



Air Force Sequencing Study to Inform Broader Genomic Medicine Implementation Among Service Members

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NEW YORK (GenomeWeb) – Anticipating a future where genomically informed care is broadly available in the military, the US Air Force is studying the impact of incorporating data from exome sequencing into its service members' medical records.

The Air Force and the US Department of Defense "want to be right up on the cutting edge as our society hopefully moves toward personalized and precision medicine," said Robert Green, a professor of medicine at Harvard Medical School who is co-leading the study called MilSeq.

The pilot study is an initial step toward broader implementation of genomic medicine in the Air Force. "The main reason we're doing this project is because we have a lot of questions about how best to integrate medical genetics into military medicine," said Capt. Mauricio De Castro, a co-investigator on MilSeq and associate director for the Air Force's Medical Genetics Center. "We hope that this study is going to be one of the pieces that helps us answer those [questions] so we can provide excellent care to our service members."

The two-year study involves a number of institutions within the Air Force, Brigham and Women's Hospital, Harvard Medical School, VA Boston Healthcare System, Baylor College of Medicine, Case Western Reserve University, Ohio State University, Partners Personalized Medicine, and the Broad Institute.

MilSeq will enroll 75 healthy, active-duty Air Force service members at Lackland Air Force Base in San Antonio, Texas, who consent to having their exomes sequenced. The study will also recruit 15 active duty healthcare providers in primary care, internal medicine, and family practice.

"We're not really trying to gather large-scale data here," said Green. The aim of MilSeq is to explore the process of presenting genomic information to providers and airmen, what they think of the consent process, why service members declined to participate, and if those reasons mirror civilians who decline to participate in genomics research.

MilSeq is a study within the Genomes2People Research Program, which Green directs. In these studies, Green and his team have been exploring the medical, behavioral, and economic impact of genetic risk information in various contexts.

Within MilSeq, doctors will receive an educational primer in genomics and on-site genetic counseling support. After exome testing is performed on patients, their doctors will get a report listing the pathogenic and likely pathogenic variants related to dominant and recessive monogenic conditions, risks for complex diseases, and response to drugs. These results will be entered into the service members' electronic medical record.

Afterwards, researchers will track how well doctors understood the genomic information and assessed their patients based on test results. They will also evaluate whether having this information in the active service members' records influences their behavior, health, life style, and family members.

The study results will help inform the Air Force's efforts to bring exome sequencing in house by next year. Such testing is happening in the Air Force but in a limited fashion. De Castro has ordered exome sequencing for only a handful of patients, mostly for the children of service members who have a congenital disorder or developmental delay. But a few times he's ordered exome sequencing for adults with complex disorders with unknown etiology.

In these cases, the Air Force's external lab partners conduct exome sequencing. But according to De Castro, his team will use the samples collected within MilSeq to validate in-house exome sequencing methods. His hope is to eventually do all genetic testing in house.

In fact, the Air Force's Medical Genetics Center serves as the reference genetics lab for the entire DoD and already conducts a wide variety of tests in house, including prenatal screening, assessments for genetic diseases, and next-generation sequencing panels for determining cancer risks and treatment options. The geneticists at the center lend their expertise to doctors in diagnosing patients, and recently launched an effort to provide telegenetics services to personnel stationed in far flung places around the world.

The Air Force also has its own Personalized Medicine Program, which is the coordinating center for the various genomics-focused projects it is engaged in. For example, the Air Force [has been working](#) for several years with the Coriell Personalized Medicine Collaborative to genotype participants for disease risks and characterize treatment response. A year ago, more than 3,000 participants had enrolled in the study and the project [has a goal](#) of enrolling 6,500 participants by year end.

Similar to MilSeq, the broader aim of this project with Coriell is to explore how genomics research might be conducted within the military and how genetic information is relayed to study participants. According to Green, the military is in many ways a "superb place" for doing high-quality research.

Service members in the Air Force are ethnically diverse, have different educational backgrounds, and may be more inclined to volunteer for research because they're already dedicated to service. And the fact that their medical information is in the same electronic health records system gets around the interoperability issues that plague researchers in the civilian world. "You have the potential to do much more vertically and chronologically integrated research with a stable population," Green said.

But the military mindset is also starkly different from civilians who aren't in the service, and there are strict medical standards for certain jobs in the military. "There's a different perception of privacy in the military, because while it may not often be acted upon, military commanders do have some discretion to evaluate medical conditions in terms of operational readiness," said Green. This, he said, may contribute to a perception that having a genetic predisposition for a disease "may be used against you in ways that could really hurt your career."

Although the Genetic Information Non-discrimination Act protects civilians against genetic discrimination when it comes to health insurance and employment, the law doesn't extend to men and women serving in the military, who rely on the DoD for both healthcare and work. The military evaluates all recruits for certain conditions as part of the assessment for overall fitness for military service. Although having a genetic predisposition for a disease can't disqualify someone from service, showing symptoms of the disease at the time of enrollment can.

Before 2008, the DoD had a policy where any injury or disease discovered after the start of active duty was treated as if it was incurred in the line of duty and so the service member was entitled to a medical discharge and disability benefits. However, this policy excluded congenital and hereditary conditions, many of which have a known genetic cause.

However, the National Defense Authorization Act of 2008 ensured that if a service member develops a condition (genetic or otherwise) that requires discharge after at least six months of service, the DoD will pay benefits unless the "disability" or symptoms were present at enrollment. Extending this policy to MilSeq, where test results will end up in the service members' health records, means that any genetic risks for diseases identified through exome sequencing by themselves can't impact a service member's career.

However, once those results are entered into the medical record, it could lead to increased screening, which in turn could help identify symptoms that factor into determinations about job fitness. As such, there is a chance that some service members will shy away from MilSeq.

"If your dream is to fly a very expensive war plane, and you learn through sequencing that you're carrying a variant for sudden cardiac death, you might legitimately worry that somehow it might be used to disqualify you," said Green.

However, any symptoms identified via greater screening prompted by genetic testing would have to be "duty disruptive," explained Megan Maxwell, a genetic counselor project manager at Brigham and Women's Hospital, who is also in charge of operations and recruitment at Lackland for MilSeq. "Not everyone in the Air Force is a pilot," she said. "What might be important for fitness for duty for a pilot is not the same as what might be important for a recruiter who sits at a desk."

Certainly, in the civilian population, the fear of genetic discrimination is one of the main reasons individuals refuse participation in the studies ongoing under the Genomes2People umbrella, such as MedSeq and BabySeq. On the positive side, Genomes2People studies looking at the impact of direct-to-consumer genetic testing have found that customers of such services generally understood the limitations of the results, and weren't particularly distressed when results indicated they had a higher risk for diseases, like Alzheimer's or cancer.

In MilSeq, Green also isn't expecting the service members will be particularly distressed by their genetic test results. "These are brave people," he said. "But I do expect the possibility of different nuances, and a different perception of the value proposition. I expect potentially different reactions from providers who are not quite so embedded in systems where specialists are easy to get to."

So far, MilSeq recruitment has been strong and people haven't expressed fears about the misuse of genetic information as a reason for not participating, according to Maxwell. Already, around 30 service members have taken the baseline survey in MilSeq, which logs their attitudes and perceptions around genetic testing, and all of them have expressed interest in getting sequenced. Those who have declined participation, Maxwell said, seem to do so out of a general disinterest in joining a research project.

Still, looking at attitudes in the military about genetic discrimination is a critical component of the study, according to De Castro. While early uptake in MilSeq doesn't yet suggest service members have strong reservations in this regard, a minority — less than 10 percent — decline clinical testing citing worrying about discrimination or misuse of their genetic data, he estimated.

However, longitudinal assessments of patients who do go ahead with testing after learning about existing legal protections suggest to De Castro that the military's existing policies are working for the benefit of service members. "There hasn't been discrimination against those individuals, they're not getting kicked out, retrained, or medically boarded," he said. "They're able to take care of the disorder they have ... and they're able to do their job and fulfill their mission."

The military's evolving policies for carriers of a genetic trait for the inherited blood disorder known as sickle cell disease offers a positive example. In the 1960s and 1970s, after four recruits who had the sickle cell trait died during training at a moderate altitude, the Navy began screening all recruits for this trait and restricted the activities of carriers. However, after studies failed to turn up convincing evidence that merely having a trait increased the risk of death, the military no longer routinely screens for the trait, but does assess recruits for a personal history of haemoglobin disorders.

Moreover, today, when recruits are carriers, the military offers counseling so they know to "avoid exertional collapse by gradually increasing activity, maintain adequate hydration, ensure proper rest between workouts, avoid exercise while ill and avoid low-oxygen and increased-air-pressure environments," wrote Green and De Castro last year in a [paper](#) on the opportunities and challenges of integrating genomic medicine into the military.

Genomic information can be a "two-edged sword," Green said. "Used the wrong way you can imagine how they can be applied against service members, and that's a legitimate concern. But you can also imagine ways in which genetic predisposition information could be used to protect people in the military."

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