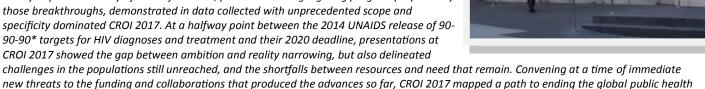
CROI 2017

Progress and partnerships

A report from

Launched in 1993 as a forum for basic scientists and clinical investigators from ground the world to share and discuss laboratory science, clinical trials and evolving practice confronting HIV and its associated impacts, the Conference on Retroviruses and Opportunistic Infections has provided the setting for presentations of landmark research heralding advances against the pandemic. Breakthroughs reported and updated at CROI have changed the course of research and responses across the landscape of implementation, vaccine and cure research and continuing progress in diagnosis, treatment, care and prevention of the virus and coinfections to control HIV.

Nearly a quarter century after the first CROI, presentations highlighting progress propelled by those breakthroughs, demonstrated in data collected with unprecedented scope and specificity dominated CROI 2017. At a halfway point between the 2014 UNAIDS release of 90-90-90* targets for HIV diagnoses and treatment and their 2020 deadline, presentations at CROI 2017 showed the gap between ambition and reality narrowing, but also delineated





threat of HIV, amid uncertainty of whether that path will be taken.

An international meeting

CROI 2017 convened in Seattle, WA, on February 13, two weeks after a new administration in Washington, DC instituted an order barring travelers to the United States from seven Muslim-majority countries. With nearly half of the roughly 4,000 delegates scheduled to attend the conference coming from outside of the U.S., CROI organizers were among the first representatives from a cross section of scientific and medical organizations to voice strong opposition to the ban. Research to confront infectious diseases must, like the outbreaks themselves, cross national borders worldwide, conveners argued, with open, unimpeded, and ongoing collaborations. The ban was lifted by a federal court judge a week before

the conference began, but organizers expressed continuing concern that the ban, and the prospect of its reinstatement present potential disincentives and actual obstacles to the work ahead, while undermining U.S. leadership of global health responses. "If policies like this are not swiftly and definitively rejected, they will have a detrimental effect on science," Conference Chair Dr. Susan Buchbinder told an opening night audience. Obstacles to international collaboration, conference leaders emphasized in a statement released on the eve of the conference, would harm health everywhere.

Two decades of cross border partnerships

The 2017 CROI N'Galy-Mann lecture, opening the conference, honoring two international scientist leaders of the global HIV response, and, at this conference, recognizing two decades of partnerships between U.S. and Zimbabwean physicians and scientists that garnered knowledge, tools, and success against a national epidemic beset by structural challenges, underscored the point. In a speech that chronicled collaborations between the sub-Saharan African nation's health ministry and research institutions with the HIV Prevention Trials Network, the AIDS Clinical Trials Group, The International Maternal Pediatric Adolescent AIDS Clinical Trials Group, the



Microbicides Trials Network, the HIV Vaccine Trials Network, and the Medical Education Partnership Initiative, Dr. James Hakim of the University of Zimbabwe unspooled the backstory of findings that changed the course of HIV prevention, care, treatment and policies worldwide, and set the stage to ensure that those advances also prepare responders at home and abroad for the next pandemic.

^{*} That 90 percent of all people living with HIV know their HIV status; 90 percent of all people with diagnosed HIV infection receive sustained antiretroviral therapy; and 90 percent of all people receiving antiretroviral therapy have viral suppression, and that meeting those targets by 2020 would end HIV as a global health threat by 2030.

Building on breakthroughs

In research and responses spanning the years preceding the advent of the U.S. President's Emergency Plan for AIDS Relief to the present, in the rural Uganda community that was home to that nation's first report of the virus, investigators documented the difference that medical interventions as well as those considered "behavioral" that include HIV counseling and testing, and condom use have made. The 17 years of data from the Rakai cohort, presented at CROI 2017 enumerated the value of steadily increasing access to diagnosis, treatment, medical circumcision and condoms with a 42-percent drop in HIV incidence. Accompanied by a 75-percent rate of viral suppression among infected individuals, the numbers from Rakai showed a community with one of the oldest recognized epidemics in Africa meeting and exceeding the treatment targets UNAIDS projects as necessary to controlling the spread of the virus. Beyond validating the returns of present and continuing investments and interventions, the data also outlined missing pieces: increased outreach to men, additional prevention tools for women, and more accessible links to health services for all people, including migrants.



Across countries and communities, in-person surveys bring answers

The conference also brought the first detailed discussion of findings from door-to-door research across Zambia, Malawi and Zimbabwe. Three countries with historically high burdens of HIV and its accompanying impacts, fragile health infrastructures, and limited medical technologies and staffing to meet the long-multiplying demands of mature HIV epidemics, all had faced challenges difficult to both meet and measure. Like the Rakai data, the data from the Population-based HIV Impact Assessment gathered by ICAP at Columbia University and local investigators through interviews and blood tests

showed promising potential for the hardest hit communities to meet the UNAIDS goals. Combined and comparable data from the neighboring nations found 87 percent of people who had already been diagnosed with HIV receiving treatment, and treatment consistent and effective enough in more than 88 percent of them to suppress the virus. But the data also revealed a bottleneck, at the apparently simple first step: roughly 30 percent of those who tested positive for HIV during the survey had not known they were infected. Most of them were male. While again illustrating the effectiveness of existing interventions, and the impact of a decade and a half of investment, the data also indicated an ongoing unmet need for HIV testing and counseling outreach, and the likelihood of future needs as added numbers of individuals diagnosed with the virus join care and treatment rolls.

Additional research presented at CROI 2017 indicated that as demand for HIV services continues to increase, immediacy, in connections to care and treatment will be critical to maximizing the effectiveness of responses. Findings from a randomized trial in Malawi showed that accelerated access to antiretroviral treatment and text message appointment reminders improved the odds of getting and staying in care for a year following HIV diagnosis by more than 25 percent, while research in South Africa found individuals diagnosed with HIV who received both text messages and peer guidance to navigate care services were three times as likely to stay in care than those receiving text messages alone, or receiving neither. New mothers who had been diagnosed with HIV were found in a Cape Town study to be about 25 percent likelier to remain in care with antiretroviral treatment suppressing their virus when that treatment was supplied in the same setting as post-natal services — an efficiency that a study author called "a simple and highly effective strategy."

Does exclusion of immigrants stall progress?

Finally, researchers in Botswana highlighted the obstacle to care, and to HIV control that borders bring. Home to one of the densest concentrations of HIV infection in Africa, but with early recognition and leadership of necessary interventions to combat the epidemic there, Botswana has served as an example of what a country-guided response could accomplish with the support of international resources. One obstacle continues to present a threat to the country's progress, however, a presentation from the U.S. Centers for Disease Control and Prevention and the Botswana Combination Prevention Project showed. While free treatment to all citizens who live with the virus has accelerated progress against the disease, immigrants must pay for the medicine that prevents illness as well as transmission, travel back to their countries of origin, or do without. While 71 percent of citizens living with HIV in the cohort studied were accessing treatment, just 29 of non-citizens were.



The findings were presented during a session highlighting factors already making immigrants vulnerable word-wide, including factors in their countries of origin and in transit that include violence, transactional sex, exploitation, language barriers and threats of deportation and arrest. To overcome those factors, and the impacts of barriers to treatment, presenters agreed, nations need to develop policies that ensure services are made available where needed.

Steps to control the No. 1 killer

Zimbabwe

Botswana

South Africa

Namibia

While advances in antiretroviral medicines and access extended the lives of people living with HIV around the world, progress against the curable disease that kills more people living with the virus than any other opportunistic infection long lagged far behind. CROI 2017 sessions highlighted promising applications of new and established tools to meeting persisting challenges in prevention, diagnosis, and treatment of tuberculosis disease.

A possible gold standard and hope, for XDR-TB treatment, and impetus for evidence-based prevention

The news with the greatest potential impact came with an update of continuing results from the trial of a new regimen that replaces what the presenter, Dr. Francesca Conradie, called "the kitchen sink" approach to treating tuberculosis that does not respond to most common medicines with a six-month regimen of two recently developed drugs and one repurposed to fight the disease. The Nix-TB regimen had already shown promising outcomes among 33 patients in South Africa who showed no signs of disease six months after treatment, in findings released at the Union World Conference on Lung Health the preceding October. The update, now of 40 patients, 31 of whom had been tracked for another six

months, point to hope, and toward a possible "gold standard" of treatment for a disease that over the last three decades has had a 75 percent mortality rate.

On the diagnosis front, results from the long-waited Xpert Ultra test indicate the new technology detects a 12 percent higher rate of tuberculosis cases among people living with HIV than the XPertRIF introduced in 2010. The promise of the advance comes with a caveat; the Xpert Ultra also detects old evidence of cured disease, and will require knowledgeable interpretation to avert unnecessary treatment.

A presentation also offered an answer to a complication that has discouraged early antiretroviral treatment for tuberculosis patients with HIV, with findings that the preventive use of prednisone lowered incidence of IRIS – TB Immune Reconstitution Inflammatory Syndrome.

And, findings presented at CROI 2017 threw the weight of new evidence behind nearly quarter-century-old guidance from the World Health Organization that people with HIV have access to six months of isoniazid therapy to prevent tuberculosis disease. The recommendation, backed over the years since by TEMPRANO findings released at CROI 2015, received further validation from follow-up among patients in Cote d'Ivoire showing a 39 percent lower risk of death among those receiving the therapy known as IPT.

The generation to come — impetus and opportunity

The progress presented at CROI offered a glimpse of a future in which HIV has ceased to be a public health threat, when children grow up in a world free of the hurdles the pandemic has thrown in the paths of rising generations over the last three and a half decades. But while the obstacles ahead may include the uncertain policies and priorities of new political leadership, the largest obstacle may loom in the next generation itself. Across the countries already most affected by the global HIV pandemic it will be "the largest group of young people ever to walk the face of the planet."

That was how U.S. Centers for Disease Control and Prevention global HIV and TB Director Dr. Shannon Hader summed up the generation of adolescents and young adults to come over the next decade even as international and domestic efforts intensify to meet the goals of UNAIDS 90-90-90 targets. In an opening mid-conference talk, Dr. Hader offered a stark, but open choice. Programmers, community members, researchers and funders, she said, can view the outcomes of that "youth bulge," she said, "as 'dividend or disaster'." The present offers a clear view of the disaster scenario, she noted, with the potential for economic, political and climate instability to displace the rural youth into urban settings where isolation, unemployment and violence heighten their risks for HIV. The other view, in which emerging technologies, embraced by the youngest members of societies lead to dividends of new opportunities for disease prevention, is one, Hader argued that is equally possible.

Sessions at CROI 2017 supplied support for both views. Findings from the HPTN 071 PopART for Youth

Study in Zambia showed a home-based approach to testing and prevention services raised rates of young people who knew their HIV status from 25 to 90 percent. A pilot project in Haiti found higher rates of treatment and care retention among teenagers who had been diagnosed with HIV and referred to peer support groups. And a study in Kenya found that social connections among women with HIV increased their chances of getting and staying in care. Finally, findings from Kenya on heightened risks of HIV infection among young pregnant women shone light on a safer path ahead, in which services for sexual and reproductive health are integrated into the care available to the next generation.



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