

# Pioneering Military HIV Research

## RV144

10 Years of Progress

MHRP.WRAIR



## WRAIR PROTECTS YOUR SIX

Protecting your brain - the most important six inches on the battlefield

CENTER FOR MILITARY PSYCHIATRY AND NEUROSCIENCE



Blast Induced Neurotrauma and Neuroprotection



Sleep & Resilience



Team Performance and Mental Fitness



Military Psychiatry

Protecting the most important six microns between you and the threat of disease

CENTER FOR INFECTIOUS DISEASE RESEARCH

Vaccines & Entomology



Viral & Bacterial Diseases



Military HIV Research Program



Experimental Therapeutics & Emerging Infectious Diseases



## WHETHER YOU'RE AT HOME STATION OR SIX THOUSAND MILES AWAY

### WALTER REED ARMY INSTITUTE OF RESEARCH'S MISSION

Discover, design, and develop solutions for military relevant infectious disease and brain health threats through innovative research protecting and optimizing warfighter lethality.

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#### PROMOTED HASHTAGS

- #WRAIRProtectsYourSix
- #DefeatInfections #WorldHealth
- #OptimizeHumanPotential
- #ForgeTheFuture #SoldierHealth



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# PIONEERING MILITARY HIV RESEARCH

MRDC develops countermeasures for HIV. WRAIR leads these countermeasure development efforts in partnership with USAMMDA to deliver solutions to the field.

## HIV THREATENS GLOBAL HEALTH SECURITY

Exacerbates social and political instability in regions with high or increasing rates of infection

2019 marked 10 years since the announcement of results from the WRAIR-led RV144 “Thai Study,” the first vaccine clinical trial to show efficacy in preventing HIV infection.



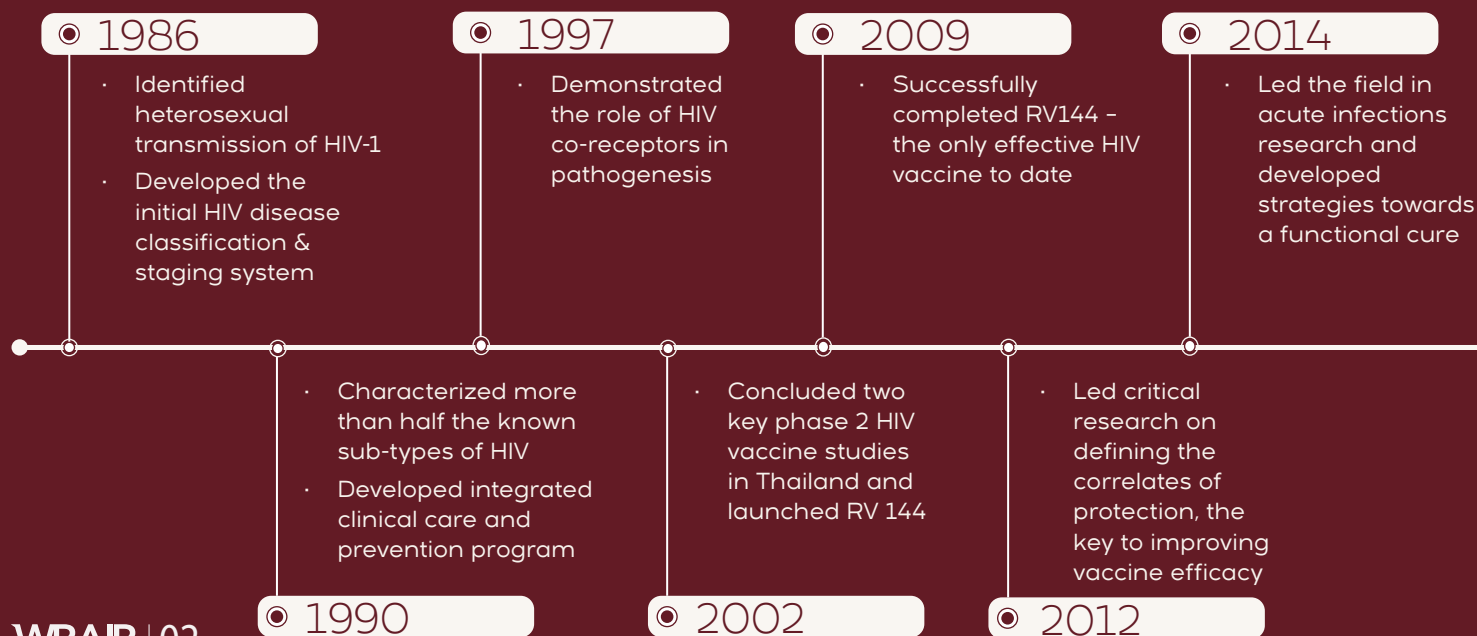
## BUILDING BIOPREPAREDNESS

- HIV research boosted WRAIR’s international network and capabilities, enabling the Institute to pivot to other emerging infectious diseases
- WRAIR’s implementation of PEPFAR ensures an ethical environment for research and serves as a cornerstone for meaningful military-to-military and cross-sector partnerships in Africa
- WRAIR was one of the first to build laboratory and clinical HIV research infrastructure and expertise throughout Africa and Asia with foundational HIV cohort studies in Thailand and East Africa and subsequent implementation of Phase 1 to 3 clinical trials

## RESPONSE TO HIV STRENGTHENS GLOBAL HEALTH SECURITY

- Strengthens mil-mil and interagency relationships
- Prevents, detects, and responds to outbreaks
- Strengthens partner country capacities
- Helps build biosafety infrastructure and biosecurity infrastructure
- Develops and improves national laboratory and surveillance systems
- Invests in human resource and workforce development
- Facilitates emerging infectious disease response operations

## LEADING THE BATTLE AGAINST HIV



## FORGING THE FUTURE



- WRAIR's Military HIV Research Program (MHRP) is a leader in international efforts to develop an HIV vaccine, find a cure and develop new diagnostics
- A safe, effective HIV vaccine is key to ending this epidemic that continues to kill nearly one million people a year
- MHRP has built a global reputation, influencing military policy and practices in addition to global health and research

## PEPFAR SUPPORTS ECONOMIC STABILITY AND DEVELOPMENT

The President's Emergency Plan for AIDS Relief (PEPFAR) is the largest commitment by any nation to address a single disease in history. It has saved more than 17 million lives and prevented millions of HIV infections.

Political instability and violence fell by **40%** in countries that received PEPFAR assistance versus only 3% in similar countries that did not.

- 2018 PEPFAR Annual Report to Congress

### PEPFAR INCREASES:

- Average life expectancy
- Ability to engage in labor
- Quality of life
- Children in school

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### 2017

- Next-gen HIV vaccine efficacy study begins, built upon early work WRAIR helped lead

### 2019

- Expanded HIV cohort studies into Kingdom of Jordan
- Published key findings into potential cure strategies
- Discovered potential new vaccine targets
- WRAIR's ALFQ vaccine adjuvant awarded a patent

### 2016

- Collaborated to launch an efficacy study that builds on RV144

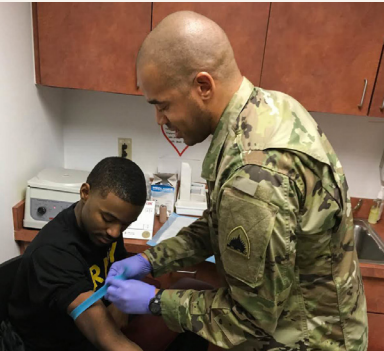
### 2018

- Informed DOD policy of use of PrEP as a prevention tool within DOD in high risk communities, which MHRP characterized



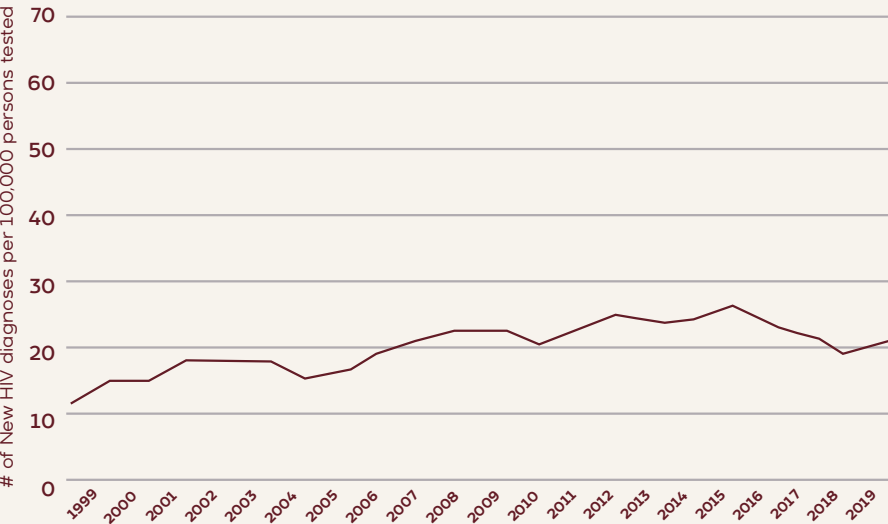
# FORCE READINESS AND MILITARY IMPACT

Although advances in science continue to mitigate the risk of HIV to Soldiers serving in the Armed Forces, exposure persists. The virus continues to threaten force readiness, force health protection and theater blood supply.



- HIV-infected Soldiers can face deployment limitations, compromising unit integrity and their ability to compete in the multi-domain environment.
- WRAIR’s MHRP’s threat assessment research informs policy development and public health practices to decrease the rates of HIV and other STIs in the military.
- WRAIR’s HIV Diagnostic and Reference Laboratory (HDRL) conducts state-of-art HIV screening and supplemental confirmatory testing, clinical and therapeutic monitoring services for U.S. military personnel.

## HIV RATES, U.S. ARMED FORCES, 1990-2019



## DOD NUMBERS

**~350**

NEW CASES OF HIV PER YEAR

**\$435,200**

ESTIMATED LIFETIME COST FOR TREATMENT PER PERSON

**\$150 MILLION**

ADDITIONAL FINANCIAL BURDEN TO THE DOD/VA ANNUALLY

## INFORMING POLICY WITH SCIENCE

<p><b>2009</b></p> <p>HIV diagnostic algorithm developed by WRAIR, adopted by U.S. CDC on July 2014</p>	<p><b>2012</b></p> <p>HIV pre-deployment data informed AR600-110 revision</p>	<p><b>2013</b></p> <p>HIV test requirement revised DODI 6485.01</p>
<p><b>2010</b></p> <p>Revised CENTCOM theater entrance policy for HIV pre-deployment screening</p>	<p><b>2018</b></p> <p>HIV Pre-exposure Prophylaxis (PrEP) DHA interim procedure memorandum published and PrEP toolkit released</p>	<p><b>2019</b></p> <p>DHA procedural instructions on HIV policy revised</p>



# HIV EPIDEMIOLOGY AND THREAT ASSESSMENT

Develop knowledge products to inform force policy and develop and implement strategies

- Recently identified at-risk groups since repeal of “Don’t Ask, Don’t Tell”
- Screening for hepatitis C makes walking blood bank safer and saves DOD money

## WRAIR’S DIAGNOSTICS

Accelerate and drive diagnostic research and product acquisitions

- Industry partnerships ensure DOD acquires the best products to support the Warfighter
- WRAIR’s MHRP conducted 61% of all pre-market applications for FDA approval for HIV assays
- Effective clinical monitoring for optimal patient care
- Key role in acute infections studies

## HIV DIAGNOSTICS TESTS FOR ACCESSION

WRAIR conducts all accession screening for entrance into the U.S. military.

- Ensures policy is informed by science (knowledge products)
- Protects blood supply from HIV and related diseases

### 27 Million

tests overseen by WRAIR’s HIV  
Diagnostics and Reference  
Laboratory between 1990-2017

### 23 Million

individuals tested with >7,000  
Soldiers identified as HIV positive



## EVALUATING PrEP IN THE MILITARY

In collaboration with the DHA HIV Tri-Service Working Group, WRAIR’s MHRP conducted an evaluation of PrEP in military populations and contributed to policy concerning its DOD rollout to ensure effective use of HIV Pre-exposure Prophylaxis (PrEP). The partnership:

- Ensures high clinical standards for HIV prevention and treatment
- Aligns clinical care policies and procedures across the military services and harmonizes administrative processes and procedures related to care of active duty Service Members with HIV infection
- Serves as the consultant laboratory for prescribing PrEP



# COMBATTING THE THREAT

## CHALLENGES GLOBALLY

- The development of antiretroviral treatments in the 1990s turned an HIV diagnosis from a death sentence into a chronic illness.

40%

of people who need HIV treatment get it

- Antiretroviral therapy (ART) is not a cure; the drugs only suppress the HIV virus to the point that it is undetectable in the blood.

30%

of new infections got it from others who did not know they had HIV

- If people stop taking their medicines, their HIV viral load rises again, which increases the risk of transmitting the virus and developing AIDS.


25%

of those living with HIV don't know their status

## ACCELERATING TOWARD ACHIEVING 90-90-90 & EPIDEMIC CONTROL

WRAIR supports the Joint United Nations Programme on HIV's 90-90-90 goal through PEPFAR. WRAIR's HIV research informs policy and diagnostics and clinical monitoring of HIV positive people.

90%  
of all



living with HIV will know their HIV status

90%  
of all



living with HIV will receive antiretroviral therapy

90%  
of all



receiving antiretroviral therapy will have viral suppression

## DOD SURPASSES TARGETS

Thanks to rigorous oversight, testing and threat assessment practices implemented largely through WRAIR, MRDC, and DHA, the DOD surpassed these targets well ahead of schedule.

1,050 NEW HIV  
DIAGNOSES  
BETWEEN  
01 JAN 2012 -  
31 DEC 2017

98.7%  
of all



living with HIV received antiretroviral therapy by 30 June 2018

96.8%  
of all



virally suppressed at last test in surveillance period

# TOWARDS A CURE

WRAIR's MHRP is testing innovative strategies for achieving long-term HIV remission, which is the control of HIV without the need for antiretroviral therapy - a functional cure through:

- Early ART, within days of infection
- Latency reversing agents
- Monoclonal antibodies
- Therapeutic vaccines

**MHRP initiated two innovative cohort studies in Thailand and East Africa, RV217 and RV254**



Thailand RV254  
East Africa RV217

We now can successfully identify HIV within days of infection

**RV217**  
Real-time screening of 320,404 samples

**RV254**  
155 acute infections observed

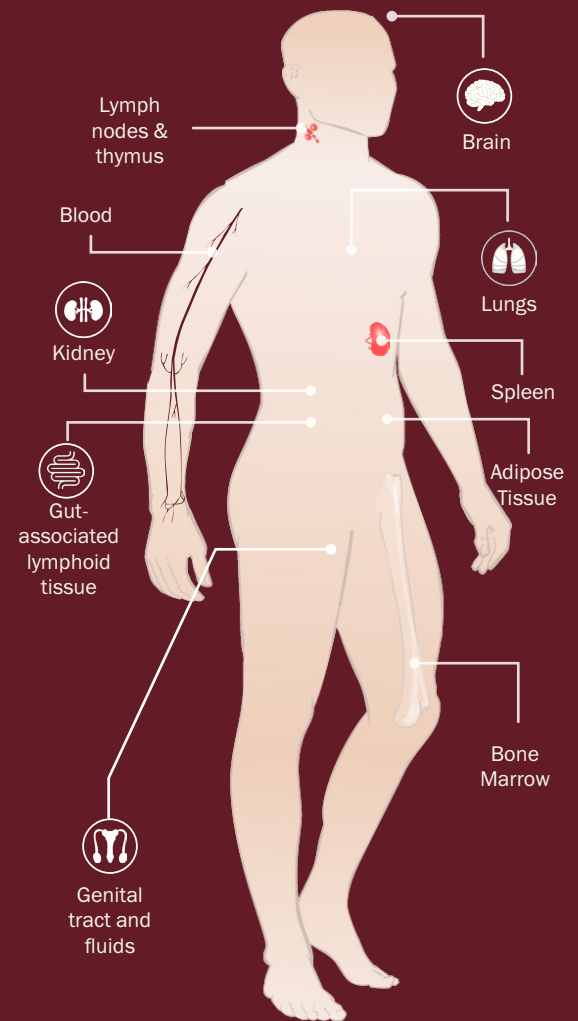
Allows WRAIR to conduct studies to test cure strategies

Resulted in an unprecedented collection of samples before and after infection, providing:

- Gold standard human data on very early infection
- Proof that disease progression is determined in the first month - weeks after infection
- Insights for an effective preventive vaccine and HIV cure interventions



## WHY IS HIV DIFFICULT TO CURE?



## BECAUSE IT HIDES IN THE BODY.

HIV incorporates itself into host cell DNA. ART can stop new viruses that might be produced from infecting new cells, but cannot eliminate the viral DNA from the host cell's genome.

Current research directions include finding a means to activate cells that are harboring viral DNA, forcing them "out into the open" where they can then be targeted by antiretroviral drugs. Researchers are also looking into ways of using genetic tools to delete viral DNA from the cell's DNA.

# VACCINE FOR PREVENTION

## Challenges

- Global genetic diversity of HIV
- Variability: HIV continues to evolve within infected individuals
- Lack of natural immunity to HIV
- HIV hides from our immune system

## Benefits



### 44% reduction in new infections

in the first 10 years, if a vaccine that stopped 70% of infections was introduced by 2027

### \$90 - 108M average savings

per year for the military in HIV-related treatment costs (ranges based on efficacy)

### \$2 billion in net savings

over 30 years for the DOD and VA by investing in a vaccine that protects against subtype B with at least 50% efficacy

## GLOBAL GENETIC DIVERSITY OF HIV SUBTYPES, A CHALLENGE FOR VACCINE DEVELOPMENT

### Americas

- B
- B, BF

### Europe

- B
- A mostly A6, CRF02\_AG/A, B
- A, B, F, B/F

■ Not Enough Data



## RV144

RV144 study results showed that a preventive HIV vaccine is possible, and the landmark trial continues to provide scientific direction to help guide vaccine development and testing. RV144 and its follow-on trials allowed researchers to:

- Discover correlates of risk
- Target optimal vaccine boost strategies
- Lay the foundation for HIV vaccine candidates currently undergoing efficacy testing

### AN AIDS VACCINE IS POSSIBLE

In 2003, RV144 HIV vaccine trial begins, involving many International partners and more than 16,000 volunteers from Thailand.



AFRIMS played a key role in the success of RV144

### 2009

U.S. Army/Thai MOPH led RV144

Thai study results announced

Year 1:  
**60.5% Efficacy**



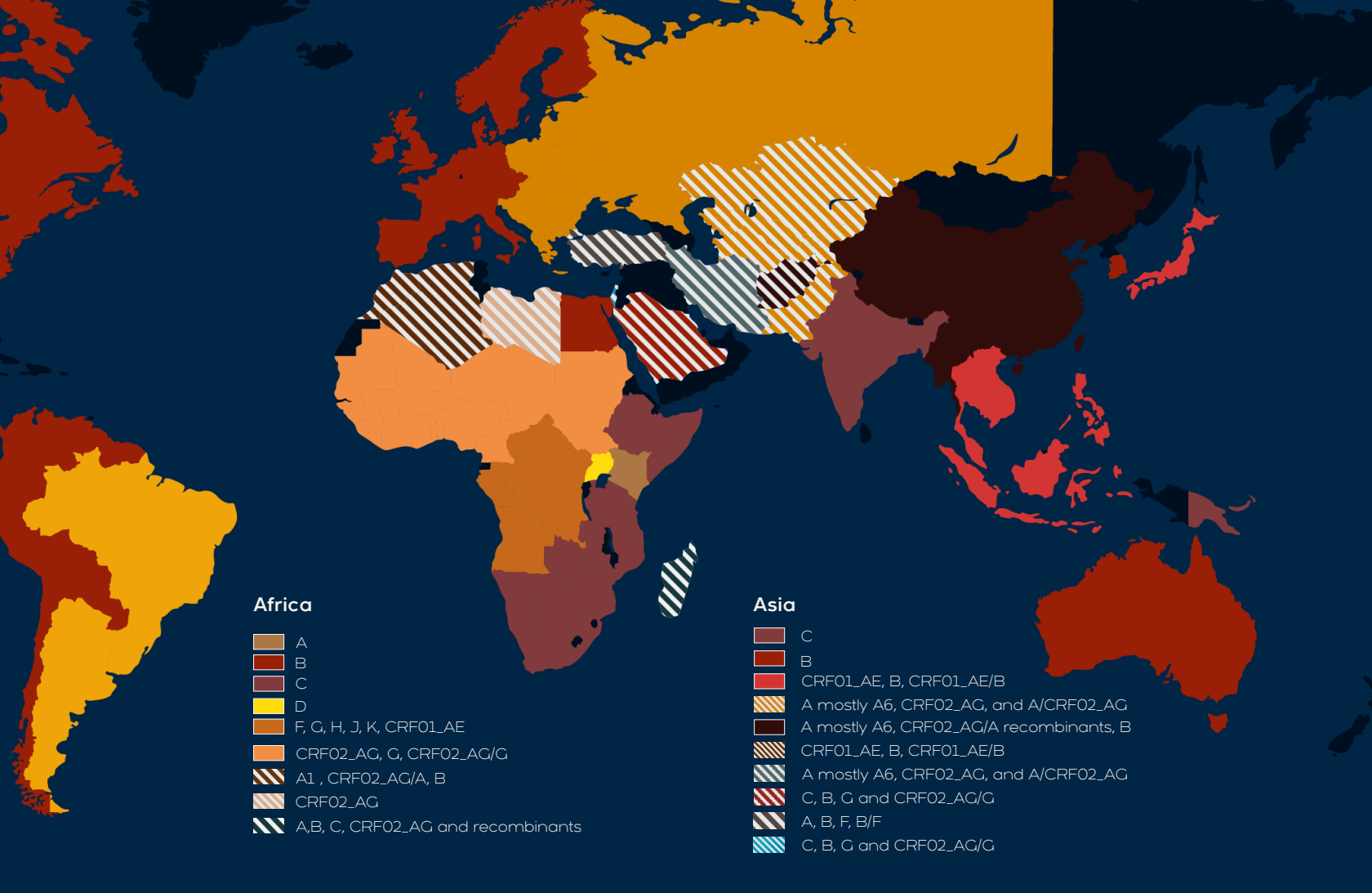
Year 3.5:  
**31.2% Efficacy**



### HOW IT MAY HAVE WORKED

In 2012, correlates of risk are identified and published in NEJM, providing clues to how the vaccine protected and informing future HIV vaccine efforts.





## CAN WE DO BETTER?

WRAIR's researchers at AFRIMS in Thailand explore effectiveness of additional boosts, announce results in 2016.

A public-private partnership including WRAIR initiates a new version of the RV144 vaccine regimen.

## BUILDING ON THE RESULTS

In 2016, the HVTN702 HIV vaccine study began in Southern Africa, using a similar pox-protein vaccine directed at sub-type C and with an additional boost.

In 2017, another vaccine study, HVTN705, began in Southern Africa using a prime-boost regimen previously tested at WRAIR.

WRAIR identified a gene signature associated with protection from Simian Immunodeficiency Virus or HIV infection which can be used to evaluate future Simian Immunodeficiency Virus and HIV vaccine candidates.



## FORGING THE FUTURE

### Mosaico HIV Vaccine Trial

The U.S. Army Medical Research and Development Command (USAMRDC) with WRAIR's MHRP technical support, is part of a global partnership that just launched Mosaico, the first large-scale Phase 3 efficacy study of an investigational mosaic-based HIV-1 preventive vaccine.

The goal of the trial is to prevent infections by the wide range of viral strains responsible for the HIV pandemic.

### Novel Vaccines

In addition to building upon the results of RV144, WRAIR's MHRP is also developing and testing novel vaccine strategies, including new adjuvants and improved protein constructs aimed at subtype B, which is common in most U.S. Service Members.

### Monoclonal Antibodies

In addition, MHRP is helping test novel broadly neutralizing antibodies to prevent and possibly cure HIV.

### ALFQ Adjuvant

ALFQ vaccine adjuvant was awarded a patent in October, 2019. In the 1990s, MHRP developed a family of new adjuvants called the Army Liposome Formulation (ALF). Adjuvants are vaccine components that help activate the immune system and improve immune responses. MHRP will be evaluating the effect of these promising new compounds on vaccine responses in various HIV vaccine clinical trials in Kenya and Thailand in 2020. It will also be tested with vaccines for malaria, enteric diseases and heroin.

# INTERNATIONAL PARTNERSHIPS FOR GLOBAL HEALTH

## INTERNATIONAL STABILITY

The impacts of HIV are widespread and include lowered life expectancy, reduced economic growth and increased health costs. These outcomes ultimately damage social and political cohesion and impede the advancement of global health objectives—posing a risk to national security and the stability of many nation-states.

PEPFAR's programs help to restore the economic productivity of those infected or affected by HIV and to protect families, communities, and societies from destabilization. Higher levels of PEPFAR funding in a country is associated with greater improvements in World Bank indicators of governance, including: government effectiveness, regulatory quality, and a 31% improvement in the rule of law.

## WRAIR'S PEPFAR PROGRAM IN AFRICA

WRAIR's MHRP works to develop sustainable PEPFAR-supported programs and clinical research within the public health infrastructure of each country. The program works closely with local government institutions and has helped develop clinical research capabilities and health care delivery systems including buildings, laboratories, central administration and data management systems. WRAIR supports:

**350,000**

People on lifesaving ART

**975**

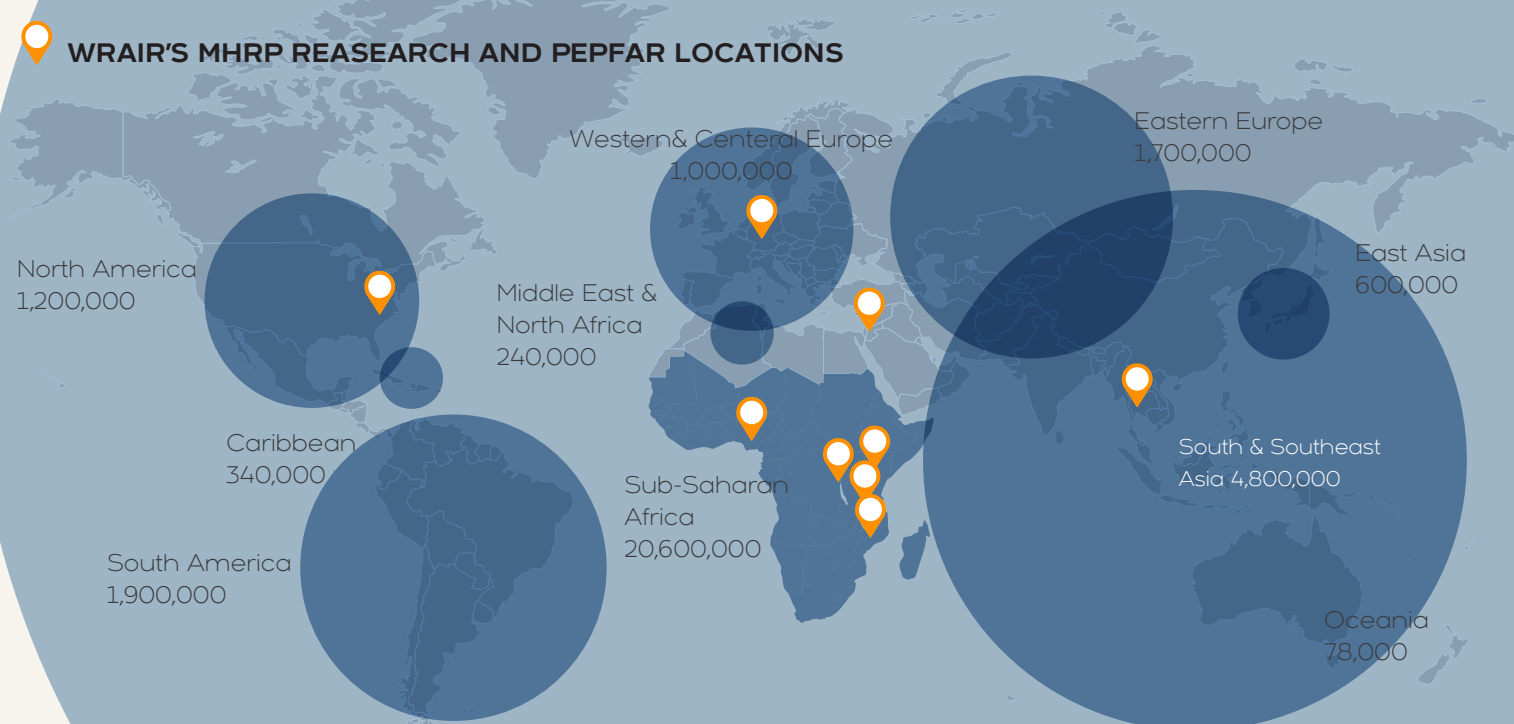
health facilities

**1.1 MILLION**

HIV tests conducted

## PEOPLE LIVING WITH HIV > 37 MILLION

### WRAIR'S MHRP REASEARCH AND PEPFAR LOCATIONS



Adults and children estimated to be living with HIV (2018)

Sources: UNAids, AVERT, HIV.gov

## KNOW YOUR STATUS

WRAIR programs include community-wide interventions to increase HIV testing, including mobile and nighttime testing, self-testing, and counseling.

30% of people living with HIV worldwide do not know their status



MHRP developed a mobile HIV diagnostic laboratory to provide HIV testing in hard-to-reach communities.

## LINK TO CARE

Ensuring people who are HIV infected have access to treatment.

4 out of 10 people know they are HIV positive but are not but on treatment



Expert clients serve as mentors to newly diagnosed people and provide practical support as new patients adjust to health impacts of HIV.

## VIRAL SUPPRESSION

People on treatment who are virally suppressed can live a healthy life and have lower risk of transmitting the disease to others.

Nearly half of the people living with HIV are not virally suppressed



WRAIR studied early warning indicators of HIV drug resistance to help identify those failing treatment.



### TRANSFORMING RESEARCH FOR BETTER CARE

WRAIR's MHRP is one of many USG partners that implement PEPFAR programs around the world. In addition to its civilian programs in Uganda, Tanzania and Kenya, WRAIR's MHRP provides HIV testing, care and treatment shoulder to shoulder with military partners in Nigeria, Kenya and Tanzania. The programs collaborate to conduct studies to characterize HIV in the populations receiving care and improve practice.



### AFRICAN COHORT STUDY (AFRICOS)

This study is the first of its kind in sub-Saharan Africa, taking place at local facilities in Kenya, Nigeria, Tanzania and Uganda.

- Long-term study with nearly 3,600 volunteers
- Enrolling at 12 HIV clinical care/treatment sites across 5 programs in 4 countries
- Providing critical data on comorbidities
- Impacting HIV policy and PEPFAR programming



### HIV PREVENTION

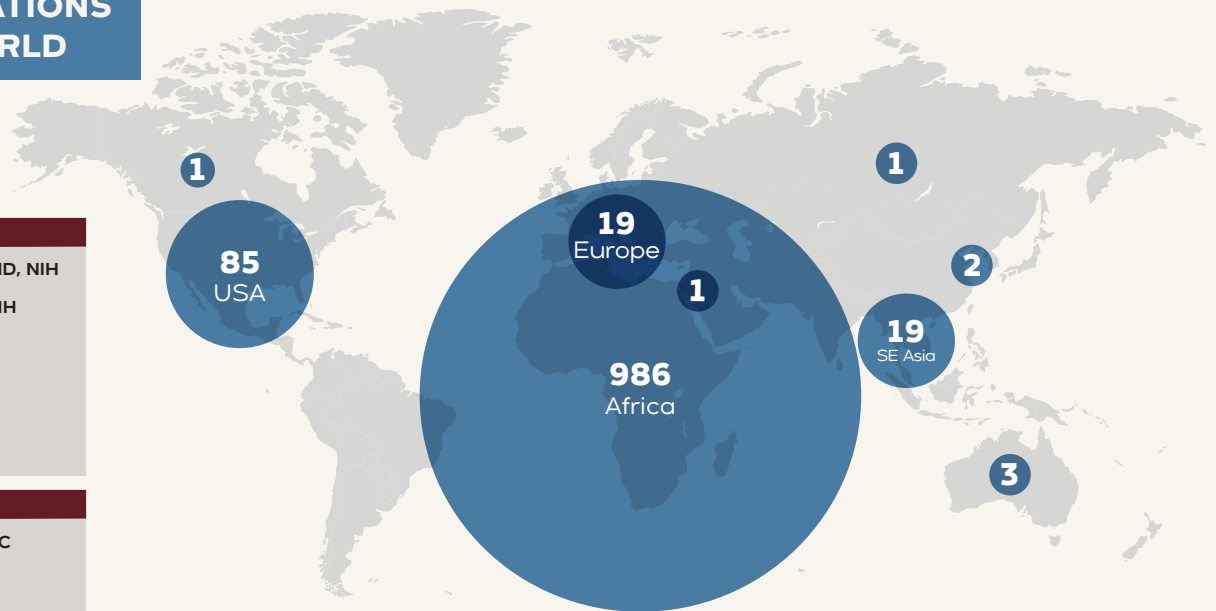
- HIV testing and counseling
- Prevention of mother-to-child transmission (PMTCT)
- Voluntary male medical circumcision
- Condom use
- PrEP
- Determined, Resilient, Empowered, AIDS-Free, Mentored, and Safe (DREAMS), a program for adolescent girls and young women

# GLOBAL IMPACT OF WRAIR'S HIV RESEARCH

WRAIR's RV144 clinical trials results paper, published in the New England Journal of Medicine, has generated nearly **1900** biomedical citations in 10 years.

## # OF COLLABORATIONS AROUND THE WORLD

KEY PARTNERSHIPS:
Vaccine Research Center, NIAID, NIH
Division of AIDS, NIAID, NIH
Janssen, J&J
Gilead Sciences
Sanofi Pasteur
HJF
ACADEMIA:
Harvard University/BIDMC
Duke University
Univ. of CA system
Mahidol University



## RETURN ON INVESTMENT

**\$175M total**

MHRP's Diversified Funding Sources:

- DAIDS/NIAID/NIH
- State Department/PEPFAR
- Congressional Special Interest
- HIV Vaccine Trials Network
- AIDS Clinical Trials Group

**DOD FUNDING**  
**\$39M (2019)**

### Force Readiness

Conduct critical research to inform policy and commands

- COCOMs, CENTCOM, SOUTHCOM, AFRICOM, DOD Armed Forces Blood Program; Army Blood Program; Army Public Health Command

### National Security

Develop key relationships; Define HIV risk; HIV Prevention

- Royal Thai Army, Kenya Ministry of Defence, Nigerian Ministry of Defence, Tanzania People's Defence Force, U.S. Missions, State Department

### Leverage Resources

Secure in-kind support and push product development

- Gates Foundation, Sanofi Pasteur, Janssen/J&J, Novartis, Harvard, University of Washington, Duke, WHO, UNAIDS, Global HIV Vaccine Enterprise, IAVI

### International Infrastructure

Established research infrastructure and relationships to conduct relevant research in endemic settings

- NIAID/NIH-Ebola, HIV, Malaria; DoD Global Emerging Infections Surveillance, President's Malaria Initiative, PEPFAR, Global Health Initiative