



Secretary of State Antony J. Blinken delivers remarks at World AIDS Day event hosted by Business Council for International Understanding, in Washington, DC, December 2, 2022 (State Department/Ron Przysucha)

The Purpose and Impact of the U.S. Military HIV Research Program

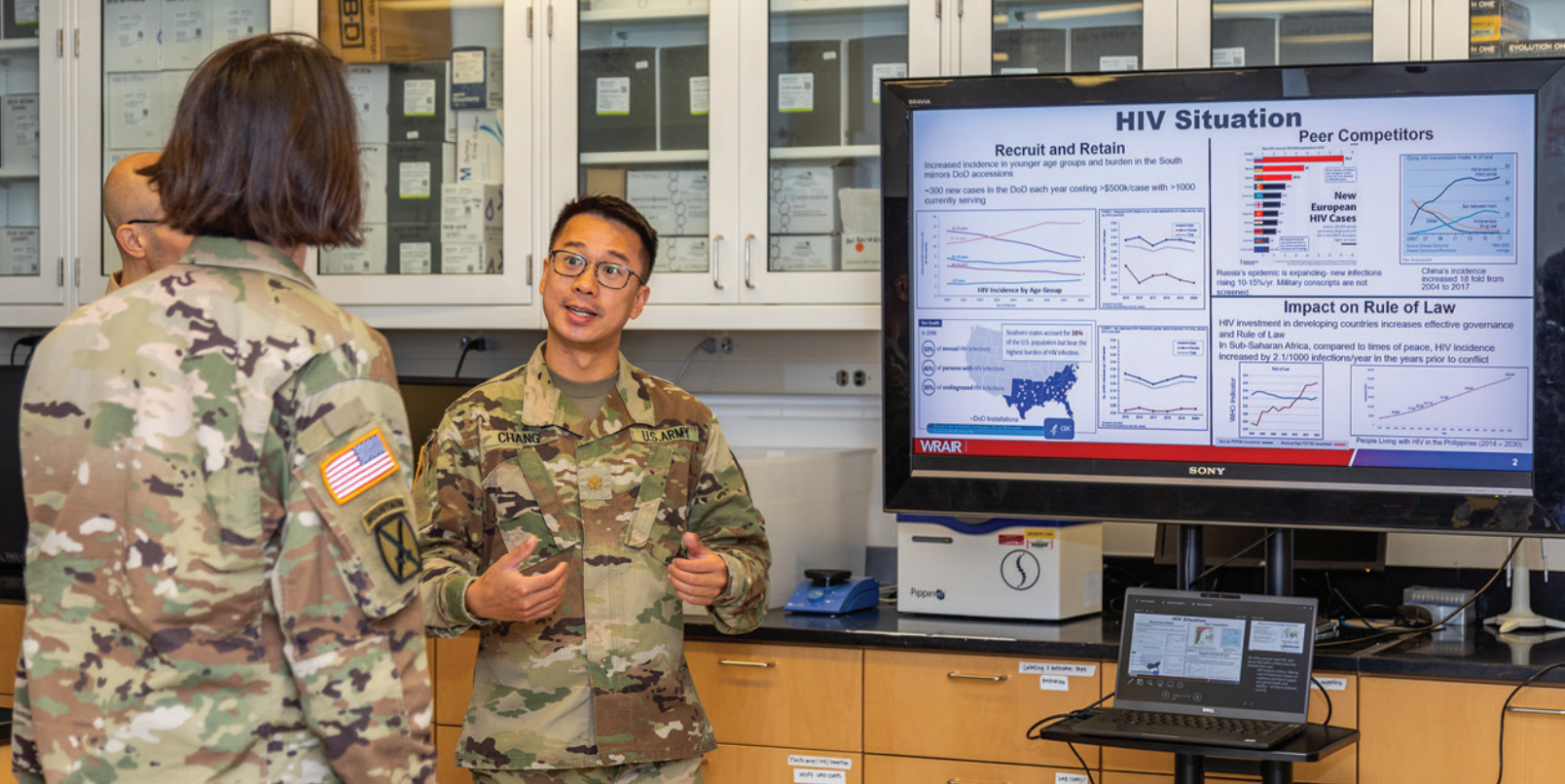
By Joseph S. Cavanaugh, Clinton K. Murray, David Chang, and Julie A. Ake

HIV, or the human immunodeficiency virus, has been acknowledged as a global epidemic since shortly after it was identified as the virus responsible for acquired immunodeficiency syndrome (AIDS) in the mid-1980s. The Joint United Nations Programme on HIV/AIDS estimates that almost 38 million people were living with HIV as of 2020, and more

than 36 million people have died from HIV-related illnesses since the beginning of the epidemic.¹ Evidence demonstrates that the prevalence of HIV is highly variable in militaries and tends to be higher than in comparable civilian populations in higher prevalence settings.² Most militaries screen for and exclude HIV-infected persons from conscription or enlisting, so detected

infections most likely occur after enlistment, suggesting that military personnel are often at substantially increased risk for acquiring and then possibly transmitting HIV.³ Researching and developing countermeasures for HIV have both operational and diplomatic benefits and are the founding objectives for the Military HIV Research Program (MHRP) at the Walter Reed Army Institute of Research (WRAIR). MHRP was established in 1986 to directly address the threats posed by HIV by conducting relevant research on prevention and treatment, evaluating the impact of HIV on U.S. Servicemembers, and developing strategies to

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Major David Chang and Captain Sean Cavanaugh brief Brigadier General Wendy L. Harter on the HIV Research Program at Walter Reed Army Institute of Research, June 29, 2021 (U.S. Army/Arlen Caplan)

protect military personnel—a mission that also addresses the global burden and consequences of HIV disease.

HIV is readily transmitted when infected body fluids break through the skin or mucosal membranes, as can happen with unprotected sexual contact or when infected needles or blood products are used. HIV spreads easily through sexual networks, especially those where barrier protection is not consistently used or commercial sex is practiced. Blood products should be universally screened for HIV, but this process takes time and is imperfect. Risks of breakthrough contamination are particularly elevated in high-volume, emergent transfusion environments, as seen during high-intensity conflict and expected during large-scale combat operations.

Untreated, HIV replicates in the human body to high viral loads, destroying the immune system as it does. High viral loads are associated with more rapid immune-system compromise and high infectiousness. The newest treatment regimens are highly effective at inhibiting viral replication and have turned HIV infection into a chronic, untransmissible condition associated with a normal or near-normal lifespan, much like other

chronic medical conditions such as diabetes or hypertension. The most widely used current treatment regimens are combination antiretroviral therapies taken as a daily pill. Successful management of HIV, however, requires diligent daily adherence, and lapses in treatment can result in progressive immune deficiency and onward transmission of the virus. Given the urgent need for rigorous adherence, and the costs associated with lifelong treatment, the most strategic approach is effective prevention for those at elevated risk of infection, including warfighters. This remains a top priority for global research efforts.

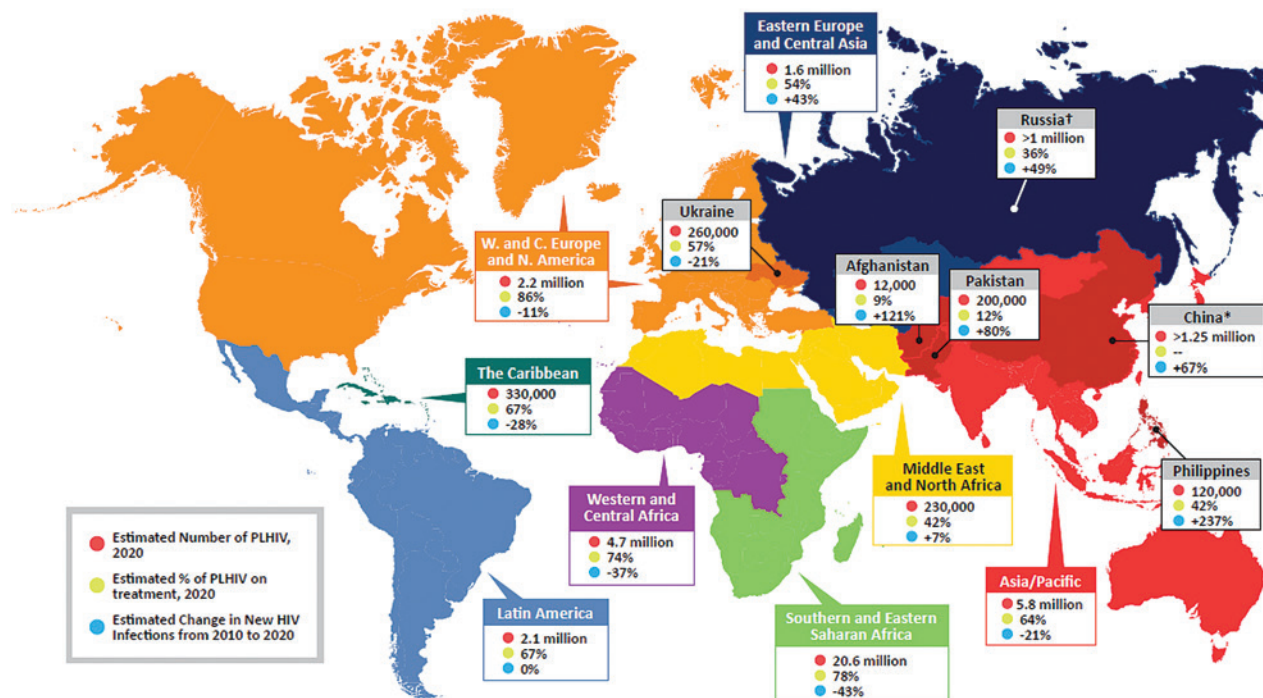
HIV is a threat to U.S. military interests for two principal reasons: the direct biomedical threat of, and the costs and consequences incurred by, infection to warfighters and the destabilizing effects that HIV may have on the sociopolitical systems of our strategic allies. MHRP has a multipronged strategy to counter these biomedical and sociopolitical threats posed by HIV.

Effective prevention of HIV infection is the cornerstone of the strategy, and MHRP has emerged as a leader in HIV vaccine research. Areas of research include both the development

of effective vaccines and “passive vaccination” approaches with monoclonal antibodies to directly neutralize HIV before infection is established. MHRP also conducts research in acute HIV infection to deepen understanding of the early events of infection. Intervening in acute infection allows for the evaluation of strategies to vastly simplify treatment or even present the possibility of a functional cure, or treatment that effectively suppresses viral replication and blocks immune decline and forward transmission without the requirement for ongoing therapy. In addition to these product development initiatives, MHRP collects and analyzes data on HIV epidemiology and threat patterns, using domestic and international observational studies of both military and civilian populations to identify opportunities to mitigate the risk of HIV and other sexually transmitted infections.

MHRP is also part of a broader Department of Defense (DOD) initiative to provide direct HIV-service delivery across the globe. DOD receives funding from the President’s Emergency Plan for AIDS Relief (PEPFAR) to support HIV services in the military health systems of countries hardest hit by the global HIV

Figure 1. HIV Prevalence and Incidence in Selected Countries



*Estimates for China are from modeled UNAIDS data in 2018

†Estimates for Russia are from UNAIDS data in 2017, some experts estimate 10–15% increase in HIV incidence each year with approximately 1.5M PLHIV in 2020

pandemic (military-to-military programs, supported principally by the DOD HIV/AIDS Prevention Program). Some of that funding goes to MHRP to provide an array of HIV services to civilian communities that participate in MHRP research (military-to-civilian programs). These activities represent a broad collaboration across the U.S. military and are a critical DOD tool to foster stability, promote goodwill, and enable strategic alliances and safer deployments.

HIV Threats to the Warfighter and Military Services

In the United States, HIV rates vary widely among groups, with the virus disproportionately affecting African Americans, Latinos, people who live in the American South, and, increasingly, those who are 25 to 34 years old—all groups highly represented in the U.S. military. These elevated infection rates have a negative impact on accessions; HIV remains a bar to enlistment because of restrictions on deployment and concerns about the ability

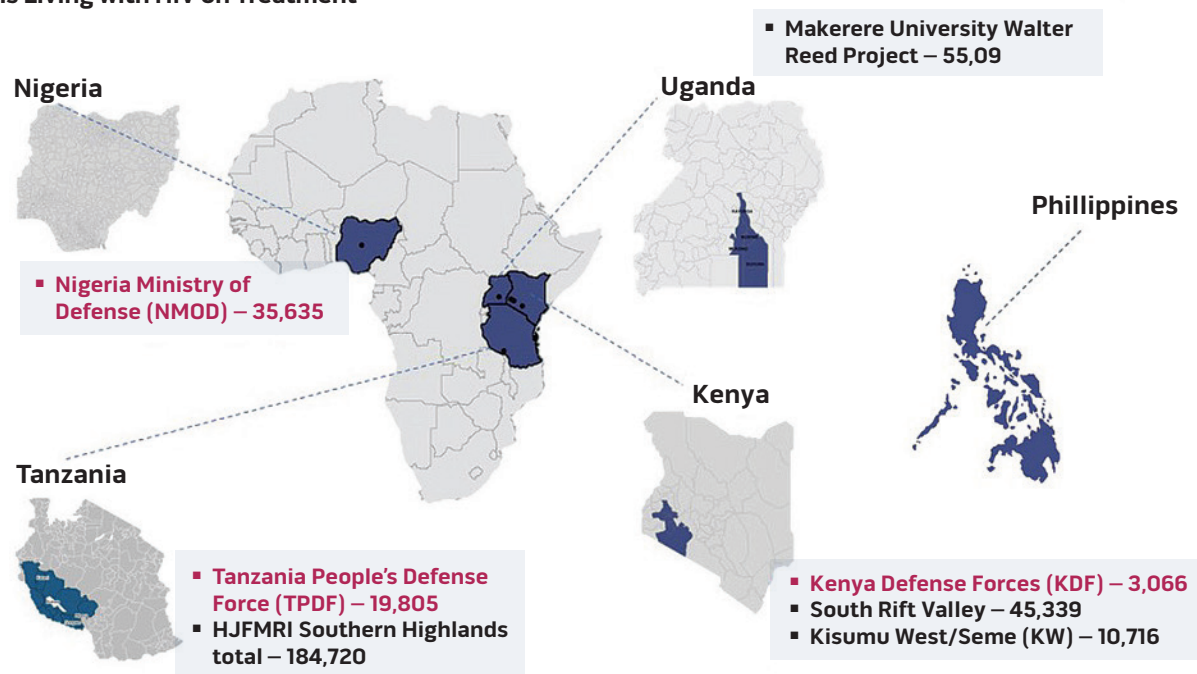
to maintain consistent treatment in battlefield conditions.

Similarly, the incidence of HIV varies widely across the globe, with particularly elevated rates of infection in many African and some Asian nations, and increasing incidence in Russia, Ukraine, China, Pakistan, the Philippines, Afghanistan, the Middle East, and North Africa, all of which are potential theaters of future military activity or strategic locations for U.S. military presence (figure 1). Of particular note, because of increasing potential for U.S. military presence, Ukraine has the second highest HIV incidence in Europe, behind only Russia, and HIV incidence in the Philippines has increased by an alarming 237 percent since 2010. In such countries, the increasing incidence of HIV and low coverage of treatment poses risks to U.S. Servicemembers through either sexual contact or exposure to blood, blood products, or sharps, which could occur on the battlefield or in forward surgical and medical units. The availability of sufficient and safe blood products during times of conflict is a growing

concern. A model run using the Medical Planners' Toolkit (and the Casualty Rate Estimation Tool) estimated that in a near-peer conflict with over 50,000 casualties in the first 4 days and 2,000 to 3,000 casualties per day after that, more than 70,000 units of red blood cells would be needed over the first 90 days.⁴ That need would rapidly deplete stocks of available blood products and overwhelm prescreened walking blood bank strategies and therefore pose risks to the supply and to effective treatment. If such a conflict were to happen in an area of rising HIV incidence, such as Russia, where an estimated 1.1 percent of the adult population is HIV-infected, breakthrough contamination to the blood supply employed in the emergent treatment of mass casualties would be likely.

There are approximately 350 new HIV infections among Active Servicemembers each year, almost all acquired through unprotected sexual activity, and it has been estimated that there are currently over 2,000 Active Servicemembers with HIV.⁵ These Servicemembers are typically not deployable given the potential

Figure 2. Countries Where MHRP Currently Implements HIV Programming, with Program Names and the Number of Persons Living with HIV on Treatment



for treatment interruption, which could compromise performance. At a lifetime treatment cost of over \$420,000 per HIV-infected Servicemember, HIV imposes a heavy financial burden on the U.S. Military Health System, a burden that could be alleviated by preventing infection and the long-term consequences of HIV disease.⁶ Preventing and treating HIV is not only a professional obligation for military clinicians, but it is also a tactical measure. Identifying and utilizing the most optimal biomedical tools yield a tactical advantage in medical readiness when facing adversaries that do not mitigate their own HIV threats.

Geopolitical Threats of HIV

In many ways, the more pervasive threat of HIV is not clinical but social and geopolitical. Like many infectious diseases, HIV is both a cause and a consequence of war and social unrest. In the 1990s and early 2000s, entire communities in certain countries were altered by the loss of their most active and productive members, which left them with unsupported orphans, a dwindling socioeconomic base, and increasing social disorder. Economic desperation and social disorder, either because of HIV itself or

as a consequence of civil unrest or war, contributed to forced and commercial sex, illicit drug trafficking, internal migration, and limited access to health care—thus creating environments even more conducive to the spread of HIV. The United Nations Security Council (UNSC) recognized HIV as an international security issue; it passed Resolution 1308 in July 2000, the first time that a health issue was acknowledged as a threat to peace and security. In June 2011, the UNSC passed Resolution 1983, recognizing the impact of HIV in conflict and postconflict environments.⁷

Health is a security imperative, central to the success of the combatant command missions. HIV threatens health security and if left unaddressed can undermine efforts to secure and stabilize volatile regions. As mentioned, military personnel may be at greater risk for acquiring and then transmitting HIV, and if those personnel do not have reliable access to affordable medications and quality health care, there is a real risk of amplifying transmission and compromising force readiness. In addition, in regions where U.S. forces serve alongside those of allies, high rates of infection can compromise the allied militaries, thus impeding U.S. strategic interests.

HIV Countermeasures

Prevention is the most cost-efficient and effective approach to the threats posed by HIV. There have been important advances in the use of medicines to reduce the risk of HIV infection, so-called pre-exposure prophylaxis (PrEP). Both daily and on-demand oral regimens and, more recently, investigational long-acting injectables have shown remarkable effectiveness at preventing infection in certain populations.⁸ MHRP has worked with Service clinical leadership to evaluate the use of PrEP in the military and identify military-specific issues. DOD is using findings from this research to identify gaps and barriers to care and to develop policy for its use; for example, currently available oral PrEP agents are now employed for HIV prevention in military treatment facilities but are not recommended as appropriate for use in deployed settings.

The most critical advance needed to protect against the threat of HIV is an effective vaccine. An effective vaccine would prevent the substantial morbidity and mortality associated with HIV without requiring adherence or exposure to medications, preserving force readiness at a cost substantially less than regular drug



Hospital Corpsman 1st Class Oliver Arceo draws blood for Sailor's annual HIV test at North Island Medical Clinic, Naval Air Station North Island, Coronado, California, January 7, 2017 (U.S. Navy/Marie A. Montez)

administration. MHRP is collaborating with government, academic, and industry partners to advance promising vaccine candidates to protect against global strains of the virus. To date, MHRP has conducted dozens of vaccine-related trials and conducted the only HIV vaccine study to show modest efficacy in reducing the risk of HIV infection. Although the higher level of efficacy needed to protect U.S. Servicemembers was not reached, MHRP's RV144 Thai trial provided proof of concept that an HIV vaccine is possible. MHRP continues to play a critical role in the international HIV vaccine field: among the eight most recent HIV vaccine efficacy trials (complete or ongoing), five included products that MHRP helped to develop. MHRP scientists are currently testing a novel adjuvant, called the Army Liposome Formulation, to improve immune responses to vaccines. MHRP participated in the early development of the Janssen mosaic vaccine candidate now being tested in two major multinational efficacy trials in a global partnership comprising the National Institutes of Health, Johnson and Johnson, major philanthropic organizations, and the U.S. military. Other planned studies will examine new vaccine products designed to optimize protection against HIV subtypes most common in the U.S. military as well as the effects of

rapid dose administration and product-sparing fractional dosing strategies.

Additional research is needed to protect the blood supply and wartime blood-product recipients from HIV infection. MHRP is researching the potential protective benefit of broadly neutralizing antibodies (bnAbs), which are long-lasting and may allow for injections as infrequently as every 3 or even 6 months. The use of bnAbs and post-exposure medicinal prophylaxis, potentially in combination with vaccine booster doses given at the time of transfusion, might mitigate infection risk for those receiving emergency blood products that were not adequately screened or that were collected from high-risk populations; such interventions require further investigation.

If prevention fails and infection occurs, provisions for lifelong therapy must be made. Effective management of HIV halts viral replication and stops forward transmission but is currently challenged by the need for daily pill adherence. Without regular adherence, HIV can replicate in the body at high levels, increasing the possibility of transmission and the likelihood that the virus develops genetic mutations that may cause drug resistance—both of which pose considerable threats to individual and public health. The need for fully reliable procurement and supply management is

therefore critical, but such management is difficult to guarantee, especially in prolonged conflict environments. Similar medicines with the same efficacy as daily pills can now be given as long-acting injectables monthly, allowing greater treatment flexibility and improving adherence.⁹ HIV might also be managed with infrequently dosed therapeutic bnAbs and/or vaccines, which MHRP is studying; if proven effective, such therapies could greatly reduce treatment burdens and allow for unrestricted deployment of HIV-infected individuals.

Countering Geopolitical Threats

Assisting other countries and foreign militaries with their own HIV responses provides an opportunity to strengthen U.S. alliances and conforms to the priorities described in the Interim National Security Strategic Guidance.¹⁰ Strategic health diplomacy is the idea that U.S. interests and foreign policy objectives can be advanced through investments in foreign health programs and the international health infrastructure. PEPFAR, established by a bipartisan congressional act in 2003, has been a cornerstone program for U.S. foreign health investment and one of the most successful strategic health diplomacy programs in U.S. history.

PEPFAR is the largest single global health program of the U.S. Government and the largest HIV prevention program in the world. PEPFAR funding, approximately \$6 billion to \$7 billion each year, is divided between the Global Fund to Fight AIDS, Tuberculosis, and Malaria and various U.S. agencies, including DOD, which direct the funding to implementing partners and ministries of health in more than 50 countries. The funding directly capacitates health systems with investments in medications; laboratory and clinical commodities; personnel and staffing; and critical surveillance, research, and evaluation efforts.

We owe a debt to the communities in which research of benefit to the U.S. military is conducted, and MHRP pays that debt by implementing HIV prevention and treatment programs in those communities, providing an ethical framework for the clinical research it conducts. This programming also builds strong relationships with host communities, including local military and civilian partners, and establishes a foundation for security cooperation in strategic locations.

MHRP channels its PEPFAR funding into eight implementing mechanisms in five countries: three in Kenya, two in Tanzania, and one each in Nigeria, Uganda, and the Philippines. Four of these are military-to-military partnerships, and four are military-to-civilian programs (figure 2).

The military-to-military programs are cornerstone elements of security cooperation with partner militaries, and the military-to-civilian programs are quite visible in their respective communities and have helped cultivate enduring goodwill among DOD, the militaries, the ministries of health, and the civilian communities in the countries where PEPFAR operates. Long-term positive and productive relationships developed through partnering for HIV service delivery provide a consistently good news story for bilateral relationships and make possible other important conversations among the militaries.

A key strategic component is the substantial investment in case-finding and sufficient laboratory capacity, including

automated molecular machines that can detect multiple diseases using various specimens. These instruments can be strategically placed near the points of care across each PEPFAR-supported country to maximize access and accelerate timeliness of results. The diagnostic platforms are crucial for HIV diagnosis and service delivery but can be utilized for other disease detection, most recently COVID-19. This will enable countries to establish sensitive surveillance to emerging infectious threats and mount appropriate and timely public health responses.

Through direct investment in clinical service delivery, PEPFAR has made possible efficient and highly effective community-level HIV treatment and prevention and has laid the groundwork for comprehensive healthcare systems. The clinical infrastructure is currently being used to diagnose, treat, and prevent other infectious diseases in the broader population and can be leveraged to support noncommunicable diseases as well. The net result has been a radical improvement in the health of the communities that were previously ravaged by HIV, with an estimated 20 million lives saved by PEPFAR-supported efforts.¹¹ The effectiveness of these investments has brought stability to entire regions and has helped promote good governance across the many nations that PEPFAR supports.

The investments in HIV prevention and treatment have clear benefits to U.S. foreign policy and military interests. By promoting force health protection among U.S. Servicemembers and members of allied military forces, we are maintaining a competitive advantage and helping stabilize communities around the world. The development of an effective vaccine for HIV will be a truly historic accomplishment that could save millions of lives, provide full protection for Servicemembers, and allow great gains in strategic health diplomacy. The U.S. military's visible programmatic investments and research successes directly support U.S. combatant commands and have fostered profound good will and helped strengthen strategic alliances across the globe. JFQ

Notes

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⁴ Edwin D'Souza et al., *Forecasting Wounded-in-Action Casualty Rates for Ground Combat Operations* (San Diego, CA: Naval Health Research Center, August 2019), <https://apps.dtic.mil/sti/pdfs/AD1105971.pdf>.

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⁶ Adrienna Bingham et al., "Estimated Lifetime HIV-Related Medical Costs in the United States," *Sexually Transmitted Diseases* 48, no. 4 (April 2021), 299–304, https://journals.lww.com/stdjournal/Fulltext/2021/04000/Estimated_Lifetime_HIV_Related_Medical_Costs_in_15.aspx.

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⁹ "FDA Approves Cabenuva and Vocabria for the Treatment of HIV-1 Infection," U.S. Food and Drug Administration, January 27, 2021, <https://www.fda.gov/drugs/human-immunodeficiency-virus-hiv/fda-approves-cabenuva-and-vocabria-treatment-hiv-1-infection>.

¹⁰ *Interim National Security Strategic Guidance* (Washington, DC: The White House, March 2021), <https://www.whitehouse.gov/wp-content/uploads/2021/03/NSC-1v2.pdf>.