded training on co-occurring substance use disorders. To date, the program has delivered the "x-waiver" training necessary to prescribe buprenorphine outside of opiate treatment programs to 526 clinicians and provided consultations to an additional 733 clinicians who already had a x-waiver or were a non-prescriber clinician. These efforts have resulted in the formation of a state-wide network of 481 clinics.

State-wide Pilot of Remote Behavioral Care. As part of the Michigan Opioid Collaborative program, we conducted a single arm clinical pilot study of remote counseling that has prepared us for statewide-recruitment

efforts. We recruited 43 patients from 13 clinics, representing a mix of geographic regions. In this sample, 95% of patients were being treated with buprenorphine, and 56% reported chronic pain, defined as a mean of 5 or greater of the worst and average pain in the last 3 months on the Numeric Rating Scale.[130] The average number of years of chronic pain was 9.3. The sample was 52% female, 34% employed, 9% Hispanic, 19% Black, 77% White; one NA/AI person was recruited. Participants were offered 8 tele-counseling sessions delivered by therapists, with 57% completing all 8 sessions, and 80% completing at least 4. Of those with follow-up data, collected 2-7 months post-baseline, 91% were still prescribed buprenorphine. This study established the feasibility of state-wide recruitment clinics and the acceptability of remote recruitment and care to the participants through our research infrastructure.

In total since 2017, the State of Michigan has awarded $2,530,877 to University of Michigan for the Michigan Opioid Collaborative. The program has been successful in meeting its objectives and in developing and maintaining partnerships. Dr. Bohnert is also a co-investigator of the Michigan Opioid Prescribing Engagement Network (M-OPEN), a University of Michigan program that seeks to improve opioid analgesic prescribing and related opioid safety practices at hospitals throughout Michigan, also funded through contracts with state government. Collectively, the two programs establish our team's capacity to responsibly manage State of Michigan funding and produce deliverables in a timely manner.

(3) Current funding source(s) and the level of funding for the current year and the previous ten years.

BEGIN APPLICANT RESPONSE

Current Support and Support over the Past Ten Years has been provided for the Principal Investigators and Co-Investigators at the University of Michigan.

CLAUW, DANIEL J., M.D.

Current

R01 DA038261 09/01/15 – 07/31/21 (10.0%) 1.20 CM
Clauw, DJ-Contact / Brummett, CM $ 369,307 Annual Direct Costs
NIH/NIDA $2,871,151 Total Award Amount
Centralized Pain Phenotype as a Predictor of Opioid Non-responsiveness
The goal of this project is to test if the degree of pain centralization as measured on a simple self-report measure strongly predicts acute opioid pain responsiveness by providing a surrogate measure of endogenous opioid function.
Role: Contact Principal Investigator (MPI)

P50 AR070600 09/20/16 – 08/31/22 (NCTX) (25.0%) 3.00 CM
Clauw, DJ-Contact / Brummett, CM $ 958,792 Annual Direct Costs
NIH/NIAMS $7,415,237 Total Award Amount
University of Michigan Fibromyalgia CORT
The goal of this program of research is to understand how fibromyalgia and other rheumatic diseases affect patients, better understand the underlying mechanisms of their pain, and personalize analgesic treatment.
Role: Contact Principal Investigator (MPI) - Program Director

R01 NR017096 05/09/17 – 02/28/22 (0.0%) 0.00 CM
Hassett, AL – Contact / Williams, DA $ 365,546 Annual Direct Costs
NIH/NINR $2,549,712 Total Award Amount
Resilience Skills Self-Management for Chronic Pain
The objective of this application is to evaluate the general effectiveness and impact on telomere health of a

resilience-based self-management intervention, the CBT self-management with resilience-enhancing activities (CBTRE) program.
Role: Consultant

UL1 TR002240 09/17/07 – 02/28/22 (10.0%) 1.20 CM
Mashour, GA $ 6,221,969 Annual Direct Costs
NIH/NCATS $48,448,400 Total Award Amount
Michigan Institute for Clinical and Health Research (MICHR)
The UM CTSA, housed in the Michigan Institute of Clinical and Health Research (MICHR), was created to provide robust infrastructure and support based on strong existing units and programs, as well as academic programs in key clinical and translational disciplines in order to provide faculty leadership, expertise, and consultation as well as high quality services.
Role: Sr. Associate Director; Co-Director, Research Development Core; Education and Mentoring Core – Predoc Programs Leader

R01 HD088712 06/01/17 – 02/28/22 (8.0%) 0.96 CM
As-Sanie, S-Contact / Clauw, DJ $ 417,481 Annual Direct Costs
NIH/NICHD $3,028,770 Total Award Amount
Peripheral and Central Nervous System Correlates of Persistent Post-Hysterectomy Pain
The objective of this study is to characterize role of peripheral and central sensitization among women undergoing hysterectomy for CPP and to explore the utility of preoperative measures of PNS and CNS factors to predict the likelihood of persistent post-hysterectomy pain.
Role: Principal Investigator (MPI)

U01 DK082345 09/15/08 – 06/30/22 (10.0%) 1.20 cm
Clauw, DJ-Contact / Clemens, JQ $ 250,525 Annual Direct Costs
NIH/NIDDK $1,172,455 Total Award Amount
University of Michigan MAPP Research Network Discovery Site
The goal this project is to study the etiology and treated natural history of UCPPS, to inform better treatments and management of symptoms through improved designs of clinical trials, and to identify clinical factors and research measurements to define clinically relevant sub-groups of these patients. The proposed three-year extension will allow the participating institutions to obtain an additional 12 months of follow-up in the MAPP-II Symptom Patterns Study (SPS), observe additional ATLAS (Analysis of Therapies during Longitudinal Assessment of Symptoms) events in the MAPP-II SPS, and analyze MAPP-II data.
Role: Contact Principal Investigator (MPI)

R01 DE024450 09/13/19 – 05/31/24 (1.0%) 0.12 cm
Cevidanes, L $ 387,873 Annual Direct Costs
NIH/NIDCR $2,545,710 Total Award Amount
Integrative Predictors of Temporomandibular Osteoarthritis
The goal of this project is to develop efficient web-based data management, mining, and analytics, to integrate and analyze clinical, biological, and high dimensional imaging data from TMJ OA patients.
Role: Co-Investigator

U19 AR076734 09/26/19 – 05/31/24 (25.0%) 3.00 CM
Clauw, DJ-Contact / Hassett, AL $1,152,504 Annual Direct Costs
NIH/NIAMS $8,969,433 Total Award Amount
University of Michigan BACPAC Mechanistic Research Center
As part of the BACPAC initiative, the mechanistic research center at the University of Michigan aims to be a team member in realizing the vision of personalized medicine for individuals with cLBP.
Role: Contact Principal Investigator (MPI)

R01 AT010381 08/01/20 – 07/31/25 (2.0%) 0.24 CM
Harris, RE-Contact / Harte, SE $ 391,848 Annual Direct Costs
NIH/NCCIH $3,489,509 Total Award Amount
Cannabinoid interactions with central and peripheral pain mechanisms in osteoarthritis of the knee
The studies proposed herein are the first attempt to understand how THC and CBD affect different chronic pain mechanisms in humans by examining the effects of these compounds on knee OA in individuals with varying degrees of pain centralization.
Role: Co-Investigator

UM1 NS118922 08/01/20 – 07/31/23 (8.0%) 0.96 CM
Brummett -Contact/Chang/Clauw/Waljee $1,410,610 Annual Direct Costs
NIH/NINDS $6,598,505 Total Award
Transition from Acute to Chronic Pain After Thoracic Surgery
The successful completion of the proposed study and supplement would provide an unparalleled resource for understanding the factors associated with CPSP and will allow for more efficient and personalized trials to prevent the development of chronic pain after thoracotomy and other thoracic surgeries.
Role: Principal Investigator (MPI)

Past Support

R01 AT007550 (Harris, RE-Contact/Napadow, V) 05/01/13 – 10/31/20 (0.00%) 0.00 CM
NIH/NCCIH $117,474
Neuroimaging Approaches to Deconstructing Acupuncture for Chronic Pain
Our overall goal is to evaluate the impact of acupuncture-induced somatosensory afference on altered neurobiology and analgesia in FM.
Role: Co-Investigator

SAV-MD-09 (Clauw, D.) 04/22/10 – 05/31/12 NCTX (4.0%) 0.48 CM
Forest Laboratories, Inc. $592,470
A single-center, randomized, double-blind, placebo-controlled, two-way crossover study to evaluate the effect of milnacipran on pain processing and functional magnetic resonance imaging activation patterns in patients with Fibromyalgia.
The objective of this study is to evaluate the effect of milnacipran on pain processing in patients with fibromyalgia and to assess the correlation between this effect and neural activation patterns during functional magnetic resonance imaging.
Role: Principal Investigator

R01 AR057808 (Lumley, M. – Wayne St. Univ.) 08/15/10 – 06/30/15 (5.0%) 0.60 CM
NIH/NIAMS $204,037 (UM Subcontract Direct Costs)
Emotional Exposure and Cognitive Behavioral Therapies for Fibromyalgia
This application combines the clinical research, pain, and FMS expertise of two research teams to conduct a 2-site, randomized, controlled trial of emotional exposure therapy (EET) against both a standard cognitive-behavioral therapy (CBT; pain coping skills training) and control condition (FMS education and support) in a design that controls for the importance of exercise, non-specific factors, and experimenter allegiance to the different treatments.
Role: Co-Investigator

R01 AR060392 (Clauw, D./Brummett, C.-MPI) 08/01/11 – 05/31/16 (20.0%) 2.40 CM
NIH/NIAMS $437,235
Central Nervous System Mechanisms in Knee Osteoarthritis (KOA)
The goal of this project is to show that simple clinical testing easily performed at the point-of-care can reliably segment chronic pain patients into those with prominent central components to their pain, that are likely to need

different pharmacologic (i.e. centrally acting analgesics) and non-pharmacologic approaches (not surgery). Moreover this study has tremendous potential to help improve broaden our understanding of the underlying mechanisms that may lead to pain and other symptoms in OA.
Role: Contact Principal Investigator

R24 DK094583 (Clemens/Clauw/Reed-MPI) 09/15/11 – 08/31/12 (10.0%) 1.20 CM
NIH/NIDDK $225,000
Sensory Sensitivity and Urinary Symptoms in the Female Population

This project will examine for clinical evidence of global pain hypersensitivity in these patients. If a global pain abnormality is identified, additional studies can be done to examine the etiology of these symptoms and design novel treatments that are focused on central, rather than peripheral, pathophysiology.
Role: Principal Investigator (MPI)

Services Agreement (Clauw, D.) 01/01/12 – 12/31/12 (0.0%) 0.00 CM
Pfizer, Inc. $402,572
Development of a Web-based Patient Engagement Tool for Chronic Low Back Pain
The goal of this project is to develop the Patient Engagement Platform (PEP), an integrated and interactive eHealth product developed for physician and patient engagement surrounding the pain management of chronic low back pain. The PEP contains 5 categories and functions (clinic assessment, guidance, tracking/reporting, self-management modules, and motivational tools).
Role: Principal Investigator

K12 DE023574 (Kapila, S-Contact/Clauw, DJ) 07/01/13 – 06/30/18 (5.0%) 0.60 CM
NIH/NIDCR $385,538
University of Michigan's TMJD and Orofacial Pain Interdisciplinary Consortium

The goal of this K12 program is to train a cadre of high caliber clinician scientists and basic scientists to enhance the number and quality of interdisciplinary researchers that can appropriately unravel the mechanisms and most effective treatments for TMJD/OP.
Role: Principal Investigator (MPI)

GM103730 (Clauw, DJ-Contact/Mashour, GA) 07/01/14 – 06/30/19 (2.50%) 0.30 CM
NIH/NIGMS $79,124
University of Michigan Anesthesiology Post-Doctoral Research Training Program

This proposed new *NIGMS T32 Postdoctoral Training Program in Anesthesiology* will provide support to post-doctoral trainees interested in careers in academic anesthesiology, and who embrace the interdisciplinary nature of our institution.
Role: Contact Principal Investigator (MPI)

R01 DK100368 (Tu, F) 04/01/14 – 03/31/19 (4.0%) 0.48 CM
Northshore University Healthcare System Research Institute (NIH Prime) $317,056
Deciphering the hormonal and nociceptive mechanisms underlying bladder pain
The objective of this proposal is to identify the hormonal, nociceptive, and psychological mechanisms responsible for COS of the bladder and determine the mechanisms underlying the ability of oral contraceptives to improve bladder pain.
Role: Co-Investigator

BOHNERT, AMY S.B., PH.D.

University yearly evaluation of the effort distribution between the UM and the VA is represented by the

calendar months reported on other support. MOU is on file.

Current Support

R01 DA039159	05/01/2016-01/31/2022	1.20 calendar
Bohnert, A	$ 353,447 Annual Direct Costs	United States
NIH-NIDA	$2,817,357 Total Award Amount	

Reducing Non-Medical Opioid Use: An automatically adaptive mHealth Intervention
This study is a phase - III clinical trial of the intervention compared to an enhanced usual care condition with 600 ED patients. This study will also involve focus groups of patients and ED clinicians in order to understand issues related to implementation of the intervention.
Role: Principal Investigator

R01 DA042859	07/01/2017-04/30/2022	0.24 calendar
Brummett, C / Waljee, J-Contact	$430,465 Annual Direct Costs	United States
NIH-NIDA	$3,557,204 Total Award Amount	

oPIOIDS: Prevention of Iatrogenic Opioid Dependence after Surgery
The purpose of this study is to better understand the factors that put people at risk of long-term opioid use so that these patients can be prescribed alternative pain management strategies when having surgery. This study will examine new prescription drug claims data with existing clinical and genetic data as well as the opioid prescription fulfillment data to assess patient characteristics associated with greater opioid ascertainment.
Role: Co-Investigator

Grant Agreement	11/12/2018-01/14/2022 NCTE	0.60 calendar
Lagisetty, P	$448,737 Annual Direct Costs	United States
Michigan Health Endowment Fund	$498,596 Total Award Amount	

Enhancing Treatment Access for Abandoned Chronic Pain Patients
This project aims to quantify primary care access for patients on long-term opioid therapy (LTOT) for their pain utilizing an audit, 'secret shopper' methodology. In addition, qualitative interviews will elicit feedback from providers, office staff, and patients on their experiences with treating pain and opioid prescribing. These findings will be used to convene a Delphi panel of experts to create recommendations to the State of Michigan for how to best care for this patient population.
Role: Co-Investigator

Bohnert, A / Sen, S	04/01/2019-03/31/2022	0.60 calendar
Internal/Precision Health	$1,800,000 Total Award Amount	United States

Precision Health - Mental Health Use Case
The overall goal of this project is to reduce the burden of mental illness by 1) increasing capacity in the mental health care system through expanding use of mobile technology-delivered interventions and 2) accelerating recovery from mental illness by better matching patients to pharmacological, psychological, and mobile-based treatments. Participants are randomized to receive specific mobile health interventions for four weeks while on the waitlist for traditional care. Analyses will seek to identify patient characteristics that predict response to specific treatment modalities.
Role: Co-Director

OPD-1511-33052	11/01/2019-10/31/2021	0.35 calendar
Krebs, E	$101,596 Annual Direct Costs	United States
University of Minnesota/PCORI	$306,846 Total Award Amount	

Veterans Pain Care Organizational Improvement Comparative Effectiveness (VOICE) Trial
This study will test which of two pain treatment strategies is better for managing pain and helping patients improve safety of opioid medication. For patients on high opioid doses who want to reduce, this study will also test whether offering an extra option for tapering (buprenorphine-naloxone) helps them succeed. Finally, the study will examine patients' and clinicians' experiences with the interventions.

Role Co-Investigator

Brummett, C 01/01/2017 – 12/31/2022 0.36 calendar
University of Michigan $665,753 Total Award Amount United States
Institute for Health Policy and Innovation (IHPI)
Precision Health Opioid Use Case
The overall goal of this project is to test and test and refine the resources and infrastructure most useful to researchers relating to opioid prescribing in the pre-surgical setting.
Role: Associate Director

Agreement 01/01/2020-12/31/2021 0.82 calendar
Bohnert, A $1,165,524 Annual Direct Costs United States
Blue Cross Blue Shield of Michigan $2,859,052 Total Award Amount
Michigan Opioid Collaborative
The primary goal of this service project is to provide mentoring to BCBS network providers related to prescribing medications to treat opioid use disorder. Target rural Michigan counties to help engage providers with medication assisted treatment with mentoring support. This includes partnering with other BCBS grantees/partners to help support PQI/PGIP.
Role: Principal Investigator

R49 CE03085 08/01/2019 – 07/31/2024 0.24 calendar
Carter, P $1,245,583 Annual Direct Costs United States
DHHS / CDC $6,507,198 Total Award Amount
University of Michigan Injury Prevention Center 2019-2024
The University of Michigan Injury Prevention Center provides the infrastructure to coordinate a collaborative injury prevention agenda focused on the prevention of opioid misuse/overdose, suicide, youth/sexual violence, concussion, motor vehicle crash, and are beginning a portfolio in older adult falls. Adverse childhood experiences are a crosscutting and underlying risk factor for all of focus areas.
Role: Co-Investigator

UH3 DA050173 09/30/2019-08/31/2024 0.60 calendar
Walton, M-Contact / Bonar, E $ 855,255 Annual Direct Costs United States
NIH/NIDA $5,870,743 Total Award Amount
Optimized Interventions to Prevent Opioid Use Disorder among Adolescents and Young Adults in the Emergency Department
This project will adapt promising remote health coach-delivered interventions, and pilot test feasibility/acceptability among adolescents and young adults. Then, we will evaluate the efficacy of interventions and their combinations to prevent/reduce opioid misuse among adolescents and young adults in the emergency department. Finally, we conduct an economic evaluation to identify the most efficacious intervention combination for preventing opioid misuse and implement it in the emergency department among adolescents and young adults.
Role: Co-Investigator

E20213472-00 / H79TI081712 10/01/2020-09/30/2021 0.84 calendar
Bohnert, A-Contact / Lin, A $333,333 Annual Direct Costs United States
MDHHS/SAMHSA $400,000 Total Award Amount
Michigan Opioid Collaborative - State Opioid Response FY21
This project will build upon the connections of the Michigan Opioid Collaborative with physicians in areas of Michigan with limited access to MAT to provide telehealth support for opioid use disorders.
Role: Principal Investigator

E20213600-00 / H79TI083298 10/01/2020-09/30/2021 1.20 calendar

Bohnert, A-Contact / Lin, A $1,057,607 Annual Direct Costs United States

MDHHS/SAMHSA $1,290,728 Total Award Amount
The Michigan Opioid Collaborative: State Opioid Response 2
This project will use telementoring and consultant services to increase access to medication assisted therapy (MAT) for individuals with Opioid Use Disorders (OUD). Specifically, the program will help to increase the workforce of physicians prescribing medications used in MAT, increase clinician access to training on counseling services that accompany those medications in MAT, and provide a process for linkages to other OUD treatment in the community.
Role: Principal Investigator

E20213443-00 10/01/20 – 09/30/21 0.36 calendar
Englesbe - Contact / Brummett / Waljee $1,796,869 Annual Direct Costs United States
$2,156,243 Total Award Amount
Medicaid/MDHHS - MA-2021 Master Agreement Program
Michigan Opioid Prescribing Engagement Network (M-OPEN) (AWD16455-SUB030)
The overall goal of this initiative is to reduce the amount of opioids prescribed to surgical patients by 50%, reduce new chronic postoperative opioid use by 50%, and reduce opioid diversion into our communities.
Role: Co-Investigator

VA HSR&D IIR 16-235 (Blow) 06/01/2018-05/31/2022 0.375 calendar
Improving Outcomes for Emergency Patients with Alcohol Problems United States
This study is a randomized controlled trial to facilitate reductions in alcohol use and to link Veterans with alcohol problems to needed primary and specialty care including other needed services such as homeless outreach and case management where needed.
Role: Co-Investigator

IIR 16-210 (Maust) 02/01/2018-01/31/2022 0.60 calendar
VA Health Administration–HSR&D $253,639 United States
Addressing inappropriate benzodiazepine prescribing among older Veterans
The aims of this project are: 1) identify high- and low-performing facilities on acute and chronic BZD prescribing among those facilities that prioritized the BZD≥75 measure; 2) assess facility-level strategies to address BZD≥75 prescribing, the associated barriers and facilitators, and acceptability of these strategies to older Veterans through semi-structured interviews and site visits; and 3) identify and pilot test context-sensitive strategies for facilities to successfully reduce acute and chronic BZD use among older adults.
Role: Co-Investigator

COR 19-490 (Ilgen) 07/01/2019-06/30/2021 2.40 calendar
Suicide Prevention Research Impact NeTwork (SPRINT) United States
Suicide prevention is VHA's number one clinical priority, and multiple, important suicide prevention research gaps need to be addressed. The mission of the "Suicide Prevention Research Impact NeTwork (SPRINT)" is to accelerate health services suicide prevention (SP) research that will improve care and result in reductions in suicide behaviors among Veterans.
Role: Co-Investigator

IIR 16-078 (Olivia) 12/01/2018-11/30/2021 0.375 calendar
VA Health Administration–HSR&D United States
Effectiveness of a Rescue Medication in Preventing Opioid Overdose in Veterans
The aims of this project are: 1) Characterize naloxone distribution within VA and patient-, prescriber-, and setting-related factors associated with distribution. 2) Assess whether naloxone distribution to at-risk Veterans compared to similar at-risk Veterans who did not receive naloxone is associated with reduced fatal and non-fatal opioid overdose.

Role: Co-Investigator

Past Support

U01 CE002780 (Bohnert) 09/01/2017-08/31/2020 0.84 calendar
CDC-DHHS $799,823 United States
Heroin use and overdose following changes to individual-level opioid prescribing
Heroin-related overdose deaths more than tripled between 2010 and 2014 in the United States. Emerging evidence has identified nonmedical use of prescription opioids as a risk factor for heroin initiation. Some have observed that the spike in heroin overdose deaths has overlapped with efforts to reduce the nonmedical use of prescription opioids; however, a causal link has not been established. Using analysis of medical records for over 50 million Americans and in-depth interviews with patients, this study will seek to inform prevention efforts by examining the association between individual-level opioid prescribing patterns – in particular tapering or discontinuation of opioids – and the risk of heroin use and overdose.
Role: Principal Investigator

(Bohnert/Lin) 10/01/2019-09/30/2020 0.66 calendar
MDHHS/SAMHSA $1,950,479 United States
Michigan Opioid Collaborative - State Opioid Response FY20
To provide this type of support to clinics in rural area of Michigan, we propose to engage in the following activities: 1. Over a period of 3 months, conduct a needs and capacity assessment with clinics and providers currently offering MAT or interested in offering MAT to their patients, and also interested in using telehealth to support MAT. 2. Provide nurse care manager-led telehealth for MAT, following the Collaborative Care Model of Office-Based Opioid Treatment developed in Massachusetts, which has been found to be effective for in-person MAT. The telehealth program will also be supported by a team of addictions psychiatrists and other University clinical staff, consistent with this model. In compliance with telehealth laws related to controlled substances, prescribers local to the patient will be a member of the collaborative care team and retain primary responsibility for prescribing. 3. Also as part of the collaborative care team. we will offer telehealth-based psychotherapy to clinics that identify this as a gap to their ability to provide MAT. 4. We will create a dissemination toolkit to ensure that the program can be replicated.
Role: Principal Investigator

IIR 13-322-2 (Bohnert) 07/01/2015-03/31/2021 (NCE) 2.25 calendar
VA Health Administration-HSR&D $324,372 United States
Primary Care Intervention to Reduce Prescription Opioid Overdoses: Prescription Opioid Safety Trial (POST)
This project aims to determine the safety of high-dose opioid use among Veterans presenting to primary care and mental health clinics, it is of critical importance to involve researchers who have expertise in overdose risk, opioid use, primary care and mental health care settings, pharmacoepidemiology, and longitudinal data analysis, as well as sufficient support staff.
Role: Principal Investigator

R03 AG042899 (Bohnert, A) 08/01/12 – 07/31/14 2.40 calendar
NIH/NIA $155,500 Total Award Amount
Safety of Opioids for Older Adults: Determinants of Opioid Overdose Risk
The primary specific aims will be to examine the relationship of specific opioid formulations, interactions with other medications (particularly other central nervous system depressants), and the timing of treatment (length of continuous opioid treatment, number of days supplied at once) in relation to the outcomes of interest.
Role: Principal Investigator

R34 DA0358331 (Bohnert, A) 03/01/2014 – 08/31/2017 (NCTX) 2.40 calendar
NIH/NIDA $677,747 Total Award Amount
Developing a Prescription Opioid Overdose Prevention Intervention
The purpose of this project is to refine a three-session brief intervention focused on reducing personal overdose

risk and improving response to witnessed overdoses among individuals in substance use disorder treatment reporting recent non-medical prescription opioid use and to pilot test randomized controlled procedures comparing the intervention to a control condition. Study findings will inform a full-scale randomized controlled trial of an intervention with the potential to reduce overdose mortality associated with prescription opioid use.
Role: Principal Investigator

BOEHNKE, KEVIN F. PH.D.

Current

K01 DA049219 07/15/20 – 06/30/24 (90%) 10.8 CM
Boehnke, K $131,921 Annual Direct Costs United States
NIH/NIDA $569,355 Total Award Amount
Cannabinoid Effects on Central and Peripheral Pain Mechanisms in Osteoarthritis of the Knee
The primary goal of this K01 award is to provide me with additional training that will allow me to unify chronic pain and cannabinoid mechanisms as an independent researcher.
Role: Principal Investigator

R01 AT010381 08/01/20 – 07/31/25 (10.0%) 1.2 CM Concurrent
Harris, RE-Contact / Harte, SE$ 391,848 Annual Direct Costs United States
NIH/NCCIH $3,489,509 Total Award Amount
Cannabinoid interactions with central and peripheral pain mechanisms in osteoarthritis of the knee
The studies proposed herein are the first attempt to understand how THC and CBD affect different chronic pain mechanisms in humans by examining the effects of these compounds on knee OA in individuals with varying degrees of pain centralization.
Role: Co-Investigator

Past Support

K12 DE023574 (Clauw, DJ-Contact/Kapila, S) 07/01/13 – 06/30/19 (NCTX) (100.0%) 12.0 CM
Clauw, DJ-Contact/Kapila, S $ 80,000 Annual Direct Costs United States
NIH/NIDCR $172,800 Total Award Amount
University of Michigan's TMJD and Orofacial Pain Interdisciplinary Consortium
The goal of this K12 program is to train a cadre of high caliber clinician scientists and basic scientists to enhance the number and quality of interdisciplinary researchers that can appropriately unravel the mechanisms and most effective treatments for TMJD/OP.
Role: Postdoctoral Fellow **(09/01/17 – 06/30/19)**

Dow Sustainability Fellow 09/01/15 – 08/31/17 (100.0%) 12.0 CM
Boehnke, K $12,500 Annual Direct Costs
Graham Institute of Sustainability $25,000 Total Award Amount
Risk of infection from waterborne Helicobacter pylori in Lima, Peru: Examining sustainable solutions through an integrated assessment approach
The purpose of this project is to train the individual to develop an interdisciplinary approach to thinking about science in society, and to bring this approach to research on characterizing risk from waterborne *Helicobacter pylori*.
Role: Principal Investigator

BERGMANS, RACHEL, PH.D.

Current

R01 AG051142 (Smith, J) 09/15/15 – 06/30/24 (10.0%) 4.20 CM
NIH/NIA $ 862,709 average direct costs United States
$5,925,104 Total Award Amount
Enhancing Retrospective Life History Data in the Health and Retirement Study
This project will enrich the stock of retrospective information about the lives of participants in the Health and Retirement Study (HRS) from childhood to study entry. We will produce user-friendly aggregated files of partnership, fertility, employment, and health histories and early-life traumatic events that have been collected in different waves of HRS since 1992. Gaps in these data will be supplemented by a Life History Mail Survey (LHMS) which we will design, test, and field in 2017.
Role: Postdoctoral Research Fellow

Previous

P30 ES017885 (Loch-Caruso, R) 04/01/16 – 03/31/21 (35.0%) 4.20 CM
NIH/NIEH $25,000
Michigan Center of Lifestage Environmental Exposures and Disease
Pilot Project *Linking atmospheric pollen and air pollution to suicide* (6/01/20 – 02/28/21)
This project links environmental data with mortality records to determine whether atmospheric concentrations of speciated aeroallergens increase the risk of suicide.
Role: Pilot Project PI

T32 MH073553 (Bruce, M) 09/01/05 – 06/01/21 (100.0%) 12.0 CM
NIH/NIMH $405,762 United States
Training Geriatric Mental Health Services Researchers
This training program responds to a nationally recognized urgent need to develop new researchers who have the necessary skills to inform the development, dissemination, and implementation of future mental health and substance abuse services for a rapidly growing older population.
Role: Postdoctoral Research Fellow (05/01/19 – 04/30/20)

UL1 TR002240 09/17/07 – 02/28/22 (100.0%) 12.0 CM
Mashour, GA $ 6,221,969 Annual Direct Costs United States
NIH/NCATS $48,448,400 Total Award Amount
Michigan Institute for Clinical and Health Research (MICHR)
The UM CTSA, housed in the Michigan Institute of Clinical and Health Research (MICHR), was created to provide robust infrastructure and support based on strong existing units and programs, as well as academic programs in key clinical and translational disciplines in order to provide faculty leadership, expertise, and consultation as well as high quality services.
Pilot Project: *Targeting the Gut Microbiome to Improve Psychiatric Treatment Paradigms*
The objective of this study is to determine how specific dietary control alters the microbiome composition to effect clinical outcome measures in a longitudinal study of individuals with bipolar disorder. Our central hypothesis is that a low carbohydrate (CHO) / high polyunsaturated fat (PUFA) diet will increase the fractional representation of specific butyrate producing members of the Firmicutes phylum in the gut microbiome, which will attenuate host inflammation, improve sleep quality, and reduce anxiety in bipolar
Role: Post-doctoral Fellow (07/01/18 – 05/31/19)

DEMPSEY, WALTER, PH.D.

Current

R01 DA039901 08/01/20-05/31/25 2.50 sum
NIH (Nahum-Shani/Almirall) USA
Annual Direct Costs: $338,525 Total Award Amount $2,913,828

Novel Longitudinal Methods for SMART Studies of Drug Abuse and HIV
The treatment of drug use and HIV often requires sequential, individualized decisions concerning the type or delivery of treatments. The methods developed in this project will improve clinical and public health outcomes by enabling drug use and HIV scientists to develop more potent approaches to guide the sequential, individualization of drug use and HIV treatments.

20SFRN35370008/20SFRN35360220 04/01/20-03/31/24 0.29 acad
American Heart Association (Nallamothu/Skolarus) USA
Annual Direct Costs: $592,182 Total Award Amount: $2,500,000
Wearables in Reducing Risk and Enhancing Daily Life-style (WIRED-L) – SFRN
The long-term goal of our research is to develop successful strategies driven by adaptive technologies that support self-management in common cardiovascular conditions.

R44 CA236557 09/01/20-08/31/22 0.60 acad
Arcascope Inc./NIH (Walch) USA
Annual Direct Costs: $265,210 Total Award Amount: $800,031
Assessing the effects of lighting interventions on fatigue in three populations of cancer patients
The goal of this project is to carry out a clinical trial to test the effects of a mobile app that recommends lighting interventions on fatigue and other quality of life metrics in a population of cancer patients.

Past Support

None

KHETERPAL, SACHIN, MD, MBA

Current Support
Michigan Predictive Activity and Clinical Trajectories Study (MiPACT); Research Agreement #042230
Percent effort (time commitment): 30.0% (3.60 CM)
Funding agency: Apple, Inc.
Period of performance: 08/17/2018 – 08/17/2024
Level of funding: confidential
Our study aims to understand disease trajectories using Apple Watch and iPhone sensors, electronic health records, blood pressure monitors, questionnaires of participant survey data, and genomic information.

MIPACT-ER: Michigan Predictive Activity & Clinical Trajectories Study Extension; Research
Agreement #042230
Percent effort (time commitment): 2.50% (0.30 CM)
Funding agency: Apple, Inc.
Period of performance: 07/13/2020 – 08/17/2024
Level of funding: confidential
Our study aims to understand disease trajectories using Apple Watch and iPhone sensors, electronic health records, blood pressure monitors, questionnaires of participant survey data, and genomic information.

Transition from Acute to Chronic Pain After Thoracic Surgery; UM1 NS118922
Percent effort (time commitment): 2.0% (0.24 CM)
Funding agency: National Institute of Neurological Disorders and Stroke / National Institutes of Health (NINDS/NIH)
Period of performance: 08/01/2020 – 07/31/2023
Level of funding: $6,410,214

The interplay between genomics, activity, lifestyle, family history, and clinical care upon long term outcomes is poorly understand. By enrolling patients and providing them with mobile wearable devices combined with electronic health record, genotyping, clinical laboratory, and electronic health record data, we will be able to advance our understanding of the value of each data stream and potential predictors of poor outcomes.

University of Michigan Anesthesiology Training Grant; T32 GM103730
Percent effort (time commitment): 2.50% (0.30 CM)
Funding agency: National Institute of General Medical Sciences / National Institutes of Health (NIGMS/NIH)
Period of performance: 07/01/2015 – 06/30/2025
Level of funding: $814,861
NIGMS T32 Postdoctoral Training Program in Anesthesiology provides support to post-doctoral trainees interested in careers in academic anesthesiology, and who embrace the interdisciplinary nature of our institution.

Wearables In Reducing risk and Enhancing Daily Life-style (WIRED-L) - SFRN;
20SFRN35370008/20SFRN35360220
Percent effort (time commitment): 2.50% (0.30 CM)
Funding agency: American Heart Association
Period of performance: 04/01/2020 – 03/31/2024
Level of funding: $2,500,000
The long-term goal of our research is to develop successful strategies driven by adaptive technologies that support self-management in common cardiovascular conditions.

COVID-19 Health Evaluation & Cardiovascular Complications (CHECC) Study; COVID-19 Rapid Response
Percent effort (time commitment): 1.0% (0.12 CM)
Funding agency: American Heart Association
Period of performance: 06/01/2020 – 05/31/2021
Level of funding: $200,000
To better understand the pathobiology and the clinical implications of the viral infection that leads to the morbidity and mortality seen with COVID-19. We propose leveraging data from two ongoing U-M mHealth studies: (1) the Michigan Predictive Activity & Clinical Trajectories (MIPACT) study of nearly 7,000 diverse participants in Ann Arbor (21% African American, 18% Asian, 12% Hispanic) and (2) the REACH-OUT Blood Pressure study of over 450 largely African-American participants in Flint.

Michigan Institute for Clinical and Health Research (MICHR); UL1 TR002240
Percent effort (time commitment): 5.0% (0.60 CM)
Funding agency: National Center for Advancing Translational Sciences / National Institutes of Health (NCATS/NIH)
Period of performance: 06/01/2017 – 02/28/2022
Level of funding: $48,548,399
The Michigan Institute for Clinical & Health Research (MICHR) of the University of Michigan (U-M) is a dynamic hub that, on institutional and national levels, catalyzes the translation of discoveries into improved health.

Past Support
Anesthesiology Control Tower: Feedback Alerts to Supplement Treatment (ACTFAST), R21 HS024581
Percent effort (time commitment): 5.0% (0.60 CM)
Funding agency: Agency for Healthcare Research and Quality (AHRQ)
Period of performance: 4/01/2017-3/31/2019
Level of funding: $103,078

This pilot study will institute an air-traffic control-like command center to facilitate increased adherence to best-practice principles and superior intraoperative care, ultimately improving postoperative quality of recovery and patient outcomes.

Analysis of Anesthesia Medications Delivered in Acute Care Hospitals, No agreement #
Percent effort (time commitment): 5.0% (0.60 CM)
Funding agency: Becton, Dickinson and Company
Name and email of Contracting/Grants Officer: Kelly Sager; Kelly_Sager@bd.com
Period of performance: 4/27/2020-10/31/2020
Level of funding: $120,000
The goals of this statement of work are the following: **1.** Develop report table shells, finalize patient inclusion criteria, confirm data quality limitations, establish project timeline; **2.** Develop, refine, execute on dose and unit of measure database queries across all MPOG sites for patients; **3.** Develop, refine, execute on medication concentration database queries for top 25 medications across MPOG sites using Cerner electronic health record; **4.** Review query results, establish plausibility, iterate on queries as needed; **5.** Collate query results into report package for sponsor

Canagliflozin: Impact on Health Status, Quality of Life, and Functional Status in Heart Failure; Protocol #28431754HFA3002
Percent effort (time commitment): 1.0% (0.12 CM)
Funding agency: Pharmaceutical Research Associates Inc. (Janssen Research & Development, LLC)
Period of performance: 03/27/2020 – 06/30/21 (Effort ended 2/28/2021)
Level of funding: $379,215
This randomized study is designed to assess whether canagliflozin therapy improves HF symptoms as assessed by the Total Symptom Score (TSS) of the Kansas City Cardiomyopathy Questionnaire (KCCQ) patient-reported outcome (PRO) scale in participants with HF and with or without T2DM in a real-world setting.

KRATZ, ANNA L., PH.D.

Current

WSU21009 (Fritz) 10/01/2020 – 09/30/2021 0.84 CM
Wayne State University (National Multiple Sclerosis Society) Country of Source of Support: USA
$23,141/annual directs $25,455/total proposed amount
Ambulatory Measurement of Perceived and Performance Fatigability
Project Goals: To use a combination of actigraphy, lab-based performance measures, and self-report of symptoms and functioning to develop and validate a whole-person measure of physical fatigability in MS.
Role: Co-Investigator

1U19AR076734-01 (Clauw) 09/20/2019 – 09/19/2024 0.60 CM
National Institutes of Health Country of Source of Support: USA
$1,244,618/annual directs $8,969,433/total award amount
University of Michigan BACPAC Mechanistic Research Center
Project Goals: The NIH BACPAC initiative is designed chronic low back pain (cLBP). We propose a single Research Project that will take patients with cLBP and use a patient-centric, SMART design study to follow these individuals longitudinally to generate new knowledge regarding phenotypes, endotypes, mechanisms, diagnostics, trial outcomes, and therapeutic responsiveness.
Role: Co-Investigator

1UG3HL145269-01A1 09/19/2019 – 08/31/2024 1.20 CM
National Institutes of Health Country of Source of Support: USA

$3,185,855/annual directs $27,515,029/total award amount
½ ICECAP: Influence of Cooling duration on Efficacy in Cardiac Arrest Patients
The overarching goal of this project is to identify clinical strategies that will increase the number of patients with good neurological recovery from cardiac arrest. We hypothesize that longer durations of cooling may improve either the proportion of patients that attain a good neurological recovery or may result in better recovery among the proportion already categorized as having good outcome.
Role: Co-Investigator

MS-1610-36980 (Kratz/Braley) 04/01/2/018 – 04/01/2023 3.60 CM
Patient-Centered Outcomes Research Institute (PCORI) Country of Source of Support: USA
$960,238/annual directs $3,706,651/total award amount
A randomized controlled trial of telephone-delivered cognitive behavioral-therapy, modafinil, and combination therapy of both interventions for fatigue in multiple sclerosis
Project Goals: This study will compare the effectiveness of a commonly used behavioral treatment strategy (cognitive behavioral therapy), a commonly used medication (modafinil), and a combination of both therapies, for fatigue in a large, representative group of patients with multiple sclerosis. The goal will be to help patients, providers, and policy makers determine which patients respond best to which treatment or combination of treatments.
Role: Principal Investigator

90ARC90003-01-00 (Murphy/Kratz) 10/01/2019 – 09/30/2024 0.90 CM
Administration for Community Living, National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) Country of Source of Support: USA
$161,937/annual directs $840,223/total award amount
University of Michigan Advanced Rehabilitation Research Training Program in Community Living and Participation
Project Goals: This 5-year, University of Michigan Advanced Rehabilitation Research Training Program in Community Living and Participation (ARRTP-CP) will train postdoctoral fellows to advance the rehabilitation field by embracing community-based and person-centered research methods.
Role: Co-Principal Investigator

MB-1706-27943 (Kratz) 07/01/2019 – 06/30/2024 0.36 CM
National Multiple Sclerosis Society Country of Source of Support: USA
$74,132/annual directs $430,255/total award amount
Training to Advance Rehabilitation Research in Multiple Sclerosis
The goal of this project is to train postdoctoral research fellows in rehabilitation research. The aim is to produce highly-competent and innovative researchers who can launch independent research programs that advance the goal of optimizing quality of life for those living with MS.
Role: Principal Investigator

(Kratz) 04/01/2021 – 03/31/2024 1.50 CM
Craig H. Neilsen Foundation Country of Source of Support: USA
$116,669/annual directs $400,000/total award amount
Acceptance and Commitment Therapy for Chronic Pain in SCI: Development and Testing of an eHealth Program
Project Goals: This grant is funding the development and pilot testing of an Acceptance and Commitment Therapy-based digital health intervention for chronic pain in people with spinal cord injury.
Role: Principal Investigator

(Iwashyna) 05/01/2020 – 04/30/2022 1.20 CM
Massachusetts General Hospital /NIH Country of Source of Support: USA
$306,434/annual directs $386,107/total award amount

COVID-19: PETAL COVID-19 Observational Study
Project Goals: This project will conduct the 1, 3, and 6 month post-admission follow-ups for a national cohort of patients with COVID-19 recruited from within the more than 40 hospitals in the NIH/NHLBI's Prevention and Early Treatment of Acute Lung Injury Network. These follow-up surveys will be conducted over the phone from a centralized location.
Role: Co-Investigator

(Murphy/Khanna) 07/01/2021 – 06/30/2023 0.60 CM
Rheumatology Research Foundation Country of Source of Support: USA
Resilience-based, Energy Management to Enhance Wellbeing in Scleroderma (RENEW): Testing of a Peer-Mentored Web-based Intervention
$199,999/annual directs $399,999/total proposed amount
Project Goals: We hypothesize that participants in the RENEW intervention will have a clinically meaningful improvement in fatigue as well as other symptoms and psychosocial issues (pain interference, depression, and resilience). We will also explore whether self-efficacy, a potential mediator of effects, is increased for participants in the RENEW intervention.
Role: Co-PD/PI

Past Support

4R01NR013658-05 (Carlozzi) 09/27/2012 – 06/30/2018 2.40 CM
National Institutes of Health Country of Source of Support: USA
$3,649,851/total award amount
Quality of Life in Caregivers of Traumatic Brain Injury: The TBI-CareQOL
Project Goals: The specific aims of this proposal are to: 1. Identify relevant HRQOL domains and item pools that are specific to caregivers of civilian- and/or military-related TBI; 2. Develop computer adaptive tests (CATs) or "smart tests" that are relevant to caregivers of civilianand/or military-related TBI; and 3. Validate the TBI-CareQOL and PROMIS in civilian and military populations and integrate the scales within large-scale studies within these populations.
Role: Co-Investigator

5K01AR064275-05 (Kratz) 04/01/2014 – 06/30/2019 9.00 CM
National Institutes of Health Country of Source of Support: USA
$652,785/total award amount
Characteristics and Mechanisms of Cognitive Problems in Fibromyalgia
Project Goals: The overarching goal of this proposal is to provide education and training to the Principal Investigator (PI), Anna Kratz, PhD, so that she has the requisite knowledge and skills to address these limitations in the scientific evidence on fibrofog.
Role: Principal Investigator

1R03NR014515-01A1 (Kratz) 07/01/2014 - 05/31/2016
National Institute of Nursing Research (NIH/NINR)
Characteristics of Symptoms and Functioning in Multiple Sclerosis
Project Goals: The goal of this study is to examine the day-to-day variability and interactions between various symptoms in multiple sclerosis and the impact of symptom burden on functioning.
Role: Principal Investigator

Craig H. Neilsen Foundation (Kratz) 04/01/2014-03/31/2016
The Dynamics of Pain Acceptance, Well-Being, and Functioning in SCI
Project Goals: This study examines the role of pain acceptance in the day to day functioning and well-being of individuals with chronic pain secondary to spinal cord injury.
Role: Principal Investigator

RG4986A 1/1 (Kratz) 04/01/2014 – 06/30/2019 1.20 CM
University of Washington/NMSS Country of Source of Support: USA
$52,441/total award amount
Life after MS diagnosis: a biopsychosocial assessment of symptom trajectory
Project Goals: Year 1: Dr. Kratz will provide the PI consultation on the selection and administration of outcomes measures and study design. She will establish data collection and data monitoring protocols and will see to it that research staff are following protocols. Once data collection has begun, she will conduct monthly data quality checks for the first three months of the study to assure adherence to study data collection protocols. Years 2 and 3: Dr. Kratz will conduct quarterly data quality checks and troubleshoot problems with data collection and/or entry. She will also conduct quarterly data analyses to ensure that study recruitment is meeting sample requirements in terms of participant demographic and clinical characteristics (e.g. to assure that appropriate numbers of racial minority participants are being recruited) and advise the research team for the need for targeted recruitment efforts. Year 4: Dr. Kratz will ensure that all data are adequately cleaned and conduct standard data integrity analyses. She will complete all primary study statistical analyses (to test the primary aim hypotheses) and will disseminate study findings through peer-reviewed manuscripts and scientific conference presentations.
Role: Site PD/PI

RG5280-A-2 (Braley) 04/01/2015 – 03/31/2021 0.12 CM
National Multiple Sclerosis Society (NMSS) Country of Source of Support: USA
$827,967/total award amount
A randomized trial of positive airway pressure therapy to treat cognitive dysfunction in MS patients with obstructive sleep apnea
Project Goals: The goals of this project are to examine the effects of OSA (obstructive sleep apnea), and its treatment - positive airway pressure therapy - on cognitive performance in MS patients who suffer from OSA.
Role: Co-Investigator

WSU16102 (Kratz) 04/30/2016 – 05/30/2018 0.48 CM
Wayne State University/Craig H. Neilsen Foundation Country of Source of Support: USA
$53,634/total award amount
Positive Psychological Traits and Psychological Flexibility in a Model of SCI Rehabilitation and Adjustment
Project Goals: 1. The University of Michigan will cover the recruitment of 80 participants for the survey portion of the study and 10 participants for the pilot intervention portion of the study. 2. The University of Michigan will collect data from the participants it recruits. 3. The University of Michigan will process participant compensation for the participants it collects data from. 4. The University of Michigan will program data collection web-sites and manage the data collected through these sites. 5. The University of Michigan will be engaged in subject recruitment, data collection, data processing and transfer, and dissemination activities. 6. The University of Michigan will engage in data analysis and dissemination activities.
Role: Site PD/PI/Collaborator

5R21AG053186-02 (Kratz) 09/01/2016 – 04/30/2020 1.20 CM
National Institutes of Health Country of Source of Support: USA
$426,250/total award amount
Development of a conceptual model of subjective physical and mental fatigability: the MI-FI study
Project Goals: The goal of this study is to address these limitations through a two-phase study to develop a foundational conceptual model of fatigability and lay the ground work for a state-of the art self-report measure of fatigability, the Michigan Fatigability Inventory (MI-FI).
Role: Principal Investigator

(Carlozzi) 04/30/2017 – 10/30/2020 0.60 CM
Craig H. Neilsen Foundation Country of Source of Support: USA

$399,187/total award amount
The Impact of Sleep Quality on Symptoms, Cognition, and Functioning in SCI
Project Goals: Using this multi-method measurement approach, we will conduct a novel study of how adults with SCI experience sleep, symptoms and cognition across a seven-day period. This study will focus on four common and troubling SCI symptoms – fatigue, pain, depression, anxiety, and cognitive concerns – assessed by self-report at five intervals each day throughout the week. We will evaluate functioning over the week through objective physical activity, assessed continuously by wrist-worn accelerometer, and by subjective report of daily participation in activities. We will also evaluate objective cognitive status through an in-person neurocognitive assessment completed at the end of the seven-day period.
Role: Collaborator

5U01DK082345-10 (Clemens/Clauw) 09/18/2014 – 06/30/2019 1.20 CM
National Institutes of Health Country of Source of Support: USA
$4,293,441/total award amount
University of Michigan MAPP Research Network Discovery Site
Project Goals: The NIDDK supplement to MAPP will modify the CMSI that is currently in use within the MAPP network. This involves expert consensus building regarding the best diagnostic criteria for each condition, cognitive interviews (focus groups) with patients to determine item relevance and understandability, and preliminary psychometric analysis of the instrument. The CMSI screener will also be updated to include trigger items for the 4 new conditions not currently in the MAPP version of the CMSI.
Role: Co-Investigator

W81XWH-17-1-0367 (Kratz) 09/15/2017 – 03/14/2020 1.20 CM
Department of Defense Country of Source of Support: USA
$209,556/total award amount
Development of a Web-Based Symptom Self-Management Program for Individuals with Multiple Sclerosis
Project Goals: The primary objective of the proposed research is to improve management of pain, fatigue, and depressed mood through an online platform that provides education, guidance, and skills-building exercises that are specifically tailored for people with MS. Access to rehabilitation care that focuses on symptom self-management is seriously limited for many individuals with MS due to geographical location, limited resources (e.g. financial, transportation), and/or disability. The objective of this proposal is to expand access to symptom self-management care to all patients with MS, with particular focus on those under-served patients with limited access to symptom management care.
Role: Principal Investigator

(Tate/Rohn) 04/30/2018 – 04/29/2021 0.60 CM
Craig H. Neilsen Foundation Country of Source of Support: USA
$200,000/total award amount
Phenomenology of Chronic Pain After Spinal Cord Injury: Experience, Adaptation and Quality of Life
Project Goals: The goal of the proposed study is to characterize the factors that contribute to the day-to-day experience of and adaptation to chronic pain and examine the relationship of those factors to QOL for those with SCI.
Role: Collaborator

KRUGER, DANIEL, PH.D.

Current

R01 HD096909 03/01/19 – 02/28/24 (5.0%) 0.60 CM
Mendelsohn, A $ 9,415 average subcontract direct costs United States
New York University / NIH Prime $76,204 Total Subcontract Award

Universal Strengths-Based Parenting Support in Pediatric Health Care for Families with Very Young Children Following the Flint Water Crisis
The goals of this project are to characterize neighborhood-level stressors and resilience factors in relation to the disaster and to poverty more broadly using geocoded, census-linked Speak to Your Health survey data before, during, and in the aftermath of the disaster. Assess impacts of promotion of parenting on responsive parenting and child development in the aftermath of a disaster in a high poverty community.
Role: Co-Investigator

Past Funding

RFP #09-013	10/01/11 – 09/30/12	(40.0%) 4.80 CM
Kruger, D	$56,092 Direct Costs	United States
Genesee County, MI	$84,997 Total Award Amount	

REACH US
The Genesee County REACH US project is designed to reduce disparities in perinatal health and infant mortality in Genesee County, MI. The project is funded by a grant from the Centers for Disease Control and Prevention to the Genesee County Health Department. The project follows Community Based Public Health principles and involves a partnership between local health infrastructures, community-based organizations and universities. The partnership promotes education and health promotion programs, community mobilization, healthcare advocacy, and other activities that address historical, cultural and structural aspects of racism.
Role: Principal Investigator

MCAFEE (GOESLING), JENNA, PH.D.

Current

U19 AR076734	09/26/19 – 05/31/24	(20.0%) 2.40 CM
NIH/NIAMS	$1,152,504 Annual Direct Costs	NIH/NIAMS
Clauw, DJ-Contact / Hassett, AL	$8,969,433 Total Award Amount	United States

University of Michigan BACPAC Mechanistic Research Center
As part of the BACPAC initiative, the mechanistic research center at the University of Michigan aims to be a team member in realizing the vision of personalized medicine for individuals with cLBP**.**
Role: Co-Investigator; Clinical Core, Behavioral Phenotyping Core, Research Project

Past Support

K23 DA038718	05/01/16 – 04/30/21	(75.0%) 9.00 cm
(Goesling, J)	$124,043 Annual Direct Costs	United States
NIH/NIDA	$690,841 Total Award Amount	

Advancing the Treatment of Chronic Pain through Individualized Opioid Cessation
The goal of this mentored career development award is to better understand why patients continue taking opioids and incorporate theory-based models of behavior change into the development of interventions for individuals who would benefit from opioid cessation.
Role: Principal Investigator

U01 CE002780	09/01/17 – 08/31/20 NCTX	(10.0%) 1.20cm
Bohnert, AB	$285,025 Annual Direct Costs	United States
CDC	$799,823 Total Award Amount	

Heroin use and overdose following changes to individual-level opioid prescribing
Heroin-related overdose deaths more than tripled between 2010 and 2014 in the United States. Emerging evidence has identified nonmedical use of prescription opioids as a risk factor for heroin initiation. Some have observed that the spike in heroin overdose deaths has overlapped with efforts to reduce the nonmedical use of

prescription opioids; however, a causal link has not been established. Using analysis of medical records for over 50 million Americans and in-depth interviews with patients, this study will seek to inform prevention efforts by examining the association between individual-level opioid prescribing patterns – in particular tapering or discontinuation of opioids – and the risk of heroin use and overdose.
Role: Co-Investigator

SHAH, NIRAV, M.D.

Current

Anesthesiology Performance Improvement and Reporting Exchange (ASPIRE) / MPOG, Master Vendor Agreement #12600
Percent effort (time commitment): 19%
Funding agency: Blue Cross Blue Shield of Michigan
Period of performance: 01/01/19 – 7/31/24
Level of funding: $940,278 Annual Direct Costs, $2,350,691 Total Award Amount
Integrating electronic health record data across dozens of centers, we are able to provide near real-time feedback to providers and hospitals regarding their adherence to accepted standards of care.

Anesthetic Induction Overdose Among Elderly Surgical Patients, R01AG 059607, GR105746(CON-80001781)
Percent effort (time commitment): 5%
Funding agency: NIH/Yale University
Period of performance: 4/1/2019 – 1/31/23
Level of funding: Total UofM Award $450,590
Dr. Shah will be integral in the completion of Aim 3 during the final two years of the projects. Both investigators will participate with Yale University researchers as they formulate the specific research questions, consulting with them in the determination of specific analytic approaches as best directed to the

MIPACT-ER: Michigan Predictive Activity & Clinical Trajectories Study Extension
Percent effort (time commitment): 2.5%
Funding agency: Apple, Inc.
Period of performance: 7/13/2020 – 8/17/2024
Level of funding: confidential
The overarching goal of the MIPACT-ER project is to integrate Apple Watch, electronic health record, genomic, and participant survey data to build a dataset for future research.

Michigan Predictive Activity & Clinical Trajectories (MIPACT) Study
Percent effort (time commitment): 15%
Funding agency: Apple, Inc.
Period of performance: 8/17/2018 – 8/17/2024
Level of funding: confidential
Institution will conduct a Research Study to [determine how wearable devices can be used to determine health trajectories in order to improve patient outcomes] as more fully described in the protocol attached as Exhibit B

COVID-19: COVID-19 Health Evaluation & Cardiovascular Complications (CHECC) Study
Percent effort (time commitment): 2.5%
Funding agency: American Heart Association, Inc.
Period of performance: 6/1/2020 - 5/31/2021
Level of funding: Total Award $200,000

To better understand the pathobiology and the clinical implications of the viral infection that leads to the morbidity and mortality seen with COVID-19. We propose leveraging data from two ongoing U-M mHealth studies: (1) the Michigan Predictive Activity & Clinical Trajectories (MIPACT) study of nearly 7,000 diverse participants in Ann Arbor (21% African American, 18% Asian, 12% Hispanic) and (2) the REACH-OUT Blood Pressure study of over 450 largely African-American participants in Flint.

Association between Intraoperative Hypotension and Patient Outcomes: A Multicenter Retrospective Observational Study, SOW#2
Percent effort (time commitment): 7.5%
Funding agency: Edwards Lifesciences, LLC
Period of performance: 3/1/2021 – 2/28/2022
Level of funding: $225,000
This study will analyze the relationship between several commonly used definitions of intraoperative hypotension and post-operative outcomes. Our primary hypothesis is that as the burden of hypotension increases, rates of AKI will increase as well.

Michigan Opioid Misuse Prevention Network (AWD016455-SUB030-Michigan Opioid Prescribing Engagement Network: M-OPEN), E20213443-00
Percent effort (time commitment): 10%
Funding agency: Michigan DHHS - MA-2020 Master Agrmt Prog
Period of performance: 10/01/2020 – 09/30/2021
Level of funding: $2,156,243 Total Award
The overall goal of this initiative is to reduce the amount of opioids prescribed to surgical patients by 50%, reduce new chronic postoperative opioid use by 50%, and reduce opioid diversion into our communities.

Past Support
Association between Intraoperative Hypotension and Patient Outcomes: A Multicenter Retrospective Observational Study, Res Svcs Agmt Protocol #2018-16
Percent effort (time commitment): 5%
Funding agency: Edwards Lifesciences, LLC
Period of performance: 04/08/2019 – 06/30/2020
Level of funding: $161,154 Annual Direct Costs, $250,000 Total Award Amount
This study will analyze the relationship between several commonly used definitions of intraoperative hypotension and post-operative outcomes. Our primary hypothesis is that as the burden of hypotension increases, rates of AKI will increase as well.

National Trends and Variation in the Reversal of Perioperative Neuromuscular Blockade -A Comparison of Cholinesterase Inhibitors and Selective Relaxant Binding Agents, Research Service Agreement PO810225
Percent effort (time commitment): 10%
Funding agency: Merck and Company, Inc.
Period of performance: 04/18/2017–12/31/2018
Level of funding: $1,795,800
The goal of the proposed study is to use a broadly representative observational dataset to compare patterns of care in the reversal of non-depolarizing neuromuscular blockade, comparing patients receiving neostigmine and sugammadex. Next, using administrative data, we will compare the impact of sugammadex use on pulmonary complications and resource utilization.

Prospective, Single-Arm, Open-Label, Multicenter Study of Hypotension Prevention and Treatment in Patients Receiving Arterial Pressure Monitoring with Acumen Hypotension Prediction Index Feature Software
Percent effort (time commitment): 7%

Funding agency: Edwards Lifesciences
Period of performance: 8/20/2019 - 12/31/2020
Level of funding: Total Award $378,654
The objective of the study is to determine whether use of the AcumenTM HPI Feature Software to guide intraoperative hemodynamic management in non-cardiac surgery reduces the duration of intraoperative hypotension (defined as MAP < 65 mmHg for at least 1 minute) as compared with a historic retrospective control group.

Pulmonary complications and mortality among high risk patients and surgical procedures; evaluating the impact of sugammadex, PO 8103110534
Percent effort (time commitment): 5%
Funding agency: Merck Sharp and Dohme Research
Period of performance: 4/24/2020 – 11/30/2020
Level of funding: $194,275
We propose to evaluate the impact of sugammadex use, compared to neostigmine, among patients exhibiting one or more of these surgical (major abdominal, thoracic, emergency, or prolonged procedure) or underlying risk factors (advanced age, morbid obesity, sleep apnea, or pulmonary disease).

Michigan Opioid Misuse Prevention Network (AWD10680-Michigan Opioid Prescribing Engagement Network: M-OPEN), E20192408-00 – Project AS
Percent effort (time commitment): 10%
Funding agency: Michigan DHHS - MA-2020 Master Agrmt Prog
Period of performance: 10/01/2018 – 09/30/2019
Level of funding: $1,625,737 Total Award
The overall goal of this initiative is to reduce the amount of opioids prescribed to surgical patients by 50%, reduce new chronic postoperative opioid use by 50%, and reduce opioid diversion into our communities.

SILVEIRA, MARIA J., M.D., M.P.H.

Dr. Silveira holds a joint appointment with the Department of Veterans Affairs (VA) and the University of Michigan (UM). Veterans Affairs 5/8 appointment and University of Michigan 6.0 calendar months.

Current

University of Michigan Palliative Care Pilot grant (PI: Silveira) 6/1/2020-5/31/2022
Annual Directs: $20,000
Centralized pain in lung cancer patients
Our objective is to measure the prevalence of central sensitization in a convenience sample of lung cancer patients in preparation for an R01 to examine central sensitization in chronic cancer pain.

University of Michigan MCube (PI: Silveira) 6/1/2019-12/31/2021
Annual Directs: $60,000
Electronic monitoring of opioid adherence among patients at risk for misuse
The primary goal of this project is to assess the ideal features of a program to electronically monitor patient opioid use among patients with cancer pain who have past histories of substance use or alcohol use disorder.

PLC-1609-35995 1/1/2018-12/31/2022 1.8 Calendar Months
PCORI (PI: Temel) Source Country: USA
Annual Directs: $45,798 Total Award: $338,800
Comparative effectiveness trial of early integrated telehealth vs in-person palliative care for patients with advanced lung cancer

Early and longitudinal involvement of palliative care (PC) in the outpatient management of patients with advanced cancer improves patient-reported and end of life (EOL) care outcomes. While recommended by national organizations as the standard of care, this early integrated care model utilizes substantial PC resources, which has limited its dissemination across care settings. Telehealth (i.e., the use of information and communication technology in health care delivery) is an effective strategy to increase patients' access to health care services when the numbers of specialty-trained clinicians are limited. We seek to perform a multi-site comparative effectiveness trial of early integrated telehealth versus in-person PC in patients with advanced lung cancer. By demonstrating the equivalence of the telehealth delivery modality, we seek to define a role for this more accessible, scalable and patient-centered approach to PC.
Role: Co-I, Site-PI

Past Support

None

WHIBLEY, DANIEL, PH.D.
Current

(Murphy/Khanna) 07/01/2021 – 06/30/2023 0.60 CM
Rheumatology Research Foundation Country of Source of Support: USA
$199,999/annual directs $399,999/total award amount
Resilience-based, Energy Management to Enhance Wellbeing in Scleroderma (RENEW): Testing of a Peer-Mentored Web-based Intervention
Project Goals: We hypothesize that participants in the RENEW intervention will have a clinically meaningful improvement in fatigue as well as other symptoms and psychosocial issues (pain interference, depression, and resilience). We will also explore whether self-efficacy, a potential mediator of effects, is increased for participants in the RENEW intervention.
Role: Co-Investigator

(Kratz) 04/01/2021 – 03/31/2024 2.40 CM
Craig H. Neilsen Foundation Country of Source of Support: USA
$116,669/annual directs $400,000/total award amount
Acceptance and Commitment Therapy for Chronic Pain in SCI: Development and Testing of an eHealth Program
Project Goals: This grant is funding the development and pilot testing of a digitally delivered Acceptance and Commitment Therapy intervention for people with spinal cord injury-related chronic pain.
Role: Co-Investigator

1U19AR076734-01 (Clauw) 09/20/2019 – 09/19/2024 2.61 CM
National Institutes of Health Country of Source of Support: USA
$1,244,618/annual directs $8,969,433/total award amount
University of Michigan BACPAC Mechanistic Research Center
Project Goals: The NIH BACPAC initiative is designed to address the need for effective and personalized therapies for chronic low back pain (cLBP). Within the initiative, we are conducting a research project that uses a patient-centric, SMART design study to follow people with cLBP longitudinally to generate new knowledge regarding phenotypes, endotypes, mechanisms, diagnostics, trial outcomes, and therapeutic responsiveness.
Role: Co-Investigator

Past Support

(Whibley) 06/02/2019 – 05/29/2020 1.00 CM
Michigan Medicine Dan Barry Grant Country of Source of Support: USA

Harnessing Participatory Action Research to guide the design of a sleep and physical activity improvement intervention for adults with osteoarthritis
$2500/total award amount
This grant funded a longitudinal qualitative focus group study to explore target user motivations, expectations, and attitudes toward a newly developed digitally delivered hybrid sleep and physical activity improvement intervention.
Role: Principal Investigator

(Whibley) 03/05/2018 – 06/04/2021 12.00 CM
Versus Arthritis (Foundation Fellowship) Country of Source of Support: UK
Investigating the role of exercise and sleep in the management of chronic pain
£178,377.00/total award amount
This grant funded an investigation of the interlinkages between chronic pain, exercise/physical activity and sleep among people living with chronic pain. Insights gained were then used to develop and feasibility test a new digital intervention that simultaneously targets exercise and sleep behaviors in people living with chronic pain.
Role: Principal Investigator

(Whibley) 08/01/2018 – 09/01/2018 1.00 CM
Scottish Universities Life Sciences Alliance Country of Source of Support: UK
The relationship between sleep, fatigue, cognitive dysfunction and chronic pain: Identifying temporal relationships and targets for treatment
£4110/total award amount
This Postdoctoral and Early Career Research Exchange grant funded travel to work in the Kratz Lab at the University of Michigan to analyze actigraphy and ambulatory assessment data to enhance understanding of the temporal associations between sleep, fatigue, cognitive dysfunction and chronic pain.
Role: Principal Investigator

WILLIAMS, DAVID A., PH.D.

Current

P50 AR070600 09/20/16 – 08/31/21 (10.0%) 1.20 CM
Clauw, DJ-Contact / Brummett, CM $ 958,792 Annual Direct Costs United States
NIH/NIAMS $7,415,237 Total Award Amount
University of Michigan Fibromyalgia CORT
The goal of this program of research is to understand how fibromyalgia and other rheumatic diseases affect patients, better understand the underlying mechanisms of their pain, and personalize analgesic treatment.
Role: Co-Director, Phenotyping and Outcomes Core (POC)

R01 NR017096 05/09/17 – 02/28/22 (16.0%) 1.92 CM
Hassett, AL – Contact / Williams, DA $ 371,906 Annual Direct Costs United States
NIH/NINR $2,549,712 Total Award Amount
Resilience Skills Self-Management for Chronic Pain
The goal of this project is to develop pilot a simple, nurse-delivered affective intervention to improve physical function and markers for biological aging for patients suffering from fibromyalgia.
Role: Principal Investigator (MPI)

UL1 TR002240 09/17/07 – 02/28/22 (20.0%) 2.40 CM
Mashour, GA $ 6,221,969 Annual Direct Costs United States
NIH/NCATS $48,448,400 Total Award Amount

Michigan Institute for Clinical and Health Research (MICHR)
The UM CTSA, housed in the Michigan Institute of Clinical and Health Research (MICHR), was created to provide robust infrastructure and support based on strong existing units and programs, as well as academic programs in key clinical and translational disciplines in order to provide faculty leadership, expertise, and consultation as well as high quality services
Role: Co-Director, Research Development Core

U01 DK082345 09/15/08 – 06/30/22 (10.0%) 1.20 CM
Clauw, DJ-Contact/Clemens, JQ $ 250,525 Annual Direct Costs United States
NIH/NIDDK $1,172,455 Total Award Amount
University of Michigan MAPP Research Network Discovery Site
The goal this project is to study the etiology and treated natural history of UCPPS, to inform better treatments and management of symptoms through improved designs of clinical trials, and to identify clinical factors and research measurements to define clinically relevant sub-groups of these patients. The proposed three-year extension will allow the participating institutions to obtain an additional 12 months of follow-up in the MAPP-II Symptom Patterns Study (SPS), observe additional ATLAS (Analysis of Therapies during Longitudinal Assessment of Symptoms) events in the MAPP-II SPS, and analyze MAPP-II data.
Role: Co-Investigator

R01 DK123164 01/22/20 – 11/30/24 (10.0%) 1.20 CM
Harte, SE / Schrepf, AE $ 392,187 Annual Direct Costs United States
NIH/NIDDK $2,594,063 Total Award
Neuroimmune Interface in Urological Chronic Pelvic Pain Syndrome
Our primary goal is to identify how inflammation interacts with the CNS to promote chronic pain and other debilitating symptoms in UCPPS.
Role: Co-Investigator

UL1 TR001857 06/01/19 – 05/31/21 (1.0%) 0.12 CM
Hanauer, D $ 25,000 Annual Direct Costs United States
University of Pittsburgh/NIH $129,000 Total Award Amount
University of Pittsburgh Clinical and Translational Science Institute - ACT Network Supplement
As a site in the network, the Michigan Institute for Clinical and Health Research will support maintenance and updates of the informatics platform and data harmonization schema for the ACT network.
Role: Co-Investigator

U19 AR076734 09/26/19 – 05/31/24 (15.0%) 1.80 CM
Clauw, DJ-Contact / Hassett, AL $1,152,504 Annual Direct Costs United States
NIH/NIAMS $8,969,433 Total Award Amount
University of Michigan BACPAC Mechanistic Research Center
As part of the BACPAC initiative, the mechanistic research center at the University of Michigan aims to be a team member in realizing the vision of personalized medicine for individuals with cLBP.
Role: Co-Director, Behavioral Phenotyping Core

RI-CRN-2020-006 (714976-3) 01/01/20 – 07/31/21 (15.0%) 1.80 CM
Williams, DE $430,968 Annual Direct Costs United States
University of Pittsburgh/PCORI $541,104 Total Award Amount
University of Pittsburgh Clinical and Translational Science Institute - ACT Network Supplement
As a site in the network, the Michigan Institute for Clinical and Health Research will support maintenance and updates of the informatics platform and data harmonization schema for the ACT network.
Role: Co-Investigator, Site Principal Investigator

NU38 OT000316 **1**0/01/20-07/31/21 (3.0%) 0.36 CM

Williams, D $50,000 Annual Direct Costs United States
Task Force for Global Health/CDE Prime $64,500 Total Award Amount
Task Force for Global Health – COVID-19 Electronic Health Data Initiative
The COVID-19 electronic healthcare data initiative project will demonstrate PCORnet sites ability to collect information on COVID data through the implementation of a nationally distributed data infrastructure. The collection of these COVID-19 data will help to answer critical questions to assist in the emergency response to the COVID-19 pandemic.
Role: Site Principal Investigator

Past Support

CNVA00062316 (713948-5) (McTigue, K) 03/30/19 – 09/30/20 (15.0%) 1.80 CM
University of Pittsburgh (People Centered Research Fdn-Prime) $90,740 United States
PaTH Network
The goal of this agreement is for UM to actively and collaboratively participate in the development of PCORnet governance, including development of PCORnet-wide policies and standards and ad hoc working groups or teams for the governance of PCORnet. The UM PI will attend and contribute to PCORnet-wide meetings, ad hoc groups and teams that support the operations, management, improvement and sustainability of PCORnet. **Role:** UM Site Principal Investigator

UL1 TR001857 (Ries, SE) 06/01/19 – 05/31/20 (2.50%) 0.30 CM
University of Pittsburgh / NIH Prime $75,000 United States
University of Pittsburgh Clinical and Translational Science Institute - ACT Network Supplement
As a site in the network, the Michigan Institute for Clinical and Health Research will support maintenance and updates of the informatics platform and data harmonization schema for the ACT network.
Role: Co-Investigator

R21 NR016930 09/26/18 – 08/31/20 (2.0%) 0.24 CM
Burgess, H $137,500 Annual Direct Costs United States
NIH / NINR $421,751 Total Award Amount
Bright Light Treatment at Home to Improve Symptom Management of Fibromyalgia Syndrome
Our pilot data suggests that morning bright light treatment can meaningfully reduce FMS symptoms. In the proposed study, we will reduce subject burden and increase innovation by testing a wearable light device (bright vs. dim Re-timer®) with objective measures of treatment compliance.
Role: Co-Investigator

U01 AR55069 (Williams, D.) 08/01/07 – 02/28/12 (NCTX) (10%) 1.20 calendar
NIH/NIAMS $128,388
A Fibromyalgia-Specific Extension of the PROMIS Network
The overall goal of this project is the development, testing and integration of a disease-specific measurement instrument to use in clinical trials for the assessment of multiple domains of relevance for fibromyalgia.
Role: Principal Investigator

R01 AR057808 (Lumley, M. – Wayne St. Univ.) 08/15/10 – 06/30/15 (20.0%) 2.16 calendar
NIH/NIAMS $566,563
Emotional Exposure and Cognitive Behavioral Therapies for Fibromyalgia
This application combines the clinical research, pain, and FMS expertise of two research teams to conduct a 2-site, randomized, controlled trial of emotional exposure therapy (EET) against both a standard cognitive-behavioral therapy (CBT; pain coping skills training) and control condition (FMS education and support) in a design that controls for the importance of exercise, non-specific factors, and experimenter allegiance to the different treatments.
Role: Site Principal Investigator

VA Merit Grant E7557R (Murphy, S.) 10/01/10 – 09/30/13 (5.0%) 0.60 calendar
U.S. VA Rehabilitation Research & Development $40,000
Effectiveness of Tailored Activity Pacing for Symptomatic Osteoarthritis

The goal of this project is to examine the effectiveness of tailored activity pacing, compared to general activity pacing and usual care, on pain, fatigue, and physical function for veterans with knee or hip osteoarthritis.
Role: Co-Investigator

R01 AR060392 (Clauw, D./Brummett, C.–MPI) 08/01/11– 05/31/16 (10.0%) 1.80 calendar
NIH/NIAMS $437,235
Central Nervous System Mechanisms in Knee Osteoarthritis (KOA)

The goal of this project is to show that simple clinical testing easily performed at the point-of-care can reliably segment chronic pain patients into those with prominent central components to their pain, that are likely to need different pharmacologic (i.e. centrally acting analgesics) and non-pharmacologic approaches (not surgery). Moreover this study has tremendous potential to help improve broaden our understanding of the underlying mechanisms that may lead to pain and other symptoms in OA.
Role: Co-Investigator

Services Agreement (Clauw, DJ) 01/01/12 – 12/31/12 (5.0%) 0.60 calendar
Pfizer, Inc. $402,572
Development of a Web-based Patient Engagement Tool for Chronic Low Back Pain

The goal of this project is to develop the Patient Engagement Platform (PEP), an integrated and interactive eHealth product developed for physician and patient engagement surrounding the pain management of chronic low back pain. The PEP contains 5 categories and functions (clinic assessment, guidance, tracking/reporting, self-management modules, and motivational tools).
Role: Co-Investigator

RSG-13-240-01-PCSM (Henry, NL) 08/01/13 – 07/31/17 (5.0%) 0.60 cm
American Cancer Society (ACS) $150,000
Centralization of pain in breast cancer survivors
The primary goals of this proposal are to investigate markers of centralization of pain and to evaluate potential predictors of response to the predominantly centrally-acting analgesic duloxetine in breast cancer survivors with chronic, treatment-related pain.
Role: Co-Investigator

(Piette, J) 10/01/14 – 06/30/19 (1.0%) 0.12 cm
VA Ann Arbor Healthcare System $2,451
Patient-Centered Pain Care Using Artificial Intelligence and Mobile Health Tools

As a member of the Expert Panel, Dr. Williams will contribute expertise on delivering CBT using m-Health technologies.
Role: Expert Panel Member

END APPLICANT RESPONSE

V-G Personnel

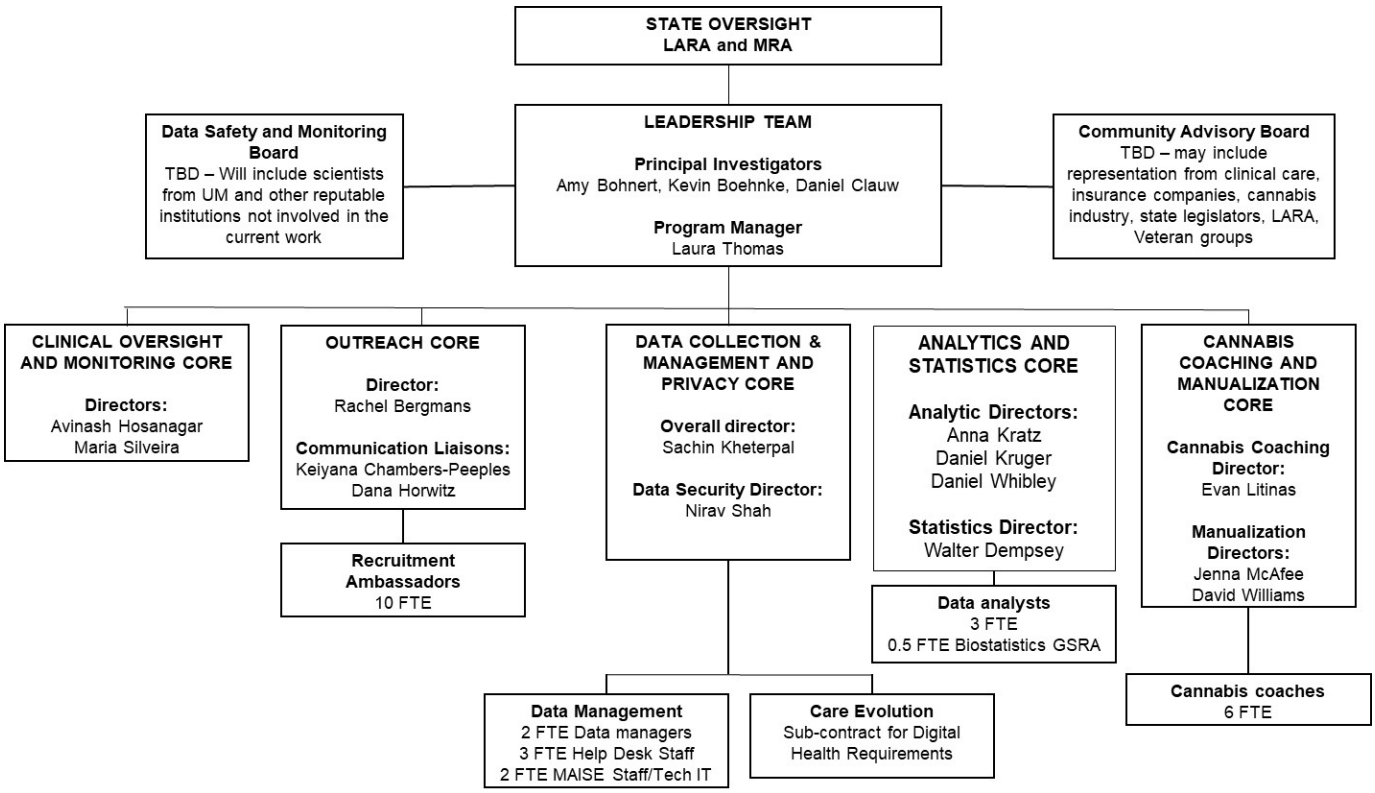
Selected applicant(s) must be able to staff a project team that clearly possesses skill and experience in coordinating clinical trials. In the narrative, identify the authorized contact person and key personnel to be involved with this project by name and title and provide a brief summary of their experience, qualifications, and the work to be performed.

If other organizations will be playing a role in the proposed project, provide sufficient background information that will give the Issuing Office a reasonable understanding of each organization's qualifications.

Include a detailed organizational chart including names, titles, and geographic location of all individuals that will contribute to the project.

Attach a copy of your confidentiality agreement and provide a list of personnel and the date that the confidentiality agreement was signed.

BEGIN APPLICANT RESPONSE



The figure above shows the organizational structure for the individuals who will contribute to this project. These individuals include the Leadership Team and Co-Investigators listed above, all of whom are based in Ann Arbor, MI.

Leadership Team

Our team of co-Principal Investigators (co-PIs) have complementary expertise to ensure that all aspects of the study can be carried out. They are Drs. Amy Bohnert, Kevin Boehnke, and Daniel Clauw, all three of whom are faculty members at the University of Michigan. Both Drs. Bohnert and Clauw have successfully managed very large grants and contracts, with Dr. Clauw alone having been responsible for over $100M in federal grant funding.

- Dr. Amy Bohnert is a Professor of Anesthesiology, Psychiatry, and Epidemiology at the University of Michigan (UM). She is an internationally renowned epidemiologist whose research team has been very involved in studying Veterans, mental health and the risk of suicide.[3,5-7,106,108-115,117-129,131-133,135,143-163,165-177,179-191,203] Her research, funded by NIH, CDC, and the VA, has been foundational in understanding the balance of benefits and harms of opioid analgesic use, and she has content expertise

in pain and substance use disorders. She currently uses the MyDataHelps and Fitbits to collect data from individuals on wait lists for outpatient psychiatry care, and has experience with all of the programs and risk management protocols necessary. She also has led the Michigan Opioid Collaborative since 2017, which is funded by contract from the Michigan Department of Health and Human Services (described more below).

- Dr. Kevin Boehnke is a Research Investigator in the Department of Anesthesiology at UM and a nationally renowned cannabis expert. He is currently involved in several NIH-funded clinical trials investigating effects of cannabinoids on pain and sleep. He has led numerous studies showing that people with chronic pain substitute cannabis for opioids and other pain medications, mostly without clinician oversight.[16-18,49,50,52-57] Dr. Boehnke has provided guidance on CBD for the Arthritis Foundation,[204] and is currently a Technical Expert Panel member for two national committees on cannabinoid use for pain, including a collaboration between the office of Veterans Affairs and Oregon Science and Health University.
- Dr. Daniel J. Clauw, MD is a Professor of Anesthesiology, Rheumatology, and Psychiatry at UM. He serves as the Director of the Chronic Pain and Fatigue Research Center (CPFRC), which is one of the world's leading pain research groups. Dr. Clauw is an internationally renowned pain researcher and expert on centralized pain syndromes, and and currently leads or has previously led numerous federally funded projects related to chronic pain including the NIH-funded UM Fibromyalgia Center for Research Translation, the Back Pain Consortium Research Program, and the Multidisciplinary Approach to the Study of Chronic Pelvic Pain network. He has extensive experience in clinical trial design, conduct, and interpretation, as well as considerable expertise in cannabinoids.[16,17,49-51,103,140,199,205-235]
- Laura Thomas, MSW, MPH is a Project Manager at the VA and a Clinical Therapist in Anesthesiology at UM. She is a licensed social worker with expertise in suicide risk management and motivational interviewing. She has over 7 years of experience in project management at the University of Michigan.

Clinical Oversight and Monitoring Core

- Dr. Avinash Hosanagar, MD, is a Staff Psychiatrist at the Ann Arbor VA Medical Center (VAMC) and a Clinical Assistant Professor in the Department of Psychiatry at UM. Dr. Hosanagar is addiction medicine-boarded and provides addiction-related services to Veterans, as well as leading the ketamine clinic for severe depression at the Ann Arbor VAMC. He will lead efforts to monitor and conduct risk assessments and treatment referrals in this project.
- Dr. Maria Silveira, MD is an Associate Professor in Geriatric and Palliative Medicine at the University of Michigan, Research Scientist at the Ann Arbor VAMC GRECC, and Director of the Supportive Oncology Clinic at the Rogel Cancer Center. She has devoted the last 10 years to developing technology to improve patient and caregiver access to safe and effective symptom management advice, including trials of web-based support for caregivers. Dr. Silveira served on the VA's Expert Panel for Long-term Opioid Therapy Guidelines and am on NCCN's panel for Anti-emesis Guidelines. In addition to her research, she has treated hundreds over Veterans clinically over the course of her career. Dr. Silveira will provide risk management for enrollees in the study, insight on the web-based intervention, and aid with Veteran outreach and engagement efforts.

Outreach Core

- Dr. Rachel Bergmans, MPH, PhD is a Psychiatric Epidemiologist and Research Fellow in the UM Institute for Social Research at UM. Her program of work investigates the influence of social factors on mood disorders and suicide-related outcomes. She has expertise in community-engaged approaches to partner with key stakeholders in addressing social determinants of health including community education centers, faith-based organizations, and health clinics. Her published work represents collaborations with members of the proposed study team over the past three years on projects examining associations of public policy with suicide-related behavior and social determinants of depression and

suicide. In this project, she will oversee outreach to and build partnerships with Veteran organizations to enhance recruitment and ensure overlap between scientific and stakeholder goals.
- Keiyana Chambers-Peeples is an Administrative Assistant in Anesthesiology at the University of Michigan. She has extensive experience in administration as well as in outreach efforts among Black communities.
- Dana Horwitz, MSW, is a Research Associate at the Ann Arbor VAMC. She has extensive clinical experience treating Veterans as well as expertise in recruiting and retention efforts for research studies with Veterans.
- TBD: We will hire 10 FTE recruitment ambassadors who will facilitate outreach with Veteran communities to enhance recruitment, build partnerships, and connect participants with the cannabis coaching intervention. We anticipate that ambassadors will be a mix of remote staff (e.g., in Flint and Detroit) as well as local staff located in the Ann Arbor area.

Data Collection, Management, and Privacy Core

- Dr. Sachin Kheterpal, MD, is a Professor of Anesthesiology and associate dean for research information technology at the Medical School at UM. He is an expert in information technology (IT) and directs the ongoing development IT infrastructure across multiple international sites using innovative techniques to integrate administrative, electronic health records (EHR), and registry data across institutions. He is also the Principal Investigator of a study (MiPACT), funded via contract from Apple, that has recruited over 7,000 participants to use Apple Watch devices to track health outcomes longitudinally and developed methods to ensure a diverse sample. In this project, he will provide technical leadership to ensure that key delivery functionality of the mobile technology is operational and maintained.
- Dr. Nirav Shah, MD, is an Assistant Professor in the Department of Anesthesiology at the University of Michigan. Within Michigan Medicine, he is the Associate Chief Medical Information Officer – Perioperative Care, and Director of Anesthesia Informatics and Systems Improvement, where he leads a team that develops software solutions for perioperative quality improvement, research, clinical and business operations, and supports the hospital's perioperative electronic health record (EPIC). Dr. Shah has deep expertise in workflow optimization, data privacy, and data management, all of which he will bring to his role on this project.
- TBD:
    - We will hire 2 FTE data managers who will oversee the project database and maintain data quality and consistency.
    - We will hire 3 FTE Help Desk Staff who will aid with maintaining the project database and providing as-needed support to study participants and the project team.
    - We will hire 2 FTE MAISE (Michigan Anesthesiology Informatics and Systems Improvement Exchange) Staff/Technical support who will be responsible for database management and programming needs.
    - We anticipate that most of these employees will be located in Ann Arbor, MI, but are flexible in allowing some to work remotely as that may facilitate a broader pool of qualified applicants.

Analytics and Statistics Core

- Dr. Walter Dempsey, PhD, is an Assistant Professor of Biostatistics and Assistant Research Professor at the Institute for Social Research at UM. His research focuses on statistical methods for digital mental health, with a particular interest in dynamic (i.e., longitudinal) treatment strategies and using sensor data to improve participant engagement and outcomes. In this project, he will guide statistical modeling decisions and oversee the activities of the project data analysts.
- Dr. Daniel J. Kruger, PhD is a Research Investigator in the Institute for Social Research at UM. He has extensive expertise in on-line survey research, program evaluation, and statistical analyses. Dr. Kruger has a collaborative research program on cannabis use and public health, focusing on the relationships

and disconnects between medical cannabis use and mainstream health systems.[52,55,253-261] His work has been funded by federal and state agencies, as well as foundations. Dr. Kruger will provide insight on statistical analyses, survey design, and manuscript preparation for this project.

- Dr. Daniel Whibley, PhD, is a UK-registered physiotherapist, a Research Assistant Professor in the Department of Physical Medicine and Rehabilitation at UM. His research is focused on the impact of sleep and physical activity on the symptoms pain, fatigue, and cognitive function. His expertise includes analysis of data collected using ambulatory assessment methods and actigraphy. He has published numerous studies in the sleep and pain fields and previously investigated cannabis use patterns among adults with Multiple Sclerosis and impacts on pain, anxiety, fatigue and insomnia. He will provide support and expertise related to the sleep, pain and measurement/analysis aspects of the project, building on prior collaborations with members of the research team.
- Dr. Anna Kratz, PhD, is a clinical psychologist and Associate Professor in the Department of Physical Medicine and Rehabilitation at UM. She leads a program of federally- and foundation-funded research that examines the characteristics, mechanisms, and treatment of chronic symptoms, including chronic pain and fatigue. Dr. Kratz has extensive expertise in ambulatory assessment techniques, including ecological momentary assessment (self-report in real time), actigraphy, app-based cognitive tests, and collection of physiological data using wearable devices. She has expertise in randomized as well as pragmatic and comparative effectiveness trial designs. She has developed digital educational and behavioral interventions for symptom management (e.g. MyMSToolkit, PainGuide). She will provide support and expertise on the areas described above for this project, which is a natural extension of her ongoing collaborations with the team.
- TBD:
    - We will hire 3 FTE data analysts who will help conduct statistical analyses for the many manuscripts produced through this project.
    - We will hire a 0.5 FTE biostatistics graduate student research assistant who will help oversee the data analysts and conduct high-level statistical analyses.
    - We anticipate that most of the individuals will be located in Ann Arbor, MI, but are flexible in allowing some to work remotely as that may facilitate a broader pool of qualified applicants.

Cannabis Coaching and Manualization Core

- Dr. Evan Litinas, MD, is the co-owner of Om of Medicine and owner of Litinas LLC. He has spent the last 9 years focusing exclusively on optimizing the clinical use of medical cannabis. He has collaborated with UM on several cannabis projects and is a co-author on several resulting publications.[16-18,49,55] Dr. Litinas has extensive clinical experience working with patients from his time as the Chief Medical officer of Om of Medicine, developing patient education materials and individualized medical cannabis usage protocols based on his extensive knowledge of cannabinoid research, methods of administration, therapeutic levels of cannabis or cannabinoids according to the scientific literature, and available cannabinoid based medicines. Dr. Litinas will help lead the intervention development, manualization, and training for this project.
- Dr. David Williams, PhD, is a Professor of Anesthesiology, Medicine, Psychiatry and Psychology at UM where he also serves as the Associate Director of the Chronic Pain and Fatigue Research Center and the Co-Director of Research Development within the Michigan Institute for Clinical and Health Research (MICHR). Dr. Williams is both a clinician and researcher with publications in the areas of chronic illness management, outcomes measurement and instrument development, mechanisms in chronic pain, and research methodologies. For the current application, Dr. Williams brings extensive experience in characterizing chronic illnesses and assessing outcomes of interventions. He also brings expertise in coaching, educational, and adherence methods associated with pharmacological and non-pharmacological interventions. With Dr. McAfee, he will oversee intervention development and manualization as well as providing insight on outcome assessment.

- Dr. Jenna McAfee, PhD, is an Associate Professor in the Department of Anesthesiology at UM. She is a licensed clinical psychologist and specializes in treating chronic pain and the associated mental health comorbidities including depression, anxiety, and PTSD. She serves as the Associate Director of Research at the Back & Pain Center. She has received NIH funding to study opioid cessation in the context of pain management, with a focus on developing tailored interventions. She is also leading a study at the Back & Pain Center exploring chronic pain patient's cannabis use patterns and attitudes towards medical cannabis and has co-authored numerous manuscripts on cannabis and chronic pain with members of the proposed study team.[17,52,53] With Dr. Williams, she will oversee intervention manualization and QA/QC measures for this process, and provide clinical expertise for risk assessments on this project.
- TBD: We will hire 6 FTE cannabis coaches who will be trained by Dr. Litinas on delivering the cannabis coaching intervention. We anticipate that most coaches will be located in Ann Arbor, MI, but are flexible in allowing some to work remotely as that may facilitate a broader pool of qualified applicants.

Community Advisory Board

In addition to our leadership team and staff, we will put together an advisory board whose purpose is to provide direct feedback to leadership. This 10-person board may include but is not limited to healthcare providers, insurance companies, large state employers, State representatives, Veteran's groups, and representation from the Department of Licensing and Regulatory Affairs.

Data Safety and Monitoring Board

The PIs will designate a Data Safety Monitoring Board to perform an independent review of ongoing study progress and safety. The Monitoring Committee for this study will be comprised of experts in the field are not associated with this research project and thus work independently of the PIs. They are not part of the key personnel involved in this grant and each are qualified to review the patient safety data generated by this study because of their unique areas of expertise.

END APPLICANT RESPONSE

V-H Budget

To enable the Issuing Office to evaluate all project costs, **applicant(s) will submit a proposed budget and corresponding budget narrative.** Please see attachment A for the required budget format. The budget and narrative must include only VMR grant funds in the budget; do not include matching, leveraged, cost share or any other type of supplemental funds. The budget narrative must identify the budget line item and number, provide a detailed description for each line, and include individual unit prices.

Selected applicant(s) will be required to provide supporting documentation for all grant expenditures incurred during the term of the grant. Accounting records must be supported by source documentation including, but not limited to, general ledgers, time sheets, payroll registers, invoices, check copies and bank statements, or cancelled checks. Expenses will be verified based on actual expenditures incurred within the grant period that are supported by source documentation, not budgeted amounts.

(1) **Budget Changes** – Any changes to the budget must be pre-approved by the Grant Administrator. Changes in the budget of less than 5% of the total line item amount do not require a formal amendment; however, a revised budget should be submitted to the Grant Administrator for approval. The allowable transfer should be calculated as less than 5% of the total line item that the funds are being transferred from.

Cumulative changes in the budget equal to or greater than 5% of the total line item amount may be permitted only upon prior review and written approval by the Grant Administrator. A formal grant amendment must be signed by both the grantor and grantee.

(2) **Disallowed Costs** – Disallowed costs include but are not limited to the following: sick pay, vacation pay, holiday pay, bonuses, overtime, tuition reimbursement/remission, vehicle allowance, seminars, conferences, meetings, subscriptions, dues, and memberships.

(3) **Administrative Costs** – Administrative costs cover expenses related to general administrative functions and coordination of functions and oversight related to VMR administrative functions. Administrative costs should include costs of goods and services required for administrative functions of the program; travel costs incurred for official business in carrying out administrative activities or the overall management of the VMR; costs of information systems related to administrative functions; and contractual services related to sub-recipients or vendors that are solely for the performance of administrative functions. **Total administrative and indirect costs must be identified, labeled clearly, and may not exceed 10% of the overall grant.**

(4) **Budget Requirements** – the proposed budget will display three (3) headings identified as the: Line Item, Budget Category, and Total. The budget line items that need to be included, at a minimum, are listed below. The budget should reflect the best estimate of actual costs using whole numbers. Please refrain from using decimals or formulas. Refer to the budget example provided in Attachment D.

- **Personnel** – In the budget, include the name, job title, and salary for each staff position to be paid for by the grant. Time sheets and payroll registers must be submitted for each staff position, and hours worked must be grant related. Fringe benefits may not exceed 35% of each employee's salary. Fringe benefits will be reimbursed based on actual expenditures per employee up to 35%, not on budgeted amounts. Allowable benefits include: health, dental, and optical insurance, employer-paid Social Security and Medicare tax, Michigan and Federal unemployment tax, and other miscellaneous fringe benefits (life insurance, long- and short-term disability insurance, worker's compensation, and retirement program contributions up to 4%). Applicant(s) must provide details on the organization's method of calculating fringe benefit expenses that will be charged to the grant including whether fringe benefits are calculated on an annualized basis or based on the length of the grant term.

  The budget narrative must include the number of weeks the individual will work on the grant; number of hours per week a full time employee of the organization is expected to work; a description of the work to be performed by each individual; the estimated hours to be worked; actual pay rate; the fringe benefit percentage being charged to the grant for each employee; the percentage of the employee's time allocated to the grant; whether each employee is salaried-exempt, salaried-non-exempt or hourly; and any other applicable information related to the individual's duties and responsibilities in connection with this grant.

  Individuals that are not on selected applicant(s)'s payroll, e.g., independent contractors, individuals receiving a Form 1099, temporary workers, etc., must be placed under the Contractual Services budget category. Only employees on the selected applicant(s)'s payroll should be included in the Personnel budget category.

- **Supplies, Materials, & Equipment:** specify item(s) and cost. The budget narrative should include the anticipated cost of each item, a detailed explanation of the item's purpose, and how it relates to the project being funded. Be as detailed as possible.

- **Contractual Services:** these services must be competitively bid. Individuals that are not on selected applicant(s)'s payroll, e.g., independent contractors, individuals receiving a Form 1099, temporary workers, etc., must be placed under **Contractual Services**. When competitive selection is not feasible or practical, the selected applicant(s) agrees to obtain the written approval of the Grant Administrator before making a sole source selection. Selected applicant(s) must provide a copy of contracts, memoranda of understanding or agreements signed by selected applicant(s) and contractors.

  Selected applicant(s) assumes responsibility to select subcontractors on a competitive basis. A minimum of three (3) bids must be solicited and proposals must include, at a minimum:
  (1) name of selected applicant(s), grant number, and grant period; and (2) the type, number, and description of projects as described in the proposal.

  Selected applicant(s) must provide the Grant Administrator with the solicitation, list of vendor responses (including amounts), and name of the selected vendor. Selected applicant(s) must maintain bids on file at their place of business according to Section II-B, Records Maintenance, Inspection, Examination, Audit and Monitoring. The Grant Administrator will reserve the right to request a copy of all bids for services that are competitively bid.

  Selected applicant(s) must award the project to the lowest bid unless the Grant Administrator has given prior written approval for selection of a higher bid. Selected applicant(s) must provide a written justification for the selection of a higher bid. When awarding subcontracts, the selected applicant(s) must ensure that preference is given to products manufactured in or services offered by Michigan-based firms.
- **Travel:** in the budget include the name, job title and official workstation for each staff member that will be traveling. Selected applicant(s) must follow the State of Michigan Standardized Travel Regulations (www.michigan.gov/dtmb/0,5552,7-150-9141_13132---,00.html). The State will reimburse for mileage, lodging, and meals, refer to the current State travel rates. Meals and lodging must be supported by itemized, legible receipts and reasons for travel. Itemized meal receipts must include a list of each item purchased; receipts for payments made by credit card that are not itemized will not be accepted.

  Mileage must be supported by travel log(s) with beginning and ending addresses, mileage total, and reason for travel. Grantees will be provided a travel log example. Out-of-state travel must be directly related to the grant project and approved by the Grant Administrator prior to travel. Travel expenses listed in the travel budget category are strictly for individuals listed on the budget under Personnel. Per Diem payments and alcoholic beverage reimbursements are not allowed.
- **Other Expenses:** This category is solely for use by organizations charging a per-case fee for work performed by subunits or internal agencies within the organization that do not require a competitive bid, i.e. contract, memorandum of understanding or any other type of signed agreement.
- **Indirect Costs:** Indirect costs are costs not directly or specifically related to the grant program. Indirect costs are costs of administering the organization and must be spread over a number of products, services, or grant programs proportionately. Examples include office supplies and equipment, utilities, rent, maintenance and repair, insurance, accounting and bookkeeping services, and legal services. Non-cash expenses like depreciation, amortization, and depletion are not allowable indirect costs

under this grant. **Total administrative and indirect costs must be identified, labeled clearly, and may not exceed 10% of the overall grant.**

Selected applicant(s) will be reimbursed for its proportional share of indirect costs. This means the MRA should be allocated a portion of the selected applicant(s)'s indirect costs and not 100% of the organization's total indirect cost.

Indirect costs should be displayed on the face of the budget on a single line item and the indirect rate should be rounded to six (6) decimal places. The budget narrative should contain a list of indirect costs, how the selected applicant(s) determined its indirect costs, and the percentage rate calculation for reimbursable indirect costs. Selected applicant(s) is not required to provide documentation supporting indirect costs; however, documentation verifying the costs must be retained by the selected applicant(s).

(5) To ensure efficient review and approval of grant expenditures, selected applicant(s) will be provided additional guidelines to assist with calculating and determining accurate and appropriate grant expenditures.

(6) Each budget category should have a subtotal displaying the total anticipated amount to be expended, and the budget should include a subtotal for total direct project costs and a sum of total project costs.

(7) After grants are approved by the MRA, modifications of proposals and budgets may be necessary. If the MRA does not approve the total amount requested in the original proposal, selected applicant(s) will be required to submit a revised proposal, budget and budget narrative for the purpose of entering into a Grant Agreement. New line items to the revised budget are not allowed.

(8) Selected applicant(s) assumes the responsibility of ensuring all unexpended grant funds are returned to the State of Michigan at the end of the grant period. Failure to do so may render selected applicant(s) ineligible for future grant awards and/or subject to legal action.

(9) Selected applicant(s) may not commingle grant award funds with current or future grant awards. All funding sources must be managed and accounted for separately.

BEGIN APPLICANT RESPONSE

BUDGET NARRATIVE

The University of Michigan (UM) calculates effort commitment for faculty based on either a 12-month calendar year (52 weeks / 2,080 hours), or 9-month academic year (38 weeks / 1,520) and 3 summer months (14 weeks / 560 hours) and FTE appointment. Staff effort is determined using a 12-month calendar year (52 weeks / 2,080 hours) and FTE appointment. Per University guidelines, all faculty and staff are required to review and certify their effort allocated to sponsored projects annually.

Fringe benefits (FB) are estimated using the University Costs for Benefits as a Percentage of Salary spreadsheet. It displays the benefits as percentages, and it is updated each year in July. As per the RFP, fringe benefits are capped at 35.0%. The only exception is the GSRA, who is eligible for gradcare at a cost of $293/month for 12 months. The cost is inflated 3.0% in year 2.

Administrative Expenses

<u>Administrative Personnel</u> ($61,781 Salary + $21,623 FB + $6,784 Other = $90,188)

M. Kathleen Majors, Grant Administrator (25.0% effort; 35.0% FB rate)

Ms. Majors is a Research Administrator Senior in the department of Anesthesiology. She has a Bachelor of business administration degree and has over 15 years of experience managing grants. She will be responsible for establishing subawards, managing project expenses, and submitting financial reports as required by the sponsor. She will meet regularly with PIs to review finances and expenditures.

Keiyana Chambers-Peeple, Administrative Assistant (25.0% effort; 35.0% FB rate)
Ms. Chambers-Peeple is an Administrative Assistant Senior in the Department of Anesthesiology Chronic Pain & Fatigue Research Center. She will be responsible for coordinating all meetings and maintaining strong lines of communication with the research team. She will provide administrative support as needed to the PIs and Project Leadership and will assist them in planning and meeting with community partners. Ms. Chambers-Peeple will coordinate and take part in take part in biweekly meetings with the Project Team.

Daniel Kruger, PhD, UM ISR Service Personnel Fee ($6,784)
The University of Michigan institute for Social Research (UM ISR) charges a fee for contributions by their faculty and staff to sponsored projects. We are requesting **$3,342** in Y1 and **$3,442** in Y2.

VMR Program Expenses (Y1 $4,503,135 + Y2 $4,406,660 = $8,909,795)

<u>VMR Program Staff</u> ($763,908 Salary + $229,165 FB = $993,073)

Daniel Clauw, MD, Contact Principal Investigator (20.0% effort; 22.0% FB rate)
Dr. Clauw is a Professor in the Departments of Anesthesiology, Psychiatry, and Rheumatology, as well as the Director of the Chronic Pain and Fatigue Research Center. He has been involved in the growth of clinical and translational research infrastructure and was the founding director of the unit at Michigan that supports translational research – the Michigan Institute for Clinical Health Research (MICHR). He is now the Senior Associate Director of MICHR and co-directs the Research Development Core and Pre-Doctoral Programs. He is currently co-PI of two NIH center grants studying the mechanisms underlying chronic pain in urological and musculoskeletal disorders and is an active mentor of clinical and pain researchers. Dr. Clauw is also a co-investigator on a NIAMS HEAL grant that aims to perform interventional response phenotyping in a cohort of chronic low back pain (cLBP) patients. Dr. Clauw has published over 400 articles related to chronic pain and pain management, including papers in *JAMA, Annals of Internal Medicine, Annals of Surgery, Journal of Pain, and Lancet.*

Amy S.B. Bohnert, PhD, Co-Principal Investigator (20.0% UM effort; 28.3% FB rate)
Dr. Bohnert is an Associate Professor in the Departments of Anesthesiology, Psychiatry and Epidemiology at the University of Michigan and a researcher with the Department of Veterans Affairs Center for Clinical Management Research (CCMR). She is Co-Director of the Division of Mental Health Innovations, Services, and Outcomes. She leads a number of NIH-, CDC-, and VA-funded projects to identify paths for reducing the burden of opioid use disorders, opioid misuse, and overdose using randomized controlled designs and electronic health records databases. Her projects include a trial of a mobile behavioral intervention to reduce opioid misuse and a State of Michigan DHHS-partnered project, the Michigan Opioid Collaborative, to provide technical assistance and peer mentoring to physicians providing medications for opioid use disorders. Dr. Bohnert has published over 100 articles related to mental health, opioids, pain, and addiction, including papers in *NEJM, JAMA*, *BMJ*, *Annals of Internal Medicine*, *JAMA Psychiatry*, and the *American Journal of Psychiatry*. She has also served in a scientific advisory role to the Centers for Disease Control and Prevention, to the Food and Drug Administration, and the Michigan Prescription Drug and Opioid Abuse Task Force.

Dr. Bohnert also has a VA appointment; however, all effort on this project will be from the University appointment. A Memorandum of Understanding is on file describing the relationship.

Kevin F. Boehnke, PhD, Co-Principal Investigator (50.0% effort; 35.0% FB rate)
Dr. Boehnke is a Research Investigator in the Department of Anesthesiology Chronic Pain and Fatigue Research Center (CPFRC) at the University of Michigan. and a nationally renowned cannabis expert. He is currently involved in several NIH-funded clinical trials investigating effects of cannabinoids on pain and sleep. He has led numerous studies showing that people with chronic pain substitute cannabis for opioids and other pain medications, mostly without clinician oversight. Dr. Boehnke has provided guidance on CBD for the Arthritis Foundation and is currently a Technical Expert Panel member for two national committees on cannabinoid use for pain, including a collaboration between the office of Veterans Affairs and Oregon Science and Health University. He has published numerous articles about chronic pain as well as cannabis, including in *JAMA, Annals of Internal Medicine* and *Journal of Pain.*

David A. Williams, PhD, (20.0% effort; 25.5% FB rate)
Dr. Williams a Professor in the Departments of Anesthesiology, Psychiatry, Rheumatology, and Psychology at the University of Michigan as well as the Associate Director of the Chronic Pain and Fatigue Research Center. Additionally, he serves as Co-Director of Research Development within the Michigan Institute for Clinical and Health Research (MICHR). He is both a pain psychologist and a researcher with publications in the areas of chronic illness management, mobile health services delivery for chronic pain, patient-reported outcomes instrument development and validation, and mechanisms of pain perception/modulation. He is the past President of the American Pain Society and serves on numerous scientific editorial boards and scientific review committees both nationally and internationally. In recognition of his commitment to students, he received the Distinguished Clinical and Translational Research Mentor Award from the University of Michigan. Dr. Williams has published over 100 articles related to pain and pain management.

Rachel Bergmans, MPH, PhD, Co-Investigator (50.0% effort; 35.0% FB rate)
Dr. Bergman is currently a Research Fellow in the University of Michigan Survey Research Center. At the time of award, she will be a Research Investigator in the Department of Anesthesiology Chronic Pain & Fatigue Research Center. Dr. Bergmans' program of work integrates multiple approaches to identify drivers of disparities in mental health and mood disorders, particularly within the context of comorbid chronic inflammatory conditions. She has 6 years of experience implementing community-engaged approaches to partner with key stakeholders in addressing social and environmental determinants of health including community-education centers, faith-based organizations, and health clinics. In this project, she will oversee outreach to and build partnerships with Veteran organizations to enhance recruitment and ensure overlap between scientific and stakeholder goals.

Jenna (Goesling) McAfee, PhD, Co-Investigator (30.0% effort; 33.5% FB rate)
Dr. McAfee is a Clinical Associate Professor of Anesthesiology at the University of Michigan, who treats patients at the Department of Anesthesiology Back and Pain Center. Dr. McAfee recently completed a K23 (DA038718) that aimed to better understand why patients continue taking opioids and incorporate theory-based models of behavior change into the development of interventions for individuals who would benefit from opioid cessation. Such work included qualitative assessment including focus groups and semi-structured clinical interviews and the evaluation of related data.

Sachin Kheterpal, MD, MBA Digital Coordinating Center Co-Director (5.0% effort; 25.5% FB rate)
Dr. Kheterpal is a Professor in the Department of Anesthesiology and the Associate Dean for Research IT for the University of Michigan Medical School. Prior to a clinical anesthesiology career, he was the lead architect of a leading commercially available electronic health record — General Electric Centricity. He led the global clinical information system product development team at GE Healthcare IT. He brings nearly two decades of informatics, software development and business administration experience to perioperative outcomes research. He is a practicing anesthesiologist, focused on high acuity surgery, including adult liver transplantation and vascular. He is the founder and principal investigator of the Multicenter perioperative outcomes group (MPOG), a research and quality improvement consortium of more than 50 anesthesiology and surgical departments across the US. The MPOG centralized research database contains more than 15 million

perioperative records with risk adjusted long term outcome data and detailed clinical intervention data. Dr. Kheterpal's current research focus is evaluating the comparative effectiveness of intraoperative anesthesiology interventions on long-term patient outcomes. Dr. Kheterpal also leads the MIPACT study, which used wearable sensors and the MyDataHelps app proposed here to collect long-term health outcomes on a diverse sample of 7,000 Michigan residents. Nationally, Dr. Kheterpal serves on the NIH Council of Councils and previously served on the Advisory Panel for the NIH Precision Medicine Initiative (All Of Us), focused on electronic health record data integration and multicenter collaboration.

Nirav Shah, MD Digital Coordinating Center Co-Director (5.0% effort; 25.5% FB rate)
Dr. Shah is an Assistant Professor in the Department of Anesthesiology at the University of Michigan. Within Michigan Medicine, he is the Associate Chief Medical Information Officer – Perioperative Care, and Director of Anesthesia Informatics and Systems Improvement, where he leads a team that develops software solutions for perioperative quality improvement, research, clinical and business operations, and supports the hospital's perioperative electronic health record (EPIC). Dr. Shah's interests lie at the intersection of perioperative care, quality improvement, research, and information technology. As Program Director for the Quality Improvement arm of MPOG, his role is to lead collaborative quality improvement efforts across its 50+ member institutions, including 20 across the state of Michigan. As co-I of MIPACT, he has helped design the MQUARK features and workflow processes to enroll 7000 patients in 18 months. Dr. Shah has deep expertise in workflow optimization.

Maria J. Silveira, MD, MPH, Co-Investigator (10.0% UM effort; 35.0% FB rate)
Maria Silveira MD MA MPH is a palliative care physician and symptom scientist at the University of Michigan and Ann Arbor VAMC. She has led or co-led clinical trials of symptom management interventions, including one VA-sponsored study which recruited Veterans with cancer from the Ann Arbor VA and their caregivers into a trial of electronic symptom assessment and advice. She has over twenty years of experience at the Ann Arbor VA where she has cared for Veterans with PTSD and complex chronic pain in primary care and palliative care settings. She is a member of the Geriatric Research Education Clinical Center, Institutional Review Board, and Pain Committee at the Ann Arbor VA, providing her with robust relationships throughout the organization to draw from in the conduct of the research proposed.

Dr. Silveira also has a VA appointment; however, all effort on this project will be from the University appointment. A Memorandum of Understanding is on file describing the relationship.

Walter Dempsey, PhD, Co-Investigator (10.0% Academic / 10.0% Summer; 32.5% FB rate)
Dr. Dempsey is an Assistant Professor of Biostatistics (School of Public Health) and Assistant Research Professor at the Institute for Social Research (ISR) at the University of Michigan. He is a core faculty member of the D3 Lab at ISR, which is made up of data scientists with expertise in adaptive mobile intervention designs and repeated randomizations (e.g., micro-randomized trials). His current work focuses on statistical methods and theory for digital and mobile health as well as more traditional areas of biomedical research involving (multi-state) survival analysis and temporal process regression. His work aims to inform decision making in health by aiding in intervention evaluation and development. His expertise in the design and analysis of innovative digital trials will be vital for the proposed project.

Anna Kratz, PhD, Co-Investigator (20.0% effort; 31.3% FB rate)
Dr. Anna Kratz is a clinical psychologist and Associate Professor in the Department of Physical Medicine and Rehabilitation at UM. She leads a program of federally- and foundation-funded research that examines the characteristics, mechanisms, and treatment of chronic symptoms, including chronic pain and fatigue. Dr. Kratz has extensive expertise in ambulatory assessment techniques, including ecological momentary assessment (self-report in real time), actigraphy, app-based cognitive tests, and collection of physiological data using wearable devices. She has expertise in randomized as well as pragmatic and comparative effectiveness trial designs. She has developed digital educational and behavioral interventions for symptom management (e.g. MyMSToolkit, PainGuide). She will provide support and expertise on the areas described above for this project, which is a natural extension of her ongoing collaborations with the team.

Daniel Whibley, PhD, Co-Investigator (20.0% effort; 35.0% FB rate)
Dr. Whibley is a Research Assistant Professor in the University of Michigan Department of Physical Medicine & Rehabilitation. He also has affiliations with the Epidemiology Group, University of Aberdeen (UK), and the Sleep and Pain Laboratory, University of Warwick (UK). He received his doctorate from the University of Aberdeen and has published in the areas of chronic pain, physical activity/exercise, and sleep health, including their intersection. Dr. Whibley is a registered physiotherapist in the UK and has clinical expertise in rheumatology and neuro-musculoskeletal rehabilitation. He was awarded a personal postdoctoral fellowship on completing his PhD from Versus Arthritis (formerly Arthritis Research UK), and was funded as Principal Investigator to develop and feasibility test a hybrid sleep and physical activity intervention for people living with chronic pain. He has undertaken extensive training in advanced statistical methods including modelling that uses momentary data collected using actigraphy, and has experience conducting qualitative research, all of which he will contribute to the current project.

Daniel J. Kruger, PhD, MS, Co-Investigator (15.0% effort; 35.0% FB rate)
Dr. Kruger is a Research Investigator in the University of Michigan Institute for Social Research, Population Studies Center, whose research interests include community-based prevention research aimed at improving health status and reducing morbidity and mortality among populations experiencing a disproportionate share of poor health outcomes. He studies several areas from an evolutionary perspective and conducts basic research as well as implementing practical applications. His applied work includes community health surveys and program evaluations conducted in partnership with health departments and community-based organizations. Projects have focused on birth outcomes, risk-taking, violence, mortality patterns, neighborhood conditions, and population factors.

Avinash Hosanagar, MD, Co-Investigator (20.0% effort; 26% FB rate)
Dr. Hosanagar is Clinical Assistant Professor of Psychiatry at the University of Michigan and a psychiatrist for the Ann Arbor VA Healthcare Center Mental Health Clinic. The VA Ann Arbor Healthcare System Psychiatry program is an integral part of the University of Michigan Department of Psychiatry.

Important goals of his clinical program include providing the highest quality psychiatric care to eligible veterans, conducting state-of-the-art basic and clinical psychiatric research relevant to veterans, and providing excellent training to the next generation of mental health clinicians and researchers.

Dr. Hosanagar's primary appointment is with the VA Ann Arbor Healthcare System and will be paid through a service agreement with the VA. ***His salary and fringe benefits (26.0% FB rate) are budgeted under VMR Contractual Services.***

<u>VMR Personnel Program Staff</u> ($3,347,935 Salary + $1,146,055 FB = $4,493,990)

Laura Thomas, Program Manager (50.0% effort; 35% FB rate)
Ms. Thomas is a project manager with a background in social work and public health. Ms. Thomas has worked with Dr. Bohnert leading human subjects research for over eight years, including working with Veterans, and starting and closing projects. Ms. Thomas will assist in the day-to-day operations of the project and oversee IRB applications and other regulatory applications and amendments..

Dana Horowitz, Study Coordinator (100.0% effort; 35.0% FB rate)
Ms. Horowitz is a project manager with a background in social work. Ms. Horowitz has worked with Dr. Bohnert on a multiple studies working with Veterans and improving their chronic pain. Ms. Horowitz will lead community outreach staff in engaging and enrolling participants into the study.

Primary appointments for Ms. Thomas and Ms. Horowitz are with the VA Ann Arbor Healthcare System and will be paid through a service agreement with the VA. ***Their salary and fringe benefits (35.0% FB rate) are budgeted under VMR Contractual Services.***

Rachel Bresnahan, Communications Specialist (25.0% effort; 35.0% FB rate)
Ms. Bresnahan is a graphic designer and communication specialist. Ms. Bresnahan will assist with developing materials for dissemination and will be in charge of marketing the program and disseminating key findings to the communities of interest as well as more broadly to the state and other stakeholders. She will also work to create, produce, and deliver a range of promotional, educational, and informational presentations, and/or resource materials related to the study activities and successes and support the community engagement activities, including website, social media, community data reports, media and press releases, and assist the communities with developing relevant and engaging materials for community outreach.

TBD, SPH Biostatistics GSRA (50.0% effort; Y1 $293/month gradcare; Y2 $302/month gradcare)
The biostatistics graduate student research assistant (GSRA) will execute the statistical analysis under the supervision of Dr. Dempsey. Please note that 50% effort is considered a full-time GSRA appointment.

TBD, Recruitment Ambassadors (10 FTE @ 100.0% effort; 35.0% FB rate)
We will hire ten (10) community health workers, community organizers, or individuals with similar experience, with deep knowledge of local resources who can serve as a bridge between research and diverse communities. CRFs will lead outreach efforts in predominantly African American and Latinx communities in the Detroit and Flint areas to support study recruitment efforts and increase sample diversity. These individuals will also facilitate bidirectional communication and knowledge transmission between the CPFRC and community stakeholders by assisting enrolled participants navigate the challenges of participating in clinical trials, thereby enhancing retention. The CRFs will take part in biweekly meetings with the Supplement Project Team, and they will be actively engaged in community dissemination efforts.

TBD, Cannabis Coaches (6 FTE @ 100.0% effort; 35.0% FB rate)
We will hire six (6) cannabis coaches to deliver the intervention for the clinical trials. These individuals will be trained and supervised by Drs. Litinas, McAfee, and Williams.

TBD, Help Desk Staff (Y1 – 2 FTE @ 100.0% effort; Y2 – 4 FTE @ 100.0% effort; 35.0% FB rate)
Informatics staff will be available to answer any questions or trouble shoot issues with the wearable activity device or MyDataHelps data collection program.

TBD, Applications Programmers (2 FTE @ 100.0% effort; 35.0% FB rate)
The Applications programmers will be responsible for development and maintenance of the database and data collection forms/applications. They will refine any data transfer processes, develop reports as needed, and specific SAE narrative management functions within the application platform.

TBD, Data Analysts (3 FTE @ 100.0% effort; 35.0% FB rate)
The Data Analysts will be responsible for developing report table shells, confirm data quality limitation and work with the Digital Coordinating Center Co-Directors and PIs on refining the project timeline, review query results, establish plausibility and collate query results into a report package for the PIs and project team to review.

TBD, Data Managers (2 FTE @ 100.0% effort; 35.0% FB rate)
The Data Managers will be responsible for data cleaning and transferring processes, query and resolution processes.

The procurement of goods and services is the responsibility of the Regents. Per Board of Regents Bylaws 3.07 (2)(d), the Regents have delegated procurement responsibility to the Executive Vice President and Chief Financial Officer, who in turn has delegated this function to Procurement Services. Purchases using sponsored funds often have unique requirements beyond that of the university's normal procurement process. This page

describes these unique requirements for federal sponsored funds from the Uniform Guidance 2 CFR 200. Non-federal sponsors may have other unique requirements when making purchases with their funds that may be found in the agreement with the sponsor.

Beginning July 1, 2018 purchases using federal sponsored funds must be made in accordance with Uniform Guidance (2 CFR 200): The Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards. The Uniform Guidance requires Sponsored Programs to review transactions meeting certain criteria to determine if they are allowable. The purpose of these federal guidelines is to verify that all expenses charged to a research project have a "direct benefit" and should be charged as "direct costs" to the project. To ensure compliance, all activity affecting a sponsored project/grant should meet the terms and conditions of the grant or contract. It is the expectation that all purchases over $10,000 be either competitively bid or a sole source justification form endorsed by an authorized signer in the school/college justifying and providing information as to why the vendor selected is the optimal choice.

VMR Supplies, Material & Equipment ($1,050,000)

Wearable Devices (Y1 $525,000 + Y2 $525,000 = $1,050,000) All participants will be selected to receive a wearable device (Apple Watch, Fitbit or Actigraph) to enable passive activity, sleep data collection and tracking cannabis use. These wearables data will be collected using the MyDataHelps app described below. We anticipate purchasing 3,000 devices at $350/device.

VMR Contractual Services ($1,041,172)

Marijuana Enforcement Tracking Reporting & Compliance (metrc) Data ($40,000) metrc is Michigan's statewide monitoring system for integrated marihuana tracking, inventory, and verification under the Medical Marihuana Facilities Licensing Act, Marihuana Tracking Act, and Michigan Regulation and Taxation of Marihuana Act. The mission of the MRA is to establish Michigan as the national model for a regulatory program that stimulates business growth while preserving safe consumer access to marijuana.

Funds are requested to purchase Michigan metrc data and analyze it to assess product use patterns among participants as well as inform MyDataHelps app development.

CareEvolution, Inc. App Development / Licensing Fee (Y1 - $300,000) CareEvolution is a national leading provider of Participant-facing Patient Reported Outcomes data collection tools. Built upon the foundation of HIEBus™, their health information exchange (HIE) technology platform, MyDataHelps is a robust Service Oriented Architecture (SOA) to enable participants to enroll in studies, complete outcome instruments, and share wearable data. CareEvolution has received federal "Authorization to Operate" as the AllOfUs Direct-to-Participant app vendor and SAFER-COVID vendor for all NIH staff. Distinct components of MyDataHelps and RKStudio (the authoring tool for MyDataHelps) include Identity Management, Record Location, Electronic Health Record Integration, Audit & Log, Visualization, Terminology, Data Mining, Data Driven Customizable Research Study Workflow and Content. MyDataHelps is available via the Google Play and Apple App Store and has been used for more than 100,000 patients already, including for eFramingham, MIPACT, and COVID-DETECT. Secure electronic data capture via CareEvolution technology will be used for feasibility and full-scale studies. All participants will be asked to download the app and receive patient reported outcome notifications. Those unable or unwilling to download the app will use the web-based desktop/tablet/phone patient reported outcome completion form.

CareEvolution, Inc. App Usage Fee ($54,000/year = $108,000) The vendor charges a monthly app usage fee of $3 per participant. Each participant **(N=3,000)** will be on the study for up to 12 months.

3,000 participants X 12 months/participant X $3 = **$108,000**

Litinas, LLC (Y1 $60,000 + Y2 $40,000 = $100,000) Evangelos Litinas, MD, MBA, is a medical cannabis expert, researcher and consultant with close to two decades of experience in various healthcare settings,

including inpatient and outpatient clinical work, management and strategic planning, research and development for academic and private drug industry with a focus in the Medical Cannabis industry.

Within the field of medical cannabis Dr. Litinas has extensive experience including research, patient outreach and support, with a focus on patient education and individualized medical cannabis usage protocols. His in-depth knowledge on the subject of Medical Cannabis includes but not limited to scientific and medical research, patient and healthcare professional education, debilitating medical conditions and symptom treatments, pharmacokinetics and pharmacodynamics of cannabinoid-based medicines, drug interactions, and methods of administration and dosing.

Within the emerging Medical Cannabis industry, he has executed projects including but not limited to the development of patient educational materials, employee training manuals, management methods specifically tailored to the Cannabis healthcare industry and experience in state-based application processes.

Dr. Litinas has training and experience in management with a healthcare focus; hospital operations, healthcare capital management, strategic planning, hospital finances, short-term and long-term financial health and resources management for the design, development, and operation of medical cannabis-based organizations.

For this project, we will contract with Dr. Litinias to provide his expertise on refining and deploying the educational intervention for use and safety of medical cannabis, training cannabis coaches, and outreach to Veterans groups and individual veterans and their families.

Community Partners (Veteran non-profit groups) (Y1 $30,000 + Y2 $30,000 = $60,000) Funds are requested to compensate community organizations that partner with us (e.g., American Legion, Disabled American Veterans, Veterans Action Council) for their contribution of time and expertise to (1) developing and refining recruitment materials, (2) refining the recruitment strategy, (3) referring study participants, (4) screening participants for initial study eligibility, (4) engaging and following up with enrolled participants who have missed 2 or more data collection points, (5) interpreting study findings, and (6) translating study findings to inform policy recommendations.

VA Contracted Service, A. Hosanagar (Y1 $49,615 salary + $12,900 FB + Y2 $51,103 salary + $13,287 FB = $126,904) Co-Investigator Avinash Hosanagar MD, whose roles is described above under VMR program staff, is a VA employee. He will be paid through a service agreement with the VA Ann Arbor Healthcare System.

VA Contracted Service, L. Thomas (Y1 $45,280 salary + Y1 $15,848 FB + Y2 $46,639 salary + Y2 $16,324 FB = $124,091) Program Manager Laura Thomas whose roles is described above under VMR personnel staff is a VA employee. She will be paid through a service agreement with the VA Ann Arbor Healthcare System.

VA Contracted Service, D. Horowitz (Y1 $66,476 salary + Y1 $23,267 FB + Y2 $68,470 salary + Y2 $23,965 FB = $182,178) Study Coordinator Dana Horowitz, whose role is described above under personnel staff, is a VA employee. She will be paid through a service agreement with the VA Ann Arbor Healthcare System

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VMR Travel (VMR Staff) ($15,680/year = $31,360)

We anticipate that all ten (10) Recruitment Ambassadors will travel throughout the state of Michigan in order to meet with Veteran's Organizations to promote and recruit for the study. We anticipate that each Recruitment Ambassador will drive approximately 2,800 miles/year. UM uses federal government GSA CONUS rates to reimburse faculty and staff for travel expenses in the continental U.S. The current mileage reimbursement rate is $0.56.

2,800 miles/year X $0.56/mile X 10 travelers = **$15,680/year**

We understand that if the State of Michigan Standardized Travel Regulations for mileage reimbursement are lower than the federal rate, and we will charge that rate to the grant.

VMR Other (Y1 654,350 + Y2 $645,850 = $1,300,200)

Participant Reimbursement ($607,500/year = $1,215,000) We anticipate enrolling 3,000 subjects into the observational study arm, who will each receive $370 for their participation. 600 of those enrolled will be randomized into the intervention arm. These individuals will receive an additional $175 for their participation. We anticipate enrolling 1,500 participants/year.

Observational Arm: 1,500 subjects X $370/subject = $555,000
Intervention Arm: 600 subjects X $175/subject = $ 52,500
$607,500

Shipping/Postage ($23,700/year = $23,700) The activity devices to be used for data capture will be shipped to all study participants using USPS Prepaid Forever Priority Mail flat rate boxes. We anticipate 1,500 shipments per year at an anticipated cost of $7.90 per shipment.

1,500 shipments/year X $7.90/box = **$11,850**

Honorariums ($20,000/year = $40,000) In acknowledgement of their time and commitment, we will pay annual honorariums to the Data Safety Monitoring Board (DSMB) and Community Advisory Board Members.

Data Safety Monitoring Board: 5 Members X $2,000/member/year X 2 years = **$20,000**

Community Advisory Board: 10 members X $1,000/member/year X 2 years = **$20,000**

Advertising and Recruitment ($5,000/year = $10,000) In order to advertise and promote the study statewide, funds are requested to create and print flyers, postcards and brochures for distribution to Veterans groups and VA hospitals and healthcare centers.

Michigan Institute for Clinical & Health Research (MICHR) IND/IDE Investigator Assistance Program (MIAP) (Y1 $10,000 + Y2 $1,500 = $11,500) The MICHR IND/IDE Investigator Assistance Program (MIAP) provides comprehensive regulatory support, guidance, and education services to investigators involved in Food and Drug Administration (FDA) regulated clinical research. MIAP's primary focus is providing regulatory assistance to sponsor-investigators of drugs, biologics, and medical devices. This includes Investigational New Drug (IND) services such as: regulatory needs assessments; exemption rationale development; assistance with FDA meeting preparation; assistance with IND application submissions, including protocol and informed consent development; assistance with regulatory compliance, document preparation, and FDA contact and correspondence; sponsor investigator training; and ongoing study assistance, including safety reporting, FDA annual report preparation, protocol amendments, and IND closeout.

The fee for MIAP regulatory support for the initial IND application submission is **$10,000**. **$1,500** is charged for each year the IND is open for preparation and submission of protocol amendments, safety reports, and annual reports. The MIAP fee also includes Clinical Trial Monitoring from the MICHR monitoring group which is required for studies under an IND.

Indirect Cost (Y1 $456,385 + Y2 $443,403 = $899,788)

The University of Michigan DHHS negotiated rate (dated 05/14/2020) for on-campus organized research is currently 56.0%. Facilities and Administrative (F&A) Costs (sometimes referred to as Indirect Costs or IDC) are the real costs of university operations that are not readily assignable to a particular project. These costs are determined by federal auditors under the guidelines of OMB Uniform Guidance. Facilities and Administrative

Cost rates are negotiated with the Department of Health and Human Services (DHHS)—the federal cognizant audit agency for the University of Michigan. These rates are applicable to all federally-sponsored projects and, in accordance with university policy, are also extended to include all non-federal sponsored projects. The federal government's longstanding recognition and payment of these costs has helped U.S colleges and universities build and support the required research infrastructure that has made the American research enterprise the best in the world.

When the government provides a grant to a university for a research project, a portion (typically 67-75 percent) of the funds are distributed directly to the research team. This "direct costs" portion supports researcher salaries, graduate students, equipment, and supplies. Another portion (typically 25-33 percent) covers necessary research infrastructure and operating expenses that the university provides to support the research. These research expenses – officially called facilities and administrative (F&A) costs – include: state-of-the art research laboratories; high-speed data processing; national security protections (e.g., export controls); patient safety (e.g., human subjects protections); radiation safety and hazardous waste disposal; personnel required to support essential administrative and regulatory compliance work, maintenance staff, and other activities necessary for supporting research.

In order to stay within the budget requirements of no more than 10% of the total budget going toward indirect and administrative costs, a reduced indirect cost rate of 9.997664% was used.

Y1: $4,564,916 X 9.997664% = **$456,385**
Y2: $4,435,067 X 9.997664% = **$443,403**
$899,788

Indirect costs plus administrative costs total **9.999999%** of the total budget, which is below the 10.0% threshold.

$899,788 indirect costs + $90,188 administrative expenses = **$989,976 / $9,899,771 = 9.999999%**

END APPLICANT RESPONSE

V-I Additional Information and Comments

BEGIN APPLICANT RESPONSE

Not Applicable / None

END APPLICANT RESPONSE

V-J Certification of Proposal

Please sign the proposal including the following language:

I certify that all information contained in the proposal is true to the best of my knowledge and belief, and that the organization is in compliance and agreement with all sections of the Request for Proposal.
Failure to comply with grant terms may result in termination.

Certified by:  07/16/2021

Kellie Buss, Sr. Project Representative, ORSP Date
Regents of the University of Michigan

ATTACHMENT A: VMR BUDGET

Submission Date: July 16, 2021

Selected Applicant's Grant Number:

Line	Budget Category	Total Item
1	**Administrative Expenses**	
2	**Administrative Personnel (Grant Administration Staff)**	
3	*Salary*	
4	Kathy Majors, Grant Administrator	$38,091
5	Keiyana Chambers-Peeple, Administrative Assistant / Community Liaison	$23,690
6	**Total Salary**	**$61,781**
7	*Fringe Benefits*	
8	Kathy Majors, Grant Administrator	$13,332
9	Keiyana Chambers-Peeples, Administrative Assistant / Community Liaison	$8,291
	UM ISR Service Personnel Fee (D. Kruger)	$6,784
10	**Total Fringe Benefits**	**$28,407**
11	***Total Administrative Personnel***	**$90,188**
12	**Administrative Supplies, Materials, and Equipment**	
13	General Office Supplies	$0
14	***Total Administrative Supplies, Materials, & Equipment***	**$0**
15	**Administrative Contractual Services**	
16		$0
17	***Total Administrative Contractual Services***	**$0**
18	**Administrative Travel (Grant Administration Staff)**	
19	Mileage	$0
20	Meals	$0
21	Lodging	$0
22	***Total Administrative Travel***	**$0**
23	**Total Administrative Expenses**	**$90,188**
24	**VMR Program Expenses**	
25	**VMR Program Staff**	
26	*Salary*	
27	Daniel J. Clauw, MD - Contact Principal Investigator	$113,438
28	Amy S.B. Bohnert, PhD - Co-Principal Investigator	$86,807
29	Kevin F. Boehnke, PhD - Co-Principal Investigator	$82,215
30	David A. Williams, PhD - Co-Investigator	$93,656
31	Rachel Bergmans - Co-Investigator	$82,215
32	Jenna McAfee - Co-Investigator	$79,977
33	Sachin Kheteroal, MD, MBA - Digitial Coordinating Center Co-Director	$24,751
34	Nirav Shah MD - Digitial Coordinating Center Co-Director	$22,373
35	Maria Silveira, MD, MPH - Co-Investigator	$33,027
36	Walter Dempsey, PhD - Co-Investigator	$28,436
37	Anna Kratz, PhD - Co-Investigator	$63,624

38	Daniel Whibley, PhD - Co-Investigator	$28,420
39	Daniel Kruger, PhD - Co-Investigator	$24,969
40	**Total Salary**	**$763,908**
41	*Fringe Benefits*	
42	Daniel J. Clauw, MD - Contact Principal Investigator	$24,957
43	Amy S.B. Bohnert, PhD - Co-Principal Investigator	$24,567
44	Kevin F. Boehnke, PhD - Co-Principal Investigator	$28,775
45	David A. Williams, PhD - Co-Investigator	$23,883
46	Rachel Bergmans - Co-Investigator	$28,775
47	Jenna McAfee - Co-Investigator	$26,792
48	Sachin Kheteroal, MD, MBA - Digitial Coordinating Center Co-Director	$6,311
49	Nirav Shah MD - Digitial Coordinating Center Co-Director	$5,705
50	Maria Silveira, MD, MPH, FAAHPM - Co-Investigator	$11,559
51	Walter Dempsey, PhD - Co-Investigator	$9,241
52	Anna Kratz, PhD - Co-Investigator	$19,914
53	Daniel Whibley, PhD - Co-Investigator	$9,947
54	Daniel Kruger, PhD - Co-Investigator	$8,739
55	**Total Fringe Benefits**	**$229,165**
56	***Total VMR Program Staff***	**$993,073**
57	**VMR Personnel Program Staff**	
58	*Salary*	
59	Rachel Breshnahan, Communications Specialist	$22,507
60	SPH-Biostatiics GSRA	$94,498
61	TBD, Recruitment Ambassadors	$1,116,500
62	TBD, Behavioral Health Consultants	$730,800
63	TBD, Digital Coordinating Center Help Desk Staff	$244,800
64	TBD, Digital Coordinating Center Programmers	$418,180
65	TBD, Data Analysts	$456,750
66	TBD, Data Managers	$263,900
67	**Total Salary**	**$3,347,935**
68	*Fringe Benefits*	
69	Rachel Bresnahan, Communications Specialist	$7,877
70	SPH-Biostatiics GSRA	$7,352
71	TBD, Recruitment Ambassadors	$390,775
72	TBD, Behavioral Health Consultants	$255,780
73	TBD, Digital Coordinating Center Help Desk Staff	$85,680
74	TBD, Digital Coordinating Center Programmers	$146,363
75	TBD, Data Analysts	$159,863
76	TBD, Data Managers	$92,365
77	**Total Fringe Benefits**	**$1,146,055**
78	***Total VMR Personnel Program Staff***	**$4,493,990**
79	**VMR Supplies, Materials, & Equipment**	
80	Activity Trackers	$1,050,000
81	***Total VMR Supplies, Materials, & Equipment***	**$1,050,000**

82	**VMR Contractual Services**	
83	Marijuana Enforcement, Tracking, Reporting & Compliance (metrc)	$40,000
84	CareEvolution, Inc.	$408,000
85	Latinas, LLC	$100,000
86	Community Partners (Veteran non-profit groups)	$60,000
87	VA Contracted Service, Aviniash Hosanagar, MD, Co-Investigator	$126,904
88	VA Contracted Service, Laura Thomas, Project Manager	$124,090
89	VA Contracted Service, Dana Horowitz, Study Coordinator	$182,178
90	***Total VMR Contractual Services***	**$1,041,172**
91	**VMR Travel (VMR Staff)**	
92	Mileage	$31,360
93	Meals	$0
94	Lodging	$0
95	***Total EAP Travel***	**$31,360**
96	**VMR Other**	
97	Participant Reimbursement	$1,215,000
98	USPS Shipping	$23,700
99	Honorarium - Community Advisory Board Members	$20,000
100	Honorarium - Data Safety Monitoring Board Members	$20,000
101	Advertising and Recruitment Materials	$10,000
102	MIAP IND Submission & Support	$11,500
103	***Total EAP Other***	**$1,300,200**
104	**Total VMR Program Expenses**	**$8,909,795**
105	**Total Direct Cost**	**$8,999,983**
106	***Indirect Cost (9.997664%)***	**$899,788**
107	**TOTAL PROJECT COST**	**$9,899,771**

REFERENCES

1. Ilgen MA, Zivin K, Austin KL, et al. Severe pain predicts greater likelihood of subsequent suicide. *Suicide Life Threat Behav.* 2010;40(6):597-608.
2. Klimkiewicz A, Bohnert AS, Jakubczyk A, Ilgen MA, Wojnar M, Brower K. The association between insomnia and suicidal thoughts in adults treated for alcohol dependence in Poland. *Drug Alcohol Depend.* 2012;122(1-2):160-163.
3. Fudalej S, Ilgen M, Kolodziejczyk I, et al. Somatic Comorbidity and Other Factors Related to Suicide Attempt Among Polish Methadone Maintenance Patients. *J Addict Med.* 2015;9(6):433-439.
4. Bonar EE, Ilgen MA, Walton M, Bohnert AS. Associations among pain, non-medical prescription opioid use, and drug overdose history. *The American journal on addictions / American Academy of Psychiatrists in Alcoholism and Addictions.* 2014;23(1):41-47.
5. Ilgen MA, Kleinberg F, Ignacio RV, et al. Noncancer pain conditions and risk of suicide. *JAMA Psychiatry.* 2013;70(7):692-697.
6. Bohnert ASB, Ilgen MA. Understanding Links among Opioid Use, Overdose, and Suicide. *N Engl J Med.* 2019;380(1):71-79.
7. Ilgen MA, Bohnert ASB, Ganoczy D, Bair MJ, McCarthy JF, Blow FC. Opioid dose and risk of suicide. *Pain.* 2016;157(5):1079-1084.
8. Bishop TM, Walsh PG, Ashrafioun L, Lavigne JE, Pigeon WR. Sleep, suicide behaviors, and the protective role of sleep medicine. *Sleep Med.* 2020;66:264-270.
9. MacCallum CA, Russo EB. Practical considerations in medical cannabis administration and dosing. *Eur J Intern Med.* 2018;49(October 2017):12-19.
10. MacCallum CA, Eadie L, Barr AM, Boivin M, Lu S. Practical Strategies Using Medical Cannabis to Reduce Harms Associated With Long Term Opioid Use in Chronic Pain. *Frontiers in Pharmacology.* 2021;12.
11. Bhaskar A, Bell A, Boivin M, et al. Consensus recommendations on dosing and administration of medical cannabis to treat chronic pain: results of a modified Delphi process. *J Cannabis Res.* 2021;3(1):22.
12. Pathiravasan CH, Zhang Y, Trinquart L, et al. Adherence of Mobile App-Based Surveys and Comparison With Traditional Surveys: eCohort Study. *J Med Internet Res.* 2021;23(1):e24773.
13. Quer G, Radin JM, Gadaleta M, et al. Wearable sensor data and self-reported symptoms for COVID-19 detection. *Nat Med.* 2021;27(1):73-77.
14. Lin H, Sardana M, Zhang Y, et al. Association of Habitual Physical Activity With Cardiovascular Disease Risk. *Circ Res.* 2020;127(10):1253-1260.
15. McManus DD, Trinquart L, Benjamin EJ, et al. Design and Preliminary Findings From a New Electronic Cohort Embedded in the Framingham Heart Study. *J Med Internet Res.* 2019;21(3):e12143.
16. Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. Pills to Pot: Observational Analyses of Cannabis Substitution Among Medical Cannabis Users With Chronic Pain. *J Pain.* 2019;20(7):830-841.
17. Boehnke KF, Scott JR, Litinas E, et al. Cannabis Use Preferences and Decision-making Among a Cross-sectional Cohort of Medical Cannabis Patients with Chronic Pain. *J Pain.* 2019;20(11):1362-1372.
18. Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. High frequency medical cannabis use is associated with worse pain among individuals with chronic pain. *J Pain.* 2019.
19. Volkow ND, Baler RD, Compton WM, Weiss SR. Adverse health effects of marijuana use. *N Engl J Med.* 2014;370(23):2219-2227.
20. Layden JE, Ghinai I, Pray I, et al. Pulmonary Illness Related to E-Cigarette Use in Illinois and Wisconsin - Preliminary Report. *N Engl J Med.* 2019.
21. Monte AA, Shelton SK, Mills E, et al. Acute Illness Associated With Cannabis Use, by Route of Exposure: An Observational Study. *Ann Intern Med.* 2019;170(8):531-537.
22. Walsh JH, Maddison KJ, Rankin T, et al. Treating Insomnia Symptoms with Medicinal Cannabis: A Randomized, Cross-Over Trial of the Efficacy of a Cannabinoid Medicine Compared with Placebo. *Sleep.* 2021.
23. National Academies of Sciences E, and Medicine. *The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.* Washington (DC)2017.
24. Russo EB, Guy GW, Robson PJ. Cannabis, pain, and sleep: lessons from therapeutic clinical trials of Sativex, a cannabis-based medicine. *Chem Biodivers.* 2007;4(8):1729-1743.
25. Ware MA, Fitzcharles MA, Joseph L, Shir Y. The effects of nabilone on sleep in fibromyalgia: results of a

randomized controlled trial. *Anesth Analg.* 2010;110(2):604-610.
26. Prasad B, Radulovacki MG, Carley DW. Proof of concept trial of dronabinol in obstructive sleep apnea. *Front Psychiatry.* 2013;4:1.
27. Cameron C, Watson D, Robinson J. Use of a synthetic cannabinoid in a correctional population for posttraumatic stress disorder-related insomnia and nightmares, chronic pain, harm reduction, and other indications: a retrospective evaluation. *J Clin Psychopharmacol.* 2014;34(5):559-564.
28. Roitman P, Mechoulam R, Cooper-Kazaz R, Shalev A. Preliminary, open-label, pilot study of add-on oral Delta9-tetrahydrocannabinol in chronic post-traumatic stress disorder. *Clin Drug Investig.* 2014;34(8):587-591.
29. Freeman AM, Petrilli K, Lees R, et al. How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. *Neurosci Biobehav Rev.* 2019;107:696-712.
30. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain.* 2005;113(1-2):9-19.
31. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain.* 2008;9(2):105-121.
32. Cella D, Riley W, Stone A, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005-2008. *J Clin Epidemiol.* 2010;63(11):1179-1194.
33. Merlin JS, Young SR, Starrels JL, et al. Correction to: Managing Concerning Behaviors in Patients Prescribed Opioids for Chronic Pain: a Delphi Study. *J Gen Intern Med.* 2018;33(9):1587.
34. Administration FaD. Marinol Drug Label.
35. Adamson SJ, Kay-Lambkin FJ, Baker AL, et al. An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R). *Drug Alcohol Depend.* 2010;110(1-2):137-143.
36. Heapy A, Dziura J, Buta E, Goulet J, Kulas JF, Kerns RD. Using Multiple Daily Pain Ratings to Improve Reliability and Assay Sensitivity: How Many Is Enough? *The Journal of Pain.* 2014;15(12):1360-1365.
37. Bastien C, Vallieres A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. *Sleep Medicine.* 2001;2(4):297-307.
38. Carney CE, Buysse DJ, Ancoli-Israel S, et al. The consensus sleep diary: Standardizing prospective sleep self-monitoring. *Sleep.* 2012;35(2):287-302.
39. HealthMeasures.net. PROMIS Profile 20+2 (PROPr). 2020; HTTP://www.healthmeasures.net/images/PROMIS/manuals/PROMIS_adult_profile_scoreing_manual.pdf. Accessed May, 20 2020, 2020.
40. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res (Hoboken).* 2010;62(5):600-610.
41. Wolfe F, Clauw DJ, Fitzcharles MA, et al. Fibromyalgia criteria and severity scales for clinical and epidemiological studies: a modification of the ACR Preliminary Diagnostic Criteria for Fibromyalgia. *J Rheumatol.* 2011;38(6):1113-1122.
42. Wolfe F, Clauw DJ, Fitzcharles MA, et al. 2016 Revisions to the 2010/2011 fibromyalgia diagnostic criteria. *Semin Arthritis Rheum.* 2016;46(3):319-329.
43. Schrepf A, Williams DA, Gallop R, et al. Sensory sensitivity and symptom severity represent unique dimensions of chronic pain: a MAPP Research Network study. *Pain.* 2018;159(10):2002-2011.
44. Hernan MA, Robins JM. Using Big Data to Emulate a Target Trial When a Randomized Trial Is Not Available. *Am J Epidemiol.* 2016;183(8):758-764.
45. Hernan MA, Robins JM. *Causal Inference: What If.* Boca Raton: Chapman & Hall/CRC; 2020.
46. Dagan N, Barda N, Kepten E, et al. BNT162b2 mRNA Covid-19 Vaccine in a Nationwide Mass Vaccination Setting. *N Engl J Med.* 2021;384(15):1412-1423.
47. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. *Epidemiology.* 2000;11(5):550-560.
48. Dickerman BA, Giovannucci E, Pernar CH, Mucci LA, Hernan MA. Guideline-Based Physical Activity and Survival Among US Men With Nonmetastatic Prostate Cancer. *Am J Epidemiol.* 2019;188(3):579-586.
49. Boehnke KF, Litinas E, Clauw DJ. Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain. *J Pain.* 2016;17(6):739-744.
50. Boehnke KF, Gangopadhyay S, Clauw DJ, Haffajee RL. Qualifying Conditions Of Medical Cannabis License Holders In The United States. *Health Aff (Millwood).* 2019;38(2):295-302.

51. Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. High-Frequency Medical Cannabis Use Is Associated With Worse Pain Among Individuals With Chronic Pain. *J Pain.* 2019.
52. Boehnke KF, McAfee J, Ackerman JM, Kruger DJ. Medication and substance use increases among people using cannabis medically during the COVID-19 pandemic. *Int J Drug Policy.* 2020:103053.
53. McAfee J, Boehnke KF, Moser SM, Brummett CM, Waljee JF, Bonar EE. Perioperative cannabis use: a longitudinal study of associated clinical characteristics and surgical outcomes. *Regional Anesthesia & Pain Medicine.* 2020.
54. Boehnke KF, Gagnier JJ, Matallana L, Williams DA. Cannabidiol Use for Fibromyalgia: Prevalence of Use and Perceptions of Effectiveness in a Large Online Survey. *J Pain.* 2021;22(5):556-566.
55. Boehnke KF, Litinas E, Worthing B, Conine L, Kruger DJ. Communication between healthcare providers and medical cannabis patients regarding referral and medication substitution. *J Cannabis Res.* 2021;3(1):2.
56. Boehnke KF. National Trends in Qualifying Conditions for Medical Cannabis. *American Journal of Endocannabinoid Medicine.* 2021;3(1):40-42.
57. Boehnke KF, Gagnier JJ, Matallana L, Williams DA. Cannabidiol Product Dosing and Decision-Making in a National Survey of Individuals with Fibromyalgia. *J Pain.* 2021.
58. Giesecke T, Williams DA, Harris RE, et al. Subgrouping of fibromyalgia patients on the basis of pressure-pain thresholds and psychological factors. *Arthritis Rheum.* 2003;48(10):2916-2922.
59. Williams DA, Farrell MJ, Cunningham J, et al. Knee pain and radiographic osteoarthritis interact in the prediction of levels of self-reported disability. *Arthritis Rheum.* 2004;51(4):558-561.
60. Petzke F, Harris RE, Williams DA, Clauw DJ, Gracely RH. Differences in unpleasantness induced by experimental pressure pain between patients with fibromyalgia and healthy controls. *Eur J Pain.* 2005;9(3):325-335.
61. Vit JP, Clauw DJ, Moallem T, Boudah A, Ohara PT, Jasmin L. Analgesia and hyperalgesia from CRF receptor modulation in the central nervous system of Fischer and Lewis rats. *Pain.* 2006;121(3):241-260.
62. Clauw DJ. Pharmacotherapy for patients with fibromyalgia. *J Clin Psychiatry.* 2008;69 Suppl 2:25-29.
63. Hsu MC, Harris RE, Sundgren PC, et al. No consistent difference in gray matter volume between individuals with fibromyalgia and age-matched healthy subjects when controlling for affective disorder. *Pain.* 2009;143(3):262-267.
64. Mease P, Arnold LM, Choy EH, et al. Fibromyalgia syndrome module at OMERACT 9: domain construct. *J Rheumatol.* 2009;36(10):2318-2329.
65. Williams DA, Kuper D, Segar M, Mohan N, Sheth M, Clauw DJ. Internet-enhanced management of fibromyalgia: a randomized controlled trial. *Pain.* 2010;151(3):694-702.
66. Arnold LM, Clauw D, Wang F, Ahl J, Gaynor PJ, Wohlreich MM. Flexible dosed duloxetine in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial. *J Rheumatol.* 2010;37(12):2578-2586.
67. Glass JM, Williams DA, Fernandez-Sanchez ML, et al. Executive function in chronic pain patients and healthy controls: different cortical activation during response inhibition in fibromyalgia. *J Pain.* 2011;12(12):1219-1229.
68. Arnold LM, Williams DA, Hudson JI, et al. Development of responder definitions for fibromyalgia clinical trials. *Arthritis Rheum.* 2012;64(3):885-894.
69. Lee YC, Lu B, Edwards RR, et al. The role of sleep problems in central pain processing in rheumatoid arthritis. *Arthritis Rheum.* 2013;65(1):59-68.
70. Brummett CM, Goesling J, Tsodikov A, et al. Prevalence of the fibromyalgia phenotype in patients with spine pain presenting to a tertiary care pain clinic and the potential treatment implications. *Arthritis Rheum.* 2013;65(12):3285-3292.
71. Hassett AL, Hilliard PE, Goesling J, Clauw DJ, Harte SE, Brummett CM. Reports of chronic pain in childhood and adolescence among patients at a tertiary care pain clinic. *J Pain.* 2013;14(11):1390-1397.
72. Brummett CM, Janda AM, Schueller CM, et al. Survey criteria for fibromyalgia independently predict increased postoperative opioid consumption after lower-extremity joint arthroplasty: a prospective, observational cohort study. *Anesthesiology.* 2013;119(6):1434-1443.
73. Brummett CM, Urquhart AG, Hassett AL, et al. Characteristics of fibromyalgia independently predict poorer long-term analgesic outcomes following total knee and hip arthroplasty. *Arthritis Rheumatol.* 2015;67(5):1386-1394.
74. Kairys AE, Schmidt-Wilcke T, Puiu T, et al. Increased brain gray matter in the primary somatosensory cortex is associated with increased pain and mood disturbance in patients with interstitial cystitis/painful bladder syndrome. *J Urol.* 2015;193(1):131-137.

75. As-Sanie S, Kim J, Schmidt-Wilcke T, et al. Functional Connectivity is Associated With Altered Brain Chemistry in Women With Endometriosis-Associated Chronic Pelvic Pain. *J Pain.* 2016;17(1):1-13.
76. Clauw DJ, Hassett AL. The role of centralised pain in osteoarthritis. *Clin Exp Rheumatol.* 2017;35 Suppl 107(5):79-84.
77. Neville SJ, Clauw AD, Moser SE, et al. Association Between the 2011 Fibromyalgia Survey Criteria and Multisite Pain Sensitivity in Knee Osteoarthritis. *Clin J Pain.* 2018;34(10):909-917.
78. Scott JR, Hassett AL, Schrepf AD, et al. Moderate Alcohol Consumption Is Associated with Reduced Pain and Fibromyalgia Symptoms in Chronic Pain Patients. *Pain Med.* 2018;19(12):2515-2527.
79. Goesling J, DeJonckheere M, Pierce J, et al. Opioid cessation and chronic pain: perspectives of former opioid users. *Pain.* 2019;160(5):1131-1145.
80. Larach DB, Sahara MJ, As-Sanie S, et al. Patient Factors Associated with Opioid Consumption in the Month Following Major Surgery. *Ann Surg.* 2019.
81. Clauw DJ. The pathogenesis of chronic pain and fatigue syndromes, with special reference to fibromyalgia. *Med Hypotheses.* 1995;44(5):369-378.
82. Clauw DJ. Elusive syndromes: treating the biologic basis of fibromyalgia and related syndromes. *Cleve Clin J Med.* 2001;68(10):830, 832-834.
83. Mease PJ, Clauw DJ, Arnold LM, et al. Fibromyalgia syndrome. *J Rheumatol.* 2005;32(11):2270-2277.
84. Kop WJ, Lyden A, Berlin AA, et al. Ambulatory monitoring of physical activity and symptoms in fibromyalgia and chronic fatigue syndrome. *Arthritis Rheum.* 2005;52(1):296-303.
85. Clauw DJ. Assessing and diagnosing fibromyalgia in the clinical setting. *J Clin Psychiatry.* 2008;69(11):e33.
86. Arnold LM, Bradley LA, Clauw DJ, Glass JM, Goldenberg DL. Multidisciplinary care and stepwise treatment for fibromyalgia. *J Clin Psychiatry.* 2008;69(12):e35.
87. Harris RE, Clauw DJ. Newer treatments for fibromyalgia syndrome. *Ther Clin Risk Manag.* 2008;4(6):1331-1342.
88. Dadabhoy D, Crofford LJ, Spaeth M, Russell IJ, Clauw DJ. Biology and therapy of fibromyalgia. Evidence-based biomarkers for fibromyalgia syndrome. *Arthritis Res Ther.* 2008;10(4):211.
89. Choy EH, Arnold LM, Clauw DJ, et al. Content and criterion validity of the preliminary core dataset for clinical trials in fibromyalgia syndrome. *J Rheumatol.* 2009;36(10):2330-2334.
90. Lee YC, Chibnik LB, Lu B, et al. The relationship between disease activity, sleep, psychiatric distress and pain sensitivity in rheumatoid arthritis: a cross-sectional study. *Arthritis Res Ther.* 2009;11(5):R160-R160.
91. Chervin RD, Teodorescu M, Kushwaha R, et al. Objective measures of disordered sleep in fibromyalgia. *J Rheumatol.* 2009;36(9):2009-2016.
92. Clauw DJ. Fibromyalgia: an overview. *Am J Med.* 2009;122(12 Suppl):S3-S13.
93. Geisser ME, Clauw DJ, Strand V, Gendreau RM, Palmer R, Williams DA. Contributions of change in clinical status parameters to Patient Global Impression of Change (PGIC) scores among persons with fibromyalgia treated with milnacipran. *Pain.* 2010;149(2):373-378.
94. Clauw DJ. Perspectives on fatigue from the study of chronic fatigue syndrome and related conditions. *PM R.* 2010;2(5):414-430.
95. Arnold LM, Clauw DJ, McCarberg BH, FibroCollaborative. Improving the recognition and diagnosis of fibromyalgia. *Mayo Clin Proc.* 2011;86(5):457-464.
96. Clauw DJ, Arnold LM, McCarberg BH, FibroCollaborative. The science of fibromyalgia. *Mayo Clin Proc.* 2011;86(9):907-911.
97. Murphy SL, Lyden AK, Phillips K, Clauw DJ, Williams DA. Subgroups of older adults with osteoarthritis based upon differing comorbid symptom presentations and potential underlying pain mechanisms. *Arthritis Res Ther.* 2011;13(4):R135.
98. Murphy SL, Lyden AK, Phillips K, Clauw DJ, Williams DA. Association between pain, radiographic severity, and centrally-mediated symptoms in women with knee osteoarthritis. *Arthritis Care Res (Hoboken).* 2011;63(11):1543-1549.
99. Ablin JN, Clauw DJ, Lyden AK, et al. Effects of sleep restriction and exercise deprivation on somatic symptoms and mood in healthy adults. *Clin Exp Rheumatol.* 2013;31(6 Suppl 79):S53-59.
100. Clauw DJ. Fibromyalgia: a clinical review. *JAMA.* 2014;311(15):1547-1555.
101. Kidwell KM, Harte SE, Hayes DF, et al. Patient-reported symptoms and discontinuation of adjuvant aromatase inhibitor therapy. *Cancer.* 2014;120(16):2403-2411.
102. Clauw DJ. Fibromyalgia and related conditions. *Mayo Clin Proc.* 2015;90(5):680-692.

103. Fitzcharles MA, Ste-Marie PA, Hauser W, et al. Efficacy, Tolerability, and Safety of Cannabinoid Treatments in the Rheumatic Diseases: A Systematic Review of Randomized Controlled Trials. *Arthritis Care Res (Hoboken).* 2016;68(5):681-688.
104. Farrehi PM, Clore KR, Scott JR, Vanini G, Clauw DJ. Efficacy of Sleep Tool Education During Hospitalization: A Randomized Controlled Trial. *Am J Med.* 2016.
105. Harte SE, Harris RE, Clauw DJ. The neurobiology of central sensitization. *J Appl Biobehav Res.* 2018;23(2).
106. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA.* 2011;305(13):1315-1321.
107. Ilgen MA, Roeder KM, Webster L, et al. Measuring pain medication expectancies in adults treated for substance use disorders. *Drug Alcohol Depend.* 2011;115(1-2):51-56.
108. Ilgen MA, Bohnert K, Kleinberg F, et al. Characteristics of adults seeking medical marijuana certification. *Drug Alcohol Depend.* 2013;132(3):654-659.
109. Birgenheir DG, Ilgen MA, Bohnert AS, et al. Pain conditions among veterans with schizophrenia or bipolar disorder. *Gen Hosp Psychiatry.* 2013;35(5):480-484.
110. Bohnert AS, Ilgen MA, Trafton JA, et al. Trends and regional variation in opioid overdose mortality among Veterans Health Administration patients, fiscal year 2001 to 2009. *Clin J Pain.* 2014;30(7):605-612.
111. Birgenheir DG, Ilgen MA, Bohnert AS, et al. Authors' response to the letter to the editor: "Pain in primary care patients with bipolar disorder". *Gen Hosp Psychiatry.* 2014;36(2):229.
112. Becker WC, Ganoczy D, Fiellin DA, Bohnert AS. Buprenorphine/Naloxone dose and pain intensity among individuals initiating treatment for opioid use disorder. *J Subst Abuse Treat.* 2015;48(1):128-131.
113. Park TW, Saitz R, Ganoczy D, Ilgen MA, Bohnert AS. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ.* 2015;350:h2698.
114. Ilgen MA, Bohnert AS, Chermack S, et al. A randomized trial of a pain management intervention for adults receiving substance use disorder treatment. *Addiction.* 2016;111(8):1385-1393.
115. Bohnert AS, Bonar EE, Cunningham R, et al. A pilot randomized clinical trial of an intervention to reduce overdose risk behaviors among emergency department patients at risk for prescription opioid overdose. *Drug Alcohol Depend.* 2016;163:40-47.
116. Ilgen MA, Bohnert ASB, Chermack S, *et al*. A randomized trial of a pain management intervention for adults receiving substance use disorder treatment. *Addiction.* 2016;111(8):1385-1393.
117. Park TW, Lin LA, Hosanagar A, Kogowski A, Paige K, Bohnert AS. Understanding Risk Factors for Opioid Overdose in Clinical Populations to Inform Treatment and Policy. *J Addict Med.* 2016;10(6):369-381.
118. Lin LA, Hosanagar A, Park TW, Bohnert AS. Opioid Overdose: Risk Assessment and Mitigation in Outpatient Treatment. *J Addict Med.* 2016;10(6):382-386.
119. Krein SL, Bohnert A, Kim HM, Harris ME, Richardson CR. Opioid use and walking among patients with chronic low back pain. *J Rehabil Res Dev.* 2016;53(1):107-116.
120. Bohnert AS, Logan JE, Ganoczy D, Dowell D. A Detailed Exploration Into the Association of Prescribed Opioid Dosage and Overdose Deaths Among Patients With Chronic Pain. *Med Care.* 2016;54(5):435-441.
121. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg.* 2017;152(6):e170504.
122. Brummett CM, Waljee JF, Goesling J, et al. New Persistent Opioid Use After Minor and Major Surgical Procedures in US Adults. *JAMA Surg.* 2017:e170504.
123. Lin LA, Bohnert ASB, Kerns RD, Clay MA, Ganoczy D, Ilgen MA. Impact of the Opioid Safety Initiative on opioid-related prescribing in veterans. *Pain.* 2017;158(5):833-839.
124. Lin LA, Bohnert ASB, Jannausch M, Goesling J, Ilgen MA. Use of non-pharmacological strategies for pain relief in addiction treatment patients with chronic pain. *Am J Addict.* 2017;26(6):564-567.
125. Bohnert ASB, Guy GP, Jr., Losby JL. Opioid Prescribing in the United States Before and After the Centers for Disease Control and Prevention's 2016 Opioid Guideline. *Ann Intern Med.* 2018;169(6):367-375.
126. Whiteside LK, Goldstick J, Dora-Laskey A, et al. Patient Preference for Pain Medication in the Emergency Department Is Associated with Non-fatal Overdose History. *West J Emerg Med.* 2018;19(4):722-730.
127. Harbaugh CM, Lee JS, Chua KP, et al. Association Between Long-term Opioid Use in Family Members and Persistent Opioid Use After Surgery Among Adolescents and Young Adults. *JAMA Surg.* 2019;154(4):e185838.
128. Lagisetty PA, Healy N, Garpestad C, Jannausch M, Tipirneni R, Bohnert ASB. Access to Primary Care Clinics for Patients With Chronic Pain Receiving Opioids. *JAMA Netw Open.* 2019;2(7):e196928.

129. Chua KP, Brummett CM, Conti RM, Haffajee RL, Prosser LA, Bohnert ASB. Assessment of Prescriber and Pharmacy Shopping Among the Family Members of Patients Prescribed Opioids. *JAMA Netw Open.* 2019;2(5):e193673.
130. Ilgen MA, Coughlin LN, Bohnert ASB, et al. Efficacy of a Psychosocial Pain Management Intervention for Men and Women With Substance Use Disorders and Chronic Pain: A Randomized Clinical Trial. *JAMA Psychiatry.* 2020.
131. Frank JW, Bohnert ASB, Sandbrink F, McGuire M, Drexler K. Implementation and Policy Recommendations from the VHA State-of-the-Art Conference on Strategies to Improve Opioid Safety. *J Gen Intern Med.* 2020;35(Suppl 3):983-987.
132. Chua KP, Brummett CM, Conti RM, Bohnert A. Association of Opioid Prescribing Patterns With Prescription Opioid Overdose in Adolescents and Young Adults. *JAMA Pediatr.* 2020;174(2):141-148.
133. Giannitrapani KF, Fereydooni S, Azarfar A, et al. Signature Informed Consent for Long-Term Opioid Therapy in Patients With Cancer: Perspectives of Patients and Providers. *J Pain Symptom Manage.* 2020;59(1):49-57.
134. Coughlin LN, Ilgen MA, Jannausch M, Walton MA, Bohnert KM. Progression of cannabis withdrawal symptoms in people using medical cannabis for chronic pain. *Addiction.* 2021.
135. Lagisetty P, Garpestad C, Larkin A, et al. Identifying individuals with opioid use disorder: Validity of International Classification of Diseases diagnostic codes for opioid use, dependence and abuse. *Drug Alcohol Depend.* 2021;221:108583.
136. Boehnke KF. When personal becomes professional. *Science.* 2017;357(6352):726.
137. Boehnke KF. Pain Management: Assembling a Tool Kit, Building a Life. *JAMA.* 2018;320(21):2201-2202.
138. Boehnke KF, Clauw DJ. Brief Commentary: Cannabinoid Dosing for Chronic Pain Management. *Ann Intern Med.* 2019;170(2):118.
139. Boehnke KF, LaMore C, Hart P, Zick SM. Feasibility study of a modified yoga program for chronic pain among elderly adults in assisted and independent living. *Explore (NY).* 2020.
140. Silveira MJ, Boehnke KF, Clauw D. Treatment of Fibromyalgia in the 21st Century. *JAMA Intern Med.* 2021.
141. Boehnke KF, Gagnier JJ, Matallana L, Williams DA. Substituting Cannabidiol for Opioids and Pain Medications Among Individuals with Fibromyalgia: a Large Online Survey. *The Journal of Pain.* 2021.
142. Ilgen MA, Bohnert AS, Ignacio RV, et al. Psychiatric diagnoses and risk of suicide in veterans. *Arch Gen Psychiatry.* 2010;67(11):1152-1158.
143. Bohnert AS, Roeder KM, Ilgen MA. Suicide attempts and overdoses among adults entering addictions treatment: comparing correlates in a U.S. National Study. *Drug Alcohol Depend.* 2011;119(1-2):106-112.
144. Webster L, Eisenberg A, Bohnert AS, Kleinberg F, Ilgen MA. Qualitative evaluation of suicide and overdose risk assessment procedures among veterans in substance use disorder treatment clinics. *Arch Suicide Res.* 2012;16(3):250-262.
145. Britton PC, Bohnert AS, Wines JD, Jr., Conner KR. A procedure that differentiates unintentional from intentional overdose in opioid abusers. *Addictive behaviors.* 2012;37(1):127-130.
146. Kim HM, Smith EG, Ganoczy D, et al. Predictors of suicide in patient charts among patients with depression in the Veterans Health Administration health system: importance of prescription drug and alcohol abuse. *J Clin Psychiatry.* 2012;73(10):e1269-1275.
147. Ilgen MA, McCarthy JF, Ignacio RV, et al. Psychopathology, Iraq and Afghanistan service, and suicide among Veterans Health Administration patients. *J Consult Clin Psychol.* 2012;80(3):323-330.
148. Blow FC, Bohnert AS, Ilgen MA, et al. Suicide mortality among patients treated by the Veterans Health Administration from 2000 to 2007. *American journal of public health.* 2012;102 Suppl 1:S98-104.
149. Bohnert AS, McCarthy JF, Ignacio RV, Ilgen MA, Eisenberg A, Blow FC. Misclassification of suicide deaths: examining the psychiatric history of overdose decedents. *Inj Prev.* 2013;19(5):326-330.
150. Conner KR, Bohnert AS, McCarthy JF, et al. Mental disorder comorbidity and suicide among 2.96 million men receiving care in the Veterans Health Administration health system. *J Abnorm Psychol.* 2013;122(1):256-263.
151. Fudalej S, Jakubczyk A, Kopera M, et al. DISC1 as a Possible Genetic Contribution to Opioid Dependence in a Polish Sample. *J Stud Alcohol Drugs.* 2016;77(2):220-226.
152. Logan J, Bohnert A, Spies E, Jannausch M. Suicidal ideation among young Afghanistan/Iraq War Veterans and civilians: Individual, social, and environmental risk factors and perception of unmet mental healthcare needs, United States, 2013. *Psychiatry research.* 2016;245:398-405.
153. Bohnert ASB, Walton MA, Cunningham RM, et al. Overdose and adverse drug event experiences among adult

patients in the emergency department. *Addict Behav.* 2018;86:66-72.
154. Lin LA, Peltzman T, McCarthy JF, Oliva EM, Trafton JA, Bohnert ASB. Changing Trends in Opioid Overdose Deaths and Prescription Opioid Receipt Among Veterans. *Am J Prev Med.* 2019;57(1):106-110.
155. Nestadt PS, Bohnert ASB. Clinical Perspective on Opioids in the Context of Suicide Risk. *Focus (Am Psychiatr Publ).* 2020;18(2):100-105.
156. Bohnert ASB, Sen S. Deaths Attributed to Psychiatric Disorders in the United States, 2010-2018. *Am J Public Health.* 2020;110(12):1825-1827.
157. Gicquelais RE, Jannausch M, Bohnert ASB, Thomas L, Sen S, Fernandez AC. Links between suicidal intent, polysubstance use, and medical treatment after non-fatal opioid overdose. *Drug Alcohol Depend.* 2020;212:108041.
158. Lei L, Strominger J, Wiechers IR, et al. Benzodiazepine Prescribing from VA and Medicare to Dually Enrolled Older Veterans: A Retrospective Cohort Study. *J Gen Intern Med.* 2021.
159. Rockett IRH, Caine ED, Banerjee A, et al. Fatal self-injury in the United States, 1999-2018: Unmasking a national mental health crisis. *EClinicalMedicine.* 2021;32:100741.
160. Maust DT, Kim HM, Wiechers IR, Ignacio RV, Bohnert ASB, Blow FC. Benzodiazepine Use among Medicare, Commercially Insured, and Veteran Older Adults, 2013-2017. *J Am Geriatr Soc.* 2021;69(1):98-105.
161. Burnett-Zeigler I, Zivin K, Ilgen MA, Islam K, Bohnert AS. Perceptions of quality of health care among veterans with psychiatric disorders. *Psychiatric services (Washington, DC).* 2011;62(9):1054-1059.
162. Bohnert AS, Ilgen MA, Galea S, McCarthy JF, Blow FC. Accidental poisoning mortality among patients in the Department of Veterans Affairs Health System. *Med Care.* 2011;49(4):393-396.
163. Bohnert AS, Zivin K, Welsh DE, Kilbourne AM. Ratings of patient-provider communication among veterans: serious mental illnesses, substance use disorders, and the moderating role of trust. *Health Commun.* 2011;26(3):267-274.
164. Zivin K, Bohnert AS, Mezuk B, et al. Employment status of patients in the VA health system: implications for mental health services. *Psychiatr Serv.* 2011;62(1):35-38.
165. Ilgen M, Edwards P, Kleinberg F, Bohnert AS, Barry K, Blow FC. The prevalence of substance use among patients at a dental school clinic in Michigan. *Journal of the American Dental Association.* 2012;143(8):890-896.
166. Bowersox NW, Kilbourne AM, Abraham KM, et al. Cause-specific mortality among Veterans with serious mental illness lost to follow-up. *Gen Hosp Psychiatry.* 2012;34(6):651-653.
167. Bohnert AS, Ilgen MA, Bossarte RM, Britton PC, Chermack ST, Blow FC. Veteran status and alcohol use in men in the United States. *Mil Med.* 2012;177(2):198-203.
168. Chermack ST, Bohnert AS, Price AM, Austin K, Ilgen MA. Substance use disorders and homicide death in veterans. *J Stud Alcohol Drugs.* 2012;73(1):10-14.
169. Bohnert AS, Ilgen MA, Ignacio RV, McCarthy JF, Valenstein M, Blow FC. Risk of death from accidental overdose associated with psychiatric and substance use disorders. *Am J Psychiatry.* 2012;169(1):64-70.
170. Zivin K, Pfeiffer PN, Bohnert AS, et al. Evaluation of the FDA warning against prescribing citalopram at doses exceeding 40 mg. *Am J Psychiatry.* 2013;170(6):642-650.
171. Bowersox NW, Bohnert AS, Ganoczy D, Pfeiffer PN. Inpatient psychiatric care experience and its relationship to posthospitalization treatment participation. *Psychiatric services (Washington, DC).* 2013;64(6):554-562.
172. Park TW, Bohnert AS, Austin KL, Saitz R, Pizer SD. Datapoints: regional variation in benzodiazepine prescribing for patients on opioid agonist therapy. *Psychiatr Serv.* 2014;65(1):4.
173. Lin LA, Bohnert AS, Ilgen MA, Pfeiffer PN, Ganoczy D, Blow FC. Outpatient Provider Contact Prior to Unintentional Opioid Overdose Among VHA Service Users. *Psychiatric services (Washington, DC).* 2015;66(11):1149-1154.
174. Ashrafioun L, Bohnert AS, Jannausch M, Ilgen MA. Evaluation of the current opioid misuse measure among substance use disorder treatment patients. *J Subst Abuse Treat.* 2015;55:15-20.
175. Larney S, Bohnert AS, Ganoczy D, et al. Mortality among older adults with opioid use disorders in the Veteran's Health Administration, 2000-2011. *Drug and alcohol dependence.* 2015;147:32-37.
176. Pecina M, Bohnert AS, Sikora M, et al. Association Between Placebo-Activated Neural Systems and Antidepressant Responses: Neurochemistry of Placebo Effects in Major Depression. *JAMA psychiatry.* 2015;72(11):1087-1094.
177. Sripada RK, Bohnert AS, Teo AR, et al. Social networks, mental health problems, and mental health service utilization in OEF/OIF National Guard veterans. *Soc Psychiatry Psychiatr Epidemiol.* 2015;50(9):1367-1378.

178. Lin LA, Ilgen MA, Jannausch M, Bohnert KM. Comparing adults who use cannabis medically with those who use recreationally: Results from a national sample. *Addict Behav.* 2016;61:99-103.
179. Bonar EE, Bohnert AS. Perceived Severity of and Susceptibility to Overdose Among Injection Drug Users: Relationships With Overdose History. *Subst Use Misuse.* 2016;51(10):1379-1383.
180. Blow FC, Walton MA, Bohnert ASB, et al. A randomized controlled trial of brief interventions to reduce drug use among adults in a low-income urban emergency department: the HealthiER You study. *Addiction.* 2017;112(8):1395-1405.
181. Haffajee RL, Bohnert ASB, Lagisetty PA. Policy Pathways to Address Provider Workforce Barriers to Buprenorphine Treatment. *Am J Prev Med.* 2018;54(6 Suppl 3):S230-S242.
182. Bonar EE, Walton MA, Barry KL, et al. Sexual HIV risk behavior outcomes of brief interventions for drug use in an inner-city emergency department: Secondary outcomes from a randomized controlled trial. *Drug Alcohol Depend.* 2018;183:217-224.
183. Bohnert ASB, Larochelle MR. Are Temporal Trends Important Measures of Opioid-prescribing Risk? *J Addict Med.* 2019;13(1):5-6.
184. Lagisetty PA, Lin LA, Ganoczy D, Haffajee RL, Iwashyna TJ, Bohnert ASB. Opioid Prescribing After Opioid-related Inpatient Hospitalizations by Diagnosis: A Cohort Study. *Med Care.* 2019;57(10):815-821.
185. Gicquelais RE, Mezuk B, Foxman B, Thomas L, Bohnert ASB. Justice involvement patterns, overdose experiences, and naloxone knowledge among men and women in criminal justice diversion addiction treatment. *Harm Reduct J.* 2019;16(1):46.
186. Haffajee RL, Lin LA, Bohnert ASB, Goldstick JE. Characteristics of US Counties With High Opioid Overdose Mortality and Low Capacity to Deliver Medications for Opioid Use Disorder. *JAMA Netw Open.* 2019;2(6):e196373.
187. Lagisetty PA, Bohnert A. Role of an Accurate Treatment Locator and Cash-Only Practices in Access to Buprenorphine for Opioid Use Disorders. *Ann Intern Med.* 2019;171(1):58-59.
188. Bonar EE, Schneeberger DM, Bourque C, et al. Social Media Interventions for Risky Drinking Among Adolescents and Emerging Adults: Protocol for a Randomized Controlled Trial. *JMIR Res Protoc.* 2020;9(5):e16688.
189. Gicquelais RE, Bohnert ASB, Fernandez AC. Opportunities to boost naloxone awareness among people who misuse opioid analgesics who have not used illegal opioids. *Subst Abus.* 2020:1-5.
190. Maust DT, Lin LA, Goldstick JE, Haffajee RL, Brownlee R, Bohnert ASB. Association of Medicare Part D Benzodiazepine Coverage Expansion With Changes in Fall-Related Injuries and Overdoses Among Medicare Advantage Beneficiaries. *JAMA Netw Open.* 2020;3(4):e202051.
191. Lin LA, Bohnert ASB, Blow FC, et al. Polysubstance use and association with opioid use disorder treatment in the US Veterans Health Administration. *Addiction.* 2021;116(1):96-104.
192. Guarino P, Peduzzi P, Donta ST, et al. A multicenter two by two factorial trial of cognitive behavioral therapy and aerobic exercise for Gulf War veterans' illnesses: design of a veterans affairs cooperative study (CSP #470). *Control Clin Trials.* 2001;22(3):310-332.
193. Williams DA, Cary MA, Groner KH, et al. Improving physical functional status in patients with fibromyalgia: a brief cognitive behavioral intervention. *J Rheumatol.* 2002;29(6):1280-1286.
194. Donta ST, Clauw DJ, Engel CC, Jr., et al. Cognitive behavioral therapy and aerobic exercise for Gulf War veterans' illnesses: a randomized controlled trial. *JAMA.* 2003;289(11):1396-1404.
195. Gendreau RM, Thorn MD, Gendreau JF, et al. Efficacy of milnacipran in patients with fibromyalgia. *J Rheumatol.* 2005;32(10):1975-1985.
196. Harris RE, Tian X, Williams DA, et al. Treatment of fibromyalgia with formula acupuncture: investigation of needle placement, needle stimulation, and treatment frequency. *J Altern Complement Med.* 2005;11(4):663-671.
197. Clauw DJ, Mease P, Palmer RH, Gendreau RM, Wang Y. Milnacipran for the treatment of fibromyalgia in adults: a 15-week, multicenter, randomized, double-blind, placebo-controlled, multiple-dose clinical trial. *Clin Ther.* 2008;30(11):1988-2004.
198. Harris RE, Zubieta JK, Scott DJ, Napadow V, Gracely RH, Clauw DJ. Traditional Chinese acupuncture and placebo (sham) acupuncture are differentiated by their effects on mu-opioid receptors (MORs). *Neuroimage.* 2009;47(3):1077-1085.
199. Mawla I, Ichesco E, Zollner HJ, et al. Greater Somatosensory Afference With Acupuncture Increases Primary Somatosensory Connectivity and Alleviates Fibromyalgia Pain via Insular gamma-Aminobutyric Acid: A

Randomized Neuroimaging Trial. *Arthritis Rheumatol.* 2020.
200. Bonar EE, Walton MA, Cunningham RM, et al. Computer-enhanced interventions for drug use and HIV risk in the emergency room: preliminary results on psychological precursors of behavior change. *J Subst Abuse Treat.* 2014;46(1):5-14.
201. Hsu MC, Schubiner H, Lumley MA, Stracks JS, Clauw DJ, Williams DA. Sustained pain reduction through affective self-awareness in fibromyalgia: a randomized controlled trial. *J Gen Intern Med.* 2010;25(10):1064-1070.
202. Lumley MA, Schubiner H, Lockhart NA, et al. Emotional awareness and expression therapy, cognitive behavioral therapy, and education for fibromyalgia. *Pain.* 2017;158(12):2354-2363.
203. Ilgen MA, Coughlin LN, Bohnert ASB, et al. Efficacy of a Psychosocial Pain Management Intervention for Men and Women With Substance Use Disorders and Chronic Pain: A Randomized Clinical Trial. *JAMA Psychiatry.* 2020;77(12):1225-1234.
204. Foundation A. Arthritis Foundation CBD Guidance for Adults. 2019.
205. Kratz AL, Whibley D, Alschuler KN, et al. Characterizing chronic pain phenotypes in multiple sclerosis: a nationwide survey study. *Pain.* 2021;162(5):1426-1433.
206. Braley TJ, Whibley D, Alschuler KN, et al. Cannabinoid use among Americans with MS: Current trends and gaps in knowledge. *Mult Scler J Exp Transl Clin.* 2020;6(3):2055217320959816.
207. Fitzcharles MA, Clauw DJ, Hauser W. A cautious hope for cannabidiol (CBD) in rheumatology care. *Arthritis Care Res (Hoboken).* 2020.
208. Boehnke KF, Clauw DJ, Haffajee RL. Medical Cannabis And Pain: The Authors Reply. *Health affairs.* 2019;38(4):694.
209. Fitzcharles MA, Ste-Marie PA, Hauser W, et al. Efficacy, tolerability and safety of cannabinoid treatments in the rheumatic diseases: A systematic review of randomized controlled trials. *Arthritis Care Res (Hoboken).* 2015.
210. Fitzcharles MA, Ste-Marie PA, Clauw DJ, et al. Rheumatologists lack confidence in their knowledge of cannabinoids pertaining to the management of rheumatic complaints. *BMC musculoskeletal disorders.* 2014;15:258.
211. Phillips K, Clauw DJ. Central pain mechanisms in chronic pain states--maybe it is all in their head. *Best practice & research Clinical rheumatology.* 2011;25(2):141-154.
212. Larkin TE, Kaplan CM, Schrepf A, et al. Altered network architecture of functional brain communities in chronic nociplastic pain. *Neuroimage.* 2021;226:117504.
213. Toogood PL, Clauw DJ, Phadke S, Hoffman D. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): Where will the drugs come from? *Pharmacol Res.* 2021:105465.
214. Fitzcharles MA, Cohen SP, Clauw DJ, Littlejohn G, Usui C, Hauser W. Nociplastic pain: towards an understanding of prevalent pain conditions. *Lancet.* 2021;397(10289):2098-2110.
215. Wallace BI, Kenney B, Malani PN, Clauw DJ, Nallamothu BK, Waljee AK. Prevalence of Immunosuppressive Drug Use Among Commercially Insured US Adults, 2018-2019. *JAMA Netw Open.* 2021;4(5):e214920.
216. Ichesco E, Peltier SJ, Mawla I, et al. Prediction of Differential Pharmacologic Response in Chronic Pain Using Functional Neuroimaging Biomarkers and Support Vector Machine Algorithm - An Exploratory Study. *Arthritis Rheumatol.* 2021.
217. Kosek E, Clauw D, Nijs J, et al. Chronic nociplastic pain affecting the musculoskeletal system: clinical criteria and grading system. *Pain.* 2021.
218. Vlisides PE, Li D, McKinney A, et al. The Effects of Intraoperative Caffeine on Postoperative Opioid Consumption and Related Outcomes After Laparoscopic Surgery: A Randomized Controlled Trial. *Anesth Analg.* 2021.
219. McKernan LC, Crofford LJ, Kim A, et al. Electronic Delivery of Pain Education for Chronic Overlapping Pain Conditions: A Prospective Cohort Study. *Pain medicine.* 2021.
220. Minhas D, Clauw DJ. Pain Mechanisms in Patients with Rheumatic Diseases. *Rheumatic diseases clinics of North America.* 2021;47(2):133-148.
221. Booth MJ, Clauw D, Janevic MR, Kobayashi LC, Piette JD. Validation of Self-Reported Rheumatoid Arthritis Using Medicare Claims: A Nationally Representative Longitudinal Study of Older Adults. *ACR Open Rheumatol.* 2021;3(4):239-249.
222. Toogood PL, Clauw DJ, Phadke S, Hoffman D. Myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS): Where will the drugs come from? *Pharmacol Res.* 2021;165:105465.
223. Sankarasubramanian V, Chiravuri S, Mirzakhalili E, et al. Quantitative Sensory Testing of Spinal Cord and Dorsal Root Ganglion Stimulation in Chronic Pain Patients. *Neuromodulation.* 2021.

224. Clauw D. Time to Stop the Fibromyalgia Criteria Wars and Refocus on Identifying and Treating Individuals With This Type of Pain Earlier in Their Illness. *Arthritis Care Res (Hoboken).* 2021;73(5):613-616.
225. Larkin TE, Kaplan CM, Schrepf A, et al. Altered network architecture of functional brain communities in chronic nociplastic pain. *Neuroimage.* 2020;226:117504.
226. Clauw DJ, Häuser W, Cohen SP, Fitzcharles MA. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain.* 2020;161(8):1694-1697.
227. McKernan LC, Bonnet KR, Finn MTM, et al. Qualitative Analysis of Treatment Needs in Interstitial Cystitis/Bladder Pain Syndrome: Implications for Intervention. *Can J Pain.* 2020;4(1):181-198.
228. Mawla I, Schrepf A, Ichesco E, et al. Natural bladder filling alters resting brain function at multiple spatial scales: a proof-of-concept MAPP Network Neuroimaging Study. *Sci Rep.* 2020;10(1):19901.
229. Fitzcharles MA, Clauw DJ, Hauser W, Cohen SP. Reply to Chaturvedi. *Pain.* 2020;161(11):2652-2653.
230. Clauw DJ, Hauser W, Cohen SP, Fitzcharles MA. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain.* 2020;161(8):1694-1697.
231. Heisler AC, Song J, Muhammad LN, et al. Association of Dysregulated Central Pain Processing and Response to Disease-Modifying Antirheumatic Drug Therapy in Rheumatoid Arthritis. *Arthritis Rheumatol.* 2020;72(12):2017-2024.
232. Fors EA, Wensaas KA, Eide H, et al. Fibromyalgia 2016 criteria and assessments: comprehensive validation in a Norwegian population. *Scand J Pain.* 2020;20(4):663-672.
233. Clemens JQ, Kutch JJ, Mayer EA, et al. The Multidisciplinary Approach to The Study of Chronic Pelvic Pain (MAPP) Research Network*: Design and implementation of the Symptom Patterns Study (SPS). *Neurourology and urodynamics.* 2020;39(6):1803-1814.
234. Bellomo TR, Schrepf A, Kruger GH, et al. Pressure Pain Tolerance Predicts the Success of Emotional Awareness and Expression Therapy in Patients With Fibromyalgia. *Clin J Pain.* 2020;36(7):562-566.
235. Delaney LD, Clauw DJ, Waljee JF. The Management of Acute Pain for Musculoskeletal Conditions: The Challenges of Opioids and Opportunities for the Future. *The Journal of bone and joint surgery American volume.* 2020;102 Suppl 1:3-9.
236. Peduzzi P, Guarino P, Donta ST, Engel CC, Jr., Clauw DJ, Feussner JR. Research on informed consent: investigator-developed versus focus group-developed consent documents, a VA cooperative study. *Control Clin Trials.* 2002;23(2):184-197.
237. Guarino P, Peduzzi P, Donta ST, et al. A multicenter two by two factorial trial of cognitive behavioral therapy and aerobic exercise for Gulf War veterans' illnesses: Design of a veterans affairs cooperative study (CSP #470). *Controlled Clinical Trials.* 2001;22(3):310-332.
238. Glass JM, Lyden AK, Petzke F, et al. The effect of brief exercise cessation on pain, fatigue, and mood symptom development in healthy, fit individuals. *J Psychosom Res.* 2004;57(4):391-398.
239. Fontaine KR, Conn L, Clauw DJ. Effects of lifestyle physical activity on perceived symptoms and physical function in adults with fibromyalgia: results of a randomized trial. *Arthritis research & therapy.* 2010;12(2):R55.
240. Geisser ME, Clauw DJ, Strand V, Gendreau RM, Palmer R, Williams DA. Contributions of change in clinical status parameters to Patient Global Impression of Change (PGIC) scores among persons with fibromyalgia treated with milnacipran. *Pain.* 2010;149(2):373-378.
241. Goldenberg DL, Clauw DJ, Palmer RH, Mease P, Chen W, Gendreau RM. Durability of therapeutic response to milnacipran treatment for fibromyalgia. Results of a randomized, double-blind, monotherapy 6-month extension study. *Pain medicine.* 2010;11(2):180-194.
242. Arnold LM, Clauw D, Wang F, Ahl J, Gaynor PJ, Wohlreich MM. Flexible dosed duloxetine in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled trial. *The Journal of rheumatology.* 2010;37(12):2578-2586.
243. Marangell LB, Clauw DJ, Choy E, et al. Comparative pain and mood effects in patients with comorbid fibromyalgia and major depressive disorder: secondary analyses of four pooled randomized controlled trials of duloxetine. *Pain.* 2011;152(1):31-37.
244. Murphy SL, Lyden AK, Clary M, et al. Activity pacing for osteoarthritis symptom management: study design and methodology of a randomized trial testing a tailored clinical approach using accelerometers for veterans and non-veterans. *BMC musculoskeletal disorders.* 2011;12:177.
245. Harris RE, Napadow V, Huggins JP, et al. Pregabalin rectifies aberrant brain chemistry, connectivity, and functional response in chronic pain patients. *Anesthesiology.* 2013;119(6):1453-1464.

246. Clauw DJ, Mease PJ, Palmer RH, Trugman JM, Wang Y. Continuing efficacy of milnacipran following long-term treatment in fibromyalgia: a randomized trial. *Arthritis Res Ther.* 2013;15(4):R88.
247. Harte SE, Clauw DJ, Napadow V, Harris RE. Pressure Pain Sensitivity and Insular Combined Glutamate and Glutamine (Glx) Are Associated with Subsequent Clinical Response to Sham But Not Traditional Acupuncture in Patients Who Have Chronic Pain. *Med Acupunct.* 2013;25(2):154-160.
248. Foerster BR, Nascimento TD, DeBoer M, et al. Excitatory and inhibitory brain metabolites as targets of motor cortex transcranial direct current stimulation therapy and predictors of its efficacy in fibromyalgia. *Arthritis Rheumatol.* 2015;67(2):576-581.
249. Becker TK, Tafoya CA, Osei-Ampofo M, et al. Cardiopulmonary ultrasound for critically ill adults improves diagnostic accuracy in a resource-limited setting: the AFRICA trial. *Trop Med Int Health.* 2017;22(12):1599-1608.
250. Lee YC, Massarotti E, Edwards RR, et al. Effect of Milnacipran on Pain in Patients with Rheumatoid Arthritis with Widespread Pain: A Randomized Blinded Crossover Trial. *J Rheumatol.* 2016;43(1):38-45.
251. Holton KF, Ndege PK, Clauw DJ. Dietary correlates of chronic widespread pain in Meru, Kenya. *Nutrition.* 2018;53:14-19.
252. Goldstick JE, Walton MA, Bohnert ASB, Heinze JE, Cunningham RM. Predictors of alcohol use transitions among drug-using youth presenting to an urban emergency department. *PLoS One.* 2019;14(12):e0227140.
253. Kruger DJ, Kruger JS. Medical Cannabis Users' Comparisons between Medical Cannabis and Mainstream Medicine. *J Psychoactive Drugs.* 2019;51(1):31-36.
254. Kruger DJ, Kruger JS, Collins RL. Cannabis Enthusiasts' Knowledge of Medical Treatment Effectiveness and Increased Risks From Cannabis Use. *Am J Health Promot.* 2020:890117119899218.
255. Kruger JS, Blavos A, Castor TS, et al. Manipulation checking the munchies: validating self-reported dietary behaviors during cannabis intoxication. *Human Ethology.* 2019;34:10-16.
256. Kruger DJ, Kruger JS, Collins RL. Cannabis enthusiasts' knowledge of medical treatment effectiveness and increased risks from cannabis use. *American Journal of Health Promotion.* 2020;34(4):436-439.
257. Kruger DJ, Moffet IM, Seluk LC, Zammit LA. A content analysis of internet information sources on medical cannabis. *Journal of Cannabis Research.* 2020;2(1):1-6.
258. Kruger DJ, Kruger JS, Collins RL. Frequent cannabis users demonstrate low knowledge of cannabinoid content and dosages. *Drugs: Education, Prevention and Policy.* 2021;28(1):97-103.
259. Kruger DJ, Korach NJ, Kruger JS. Requirements for Cannabis Product Labeling by US State. *Cannabis and cannabinoid research.* 2021.
260. Kruger DJ, Kruger JS, Bednarczyk EM, Prescott Jr WA. Cannabis education in United States Pharmacy Colleges and Schools. *Journal of the American College of Clinical Pharmacy.* 2021;4(5):616-621.
261. Kruger JS, Kruger D, Collins RL. Knowledge and practice of harm reduction strategies among people who report frequent cannabis use. *Health promotion practice.* 2021;22(1):24-30.

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