Genomic Medicine Program Advisory Committee
April 29, 2020 Meeting
Executive Summary

The latest meeting of the Genomic Medicine Program Advisory Committee (GMPAC) took place virtually via Webex on April 29, 2020. The meeting began at 11am ET with Dr. Jennifer Moser presiding as the committee Designated Federal Officer with a quorum of members present. Dr. Dan Roden, Dr. Andrea Ferreira-Gonzalez, Dr. Adam Berger, Dr. Richard Mooney, Dr. Victoria Pratt, and Ms. Kimberly LeBlanc were on the call. Dr. Rachel Ramoni, Chief Research and Development Officer of the Office of Research and Development welcomed the committee and all attendees and gave an overview of the priorities of the office of research and development. She also outlined effects that SARS-COV-2 has had on VA researchers, including a pause on non-critical in person research visits and new research initiatives. Dr. Dan Roden, Chair, welcomed the committee and members of the public and VA to the meeting, which consisted of general Million Veteran Program (MVP) updates, an overview of a new mental health cohort, update on an MVP return of results pilot project, and a summary of a newly formed subcommittee on VA genomics services and genetic counseling.

Dr. Mike Gaziano of the Boston VA Medical Center and Co-Principle Investigator (PI) of MVP discussed the enrollment progress since the last meeting. MVP enrollment is up to over 840,000 participants, with online enrollment well underway. In-person enrolment was paused in early March across the country due to the SARS-COV-2 pandemic. During this time, MVP staff are calling potential participants, answering questions, and directing them to the online portal. Dr. Gaziano also highlighted SARS-COV-2 specific efforts underway, including a new survey instrument and potential piloting of novel biospecimen collection to assess seroprevalence in MVP participants. Additionally, several rapid response projects and new protocol to use SARS-COV-2 data for core projects have been approved. The phenomics library will also be used as a platform for the new SARS-COV-2 projects.

Dr. Chris O'Donnell, Boston VA Medical Center and co-PI of MVP, gave the committee an update on the MVP data usage. He mentioned the increasing number of publications resulting from MVP data analyses. Ongoing and new analyses will be presented at the upcoming virtual MVP science meeting in September 2020, with an eye on an in-person event for 2021.

In the discussion following Dr. O'Donnell's presentation, he reiterated that plans for collaborations with other large data sets, like UK Biobank. Additionally, MVP has coordinated with NIH's ALL of US program on the SARS-COV-2 questionnaire to ensure considerable overlap in content for future collaborations. The MVP survey will be mailed out beginning on May 5, 2020.

Dr. Phil Tsao of the Palo Alto VA Medical Center and co-PI of MVP gave the committee an update on data generation from MVP biospecimens. There are over 810,000 blood samples been stored in the biorepository; 789,000 of those have had genotyping analysis and have undergone or are undergoing quality control analysis. As of this summer, 600,000 high quality genotypes will be available to approved researchers. Additionally, almost fifty thousand samples have been sent out for methylation analysis. MVP is using the Broad Institute's GATK pipeline for processing whole genome sequence data, with a current capacity of 10,000 samples per month. The goal for release of this data to researchers is early spring 2021. Dr. Tsao confirmed that there is a plan to integrate multi-omics within MVP.

Dr. Joel Gelernter of the West Haven VA Medical Center and Yale University described the new initiative known as MVP-MIND (Measures Investigating Neuropsychiatric Disorders) project, which will be the first targeted cohort collection utilizing the MVP backbone. He is collaborating with Dr. Murray Stein at the San Diego VA Medical Center as co-Principle Investigator. Until now, MVP enrollment has not focused recruitment efforts any specific populations or Veterans. While MVP is still accepting all Veterans regardless of health status, this MVP-MIND cohort collection will focus on Veterans with mental health and substance use conditions. The investigators plan to recruit at specialty VA clinics, including substance use clinics across the country with the goal of fifty thousand participants over the next five years. Increasing enrollment from these clinics will allow for well-powered genetic studies on less common psychiatric traits that impact Veterans. The pilot sites will be identified in the coming months, and the team is currently piloting a new mental health-specific survey instrument in West Haven. Future goals of the study include genome wide association studies targeting the pharmacogenetics of antipsychotic and anti-depressant drug responses, as well as collaborative efforts with other large cohorts like UK Biobank and the Psychiatric Genomics Consortium (PGC).

Following the presentation, the committee expressed enthusiasm for the targeted cohort, and recommended a Certificate of Confidentiality be maintained for this new cohort, as it is for MVP participants. The committee also raised concerns about the study's ambitious recruitment goals, but Dr. Gelernter and Stein's study team has had considerable experience recruiting in these clinics.

Dr. Jason Vassy of the Boston VA Medical Center described progress of the MVP return of results pilot in familial hypercholesteremia (ROAR-FH). FH is an excellent candidate for a return of results genetics study because it is common, has a significant impact on health, is currently underdiagnosed and is actionable. The objectives of this pilot study are to 1) develop process for re-contacting MVP participants for clinical confirmation of FH variants 2) promote effective treatment. The clinical test used to identify genetic variants for FH is from Invitae. Dr. Vassy described the primary clinical outcome as a 6 month change in Low density lipoprotein levels, and to date, nine people have completed the process from recontact to consent to genetic testing to counseling to reporting.

Following Dr. Vassy's presentation, the group raised questions about the how and when to hand off this information to the clinical side of VHA. They also queried which version of the genetic variants interpretations are being returned to participants, to which Dr. Vassy clarified that it is the ClinGen version. These interpretations will likely change over time, so MVP-ROAR participants are consented for future contact for updates. The committee also expressed concern for the implications to family members of tested and affected participants, including informing family members and the possibility of cascade testing. The committee recommended that the pilot continue with consideration for the possibility of remote blood collection and testing, and recommendation for cascade testing for family members.

Dr. Doug Ball from the Salt Lake VA Medical Center and co-chair of the GMPAC subcommittee on genomic services and genetic counseling in the VA, described the charge of the group and their progress to date. The subcommittee is made up of clinical geneticists, advanced practice RNs (APRNs), and certified genetic counselors. Genetic services in the VA provides care for those Veterans who need genetic testing now, anticipates the resources associated with an increase in genetic testing in the future. The subcommittee will focus their recommendations on three key areas, with metastatic prostate cancer testing and treatment as the use case. Dr. Ball described the current phased draft

recommendations for the larger committee as follows: 1) retain existing genetics specialists in the VA 2) fully engage existing providers 3) train medical oncologists and oncology APRNs to do some of the pre-test counseling.

Following with presentation by Dr. Ball, the parent committee made several recommendations to the subcommittee as they continue their work, including:

1. Include a genetic counseling intern and student model to increase the number of genetics professionals in the VA. The interns and students can help with things like pedigrees and data entry.
2. Highlight the use and effectiveness of telemedicine in genetic counseling services
3. Underscore the return on investment of genomics services and genetic counseling in the VA

Following the presentation, there was a public comments session, and Dr. Sam Shekar asked what the VA clinical genetic services model looks like compared to other large hospital systems like Kaiser, and suggested the subcommittee look at those companies' best practices. There were no other public comments.

The virtual meeting adjourned at 3pm.

Dan Roden

Dr. Dan Roden, Chair GMPAC

6/8/2020

Date

Jennifer Moser

Jennifer Moser, DFO GMPAC

6.8.2020

Date