MVP INSIDER

A newsletter for Million Veteran Program partners

Issue 9 | Summer 2021

THANK YOU TO MVP PARTNERS

Since the Revolutionary War, the U.S. military has used pins to promote a sense of unity amongst its members and to recognize distinguished service and acts of bravery. As a token of our deep appreciation for the commitment of MVP partners, and to recognize your continued acts of service, **we have included an MVP partner lapel pin in this newsletter mailing.**

As we celebrate 10 years of MVP together and strive towards that 1 million participants goal, please wear your MVP partner pin with pride, knowing that you are helping to advance research that will improve health for future generations of Americans.

If you haven't already, please be sure to fill out the MVP surveys, as they can offer researchers information your medical records can't capture. You can call to request them by mail or you can go to **mvp.va.gov** to complete them online.

Thank you for partnering with MVP and sharing the great research that you make possible.

Recently Published MVP Research Made Possible Thanks to You

"When Veterans become MVP partners, they are joining an effort to advance scientific understanding of the genetic roots of many conditions and diseases," said Jennifer Huffman, Senior Research Scientist, VA Boston Healthcare System. "MVP puts priority focus on studying illnesses that are more commonly experienced by Veterans, like tinnitus, which can occur after exposure to live fire." This year, MVP researchers published findings on how genetic variants might link to a broad variety of conditions including breast cancer, peripheral artery disease, and schizophrenia. MVP has also published findings on COVID-19 and joined an ongoing global collaborative research effort to advance understanding of the virus.

Read more about published MVP research on page 7. For a list of current MVP publications, visit Science Corner at mvp.va.gov

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For more MVP stories, visit us online at mvp.va.gov.

We want to hear from you!
If you have an MVP story to share, please contact us at askMVP@va.gov or **866-441-6075**.

MVP LEADERS REFLECT ON THE PROGRAM'S TENTH ANNIVERSARY

Dr. Sumitra Muralidhar, Ph.D., Director of MVP and Dr. Michael Gaziano, M.D., M.P.H., MVP's Principal Investigator, share their thoughts on the MVP journey over the past decade.

Q What makes you proud about your work at MVP?

A When Veterans sign up with MVP, they are signing up to help the future generations of Veterans. I'm proud of many things about MVP, but most of all, I'm proud of the people. Every single person who is involved in the program truly believes in MVP's mission. That makes me proud.

I'm proud of the legacy we continue to build together.

MVP has offered an opportunity for us to be transformative with our research and what comes of it. Not only are we on the cutting edge of great science that will transform the way we think about the structure of disease and help us develop new therapies, but also the extent to which we can help Veterans has been inspiring.

Q Tell me about an important innovation within MVP.

A MVP Online is an important innovation, and we haven't yet fully realized its potential. For years, MVP has been a success thanks to face-to-face interactions between Veterans and staff. But if we want to reach *all* Veterans – including those in rural areas, and those in places without a nearby MVP site – we have to take MVP to the Veteran, instead of asking the Veteran to come to us.

We will soon launch one of the world's largest genomic analyses on the country's biggest computer: Summit. Summit will hold all of our data on genes and disease – including several thousand diseases and traits MVP Veterans have, as well as tens of millions of gene variations. While this kind of work has been done before, it's never been done at this scale. I'm excited to make the data available to VA Investigators.

Q Where do you see MVP ten years from now?

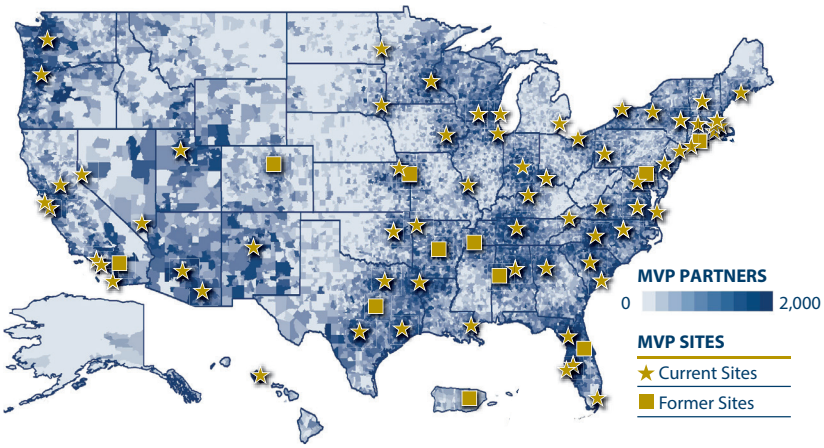
A In ten years, I would want to see MVP fully integrated into healthcare delivery, serving as a platform to expedite biomedical discovery, and turning these discoveries into improved healthcare for our Veterans and all people.

In the future, when a Veteran visits a VA doctor, that doctor will have information not only about their health and health history, but also their genetic profile, lifestyle, military exposure, and more. Providers will be able to tell patients what drugs they will best respond to, and what illnesses they are at risk for. I see MVP driving and advancing precision medicine for Veterans. That is my dream for the future.

MVP is not just a cohort, it's a platform for innovation. Over the next decade, I want to continue to grow our recruitment online, develop new areas to study, and make our data available to researchers for the next round of innovative science. I want MVP to conduct cutting-edge research, and then have that research bleed back to inform patient care.

For the full interview, please visit us online at mvp.va.gov.

MVP PARTNER & SITE LOCATIONS



"THANK YOU" TO OUR MVPs

TIMOTHY O'LEARY, M.D., PH.D. is an MVP Veteran partner and served as Chief Research and Development Officer at the Department of Veterans Affairs. During his tenure, he was instrumental in creating and growing MVP into one of the largest genetic research programs in the world.

I've heard your reasons expressed in many ways: "I'm doing it for tomorrow's Veterans"; "I'm doing it for my children and grandchildren"; "I'm doing it for other Veterans."

You joined the Million Veteran Program (MVP) to serve again, as research participants, without compensation or reward. This generosity sets you apart. For you, duty to country extends far beyond the battlefield and into the research lab.

You are from every race, creed, and color. Some of you grew up rich, some poor. Some are liberal and some conservative. But each of you shares a love of country and a deep respect for anyone who bears that proud title of "Veteran."

The truth is, diversity is not a "nice to have," but a "need to have" for MVP. To reach our full potential, we need to reflect the diversity that we see in the men and women who have served.

"The truth is diversity is not a 'nice to have' but a 'need to have.' "

With your data, we've built the largest database in the world of genetic and health information that researchers around the globe are using to unlock the mysteries of our genes and how they relate to our lives and military exposures.

With this new knowledge, physicians can finally prescribe treatments that work. Veterans who inherited high cholesterol and feared early-onset heart disease now see a brighter, more vibrant future, thanks to you, and the research you made possible.

I have been fortunate to be a part of MVP since it was first conceived.

I've seen the enthusiastic support from every subsequent VA Secretary, Deputy Secretary, and Under Secretary for Health to weave this program into the fabric of VA health care, and to create a research infrastructure to support MVP – but more importantly MVPs (most valuable partners).

I have been fortunate to have a role in building this program, but even more fortunate to be a participant.

It is good to be "one in a million." Thank you for your service, both in uniform and as an MVP.

94-YEAR OLD MVP VETERAN PITCHES IN DURING PANDEMIC

"We have to work together if we ever want to get control of COVID-19," said 94-year old Navy Veteran and Million Veteran Program partner James Nayes in a letter to Dr. Michael Gaziano, MVP Principal Investigator, last year. He added, "I have been sewing face masks, thousands so far."

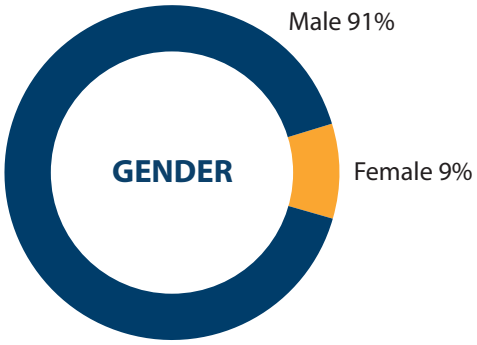
"Before she passed away six years ago, my wife was a Home Economics teacher," he said, "so, I had a good sewing machine." Nayes and friends convened to form a mask assembly line, being sure to stay six feet apart from each other for protection. The group produced thousands of masks for local distribution.

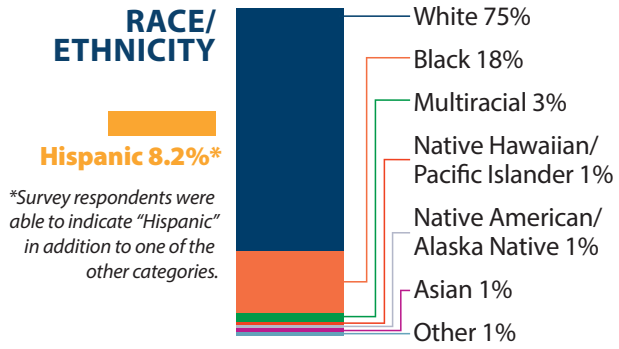
Helping out during a national crisis was important to Nayes, whose two-year enlistment in the U.S. Navy in the 1940s included accompanying Admiral Byrd's fourth expedition to the South Pole.

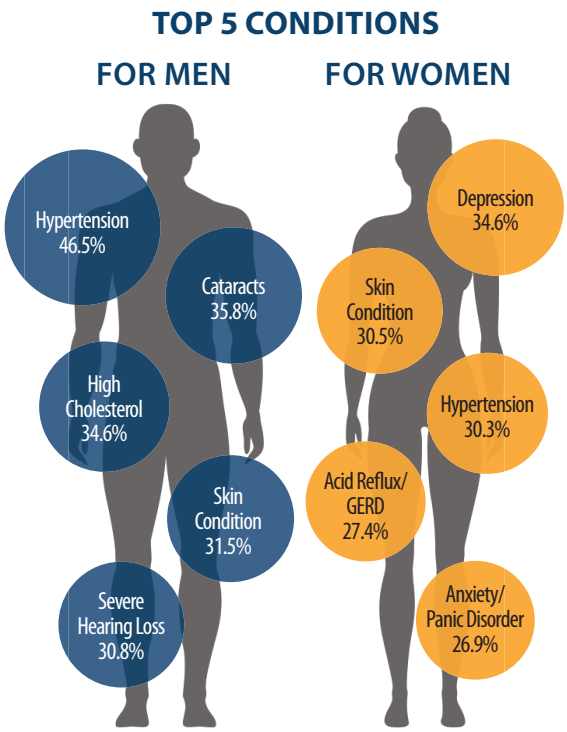
In 2013, when he was at the Clement J. Zablocki VA Medical Center, Milwaukee, WI to meet with doctors, Nayes was introduced to MVP by local site staff and signed up as "a way to help Veterans."

"It's heartening to see Veterans of all ages pitch in to fight the spread of COVID-19," said Dr. Gaziano. "And by joining MVP, Mr. Nayes has ensured that he will continue to make a difference in the lives of Veterans for generations to come."

WHO'S IN MVP?







The Drive to Diversify the Million Veteran Program

SINCE ITS LAUNCH A DECADE AGO, MVP has focused on building a diverse group of Veteran partners – and with that a varied set of genetic and health data to offer insight into all people's health. Today, MVP Veteran partners roughly mirror the demographic of Veterans who use the VA (75% White, 18% Black, 8% Hispanic, and 1-2% Native American and Asian).

But MVP is eager to include more Veterans in the program and grow its diversity.

Shakeria Cohen, American Association for the Advancement of Science (AAAS) Fellow at MVP, said, "Historically, a lot of research has been based on studies of individuals of European descent, and we just don't have as much information about minority populations. For instance, while we know that triple-negative breast cancer prevalence and mortality is higher in African-American women than in White women, we don't know exactly why that is. Is there a genetic marker for that disease? This is the kind of question we want to answer within MVP."

MVP's Outreach to Women

In March – Women's History Month – MVP launched a campaign to increase the number of women enrolled in the program.

"We are encouraging women Veterans to help other women Veterans by enrolling as an MVP partner," said Jennifer Deen, Associate Director of Cohort and Public Relations at MVP. "With more women in the cohort, we can do impactful research that addresses women's specific health needs."

The campaign to recruit women has yielded promising results. In March alone, MVP recruited more women than men into the program for the first time in its ten-year history.

GENETICS EXPLAINED

GENETICS ALONE CAN'T DETERMINE a person's risk of disease – environment plays a role too. "The air we breathe, the food we eat, the exercise we do – these also impact our risk," said Dr. Phil Tsao, MVP Co-Principal Investigator.

Ethnic-Focused DNA Chip

"While the technology exists to map an individual's genome, doing so would be expensive and highly labor-intensive. Instead, scientists study a DNA micro-array – or a DNA chip – which is like the CliffsNotes version of your genome," Dr. Tsao added.

MVP has developed an ethnic-focused DNA chip that is enriched to test for 300,000 genetic variants more common in minority populations. "It's really about getting better tools in order to promote understanding of populations that are under-represented in research," said Dr. Jennifer Moser, Ph.D., Associate Director of MVP Scientific Programs.

Scientists hope the ethnic-focused DNA chip will help advance understanding of conditions like heart disease and diabetes, which are more common in African-Americans than European-Americans.

How Proteomics and Metabolomics Enrich the Study of Genetics

"By studying genes we are looking at an architectural plan for a human being," Dr. Tsao said. "By studying proteomics and metabolomics – the proteins and small molecules within a cell – we are looking at how environmental factors impact that plan."

"By studying genomics, proteomics, and metabolomics, MVP scientists are continuing to add to a broader understanding of diseases, and how to prevent and treat them," Dr. Moser said. "I hope that in the coming years, we can teach doctors and healthcare providers how to implement this knowledge so that it has a real-life impact on Veteran patients."

MVP's INNOVATION & RESILIENCE DURING THE PANDEMIC

THE PANDEMIC CREATED OPPORTUNITIES FOR MVP to do new, important work. MVP encouraged Veterans to enroll online instead of in-person and asked MVP partners to participate in a new activity: the COVID-19 survey.

"We knew it was especially important during that difficult time to foster a sense of community among our staff and Veteran partners and to innovate new ways to fulfill our mission," said Jessica Brewer, M.P.H., Director of MVP Recruitment and Enrollment. The COVID-19 survey calls enabled MVP staff to help Veterans in unexpected ways. "Often, there were services the Veteran needed that MVP staff could connect them to, like caregiver support or benefits information," Brewer said. "In many cases, the phone calls became bright spots in an otherwise challenging time for both MVP staff and Veterans."

Participation in the COVID-19 survey was strong, with over 250,000 Veterans responding to email, direct mail, and phone call solicitations from MVP.

Collecting blood samples from online enrollees and for COVID-19 research during a pandemic spurred new challenges. "We'd been planning for years to adopt new ways to collect blood samples from Veterans who could not get to MVP offices," Brewer said. MVP piloted two new ways for Veterans to take their own blood specimens from home. "Our experience during the pandemic has given us important data for scaling up blood sample collection options in the future to provide more ways for Veterans to contribute to MVP research."

"In high-pressure situations like what we faced in 2020, a team either falls apart – or it grows; MVP grew to new heights." Brewer said.

MVP Research Advances Understanding of COVID-19

"LAST YEAR WE IDENTIFIED AN URGENT NEED to find drugs to treat people in the early stages of COVID-19," said Dr. J.P. Casas, M.D., Ph.D., Executive Director of MVP. "We wanted to identify drugs that, given early in a patient's infection, could keep that patient from severe illness."

"The fastest way to detect effective treatments and get those treatments to patients is to repurpose medicines that are already in clinical use," Dr. Casas said. "Human genetics can serve as an instrument to help us infer whether certain drugs might be effective for other uses."

"We learned that drugs targeting two genes, IFNAR2 and ACE2, could be effective for early management in COVID-19 patients. Drugs targeting IFNAR2, known as Type-I interferons, are now being tested in clinical trials for early management of COVID-19," said Dr. Casas. "Drugs targeting ACE2 were being tested in clinical trials pre-pandemic in patients with severe respiratory disorders. There are multiple medications that modulate ACE2 and some of those medications are now being tested in phase two clinical trials for treating COVID-19," he added.

MVP and the Ongoing Battle Against COVID-19

"MVP will continue to collect self-reported data from MVP partners," Dr. Stacey Whitbourne, Ph.D., MVP Director of Cohort Management, said. "Researchers are just beginning to understand the longer-term effects of COVID-19, and we believe we can help grow their knowledge," Dr. Whitbourne added.

"We are thankful to the Veterans who continually respond to our requests for help in terms of research," Dr. Casas said. "Their payback will be in knowing that they've made significant contributions to the scientific community, to other Veterans, and to the public."

MVP-MEASURES INVESTIGATING NEUROPSYCHIATRIC DISORDERS (MVP-MIND)

"BY ASSESSING A FULL RANGE OF PSYCHIATRIC TRAITS and behaviors, we hope to create a better picture of Veterans' mental health," said Dr. Joel Gelernter, M.D., Director of the Laboratory of Psychiatric Genetics at VA Connecticut Healthcare System. Dr. Gelernter is describing MVP-MIND, a new MVP study set to pilot in late 2021.

Dr. Kelly Harrington, Ph.D., MVP-MIND Director, said, "We determined that while MVP was doing a good job identifying risk factors for the most common mental health conditions experienced by Veterans – including posttraumatic stress disorder (PTSD), alcohol use disorder, and depression – we didn't know as much about less common disorders that impact Veterans, including schizophrenia, bipolar disorder, opioid use disorder, and obsessive-compulsive disorder (OCD)."

How MVP-MIND Can Help Veterans

MVP-MIND is poised to advance knowledge of conditions that are common among Veterans, like depression, anxiety, and PTSD.

Dr. Murray Stein, M.D., Staff Psychiatrist at VA San Diego Healthcare System, said, "MVP-MIND will offer a very detailed, comprehensive assessment of PTSD, including questions around different kinds of trauma – both military and non-military."

"I'm hopeful that we can uncover existing medications that can be re-purposed to treat mental illness," Dr. Stein added. "Prazosin, which treats hypertension, is also now used to treat symptoms of PTSD, like nightmares and sleep problems. More discoveries like that will lead to better treatments for Veterans with PTSD."

How Veterans Can Help

Eligible Veterans will be invited to participate in MVP-MIND.

Dr. Stacey Whitbourne, Ph.D., MVP Director of Cohort Management, said, "By participating in the MVP-MIND survey, Veterans will be contributing vital information that will allow the VA and researchers to examine the genetic and environmental factors that contribute to mental health conditions."

MVP DATA HELPS VETERANS LEAD HEALTHIER LIVES

Understanding PTSD

"ANALYSIS OF 250,000 VETERANS with posttraumatic stress disorder (PTSD) revealed a number of genetic variants that are more common among people with PTSD," said Dr. Murray Stein, M.D., Staff Psychiatrist at VA San Diego Healthcare System. Findings from the study, the largest effort of its kind, were published in *Nature Genetics* in January 2021.

"We were able to make predictions about the effectiveness of some drugs currently being studied and pointed to other classes of drugs that could be useful to people with PTSD," said Dr. Joel Gelernter, Director of the Laboratory of Psychiatric Genetics at VA Connecticut Healthcare System.

"The data are advancing scientific understanding of many conditions experienced by Veterans," Dr. Gelernter said. "I believe they will have a positive, near-term impact for Veterans as well as many long-term positive impacts for generations to come."

Predicting Patterns of Smoking Behavior

"Smoking is the single greatest preventable health risk to the population at large – and it is especially common among Veterans," said Dr. Ke Xu, Staff Psychiatrist at VA Connecticut Healthcare System. "In our most recent study (published in *Nature Communications*, October 2020) we learned that certain genetic variants are more common among persistent smokers than those who smoke only occasionally, and those who smoke and quit."

Dr. Henry Kranzler, Staff Physician at Michael J. Crescenz VAMC in Philadelphia, said, "The nearest-term impact of this work will be through the development of polygenic risk scores, which are a cumulative measure of the genetic risk for a specific condition. We hope to use genetic data to predict risk for persistent smoking."

"If a patient's genetic profile indicates they are at risk for persistent smoking behavior, a health care provider could proactively inform and educate the patient of their risk, and encourage multiple routes to treatment," said Dr. Amy Justice, Staff Physician at VA Connecticut Healthcare System.

Measuring Suicide Risk

How do we use data to help drive care? That is the question behind the MVP Suicide Exemplar project, currently being conducted in partnership with the U.S. Department of Energy. Project researchers are performing sophisticated data analyses with a mission to reduce suicide risk among Veterans. Dr. Nathan Kimbrel, M.D., Co-Director of the Clinical Core for VA Mid-Atlantic Mental Illness, Research, Education, and Clinical Center (MIRECC), said, "Suicide is remarkably challenging to predict and prevent; however, by using advanced computer science to analyze the VA's 22 million electronic health records along with genetic data from more than 840,000 MVP partners, we believe that we can make real advances in the scientific understanding of suicide and how to prevent it."

Dr. Jean Beckham, VA CSR&D Senior Research Career Scientist, said, "The Department of Energy brings new perspectives to our data, as well as cutting-edge statistical modeling to help us make use of a large amount of information." "While an algorithm currently used by the VA on patient data identifies Veterans at imminent risk, the hope is to make that model much more precise," Dr. Dave Oslin, Chief of Behavioral Health, Michael J. Crescenz VAMC in Philadelphia, said. He added, "We hope to be able to identify very accurately who is at risk and then to develop interventions that would be effective in changing that risk profile."

Go to mvp.va.gov to read more about MVP-published research.

Million Veteran Program
Department of Veterans Affairs
Million Veteran Program
PO Box 6378
Chicago, IL 60680-9919

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