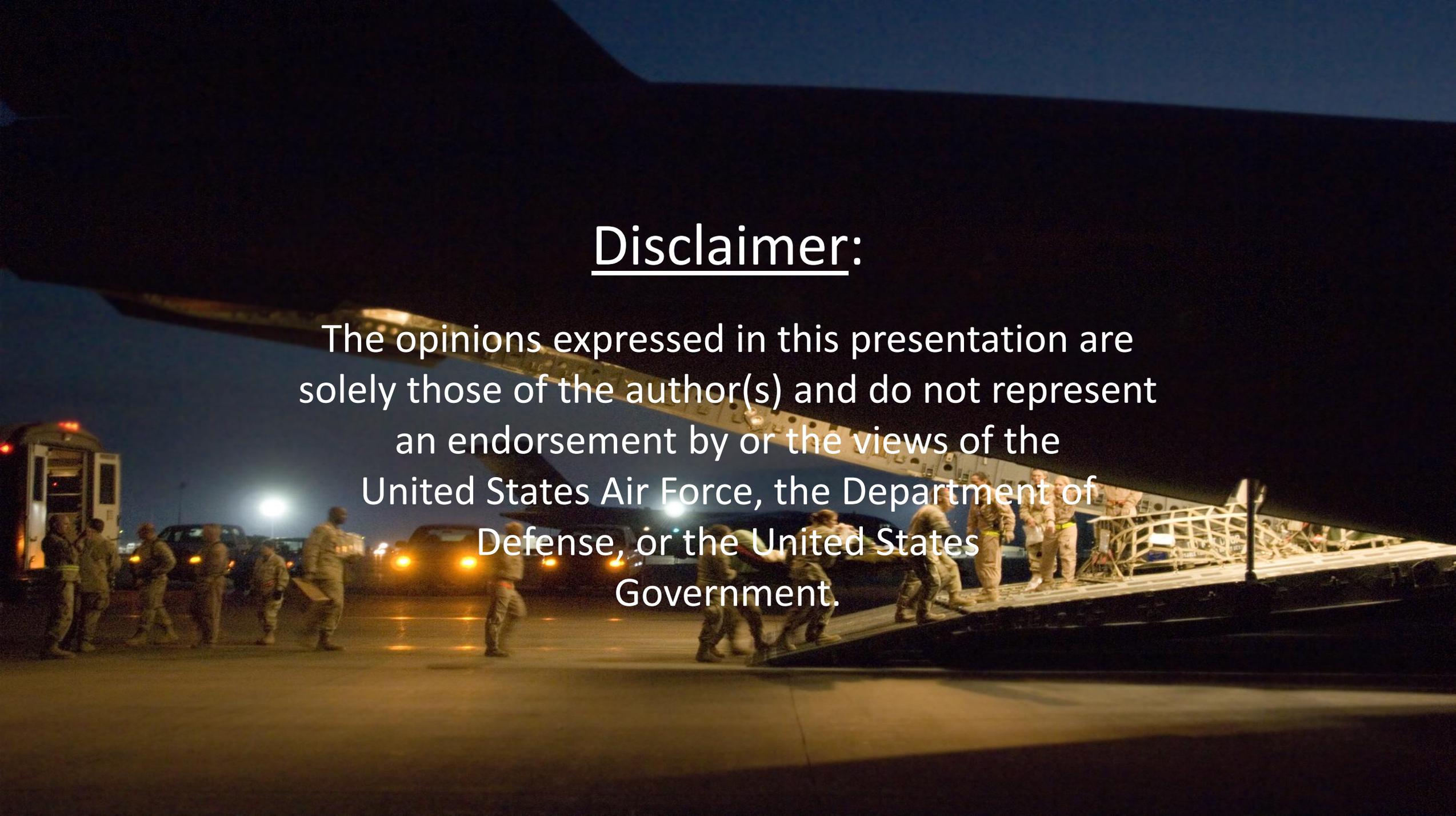




Joint Base San Antonio, Texas

Precision Medicine Research: Optimizing Warfighter Healthcare and Readiness

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Chief Scientist
59th Medical Wing
Wilford Hall, JBSA, TX
25 June 2020**

A large military aircraft, possibly a transport plane, is parked on a tarmac at night. The aircraft's cargo door is open, and a ramp is extended. Several ground crew members in flight suits are visible, some standing near the aircraft and others near a vehicle. The scene is illuminated by ground lights, creating a high-contrast environment against the dark sky.

Disclaimer:

The opinions expressed in this presentation are solely those of the author(s) and do not represent an endorsement by or the views of the United States Air Force, the Department of Defense, or the United States Government.

Introduction

Program Goal: Seek evidence to enhance utilization of genetics, genomics, pharmacogenomics, proteomics, and bioinformatics tools to optimize prevention, diagnosis, early intervention and treatment strategies in the Military Health System.

Panel members will describe studies in Disease Management, and the technologies used to provide evidence for the integration of personalized data into clinical decision-making, especially during the prevention and treatment of complex disorders to maintain health and improve healthcare outcomes.



Panel Members

- Carl Brinkley, Ph.D.
- Major Adam Willis, M.D.
- August Blackburn, Ph.D.
- Kumar Sharma, M.D.



Overview

- Military Relevance
- Strategic Priorities and Objectives
- Key Implementation Considerations
- Panel Member Presentations



Military Relevance



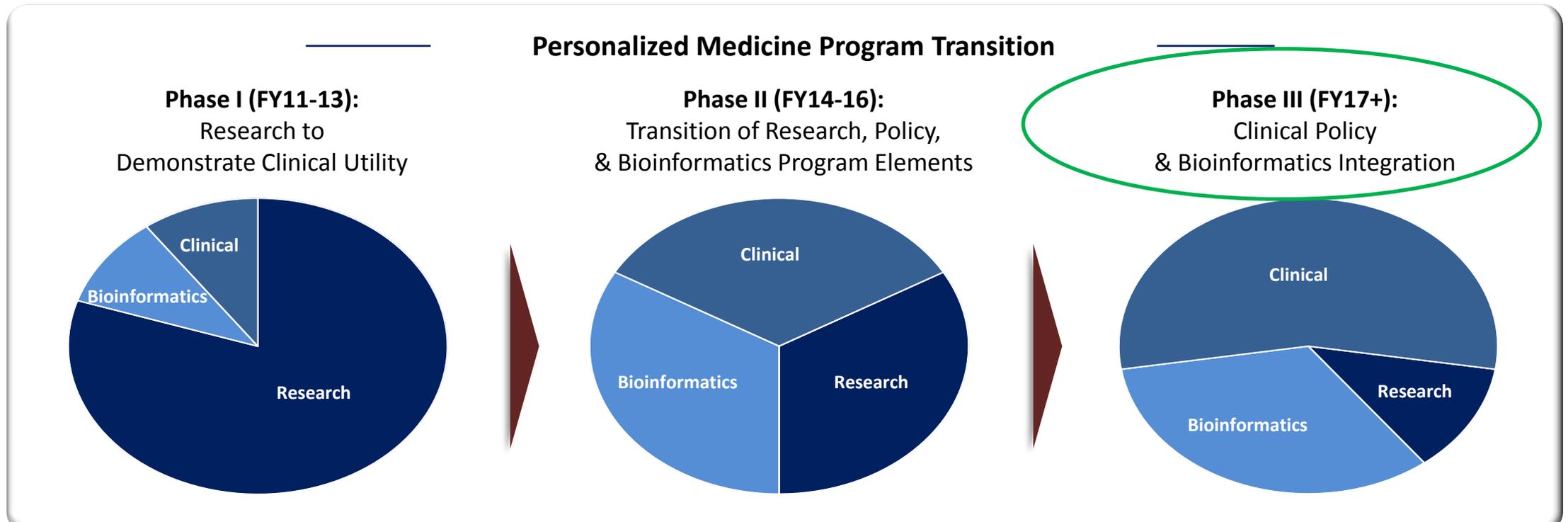
- **Sleep deprivation** costs U.S. economy as much as \$411B / 1.2M working days lost in productivity every year
 - Insomnia cases have quadrupled, and sleep apnea cases increased 5-fold in U.S. military over a decade
 - Sleep disorders six times more likely among U.S. military veterans than in the general population
- DoD spent \$294M and VA \$3B on **PTSD** care for service members and veterans
 - Veterans with PTSD (\$8.3K for 1st year of treatment), TBI (\$11.7K) or both (\$13.8K), cost the VA five times more to treat than those without PTSD or TBI (\$2.4K)
- In Military training, ~25-50% of trainees suffer **injuries**
 - ~\$23K to recruit and medically clear 1 trainee (MSK injury discharge cost)
- **Top Veteran disorders** include PTSD, Sleep Disorders, Substance Abuse, T2DM and MSK issues
 - 1st-year **PTSD** treatment for Iraq and Afghanistan veterans is \$2+B
 - \$350M on **substance use disorder** annually

A Service Strategic Priority

AFMS Vision—Trusted Care: “Our supported population is the healthiest and highest performing segment of the U.S. by 2025.”

AF Global Horizons Final Report: “The game changer for the Air Force is personalized health and performance.”

59MDW Vision: Developing Warrior Medics Through Patient-Centered Care.

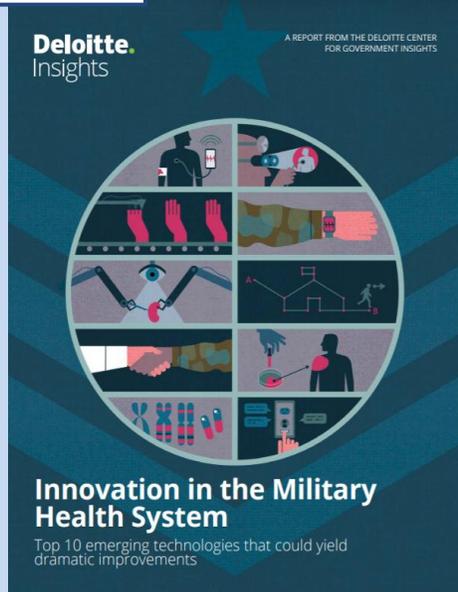


To facilitate the translation of genomic medicine research into efficient and effective healthcare

A DoD Medical Strategic Priority

“Precision Medicine... one of the top ten innovations most likely to promote the quadruple aim and drive innovation within the Military Health System”

- “Strategic Medical Research Plan,” (NDAA Fiscal Year 2019, Section 736; Public Law 115-232), "Strategic Medical Research Plan," 2019, Representative precision medicine programs.
 - DoD, and NHLBI applying precision medicine to tackle high-priority cardiovascular, pulmonary and sleep problems of relevance to military service members, retirees and family members
 - DoD Congressionally Directed Medical Research Program – Ovarian and Prostate Cancer, TBI
- Defense Health Agency Privacy Board Meetings include presentations and discussion about topics and articles related to privacy issues that impact operations and review procedures.
 - Updates from the Cancer Moonshot, Precision Medicine, and Global Genomic Data Sharing sessions held at the *Global Privacy Summit*
 - *Precision Medicine Initiative and Precision Care Advisory Panel (PCAP)* provides policy, scientific and operational recommendations on emerging topics in genomics, multi-omics, and precision medicine



Critical National and Local Resource

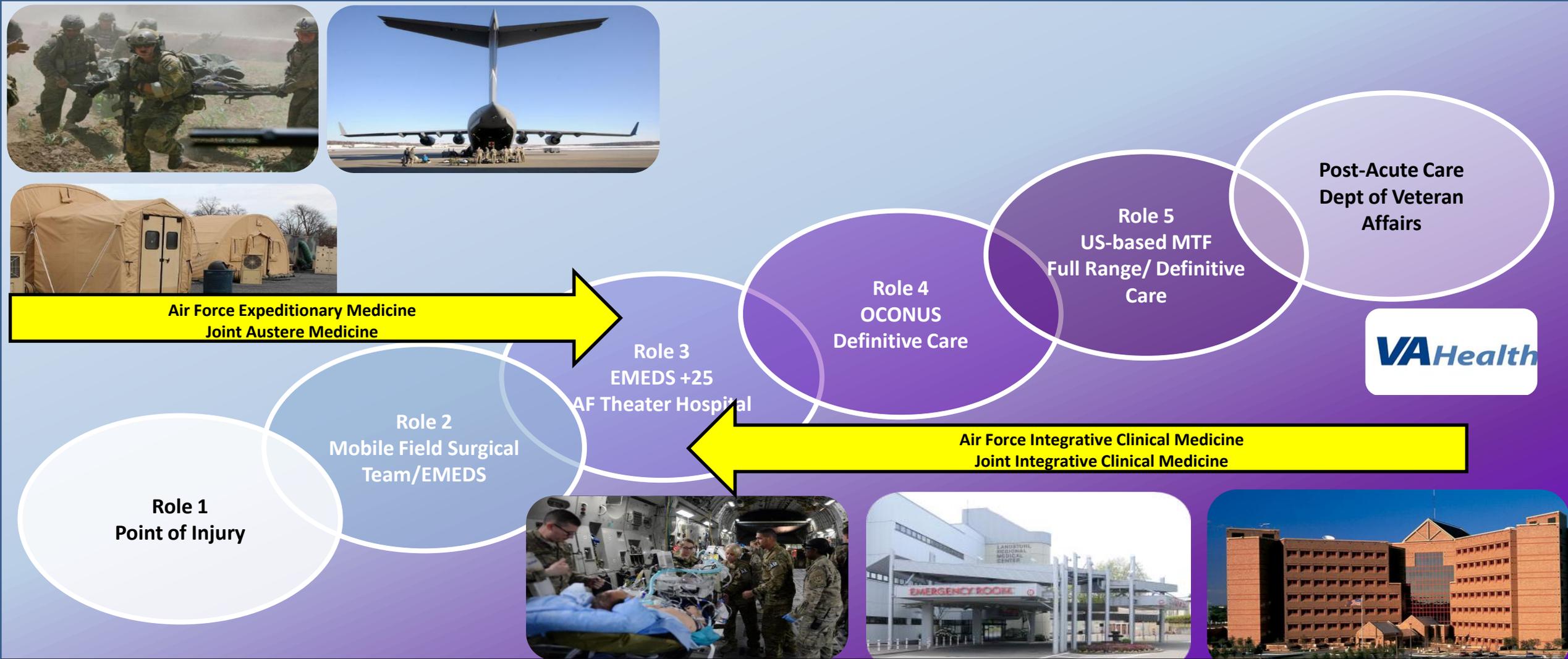


- **Strategic Asset**

- **History of Excellence in conducting Human Subjects and Animal Research**
- “Home of Military Medicine”—SA Chamber of Commerce assessed \$4B direct, \$1B indirect economic impact
- Joint Medical Readiness Training Platform
- 12 MTFs/\$1.2B Budget--12,000 staff/250,000 beneficiaries
- 37 GME programs--600 residents, 22 GHSE programs--78 residents
- Contingency/Humanitarian response -- Teams on call 24/7 and ~150 Service Members deployed
- Brooke Army Medical Center
 - DoD’s most productive inpatient facility
 - DoD’s only CONUS Level 1 Trauma Center
 - DoD’s only Bone Marrow Transplant Unit
 - DoD’s only Burn Center
- Wilford Hall Ambulatory Surgical Center and Clinics
 - DoD’s largest outpatient facility
 - DoD’s largest Blood Donor Center
- DoD’s largest centralized appointment/referral management system
- **Significant Medical Innovation, Research, Education and Training**



Theater of Operations ↔ Garrison Care



Performing Research and Providing Deliverables to Address AFMS and Joint Medical Priorities across the Continuum of Care



MilSeq Project: Enabling Personalized Medicine in the US Air Force through Whole Exome Sequencing



Megan D. Maxwell, MS, CGC¹, Jason L. Vassy, MD^{1,2,3}, Cubby L. Gardner, FNP-C, PhD Maj, USAF⁴, Carrie L. Blout, MS, CGC¹, Stacey Pereira, PhD⁵, Maxwell J. Mehlman, JD^{6,7}, Efthimios Parasidis, JD⁸, Kurt Christensen, PhD^{1,2}, Jill O. Robinson, MA⁹, Amy L. McGuire, JD, PhD⁸, Matthew Lebo, PhD^{2,9,10}, Mauricio De Castro, MD, FACMG, Capt, USAF¹¹, Ruth Brenner, MD, MPH, Lt Col, USAF¹², Brenda Morgan, PhD, Lt Col, USAF⁴, Robert C. Green, MD, MPH^{1,2,10,13}

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Purpose

The Genetic Information Nondiscrimination Act (GINA) of 2008 protects against health insurance and employment discrimination among civilians who undergo genomic sequencing (GS), but does not apply to active-duty military personnel. In its place, the Department of Defense (DoD) has distinct and robust protections against unlawful genetic discrimination for service members. With increased use of advanced GS in medical practice, we aim to explore a range of considerations unique to GS in the Air Force. In collaboration with United States Air Force (USAF), we have developed a pilot research protocol, the MilSeq Project, designed to explore procedures and outcomes associated with clinical whole exome sequencing (WES) of active-duty Airmen.

Methods

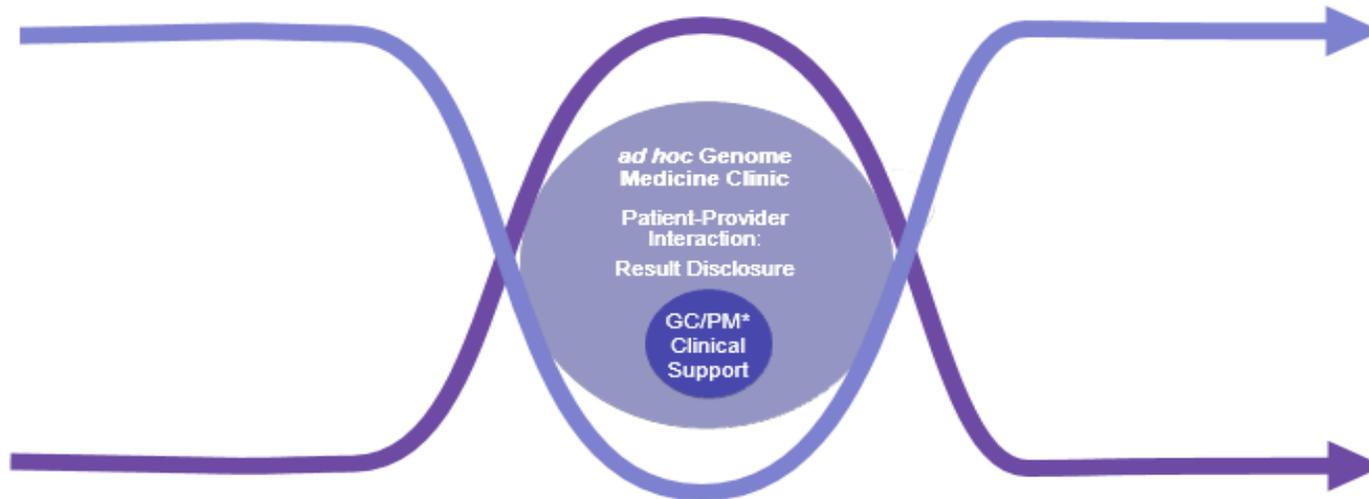
- Clinical WES on 75 ostensibly healthy, active-duty Airmen
- Monogenic pathogenic and likely pathogenic variants
- Autosomal recessive carrier status
- Pharmacogenomic (PGx) variants
- Disease-associated risk alleles
- Result disclosure by USAF healthcare providers
 - Genetic counselor-provided military-specific genomics training and clinical support
 - Permanent incorporation into Airmen's military medical record
- GINA, National Defense Authorization Act (NDAA), DoD and USAF Instructions, federal regulations, and basic human subject research rights examined to maximize safety of research protocol

Patient-Participants

- 75 ostensibly healthy, active-duty Airmen
- Clinical Whole Exome Sequencing (WES)
 - Monogenic pathogenic variants
 - Monogenic likely pathogenic variants
 - Autosomal recessive carrier status
 - Pharmacogenomic (PGx) variants
 - Disease-associated risk alleles

Provider-Participants

- 10-20 USAF healthcare providers
- Military-specific genomics training



Patient-Participants

- Permanent incorporation into medical record
- Downstream behavioral implications
 - Health and lifestyle changes

Provider-Participants

- Competence and accuracy assessment
- Downstream behavioral, medical, and economic implications
 - Practice changes and recommendations

*GC/PM – Genetic Counselor Project Manager

Precision Medicine

Objectives and Strategic Vision

- Optimize patient diagnosis, treatment and intervention through the use of genomics and pharmacogenomics
- Develop personalized (precision) diagnostic and risk mitigation methods

Near-Term (1+ yr)

- Develop a pharmacogenomics-driven predictive risk profile for the patient will result in improved management of chronic disease
- Develop evidence-based personalized treatment plans
- Personalized health assessment tools/methods



Mid-Term (3-7 yrs)

- Revised clinical care guidelines
- Genetic/Bio-markers (detection and treatment)
- Diagnostic/risk-mitigation tools and methods
- Expanded stem cell research



Far-Term (7+ yrs)

- More cost-effective and user-friendly precision-medicine tools that decrease analysis time
- Advances in disease/condition management (i.e. pharmaco-genetics; proteomic response; point of care testing)
- Gene-environment interactions for tailored treatments (First/unique gene-interaction analysis of disease associated gene markers)



On-going Program Implementation



- Continually *Watch* external research and *Leverage* technology
- Execute Research Specific to Military Medical Needs
- Translate Results into *Best Clinical Practice* and *Policy*
- Provide Education for and Support to Practitioners and Patients
- Ensure Relevance to the Military Operational community

Wartime Skills Sustainment Platform

Burn Center and Level I Trauma Center

- Both verified at highest National level
- Integrated Battlefield Health & Trauma Research
- Growing Research Education and Training Programs
- Support both Military and Civilian Fellowship training programs in Emergency Medicine, Trauma & Critical Care

PANEL PRESENTATIONS

“Drive innovations in patient care and readiness”

