

The United States President's Emergency Plan for AIDS Relief (PEPFAR)
PEPFAR Scientific Advisory Board (SAB) Meeting
April 19, 2016
US Department of State, Washington, DC

PEPFAR Scientific Advisory Board Members in Attendance

Quarraisha Abdool Karim—University of KwaZulu-Natal; Associate Scientific Director, Centre for the AIDS Programme of Research in South Africa (CAPRISA); Professor of Clinical Epidemiology, Mailman School of Public Health, Columbia University; Professor of Public Health, Nelson R. Mandela School of Medicine, University of KwaZulu (South Africa)

Judith Auerbach—Independent Science and Policy Consultant; Professor, Center for AIDS Prevention Studies, University of California San Francisco School of Medicine

Peter Berman—Professor, Global Health Systems and Economics, T.H. Chan School of Public Health, Harvard University

Connie Celum—Director, International Clinical Research Center, Department of Global Health, University of Washington School of Medicine

Judith Currier—Division Chief, Infectious Diseases and Associate Director, University of California Los Angeles (UCLA) Center for Clinical AIDS Research and Education (CARE); Professor of Medicine, UCLA School of Medicine

Carlos del Rio—Chair, Department of Global Health, Rollins School of Public Health and Professor of Medicine, Division of Infectious Diseases, Emory University School of Medicine

Mark Harrington—Executive Director, Treatment Action Group (TAG)

Mark Heywood—Executive Director, SECTION27, O'Neill Institute for National & Global Health Law; Chairperson, UNAIDS Reference Group on HIV/AIDS and Human Rights

Jennifer Kates—Vice President and Director, Global Health and HIV Policy, Kaiser Family Foundation

Lejeune Lockett—Operations and Program Manager, Global Health, Charles Drew University of Medicine and Science; Angola Military HIV Prevention Program, Drew Cares International

Ruth Macklin—Professor of Bioethics, Einstein School of Medicine

Celia Maxwell—Associate Professor of Medicine and Associate Dean for Research, Howard University College of Medicine; Infectious Disease Specialist, Howard University Hospital

Kenneth Mayer—Co-Chair and Medical Research Director, Fenway Health; Director, HIV Prevention Research and Attending Physician, Beth Israel Deaconess Medical Center; Professor, Harvard Medical School and Harvard School of Public Health

Jesse Milan—Fellow, Altarum Institute; Chair Emeritus, Black AIDS Institute

Angela Mushavi—Coordinator, Mother-to-Child HIV Transmission Prevention and Pediatric HIV Care and Treatment, Ministry of Health and Child Welfare, Zimbabwe

Christine Nabiryo—Public Health Consultant, Uganda

Jean William Pape—Professor, Weill Medical Cornell College; Director, GHESKIO (Haiti)

David Peters—Chair, International Health, Johns Hopkins University School of Public Health

Rev. Edwin Sanders—Senior Server, Metropolitan Interdenominational Church of Nashville;
Chair, The Legacy Project, a collaboration with the HIV Vaccine Trials Network; Member,
Presidential Advisory Council on HIV/AIDS (PACHA)

Fredrick Sawe—Director, HIV/AIDS Research, Walter Reed Project, Kenya Medical Research Institute

Albert Siemens—Chair, FHI Foundation

Carole Treston—Chief Nursing Officer, Association of Nurses in AIDS Care

Mitchell Warren—Executive Director, AVAC: Global Advocacy for HIV Prevention

PEPFAR Scientific Advisory Board Members Not in Attendance

Sofia Gruskin—Director, Program on Global Health and Human Rights, Institute for Global Health, University of Southern California; Harvard School of Public Health

Musimbi Kanyoro—President and CEO, Global Fund for Women

Etienne Karita—Site Leader, Project San Francisco, Rwanda Zambia HIV Research Group

Nyambura Njoroge—Project Coordinator, Ecumenical HIV and AIDS Initiatives and Advocacy, World Council of Churches

PEPFAR Implementation Team

Ambassador Deborah L. Birx—United States Global AIDS Coordinator

Julia Mackenzie—Senior Technical Advisor, Office of Research; Science and Analyst/Advisor;

AAAS Science and Technology Policy Fellow, Office of the Global AIDS Coordinator (OGAC)

Douglas Shaffer—Chief Medical Officer, Office of the Global AIDS Coordinator (OGAC)

Opening Remarks

Welcome and Meeting Overview

Douglas Shaffer

Dr. Shaffer addressed Ambassador Deborah Birx, Science Advisory Board (SAB) Chair Carlos del Rio, and esteemed colleagues, welcoming everyone to the second face-to-face meeting of the PEPFAR SAB. He expressed appreciation at the presence of members of almost 20 non-United States Government (USG) partners, along with representatives of USG departments and agencies including the Department of Defense (DoD), Peace Corps, United States Agency for International Development (USAID), Department of Health and Human Services (HHS), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Office of the Global Affairs (OGA), and Substance Abuse and Mental Health Services Administration (SAMHSA). Dr. Shaffer thanked members of the public for their interest and participation, with over 50 national and international call-in lines.

Dr. Shaffer explained that PEPFAR's teams have been quite busy since the fall SAB meeting in October 2015. At the board's recommendation, PEPFAR convened an HIV epidemic control conference in February; the session went beyond consideration of combination prevention implementation science to include current and upcoming prevention, data analyses, and sustainability, among other topics. Two expert working groups (EWGs) were activated: the Finance and Sustainability EWG and the TB/HIV EWG.

PEPFAR teams internationally have been working diligently on 2016 implementation and are in the midst of planning activities for 2017; Ambassador Birx will share her thoughts and positions on these. Dr. Shaffer noted that he and AMB Birx welcomed consideration and discussion of that planning as well as of new business later in the day, and, ultimately, for the SAB to advise AMB Birx concerning scientific, communication, and policy issues. Dr. Shaffer explained that he would support Dr. del Rio throughout the day-long meeting, and that Julia MacKenzie would serve as the designated federal official (DFO).

Dr. Shaffer thanked AMB Birx for her time and continued commitment to see an AIDS-free generation, Dr. del Rio for his leadership as SAB chair, and members of the board who serve as co-chairs of the new EWGs as well as others planning to be present during the meeting.

FACA Review

Julia Mackenzie

Dr. Mackenzie reminded the SAB that it is an advisory body chartered under the Federal Advisory Committee Act (FACA); the three elements that allow this body to serve in such a capacity are its independence of the US government, its clear scope of mission, and its balance of representation.

Dr. Mackenzie noted that, through the SAB's independence, PEPFAR asks for and receives the board's evaluation of the program from a fresh perspective. Regarding the clear scope of mission, the board charter notes that it "serves...in a solely advisory capacity concerning scientific implementation and policy issues related to the global response to HIV/AIDS. These issues will be of concern as they influence the priorities and direction of PEPFAR evaluation and research, the content of national and international strategies and implementation, and the role of PEPFAR in the international discourse regarding appropriate and resourced responses."

Concerning the balance of representation, the PEPFAR charter states: "The membership will be representative of the HIV/AIDS community, including representatives from academia, international experts, partner government representatives, multilateral and bilateral agency representatives, foundation representatives, advocates, and non-governmental organizations. Members who are not US employees are representative members." Dr. Mackenzie pointed out that members serve in a representative capacity, and that membership is balanced fairly in terms of the points of view represented.

Dr. Mackenzie echoed Dr. Shaffer's expressions of welcome and gratitude to all SAB members for giving of their time and for attending the meeting in person. She noted that some board members would be joining the meeting by phone as able, and that some non-board EWG members would be calling in as well. Others who would be joining by phone included members of the public.

Introductory Business

Dr. del Rio welcomed all in attendance and expressed his appreciation for their willingness to travel and to spend the day in the meeting. He remarked that much had occurred since the previous

meeting and that the group would hear updates on activities and progress. He noted the significance of the moment, as a change of US government administration is imminent. He added that, in order to lead with a very clear mandate, the SAB needs to view PEPFAR not as an administration program but as a national and a global one that garners the respect of any administration.

PEPFAR 2016 and Beyond

Ambassador Birx, US Global AIDS Coordinator

AMB Birx welcomed all SAB members and conveyed her feeling of continued humility in the presence of so many innovation solution seekers. She added that such creativity is needed at this time, when many believe that AIDS is extinct and that no challenges exist to gaining control of the epidemic.

The Challenge of Ending AIDS: Innovations from the Field

AMB Birx shared selected insights from PEPFAR-funded countries as they have utilized data in a new and granular way, as well as its ideas of perceived challenges for efforts over the next 12 to 24 months.

Challenge 1: Low Testing Yield in Concentrated and Generalized Epidemics

PEPFAR HIV programs in the field had experienced significantly low testing yield. PEPFAR has focused on concentrated epidemics with high-risk, vulnerable populations, and it works in some of the highest-burden countries in a generalized epidemic in sub-Saharan Africa (SSA).

PEPFAR supported 68 million tests in 2015, 45 million of those directly through buying the commodities or directly delivering the services at clinics. Looking across PEPFAR countries, one finds a 4.1% prevalence (45 million tests, 1.8 million positive results). PEPFAR posed a challenge to its supported countries to find solutions to raise the testing yield.

AMB Birx shared data outcomes from the Chiang Mai (Thailand) Community Performance program and PEPFAR's new USAID LINKAGES project. Prior to receiving this data, the perception in the HIV/AIDS world was that paid community support outreach workers were the optimal way into networks such as men who have sex with men (MSMs), injectable drug users, and sex workers; in Northern Thailand, their testing yield was 4.92%. As a new way of operating, the team turned to incentivizing peers within the networks (using cell phone minutes as rewards) to provide referrals; their yield was 10.6%. It became clear that being in the network resulted in significantly better referrals, as well as higher linkages to treatment (case in point: 44 positives, 36 started on ART).

AMB Birx noted that the format of PEPFAR management meetings shifted once this exciting data became available, with teams presenting their data to all other 10 countries in attendance; meetings thereby became sessions for data sharing from and insight into real-life programs and practices, as well as analysis of the current data. This changed PEPFAR's perception of best practices by having comparative information and learning the steps needed to achieve success.

Challenge 2: New Infections in Adults—Testing and Treating Men

With the clear gains made in the peer incentive program, PEPFAR hoped this practice also would be helpful in accessing the male network, as testing and treating men has presented a considerable challenge of its own.

AMB Birx again shared the great progress made in prevention of mother-to-child transmission (PMTCT), with many countries having less than a 4% transmission rate. She also discussed the problem of a 100% increase in adult transmission in Uganda.

AMB Birx next presented data from Kenya that had been disaggregated to the site level. While she had thought that men were being found to be HIV positive, they were infecting women, and leaving the system before being treated, the reality is considerably different. She pointed out that the female and male clinical cascades, involving people living with HIV (PLWH), diagnosis, linkage to care, ART treatment, and viral suppression, are highly similar; the difference lies in the number of people being tested. After three years of B+, 95% of women have been tested; in comparison, only 74% of men have been tested. However, when men are found and diagnosed as HIV+, they do go on treatment if they can access that treatment. AMB Birx noted that this is groundbreaking as it relates to the new World Health Organization (WHO) recommendations and enables the use of a simple, uniform public health message to women (pregnant or not) and men: “A deadly virus is destroying your immune system, even though you cannot see it, and you need to go on treatment immediately. Treatment will help you by decreasing your viral load and will help others by decreasing transmission.” PEPFAR is excited about this, as it means that men are as likely to stay in treatment scenarios as women even without adherence boosters related to pregnancy.

AMB Birx shared clinical cascade data from Swaziland with comparisons to the UNAIDS 90-90-90 strategy (90% of people with HIV diagnosed, 90% of them on ART, and 90% of them virally suppressed, all by 2020). Looking at adults, the chart showed PEPFAR targets for 2016 and 2017. She noted that 90-90-90 will be achieved for women by the end of this year and 95-95-95 should be attained by September 2017. Men’s targets will be either achieved or very close to achieved by 2017. AMB Birx asserted that the data demonstrate that testing and coverage can be accomplished, and are well on the way to being so, within the next 18 months.

Data from Namibia show the percentage to achievement in the clinical cascade by gender across the country. One high-burden area with very low coverage of services—Kavango West—remains behind in terms of treatment and viral suppression. Parity between men and women varies by area. AMB Birx noted that this detailed data allows countries to customize messages at the district level.

Challenge 3: Dramatic Increase of 10-24 Year Olds Across Sub-Saharan Africa

AMB Birx noted that the World Bank is preparing a report on this issue that will include some of the information she is sharing here.

AMB Birx called attention to the eight Millennium Development Goals (MDGs), particularly MDG #4: Reduce Child Mortality. PEPFAR's PMTCT-reduction efforts as well as work around malaria with PMI and The Global Fund, immunizations, and maternal-child health efforts to which USAID contributed, were extremely successful in the reduction of child mortality. The MDGs began in 2000; 16 years later, the children survived due to reduced childhood mortality are now 12, 13, and 14 years old. South Africa has seen a demographic shift, from 7 million to 10 million girls and women ages 10 to 24 years. Due to a decrease in fertility rates, Southern Africa (Namibia, Botswana, and South Africa) truly has a "youth bulge"—the number of adolescents will begin to decline in 10 years—and needs a very focused strategy.

Southern Africa differs substantially from the rest of SSA. According to the World Bank, the number of women in SSA besides Namibia, Botswana, and South Africa in 1950 was 25 million girls and women ages 10-24 years; by 2050, that number will be close to 300 million; this translates to almost 275 million additional young women. And, SSA fertility rates will not decrease to the levels of those in Southern Africa. High youth unemployment and low school enrollment already exist, and a strategy is needed to address the increased numbers of adolescents and young adults who were prevented from becoming infected as infants, so as to ensure they do not become HIV+ in their teenage and young adult years. This demographic issue has given the HIV/AIDS community pause over the last two years, and it is the reason for the increase of a .5 million increase in new infections annually, despite lower incidence rates. This issue is why PEPFAR launched the DREAMS partnership and why it has been strongly focused on preventing infections in young men through voluntary medical male circumcision (VMMC).

Age and Gender as Indicators

Girls and young women account for 71% of new HIV infections among adolescents in SSA; this translates to approximately 1,000 new infections each day. An age-gender disparity in new HIV infections exists globally, driven by infection of young women in the following way: Men between 25 and 30 years are infecting young women ages 15-20 years; these women at ages 22-24 years later infect young men of 25 years. This cycle alone accounts for about 720,000 new infections a year in SSA.

AMB Birx shared a three-part strategy that PEPFAR has developed in order to break this cycle:

- Place the men in their late 20s on treatment to reduce their viral load
- Have younger men circumcised to protect them from infection
- Empower young women

In DREAMS countries, PEPFAR is focusing on placing the absolute number of men on treatment and on getting closer to the absolute number of women on treatment.

Education as Risk Reducer

Education has been shown to reduce risk of HIV acquisition. Recent publications have demonstrated protective effects of education in this area.

Botswana Study

An ecological study in Botswana—the Botswana AIDS Impact Survey (BAIS)—compared young women and men completing nine and 10 years of education; results demonstrated that one additional year of education for adolescents can reduce HIV acquisition before age 32 years by one third. The protective effect of education is even stronger among young women, for whom the risk of HIV acquisition was cut nearly in half.

Botswana has conducted BAIS over the past 20 years, providing age- and gender-disaggregated data every two to three years. Between the group that received nine years of education and the subsequent group that had 10 years of education, the prevalence rates dropped by one third, with young women down by 50%.

Los Angeles County: HIV Prevalence and High School Education

PEPFAR is able to learn from domestic programs as well. In Los Angeles County, the high school education levels of PLWH have been documented. In South LA, a correlation has been shown between lower levels of high school education and higher HIV/AIDS prevalence.

Cross-Population Information and Strategies

AMB Birx noted that similar risk factors may exist for some young men of color and young women around sexual violence and issues related to education, homelessness, and ability to access prevention messages. It is exciting to learn from one another, and this kind of helpful information is what allows PEPFAR to communicate to the minister of education in Malawi, for example, that the Sustainable Development Goals (SDGs) apply to everyone; shared issues exist globally, and together, we can develop solutions.

Right Places: Country Examples

Context

AMB Birx shared examples of PEPFAR-supported countries' efforts to work in the right places, with a goal of clarifying what "right places" means. She explained that "sustained areas"—often with 75-80% coverage of services—are expanding treatment more quickly than they ever have in the history of the program; they have added resources to the high-burden areas (40% coverage) in order to bring them up to the coverage that the sustained areas possess. This is to ensure that an entire country attains 90-90-90 by 2020.

PEPFAR is working to meet those goals in a relatively flat budgetary situation. In 2014, Congress appropriated an extra \$300 million; this represented the first time the program received a funding increase in the past five years. The funding amount has been maintained, and there has been a slight increase in the bilateral program. Essentially, funding has remained flat despite increasing need.

PEPFAR representatives have been engaged in significant lobbying efforts on Capitol Hill, communicating that they are working to make the program as fit for purpose as possible—that is, doing all they can with the available resources to focus on prevention and on core treatment issues—due to the constraints of the federal budget. Very recently, a senior appropriations leader responded that the committee is aware that PEPFAR will need more money to achieve the coverage that it works to put in place. AMB Birx remarked that such feedback marks a sea change and reflects the impact the program and the SAB are having.

Rwanda: Smaller Country, Lower Burden of Disease

AMB Birx showed three maps representing the past, present, and future clinical cascade results, expected results, and targets in Rwanda. All FY17 targets meet or exceed 90-90-90. Additional slides depicted that saturation of service coverage. Finally, a chart showed viral load coverage and suppression by district. The Rwanda results represent the ideal.

Zambia: Larger Country, Larger Population, Larger Burden of Disease

AMB Birx shared a map of Zambia showing PLWH by burden of disease, with priority regions highlighted. Three additional maps displayed past, present, and future coverage in those regions, with complete epidemic control by FY17. By 18 months from now, Zambia will have 77% coverage of ART, extraordinarily close to the 90-90-90 goal of 81% by 2020.

Right Things, Right Way

The above examples, as well as that of Swaziland (mentioned earlier) convey the progress that in-country teams are making with governments and with implementation partners, all while ensuring services remain in sustained areas and the entire country achieves 90-90-90. This shows what is possible with treatment and viral suppression along with countries' expansion of circumcision and DREAMS. Adding resources to high-burden areas to ensure coverage throughout a country has proved a highly successful model, and the countries are using the data to drive their progress.

AMB Birx noted that the WHO guidelines simplify the public health message and ensure that no man will be turned away because his CD4 count is too high.

PEPFAR is working with partners in SSA toward creating and supporting a health system for the 21st century—one that is responsive to the SDGs and utilizes a human rights approach. The program has integrated everywhere there has been a place to do so. In most of Southern Africa and the rest of SSA (perhaps excepting of South Africa), the primary health delivery system was in maternal and child health (MCH); a constituent younger than five years old or pregnant had a wellness approach. If s/he was past the age of immunization, a young woman, or a male, acute care was available, but no wellness and preventive care approaches existed.

Treatment for All

PEPFAR believes that a clinic must accept all individuals, including vulnerable young women, MSMs, and sex workers. The program has been working with multiple countries, and Zimbabwe has

already begun implementing the new service delivery that involves six-month follow-up and longer duration of refills.

AMB Birx asserted that, if a policy of Test & START was immediately rolled out with the alternative service delivery as what is being used in Zimbabwe, 28 million men, women, and children could potentially be on ART by 2020; that is nearly twice as many as today. It would require some additional resources; PEPFAR is currently costing these, as none of its programs have rolled out the alternative service delivery. Actual cost savings will not be clear until implementation has occurred.

A model from Botswana demonstrates that an increase in ART would translate to a decrease of new HIV infections and of deaths by 50% over four years; new tuberculosis (TB) cases would decrease far more greatly, as people would be treated before they become susceptible.

Potential Cost Scenario

The decrease in TB alone leads to a cost savings of almost \$33 million in Botswana. AMB Birx called this an exciting strategy that has a return rate related to the TB element even though a cost exists by adding people to treatment.

PEPFAR has developed models related to cost savings by replacing the three-month ART refill policy with a six-month one. The savings get close to the cost of seeing clients every six months. PEPFAR is asking countries to implement the changes in partnerships with ministries of health, and it should have data on the alternative service delivery within six months. Cost saving models include the 10-15% of clients who are fragile asthmatics, hypertensives, and diabetics.

The major key to this implementation is the six-month supply of medication. AMB Birx attended a Vatican-led meeting chaired by Cardinal Turkson and including people working on HIV/AIDS in the private sector. A discussion was held about the six-month supply, and it looks like a reasonable volume of pills.

For purposes of cost, convenience, and retention, manufacturers are working to develop a single, smaller container that looks similar to multivitamin packaging.

ARV refill policies affect the cost of treatment. Mozambique currently employs monthly refills, and Malawi and Zambia offer three-month refills. Nigeria, Kenya, Tanzania, Uganda, Ethiopia, South Africa, and Zimbabwe all offer two-month refills.

Feedback from clients is that they are unable to leave work once a month or even once every two months to stand in a pharmacy line. This issue is dramatically negatively impacting adherence. US data show that adherence improves when people are seen once every six months. AMB Birx circled back to the development of a 21st century health system, purporting that creating such a model for HIV will benefit (and be usable for) routine diabetes and hypertension as well.

Shared Responsibility

In order to eliminate HIV as a public health threat:

- Policy changes, more than money, are essential;
- Country leadership on policies and adoption of WHO guidelines must be within weeks and months, and not years ;
- Nearly two-thirds of the cost of treatment needs to be service delivery, not the cost of drugs; and
- Change in policy to every six-month appointments and tendering to a three-to-six-month supply of drugs will allow each treatment site to add 75% more clients on treatment with the same facility personnel and cost.

PEPFAR has been working with in-country teams over the last three months. All of the permanent secretaries in all of the high-burden countries have agreed to begin Test & START by September. Even slower-adoption countries have signed on, and this has potential for real change.

Summary

AMB Birx explained that PEPFAR supports the following SDGs, through its economic work with women in families and communities, with young women in DREAMS, with faith-based organizations (FBOs) around gender-based violence, access to medical care that meets one's needs, and more:

- SDG 1: No Poverty
- SDG 3: Good Health
- SDG 4: Quality Education
- SDG 5: Gender Equality
- SDG 8: Good Jobs and Economic Growth
- SDG 10: Reduced Inequalities
- SDG 11: Sustainable Cities and Communities
- SDG 17: Partnerships for the Goals

Sobering Numbers

This week, over 2,880 children and over 20,000 adults died from HIV. More than 4,230 babies and over 34,615 adults, of whom more than 7,000 were young women, were infected with HIV. The last number represents the current number of young women at risk; AMB Birx asserted that, unless we impact incidence in young women, the numbers will grow year after year simply because of the vast number of those who are entering the vulnerable age group.

Successful Results

The accelerated children's treatment that was disseminated through PEPFAR about 15 months ago has already resulted in nearly 200,000 new children on treatment, bringing the total to over 800,000. While the big shifts occurred in nine countries, children's treatment increased and changed slope in the other 10 PEPFAR countries. AMB Birx remarked that these initiatives both affect change in the countries in which they are implemented and also capture the imagination of the PEPFAR teams and implementing partners, and expand the network.

US Global AIDS Coordinator Presentation Q&A

Dr. del Rio thanked AMB Birx for her presentation and opened the floor to questions.

Question 1: Judith Auerbach

Regarding the 90-90-90 goals, who are the other 10%? What do we know, particularly from PEPFAR programs, about who is not being reached or are choosing not to access services? Is it disproportionately populated by those we are most concerned about in this epidemic other than vulnerable girls and women? Is that group MSM, drug users, sex workers, men, women?

Answer: AMB Birx

We are trying to learn from epidemics driven by MSMs, intravenous drug users, and sex workers in the Asia and Ukraine areas. The gap in those areas was linkage to care; people were getting tested but not linking to treatment. This was true in the Caribbean as well. Gaps vary greatly from region to region.

In the generalized population, we know that the gap is men. We have been pressing countries to establish more consistent tracking of key population data of the epidemics, and this is now occurring in every PEPFAR country. Key population data is weaker than the general population data. We are now developing cascades for each of the groups, along with surveys to obtain population estimates so as to understand the size of the risk, the size of each group, and what risk behaviors specifically need to be addressed. We will have detailed data on those key populations at this year's World AIDS Day (December 1) that will answer the question of who is being left behind.

Question 2: Connie Celum

Please provide your interim perspective on successes and challenges of DREAMS and its highly ambitious targets.

Answer: AMB Birx

The DREAMS targets were set based on two parameters. The first was that the youth bulge and the youth wave were the minimum to keep from exceeding 2 million new infections a year. Implementers and the US team advised against that target, but I felt the need to set targets that would impact new infection rates to at least to stay in place; a 40% reduction merely treads water and does not get us under the 2 million new infections.

Our wildly aspirational targets have captured the imagination of the private sector and of implementers. Very strong monitoring and evaluation is in place in the DREAMS districts. One country—South Africa—has added its own funding and its Global Fund money to bring DREAMS to 100% in the country. DREAMS is planned at both the local and national levels; and South Africa will be the first country to nationalize the program. The Bill & Melinda Gates Foundation is working with OGAC on additional monitoring and evaluation to inform course correction and to gauge impact.

PEPFAR combined the evidence base from the literature on single implementations of single approaches (examples: education, conditional or unconditional cash transfer), with the hope that they would be synergistic. The impact of the combination of interventions will be known in the next 12 months. This is reminiscent of HIV vaccine development, with those who believed in the power of antibodies and those who believed in T-cells, and now those who believe in a combination of the two. Trials conducted around both show that they are more effective together. DREAMS is in that trial process.

We worked hard to develop targets that transcend US administrations. Much of the targets are based on Quarraisha Abdool Karim's data, which we regard as very strong. As I have done in the past while conducting the Thai trials, I am willing to push the field to address a very large issue.

Question 3: Peter Berman

Please elaborate on how you envisage PEPFAR's role in strengthening health systems and healthcare delivery at the lower levels. I am involved in Countdown to 2015: Maternal, Newborn & Child Survival, which has been monitoring progress on the MDGs for maternal and child health. The collaborative project recently completed a set of country case studies for the purposes of determining why change was occurring. One preliminary finding of the studies is that the MDG push seems to have done very well in strengthening simple services that are delivered at the community, lower-level health worker interface. It has also done well with some disease control programs, such as around HIV and TB, which had fairly distinct service delivery models; however, it has not done well in providing services that require a more sustained engagement at the first-level clinic (multiple visits, chronic or noncommunicable disease, etc.). These results highlight a large agenda to create that kind of a service delivery system. If HIV and TB programs are going to transition more to national systems, a hard look will need to be taken at this issue, particularly as when resources may be flat and scope is expanding to many new kinds of problems. In my experience, in some countries, funding from The Global Fund has been flexible in its ability to support these kinds of investments.

How do you visualize how PEPFAR will be able to help with this in the future?

Answer: AMB Birx

We learned from the HIV model that we got locked into a system that was dealing with very sick patients early on in the epidemic and that did not adapt to wellness. Local health centers or health posts are very much engaged around acute emergency care that has a very short delivery model of services and is not sustainable for any of the SDG goals. I believe that it is part of our mandate to work on a system of care with what are termed alternative service delivery models in order to move forward to every-six-month healthcare delivery as wellness visits for non-communicable disease (NCD) and HIV. It is incumbent upon us, as PEPFAR moves its thinking from emergency services to sustainability, to bring the system along in the same way. We have invested around \$1 billion into the laboratory health systems in Africa, and we are proud of the result. Investments

have included brick-and-mortar health centers; however, PEPFAR and Global Fund rollout has demonstrated that, as Africa has urbanized, the district hospital/health center model does not work in many of the newly low-population areas. There is a discussion around whether to develop mobile health centers with text messages for acute issues in districts with very low populations and very low burden of disease, as these are becoming more common. The district health centers may not be sustainable for any of the next 15-year goals, and we now have the ability to reach clients with acute issues through the use of cellphones and text messages without long-term, sustained brick-and-mortar health centers. PEPFAR is strongly embracing the WHO alternative service delivery models, as it sees them as its roadmap to NCD care.

The goal is to ensure that urban areas have the capacity to deal with the ever-increasing population, and that the more rural areas have a model of health care that meets their needs.

Question 4: Albert Siemens

Thank you for your demonstration of how PEPFAR is using data to bring focus to the problem. The World Bank's population data shows a scary order-of-magnitude growth in the vulnerable population and makes clear that the challenge will continue to grow. Where is PEPFAR on the issue of family planning, as this is one way to address the youth population bulge?

Answer: AMB Birx

We listened to young women and learned that their biggest concerns are twofold:

1. Becoming pregnant and not being able to finish high school and have a career.
2. No access to commodities due not to a lack of commodities but instead to a dearth of youth-friendly service providers.

Part of PEPFAR's interest in high school education relates to sexual education. If we work with countries to lower school fees and provide subsidies, funding will require schools to teach an approved, available sex education curriculum and provide health services on site. We need to find some place for young girls and boys to receive honest health messages and the commodities they need in a non-stigmatizing, non-discriminatory way.

PEPFAR is very concerned about population growth and works closely with USAID and its reproductive health programs in Uganda and Malawi. Youth unemployment of 35-40% already exists in many countries, and many young people already do not have access to high schools; now, the numbers in that age group will rise. The MDG planning did not include addressing the young people who survived infancy and youth; I hope the same gap does not exist in the SDG planning.

Question 5: Mitchell Warren

How, both centrally and with country and implementing partners, is PEPFAR thinking about how tested and uninfected individuals are linked to services to maintain their HIV-negative status? As PrEP use and DREAMS support rise, with quarterly testing in place, how do we maintain a high yield in the HIV-negative setting?

Answer: AMB Birx

Once we get close to saturation on the HIV+ yield, the key goal is to maintain the eventually 98% persistently HIV-negative yield. We now have longitudinal data down to the site level, and we can already find programs that are successfully achieving such maintenance and can be documented by the impact surveys we have in the field. Solutions already have been found in which communities have persistent negativity even in the face of high burden. We believe that granular data analysis will reveal those positive, innovative solutions as well as trend lines of decreasing yields due to having reached saturation and are persistently negative.

The question is, what are the preventive service delivery packages we need to put in place? The reality is that the current approach is quite rudimentary. We do not have refinement of what keeps men HIV-negative in the US, as we had in early studies of MSMs and sex workers; therefore, we cannot put forth an evidence-based program recommendation.

Question 6: Carole Treston

I am wondering if you have had conversations with nurses along the lines of those in which you have entered with educational and faith-based organizations. How do we keep the pipeline active: hold conversations with schools of nursing, universities, and councils of nurses? Numerous barriers exist to current nursing practice, and, with the youth bulge coming, there will be a “reverse bulge” in nurses as they compare in number to the expanding youth population. Experience shows that councils of nurse leaders are critical to the effort and need to be encouraged in that vein, including by each other.

Answer: AMB Birx

PEPFAR has worked hard to increase the supply chain, or pipeline, by training hundreds of thousands of nurses; however, it did not plan for or work toward retention or meeting the long-term training needs of those nurses as well as task-shifting to the lower health cadre to avoid burnout. Many nurses trained by PEPFAR left their countries for better opportunities in places such as England and South Africa.

At the next PEPFAR Nursing Education Partnership Initiative (NEPI) meeting, I hope that we connect with nurses with less than five years of experience, in order to learn what is making them stay or leave. One of NEPI’s goals is to support innovative nursing retention strategies to ensure adequate coverage in SSA.

The next International AIDS Conference (AIDS 2016) will take place in July in Durban, South Africa. Nurses engaged in HIV care will be in attendance, and we will begin working now to set up that first meeting so we can start the listening process around how PEPFAR can better support them.

Question 7: Mark Heywood

I always try to square the data with what I see on the ground, specifically in South Africa, and I have a concern related to the youth bulge data presented today. Given our dependence on quality education, employment, and access to public healthcare services for young girls, if indicators of those are pointing in the wrong way, what are implications of HIV prevention? Just yesterday, data was released showing poorer education outcomes as compared to 20 years ago and that youth unemployment has approached 60% with no prospect of improvement. Anecdotally, the quality of the public healthcare system is in serious decline. New factors have entered into issues like HIV control that are not getting the attention they might deserve. Fifteen years ago, South Africa did not have a serious epidemic of drug use; there is growing evidence of very significant drug use among young people that involves “nyaope”, a mixture of low grade heroin, marijuana, cleaning detergents, rat poison, and chlorine. The drug has not been studied in relation to HIV. More and more, our approach to HIV treatment and prevention needs to take more account of these deep social determinants and drivers of the HIV epidemic. If it does not, any progress will see significant pushback, some of which is already occurring. How can we think about that approach?

Answer: AMB Birx

What you have articulated is our basic fear and is what puts the \$70 million at risk. In South Africa, you have 6 million more young people, but without the facilities, capacity, teachers, or jobs to meet the needs of those individuals. On top of this, we know that these are the groups at increased risk of contracting HIV. Now the risk will be greater because those very basic elements will not be in place; we know how important they are to prevention of infection. We believe this could unravel all of the success, because that is what puts us at over 2 million new infections a year.

At the high level, meeting documents that are being prepared are costing out the funding requirements for a steady state or improvement of incidence. We believe neither is possible given the social factors we see, and those have not been discussed or attended to, and our talks now include such information.

Young people urbanize when opportunity is not present. We will have high transmission sites and waves of individuals seeking a better lifestyle. I have been pressing economists to write about this issue, because we need to create an awareness of the severity of the situation. This is not a ministry of health or education issue; this is a presidential issue that needs to be dealt with across all ministries. Social factors that put young people at risk are expanding, and we have an increased population at risk along with less of a social safety net. This combination is particularly deadly to our 15-24 year olds.

I have taken this information to venture capitalists and frontier investors, as they see 3 million more young men as a huge opportunity to sell them products. We need to get the private sector on our side, helping them to understand that young people cannot buy beer if they are unemployed.

This issue is going to be much broader than a health issue and much larger than any one of us can solve.

Question 8: David Peters

Please reflect on areas having problems, particularly those areas in countries that are doing well generally. Are you finding any patterns vis à vis obstacles? Are the ability to have data or opportunities for learning affecting them? Are there broader institutional management issues involved? Is community engagement playing a role? During the Ebola outbreak, it was community engagement that brought the public health preventive and clinical aspects together and turned the epidemic around.

Answer: AMB Birx

PEPFAR's work in Nigeria—including its now-nearly \$5 million investments, its 29% coverage of PMTCT, and its 15% coverage in treatment—has demonstrated that fighting and beating the HIV epidemic is about more than money; district and local governments must be willing to lead on these issues. A structure is needed that supports efforts and decreases stigma and discrimination, such as the church, the chiefs, or another community system.

Other countries have been left behind not because of a lack of leadership but due to low funding. We analyze every country by its total HIV investment and divide that number by the total number of PLWH. At one point, Rwanda, Haiti, and Ethiopia all had funding of over \$1,000 per PLWH. At this time and after reductions, Ethiopia is around \$450 per PLWH, Rwanda is around \$500 per PLWH, and Haiti remains at \$1,000 per PLWH. In comparison, two years ago, Mozambique had \$170 per PLWH; that takes into account money from The Global Fund, PEPFAR, and all other sources.

There is significant inequity in the HIV investment, and this needs to be corrected. I am working together with Global Fund Executive Director (and former US Global AIDS Coordinator) Mark Dybul regarding right-sizing the investment.

The reality is that both money and leadership matter in this work. Leadership enables communities to communicate on and manage these issues and to support the individuals who are at risk.

Question 9: Ruth Macklin

Is there any thinking about how to achieve equity in terms of money and related to other resources, including human capital? Is that on the agenda? If not, I would suggest that it be added.

Answer: AMB Birx

You taught me that equity is more important than equality, and we have been trying to discuss equity over last 24 months. Initially, partners were funded equally, regardless of level of burden of disease. In certain locations, there were 100% of necessary goods and services, while others only had 50%. PEPFAR has now moved money around to create equity, which we feel is enormously important to create the necessary access. Needless to say, some partners have lost some of their

funding in order to create that equity. It has been a difficult road to make the shift to equity, as the rollout was built on a sense of equality, but PEPFAR has stayed true to this principle, and progress has been made. That said, some will say “you left us behind” even though we are sustaining services in their country. This issue affects more than treatment services; it affects prevention services as well as programs that provide the services around the orphans and vulnerable children who are most at risk. A positive outcome of reallocating money is that every US ambassador in every PEPFAR country snapped to attention, learned the details of PEPFAR programming, came to understand the decision-making from an equity base, and carried that message. Even South Africa has adopted the approach after much objection. The data are allowing us to see that countries rolled out in a hub-and-spoke manner, and this did not provide equitable resources.

Question 10: Celia Maxwell

I was very pleased to hear you refer to wellness visits, as I believe that is how we need to look at HIV. I spent a week last month with Christine Nabiryo and the clinic team and saw firsthand that the brick-and-mortar approach does not work when 200 clients are in line by 10:00 a.m., with 400 queued up by noon. Providers are stretched, but I saw the use of nurse clinics very effectively easing that burden. While I saw numerous innovative innovations in Uganda, I like the idea of shifting the service delivery model; however, I wonder how to deal with the belief of, “Since I am being seen only every six months, I must be okay; I am going to drop out.” Is there a plan to ensure that we do not run into the issues of attrition and re-linkage to care?

Answer: AMB Birx

The dropping out you mention was very much facilitated by public health messages in the community. When you turn away 50% of HIV patients and tell them they do not need treatment, they take that message back to the community and question others’ treatment protocols. The message we are working towards and need to carry to clients is a unified one: “You have a disease you cannot see.” This needs to be consistently reinforced.

PEPFAR shares your concerns and therefore has gone to quarterly data analysis. The analysis includes five core parameters to determine how many are retained on ART and to identify communities that are struggling or are solidly succeeding. The data show that, in the US, moving to six-month delivery strengthened retention; this was due to a program focus shift to wellness. We look forward to finding out whether that impact is mirrored in Africa.

Question 11: Jennifer Kates

Next week, the Global Fund board will likely adopt a new strategy in the allocation formula and a new sustainability approach. What should we be thinking about related to this?

Answer: AMB Birx

Thanks to Dr. Dybul, we have changed the PEPFAR-Global Fund working relationship from a reactive one to one of collaboration. At the board meeting, we will likely raise issues about an intervening step after the technical reviews in high-burden, high-investment PEPFAR countries; we would sit

with the secretariat and together ensure we are collaborating maximally so as to avoid wastage of dollars or duplication of efforts. This collaboration, which has grown significantly, will become more critical over time.

Dr. Dybul identified 20 countries that had performance problems in their grants—65% were burden-of-disease issues and 60% were resource issues—and he came up with 357 activities with clear outcomes. The Global Fund's granular work around issues is allowing PEPFAR to respond to them with our people on the ground in a timely way. Additionally, The Global Fund is providing all first-line drugs and most of the test kits, and while PEPFAR is providing service delivery. Beyond the collaborative benefit, this allows for one data system that reflects the two organizations' information in tandem and allows us to evaluate pieces together in real time. We are working diligently to make data visible and actionable through the PEPFAR website.

Question 12: Judith Currier

To follow up on the subject of health systems for chronic care, are there any plans to inventory and collect data on sites that have been set up to provide that chronic care? Monitoring and evaluation would help show some of the progress that has been or can be made by using scaffolding for primary care in the future.

Answer: AMB Birx

PEPFAR has entered into an agreement with the Millennium Challenge Corporation (MCC) to work with a group of countries (Tanzania, Zambia, and hopefully Kenya) to develop a universal data system looking across health issues. Once the system is established, it could be used in multiple areas. PEPFAR is funding the system because it believes that such a solution of wellness care is what we need as well. We have been working with MCC on the data piece; at the same time Dr. Shaffer has been in negotiation with the private sector around exploring how the platform can be leveraged for hypertension and cardiovascular disease. Physicians and nurses do not have much trust in clients to handle a six-month drug supply plan; cultural and normative changes need to occur in order to move to this wellness model.

Question 13: Angela Mushavi

I would like to chime in on the issues of human resources and retention. Money is a big issue for healthcare workers; however, so is the work environment. In Zimbabwe, we experienced migration over the past decade due to socioeconomic challenges, and we have received support from The Global Fund and the Zimbabwe Health Transition Fund to retain workforce; some positive gains have been made.

On the topic of community work, we have been trying to get men involved in programs and have developed focus groups. Men have noted that the healthcare environment is dominated primarily by nurses, who are, in most instances, female. They also commented that they wait in lines that are filled mostly with women. In order to make the environment more male friendly, could there be more men on the front line who could talk to issues around HIV and also about wellness? To what

extent is PEPFAR looking into ways to answer men's concerns and increase their participation in their health care? Looking at the male clinical cascade, it appears that getting men to test is the issue to be addressed.

Finally, regarding PEPFAR's work to support integration of gender into the SDGs, how does PEPFAR funding come in to support integration and SDG 3, which speaks to universal health coverage?

Answer: AMB Birx

The absolute issue we are facing is that most of the healthcare delivery into which we have integrated has focused on the maternal-child health block. This female-oriented approach does not lend itself particularly well to men. When we discuss creating a healthcare system for the 21st century that is based on wellness rather than acute care, we need to determine what that care looks like. Currently, some clinics in Botswana have male nurse prescribers; we can look at data to find out whether more males visit that clinic.

We have this very discussion with our teams: How are we creating a health system that can address the issues of the entire community, including men and key populations including young women? The churches may have a whole-community approach we can study to see what they have done to keep men in the system. There is really no male clinic or adolescent clinic to which we can integrate. We need to find and build that place together so that there is a place in which to integrate to other health services.

Question 14: Jean Pape

When you compare cost per patient across countries, are you also looking at different costs among providers within a country?

Answer: AMB Birx

PEPFAR conducts expenditure analysis at the partner level and is working that down to the site level in order to truly understand performance in that detailed way.

Question 15: Jean Pape

As Ms. Maxwell cautioned, I too would suggest not moving too fast to the six-month service delivery model. We have analyzed this issue and have found that patients who are most adherent are those with the most education and with higher income levels. That group likely will not have a problem moving to the six-month service delivery; however, not all patients will remain adherent in the face of that shift.

Answer: AMB Birx

We want countries to move to three-month visits and to pilot six-month delivery. We are aware that the latter is something to be studied very carefully. What we do not want to allow to occur is the potential disconnect between retention and adherence. If a patient is to collect medication every month but only sees the physician or nurse every three months, the perception could easily

exist that the patient is adherent and retained; however, while the patient could be on and off treatment during those three months if, for example, s/he was unable to pick up the medications monthly. We currently have no ability to track this except by drug usage.

Question 16: Dr. Pape

Has PEPFAR attached as much importance to neonatal circumcision as it has to VMMC?

Answer: AMB Birx

We had to make a decision based on budgetary realities and have asked countries to reach 80% circumcision saturation in the 15-29 age band, as that is the group currently at highest risk. Kenya is close to that saturation; we directed that country's team during its most recent visit to begin discussions about neonatal circumcision.

Question 17: Jesse Milan

I am concerned about the youth bulge. Please share PEPFAR's vision for inspiring the churches and the faith-based community to properly address this critical issue.

Answer: AMB Birx

PEPFAR believes that, at a time when the churches are splitting over dogma and doctrine, the issue of the youth bulge, along with gender-based violence and the community needs of women, could be a uniting piece. PEPFAR Deputy Coordinator for Affected Populations and Civil Society Leadership Cornelius Baker and PEPFAR Chief Strategy Officer Sandy Thurman are working on how to bring the faith-based community back to the table, whether in South LA dealing with young men of color who are now homeless because they were kicked out of their families' homes, or whether in Kenya. We need uniform church engagement once again. I am deeply concerned about the church divide in SSA, as 80% of the population (rural and urban) is church-going, and stigma and discrimination is driving everyone away from the clinics. The goal is to find common ground in which people can see themselves as having a role in the community. In the ecumenical Vatican meeting, I suggested providing fact-based messages to youth about their risk. Currently, young people are getting no information from any source. Many churches are dealing with HIV in a real way day to day, but no systematization has occurred.

Everywhere we go, young women tell me that they are not at risk of HIV because they can tell who is infected. This sense of lack of risk is very real, and the churches can take an active role, as the young people may still be connected there.

Question 18: Dr. Nabiryo

I am wondering about ongoing efforts about sharing innovations and about program documentation that could be used as lessons learned and best practices and that could be shared from country to country. What is on the horizon for such sharing efforts?

Separately, how much leveraging of other USG agendas such as economic development and governance is ongoing at the country level, as was put forth as a strategy?

Answer: AMB Birx

We are open to any suggestions of how better to share information and are working on a way to virtually share things such as our findings in Chiang Mai and our cascade data. While we can submit it to the scientific literature, that will take months rather than days to be released.

There will be a brief PEPFAR gathering before IAS to share all of this information in a clear way. It can then be placed on the PEPFAR website to include point-of-contact details.

At the country level, the ambassadors and deputy chiefs are the only representatives that have an ability across all programs to understand what can be leveraged and how, and to make those connections. They have used their positions to speak with ministers of finance and foreign ministers about the issues in the countries, and they thereby have made policy movements possible.

October 2015 Meeting Follow-Up

Dr. Shaffer

Dr. Shaffer reminded the group that the SAB had initially met in October 2015, an exciting and busy time following the eighth IAS Conference on HIV Pathogenesis, Treatment & Prevention (IAS 2015) that took place in Vancouver that July. At IAS 2015, the Strategic Timing of Antiretroviral Treatment (START) study results were presented, providing definitive data supporting earlier intervention of HIV treatment regardless of CD4 count, and there was a growing enthusiasm around Pre-Exposure Prophylaxis (PrEP). This was all in the context of AMB Birx giving her commitment to dramatically move forward with these important innovations; however, we were uncertain when WHO would release its formal guidelines.

Expert Working Groups (EWGs)

The first EWGs were formed immediately following IAS 2015 and were charged with questions around the body of evidence supporting implementation of PrEP and Test & START prior to the release of WHO guidelines. The PrEP EWG was chaired by Dr. Karim and Dr. Celum and the Test & START EWG was chaired by Dr. del Rio and Dr. Currier. Reports from those working groups were a focus of the October meeting.

Fortunately, WHO released the formal guidelines in late September and early October, both before the SAB met. The board had very important feedback from the EWGs. Dr. Shaffer reported the feedback was ultimately endorsed by the SAB and immediately posted on PEPFAR.gov for public access. The SAB's feedback was critical to technical considerations that laid the foundation for PEPFAR's ongoing planning. Dr. Shaffer expressed PEPFAR's appreciation to the EWGs for their efforts.

Combination Prevention Trials

Another key activity at that time was the work around PEPFAR's combination prevention trials (CPTs). WHO's recommendations on Test & START moved the standard of care in the CPTs; therefore, the CPTs needed to be brought up to that standard, with treating all regardless of CD4 count. The SAB recommended convening a conference of stakeholders to address this question. PEPFAR convened such a meeting with consultation from Mr. Warren—who co-chaired the conference along with Myron Cohen, MD of the University of North Carolina Medical School at Chapel Hill—so as not to miss the opportunity to focus on current and future prevention finances, sustainability, and data. The conference took place at the State Department with over 100 representatives from a variety of backgrounds.

Dr. Shaffer turned to Maureen Goodenow, Fredrick Sawe, and Mr. Warren to provide an in-depth report on the conference, to update the board on the research science, and share the formal recommendations that were developed.

HIV Epidemic Control Conference Readout

Dr. Goodenow shared the framework and planning for the “HIV Epidemic Control in a Time of Constrained Resources for PEPFAR” conference. She explained that PEPFAR convened the conference based on the SAB's recommendation. It was held at the State Department on February 8-9, 2016, and was co-sponsored by:

- US Global AIDS Coordinator and Health Diplomacy
- Bill & Melinda Gates Foundation
- NIH Office of AIDS Research

Objective

The overall objective of the conference was to provide the opportunity for thought leaders to brainstorm about PEPFAR in the context of the new WHO normative guidelines, UNAIDS 90-90-90, and current and future prevention modalities in an environment of constrained resources.

Attendees

The conference was originally envisioned as including 60 individuals; organizers were inundated with requests for invitations. The conference's 109 participants included representatives of ministries of health and finance, civil society organizations, clinical trials networks, UNAIDS, the Bill & Melinda Gates Foundation, Combination Prevention/TasP Trials Study Teams, and NIH, as well as PEPFAR deputy principals.

Outputs

Outputs of the conference were a conference summary, time-dependent action items, and a report back to the SAB.

Description

Co-Chairs Mr. Warren and Dr. Cohen were greatly influential and helpful to the evolution of the program agendas for the highly interactive, two-day conference. There were three major presentations and the following five breakout sessions:

- Implementation of Current HIV Prevention Tools (Facilitators: Mark Harrington and Yogan Pilay)
- Future HIV Prevention Tools in the Pipeline (Facilitators: Mary Marovich and Fred Sawe)
- PEPFAR and Secondary Data Analyses (Facilitators: Donna Spiegelman and Basia Zada)
- Ongoing and Future Population-Based Studies (Facilitators: Meg Doherty and Shenaaz El-Halabi)
- Finance and Affordability (Facilitators: Brian Williams and Harsha Thirumurthy)

Themes and Reflections

Dr. Sawe and Mr. Warren shared the following themes and reflections from the conference:

PEPFAR: Finance and Affordability

It is clear that “flat budgets are the new increase”, and programs are expected to do more with the same amount of funding. We need to find efficiencies and gains and must stop what is not working.

- Collaborations with various donors and governments are necessary to bring in more resources and/or to find ways to reduce expenses.
 - This involves reducing waste and addressing policies.
- Host country governments need to be active participants and heavily involved in the allocation of costs.
 - Example: Donors pay for commodities and other external costs, while countries pay for infrastructure, personnel, service delivery, and internal costs.
 - Such integration makes sense, as governments are already responsible for other health care delivery services.
- PEPFAR needs to work with countries to explore policy changes that can reduce costs.
 - Example: Reduce taxes on imported supplies or ability to task shift and transfer or share
- Non-governmental organizations (NGOs) have a key role, but good management and coordination are essential to ensure the money is spent correctly.
- The conference attendees considered performance-based financing as one option to create efficiencies.

PEPFAR and Secondary Data Analysis

- PEPFAR already has a lot of data generated from its various programs, and those data should be accessible for viewing and analysis.
- Needs exist for capacity-building for data analysis and data use.
- Many in-country decision makers require technical assistance mechanisms to utilize data to identify key questions needed for evidence-based decision-making.

- The available data should be leveraged immediately to provide empirical evidence concerning key programmatic questions.
- Available data, such as those from expenditure analyses, should be linked to costs in order to find efficiencies and thereby increase cost-effectiveness.
- Countries need support for annotating and curating data, providing quality assurance, managing databases in varying formats and stages, and developing in-country data analytical skills for optimal data use by all providers and facilities.
- PEPFAR needs to guide current secondary analysis efforts with existing data through prioritization of key questions that could be addressed with these data.

Implementation of Current HIV Prevention Tools

The group based its review around the UNAIDS mantra: “Know your epidemic; know your response”.

- It is critical to know how to engage with the people PEPFAR seeks to serve, and this requires a fundamental reboot of prevention and treatment literacy efforts with a wide range of communities and stakeholders. This includes messaging around treatment for all as well as packaging PrEP in a way that makes it fashionable to use and eliminate potential for stigmatization.
- PEPFAR should increase understanding of transmission within local populations (by population-based surveys and phylogenetic analysis) to identify different groups and to provide differentiated prevention packages; “Who is infecting whom?”
- Integration of HIV services with other key health areas, i.e. TB services need to be improved.
- PrEP should be self-selected (people should be able to perceive their risks and be willing to use it to protect themselves), simplified, and included as part of a comprehensive combination prevention package.
- Government entities need to work across sectors and with all stakeholders to prevent stovepipes/silos.
- PEPFAR should develop organizing frameworks for national HIV-prevention strategies that are well coordinated with care and treatment.
 - Engagement and demand from communities is instrumental to success of strategies and will require an increase in education on current HIV prevention, care, and treatment guidelines (particularly PrEP and Test & START).

Future HIV Prevention Tools in the Pipeline

Mr. Warren explained that a driving force for this conference team was the importance of knowing the audience, the market, and the user, with a focus on user-centered design and “beginning with the end in mind.”

- Scientific development must understand early and throughout the process what potential users will want to use and how they will use it.

- Community engagement must be prioritized, integrated, and sustained in the product development process. A mark of success of every program should be that it starts with community engagement.
- PEPFAR invests in research and development through USAID primarily and can help advocate user and health system perspectives much earlier in the process among stakeholders.
- PEPFAR should be more involved in the early development of the tools needed for prevention and treatment activities.
 - Identify where clinical trials are happening and map that with PEPFAR’s investments, specifically with DREAMS
 - If PEPFAR is spreading products for young women, why not think about the platform of DREAMS and link those communities to clinical trial sites?
 - Such connections were made around treatment and should be made around prevention delivery.

The following key pipeline products will be available over the next 1-2 years:

- Microbicides
- Widespread oral self-testing
- Widespread viral load discovery and monitoring

The following key pipeline products will be available over the next 5-10 years:

- Long-acting microbicides
- Long-acting antiretrovirals
- Potentially vaccines

Ongoing and Future Population-Based Studies

One of the main drivers of this effort is to determine the status of the current combination prevention studies that are funded at least in part by PEPFAR and that were discussed at length in the October 2015 SAB meeting.

- PEPFAR needs to clarify what is meant by “combination prevention” in the trials; they are increasingly becoming “Test & Offer” (vs. Test & START), as they should be given the WHO guidelines. To create that clarification, PEPFAR should:
 - Define the prevention interventions (very few of the formal clinical trials have integrated PrEP, although it is a core part of the WHO guidelines).
 - This speaks to the evolution of practice and care and how that influences clinical trial design, as well as, perhaps, adaptations in conduct.
 - Map their geographic services delivery coverage.
 - Define what will be learned.
 - Gain operational insights on how study results with influence policies and programs.
 - Make sure analysis plans are in place prior to completion of studies.
- Large trials provide opportunities to:

- Learn how to deliver universal test & start services.
- Better understand how to deliver the last 90.
- Determine how to scale viral load testing.
- Figure out how to deliver differentiated care.
- PEPFAR needs to create a prevention care cascade.
 - Such a cascade tracks what works to keep a person negative.
 - Benefits and challenges exist, as prevention is not as linear as treatment.
- The implementation science research agenda is constantly evolving and needs to include:
 - Rigorous methods
 - Input from end users
 - Assessments of feasibility and acceptability
 - Community feedback in the prioritization process
- Mechanisms to provide data and “lessons learned” in real time are critical to justify investment and inform PEPFAR programs in country.
 - Waiting for trials to finish and to receive report-outs years later is not adequate or effective.
- Data generated must be high quality, true, distributed, and available to all stakeholders.

AMB Birx 30- to 90-Day Action Items and Statuses

AMB Birx attended the entire conference and laid out the following action items:

1. Launch a task force to generate key questions that need to be answered through analyses of existing data
 - a. Prioritize key questions and link questions with the available relevant data platform options
 - b. Use an allocative efficiency and/or cost-effectiveness analytic framework to inform strategic decision making.
2. Support capacity for country-hosted data curation and analyses linked to country-specific allocative efficiency and/or cost-effectiveness analyses
3. Consider country-specific approaches to expand HIV self-testing and HIV viral load monitoring
 - a. This was completed during PEPFAR Country Operational Plan (COP) DC management meetings in March
4. Develop and post a clear data dictionary of all the prevention activities within the ongoing PEPFAR-funded CPTs in order to ensure harmonization of definitions and common understanding of the language across investigators, funders, trial participants, and advocates
 - a. Track ART coverage in the interventions in real time.
 - b. Evaluate the ability of the current PEPFAR-funded CPTs to answer the key policy and implementation questions for Test & START and differential service delivery models.
 - c. Ensure there is a costing component to the current PEPFAR CPTs.

5. PEPFAR will post all the implementation science and research activities on the AVAC trials website
 - a. That collaboration is in process.
 - b. PEPFAR will post the results of all the implementation science and research activities on its website.
6. Harness the knowledge of the adolescent girls and young women (AGYW) from DREAMS intervention communities
 - a. At the next DREAMS meeting, PEPFAR will provide a forum for priority populations, such as AGYW and men, to inform program leadership about DREAMS implementation progress and suggested improvements.
7. Analyze current host government administrative ability to fund community-based organizations (CBOs) in PEPFAR countries.
 - a. Disseminate the information through creation and posting of a dashboard (DREAMS).

Discussion

Social Science Input

Ms. Auerbach commented that a multidisciplinary group of social scientists is working as part of five large-scale “universal test-and-treat” (UTT) trials being implemented across six African countries and she noted that multiple presenters in today’s meeting mentioned the need to understand people from their own points of view. She asked if the UTT network was involved in the conference and, if not, whether it could be moving forward.

Mr. Warren commented that he did not know about that network. Conference attendees included representatives from all four of the CPTs, as well as other researchers, implementers, donors, and delegates from civil society and social science organizations. The organizers maintained a small enough size meeting to be productive and every discipline was represented in some way. Mr. Warren suggested that perhaps a ninth action item should be added: “Ensure that the readout of this meeting is clearly described and engaged with a number of the social science networks.”

Prevention and Treatment Literacy

Mr. Heywood wants PEPFAR to unpack what “a reboot of prevention and treatment literacy efforts” means and how it will be done, as it is very necessary. He shared his observation that the drive for 90-90-90 is leading to reduced quality in services. The quality of counseling is deteriorating, as is the quality of understanding what it means to be diagnosed with HIV. This leads to less autonomy and an understanding of one’s HIV is critical to adherence. If clients do not understand the medicines they must take, the probability of adherence is lowered, particularly in circumstances in which the health system does not assist with adherence.

Financing for NGOs

Mr. Heywood remarked that the problem with funding “external NGOs and civil society” is that the term is amorphous. Money spent on commodities will have better results if there is an effective, activist civil society that can ensure accountability, find waste, and ensure that the reporting is balanced. This is about an investment role, not just charity, for civil society.

Workforce Needs

Dr. Mayer questioned how much discussion was held around workforce needs in various settings to optimally provide prevention services. He specifically noted the roles of ARV providers and clinical organization of treatment.

Primary Prevention

Dr. Celum asked if there was much discussion about investment for primary prevention. In light of the youth bulge, she expressed the importance of determining where it makes sense to use the available current prevention tools while waiting for better ones. Oral PrEP, with its imperfections, may still be cost effective for young women; if that is the case, why is so little being done in DREAMS and elsewhere?

Anecdotal Information

Rev. Edwin Sanders appreciated the significant amount of anecdotal information that appeared to have been included in the conference readout presentation.

Caution Around Civil Society

Dr. Pape remarked that it could prove dangerous if responsibilities are too quickly transferred to civil society, as it is loosely characterized. Defining civil society more specifically would be beneficial.

Reaching Youth through Technology

Ms. Lockett asked if the conference included discussion around utilizing cell phone technology and/or social media to reach populations, especially the youth in the DREAMS initiative, to raise awareness and create behavior change.

Wrap-Up

Mr. Warren commented that the issues and questions raised here were very much in tune with conference discussions involving civil society, NGOs, and literacy. He explained that the framing of the meeting was very much around technology; discussion focused on new prevention options and pointed out the fundamental issues of delivering prevention and treatment. It became clear that people have very different definitions of such things as building capacity of civil society and community-based delivery.

Mr. Warren noted that many metrics exist to monitor treatment scale-up and service delivery, and he suggested that there is a potential need for metrics to monitor around civil society, capacity

building, and treatment literacy. We need to be far more literate than we are in the face of exciting science.

Mr. Warren reported that a lot of the conversation was focused on platforms for delivering innovations and promoting adherence and engagement. This and other issues were not fully addressed over the course of the two days, but incremental steps were made and need to be followed up on and reported back to the SAB.

Dr. del Rio commented that the conference was the result of the SAB's suggestion that a broader conversation be undertaken. It also clearly went beyond CPTs to make more expansive recommendations. Dr. del Rio suggested that the SAB carefully review the documents it has been provided and provide feedback in two weeks. Such questions as when to use new strategies need to be addressed. At what point in time should they actually incorporate available prevention interventions into ongoing programs? For example, do we have enough data to implement prevention strategies such as the vaginal ring?

Dr. del Rio remarked that the SAB needs to consider how to provide advice and recommendations given the fact that known interventions have not worked in the population that is about to bulge. What approaches should be taken, and who needs to be involved, in order to keep adolescents from getting infected and in need of therapy? Opportunities exist for the SAB to set up those questions to address the current state of the epidemic.

The issue of financing arises often. Can we continue to squeeze water out of rocks? What can we achieve, and what are the most effective and efficient approaches? What advocacy needs to occur at the global and community levels to obtain resources? A presentation from the Finance & Economics EWG will follow. PEPFAR benefits from the SAB's discussions around this topic and others.

AMB Birx added that the action items from the conference were the first-step action items; the SAB has raised a whole added layer in this discussion. She explained that PEPFAR expanded PrEP before the WHO guidelines were approved and has now gone back to the countries to talk about potentially expanding PrEP.

AMB Birx agreed that PEPFAR and its partners are dealing with an at-risk group that represents the bulk of new infections, and such interventions as the vaginal ring and microbicides have not been effective in that under-21 age group. She asked that SAB members review the conference readout document and send quick comments; PEPFAR can then identify gaps emerging from the COP reviews that will take place over the next two months. The ideas raised today will help inform those COP discussions.

Finally, Dr. del Rio commented that making data available for use at the program and local levels needs to be the hallmark of moving forward.

Finance & Economics EWG Draft Recommendations

Jennifer Kates and Peter Berman, EWG Co-Chairs

Dr. Kates presented on behalf of herself, Dr. Berman, and all of the SAB and non-SAB members of the Finance & Economics EWG, some of whom may be joining by phone. She explained that the EWG is in the very preliminary stages of its work. It welcomes today's discussion, which it needs in order to move forward and eventually provide useful feedback to the SAB and OGAC. The overarching purpose of the EWG is to acknowledge that every issue with which OGAC is grappling is going to be affected by the resources available. It can solve issues, such as how to reach adolescents; however, financing is critical to getting anything accomplished.

Guiding Questions

The EWG was presented with the following three guiding questions and directive:

1. What is the projection for aggregate funding available for HIV (PEPFAR, The Global Fund, and other bilateral and domestic resources) in PEPFAR countries over the next five years? What are annual and five-year estimates for the top 20 PEPFAR countries (by size of USG program)?
2. Prepare case studies for two to three countries to illustrate how new program goals and policies will be affected by available resources.
3. With fixed goals and timeframe (90-90-90 by 2020) and with fixed resources, how can PEPFAR achieve maximum return on investment (ROI)? What are the implied efficiencies needed to achieve program goals?

The group reviewed and discussed the guiding questions in the context of what it would be able to accomplish prior to or in time for the next SAB meeting and it revised them as the goals listed here:

1. Project aggregate funding available for HIV in PEPFAR countries based on three scenarios: pessimistic, optimistic, and flat-line funding.
2. Provide design expertise and direction in support of PEPFAR conducting case studies of two to three countries to illustrate how new program goals and policies will be affected by available resources.
3. Starting with PEPFAR's proposed level of achievement by 2020 (its contribution to 90-90-90), identify two to three scenarios based on different programming or efficiency assumptions that can be used to assess ROI.

Dr. Kates reported on the status of the three goals and shared issues for consideration around each of them:

1: Project Aggregate Funding for HIV

Status

- Data collection of HIV expenditures is underway

- EWG members have gathered expenditure data on the top 20 USG investment countries, including Global Fund and other donor expenditures, as well as domestic expenditures.
- We still do not have a good sense of what countries are spending on HIV, and collecting these data is very challenging.
- UNAIDS is no longer collecting these data on a regular basis.
- Working with OGAC, the EWG has collected what it was able to.
- The next phase will be to review the data collected to determine if they are complete enough for the EWG's use.
- The EWG still needs to specify scenario parameters and define the meanings of "pessimistic", "optimistic", and "flat-line" funding, and to address data issues and gaps.
- The EWG will seek to identify other efforts to catalogue HIV expenditures.
 - The goal is to develop an inventory of efforts, not to recreate those efforts.

Issues for Consideration

- No standardized or complete data source exists for domestic HIV expenditures.
- More broadly, no institutionalized or formal mechanism exists for routinely capturing HIV budget and expenditure data across funding channels.

The information the EWG seeks to collect is even more essential in light of the recent UNAIDS report, "Fast-Track Update on Investments Needed in the AIDS Response". The fast-track approach relies on significant increases in domestic resources by 2020. One question with which the EWG is contending is whether that approach would be considered an/the optimist one.

2: Design Case Studies

Status

- The EWG will consider the optimal way to provide guidance to PEPFAR on how feasible case studies could be conducted and to produce suggestions for countries that could be included.
 - The goal would be for the SAB to endorse the EWG's eventual recommendations and for OGAC to carry them out.
 - Some members of the EWG are experienced and skilled with regard to case study design and analysis.
 - Case studies may be the only way to obtain current and verified data on domestic spending as well as realistic parameters for projecting that spending forward.
 - This work is in the very preliminary stages.

Issues for Consideration

- If the goal is to illustrate how new program goals and policies will be affected by available resources, countries will have to be chosen carefully, to balance between those that might be easiest to assess and representativeness.

3: Scenarios for Assessing ROI

Status

- The EWG will work with OGAC to determine PEPFAR's proposed level of achievement for 2020 (its contribution to 90-90-90).
 - One question is whether we can look ahead of the 2017 goals to delineate what PEPFAR hopes to contribute to the ambitious 90-90-90 goal by 2020.
- Varied programming and efficiency assumptions will be identified based on examination of PEPFAR data, literature review, consultation with OGAC, and expert input in order to determine the best way to achieve the goals.
- This work is in the very preliminary stages.

Issues for Consideration

- New studies are expected in the literature that could provide important input.
- Implications of UNAIDS fast-track update, discussed above

Dr. Kates flagged other points that have been raised in the EWG's discussions, as they may affect scenarios and outcomes:

Transitions: How does the potential withdrawal or scaling back of funds from donors in countries play into these equations?

Innovation: Where does innovation fit in, and will it really achieve significant gains we may not anticipate? How do we account for that?

Dr. Berman reinforced Dr. Kates's emphasis on the lack of data, particularly on domestic funding; this makes the first area of the EWG's work particularly difficult. He asserted that case studies can potentially serve in the short term as intelligence on potential funding scenarios. It is not ideal, as it is only possible to conduct case studies in limited locations; however, it may be the only source of "data" that can inform accurate, deep, prompt analysis.

Regarding efficiency, Dr. Berman suggested that it would be useful to dive more deeply to figure out where assumptions of efficiency have originated.

Finally, the issue of transition is being studied by other organizations, such as The Global Fund. Numerous African countries are concurrently facing transition in multiple areas including HIV, maternal and child health, and more. This question of transition relates to priorities across health problems and is not exclusive to HIV funding allocation.

Dr. del Rio noted that countries may choose to apply resources provided for HIV differently, such as supporting the child health program, for example. This depends on what a country prioritizes for health; we may view programs as specifically HIV programs, but they may be viewed differently in country.

Dr. del Rio acknowledged that PEPFAR does not know if countries have the resources to get to 90-90-90 or if they need more money. The EWG may not be able to answer that question but may be able to provide at least a rough idea, which is needed, if even for communication with political leaders.

AMB Birx purported that the case studies could serve to extract intelligence to inform the optimistic scenarios, as countries on single commodities inflate their gross national product (GNP) numbers. For example, PEPFAR maintained and even increased its investment in South Africa against the country agreement due to the breadth and depth of the need and in view of the country's actual economic conditions. Case studies could show the reality of economies that are not quite as robust as has been suggested or that have shifted due to the impact of China's economic slowdown and/or a lower valuation of a country's large export, such as oil. Case studies done well can help to articulate economic realities and program needs in order to help global funders, such as USG, understand cost drivers.

Dr. Berman agreed with AMB Birx's comment regarding future growth scenarios are important to keep in mind. No country, to his knowledge, has ever achieved its optimistic objectives for their economies.

Finance & Sustainability EWG Draft Recommendations Discussion

Importance of Quality Data

Dr. Peters expressed skepticism that the EWG will be able to identify 20 countries for which it will find analyzable data. However, starting the effort in a few places could be worthwhile for highlighting difficulties and need in order to collect national government data on health and HIV spending, as well as on household spending and NGO funding. This information is critical to assumptions and can describe more effectively what is needed.

Service Delivery Cost Efficiencies

Regarding efficiency around service delivery costs, Dr. Peters remarked that it is critical how one defines and accounts for the service delivery component and its underlying costs, as much of service delivery is needed for the health system in any event around other conditions and therefore is a cost to the country regardless and is not specific to HIV.

Dr. del Rio agreed that, when you integrate health programs for such issues as diabetes and HIV, costs are commingled.

Spending Realities

Dr. Mushavi asserted that, as we move forward, we need to understand the cost of the work. Do we know at this point whether countries are keeping National AIDS Spending Accounts and, if not, how countries can be supported to ensure that work is going on?

The cost of doing business across countries can be very different. For example, conducting training in Zimbabwe may be higher or lower than conducting one across the border in South Africa. Dr. Mushavi wondered how the EWG will take into account the purchasing power parity and the differences in costs across economies.

Dr. Berman contended that we should not expect costs to be the same across countries. Some of the costs, such as external commodities, might be standardized; however, many operating costs are not. Wage levels, exchange rates, and other elements drive those costs. Global projections work from averages and from norms (estimated average costs); what happens on the ground is quite different. The case studies will illustrate some of that variability.

Out-of-pocket expenditures can be quite significant in some countries where accessing health translates to significant up-front costs for the client. For example, a client may not be responsible for HIV care costs but may have to pay for TB diagnostics. Dr. Mushavi is curious to know how the EWG will tease out costs, as some significant costs that could be considered as related to HIV (for example, an X-ray associated with a sputum test) may be labeled as out-of-HIV-expenditure costs.

Dr. Kates explained that the EWG is looking at the National AIDS Spending Accounts. UNAIDS was able to support that project for some time, but it does not appear to be continuing; the data she has seen stop after 2012. It is possible that the EWG will recommend that some entity (possibly PEPFAR) continue to fund that very valuable effort.

Dr. Berman will apply his economics expertise to exploring purchasing power parity. It must figure into an overall analysis that includes how costs vary across countries and what economic conditions are likely to occur.

To some extent given the lack of available data, the EWG will have to use prior expenditures to predict future spending. The largest and most comprehensive study of health expenditures known to Dr. Kates, by the Institute for Health Metrics and Evaluation (IHME), was very recently released. While it is not HIV specific, it does include HIV data. The researchers as yet have been unable to reach out-of-pocket expenditures within country.

Mr. Heywood questioned how the EWG will factor in the impact of declines in per-capita public health expenditure in areas other than HIV. In South Africa, the HIV budget is increasing, and health funding is decreasing.

Dr. Sawe asked how the EWG will factor in in-kind contributions from infrastructure to HIV care, and whether it is costing as part of domestic resources.

Dr. del Rio spoke to Mr. Heywood's and Dr. Sawe's questions, affirming that case studies will help, as they will be able to look at such elements.

Dr. del Rio mentioned the value for a country or provider to know how it compares to others regarding costs. He also noted that it is possible that the easiest to treat are those who have already been reached. New populations will be harder to reach, and it will cost more to do so. He noted that this is an existing tension around financing: We do not really know how many people can be treated with a fixed amount of money. On top of this, the first number of people may be less expensive to treat than the remainder.

Case Studies

Mr. Heywood suggested that case studies could be used to assemble evidence favoring investment in the community healthcare workforce. Downstream benefits received from upfront investments might challenge the view that such a workforce is an unaffordable component of healthcare.

Dr. Berman expressed his appreciation for the SAB's support for case studies. However, as Dr. Kates explained, the EWG will not conduct the case studies. It is not clear what mechanism exists for making it happen. The working group requests that OGAC/PEPFAR helps to think through this in practical terms.

Transitions

PEPFAR is one of the only large donors that does not scale back funding support when countries reach specific income levels, as happens with The Global Fund, GAVI: The Vaccine Alliance, IDA Foundation, and others. Dr. Kates urged the EWG considers what will happen when those funding cliffs are reached and its projections going forward will be critical. to consider whether transition planning is indicated.

Survey of Experts

Mr. Siemens agreed that the overall analysis of cost is important, and the case studies should answer the challenges and questions that exist. He asked whether it would be worthwhile to do an additional survey, asking experts in healthcare delivery and in community development to describe what they see as the ideal approach to transitioning existing programs in a manner that ensures their sustainability. He remarked that the EWG will end up with information on what a situation costs; this assumes the arrival at the best healthcare or community engagement scenario. Could we model an idealized approach that would address sociological and economic issues?

Including a Commercial Perspective

Along those lines, Mr. Siemens commented that the February conference seemed not to include a consumer-oriented commercial perspective. It is astounding how commercial companies figure out how sell things to us. He asked if PEPFAR is considering strategies used by companies to understand and influence consumer perceptions and behaviors

Working Across Silos

Mr. Milan applauded the case study approach, particularly in exploring domestic financing. He also appreciated the description of combatting HIV as a presidential issue. The Altarum Institute

recently completed a study for the HHS Office of HIV/AIDS and Infectious Disease Policy (OHAIDP) assessing the resources invested in addressing HIV among Black MSM in the US. In order to do this, the institute assembled expenditure data across the USG, including the Departments of Health and Human Services, Justice, and Veterans Affairs. For Mr. Milan, this was critical to understanding the full scope of the USG response to the epidemic in these men.

Wrap-Up

Dr. Kates noted that the EWG would welcome any studies or other information SAB members think would inform its work.

TB/HIV EWG Draft Recommendations

Mark Harrington and Bill Pape, EWG Co-Chairs

Mark Harrington began by noting that the global response to TB/HIV trails the response to HIV and represents an emergency that has not been addressed by domestic or TB programs. According to OGAC, in SSA alone, an estimated 870,000 new TB/HIV cases occur each year, 47% of whom are coinfecting with HIV but only 36.5% receive ART. This translates to 64% of TB/HIV-infected people in SSA not being treated with ART. The EWG argues that we can do better.

The SAB commissioned the TB/HIV EWG after its last meeting in October 2015, and the working group was convened in January. The EWG has a broad and committed membership of experts from around the world. Mr. Harrington expressed appreciation to the OGAC team—comprised of Lisa Nelson, Carol Langley, Julia MacKenzie, and Ishani Pathmanathan—for its excellent work in staffing the working group.

Between February and April 2016, the EWG held six teleconferences and numerous separate discussions, and it developed recommendations to address the questions posed by OGAC. Many of the recommendations will require collaboration with host countries and other donors' TB programs; a number of them frame OGAC's role as a catalyst for improving TB/HIV screening, diagnosis, and treatment.

Guiding Questions

OGAC presented the EWG with the following four guiding questions (some include additions from the EWG):

1. What is needed to ensure that all HIV-infected TB patients benefit from timely ART? What is needed to ensure those without TB benefit from preventive therapy?
2. How do we need to re-imagine service delivery and partnerships to reach those left behind and most vulnerable to TB/HIV, such as prisoners, migrant workers, drug users and other key populations for HIV, children, and community health workers (CHWs)?
3. How can we use global data (TB, HIV, TB/HIV, and other) to most effectively target resources—e.g., what are TB prevalence services telling us about the unmet need for

TB/HIV? How can we better find and retain TB/HIV cases in large urban settings? What are the implications of PEPFAR's pivots on supporting the TB/HIV response?

- a. An untapped resource for TB/HIV likely exists in the data and mapping resources presented by AMB Birx.
4. How can we collaborate more effectively to ensure better coordination of laboratory investments for TB diagnosis and HIV services?

Critical Gaps and Missed Opportunities

- Only two thirds of TB cases globally are identified or reported
 - This is the reason why more people are now dying from TB than from AIDS.
- Only a fraction of those living with TB/HIV co-infection are dually diagnosed
- HIV testing rates are low among presumed TB and diagnosed TB patients
- Less than one third of TB/HIV patients receive ART
- There is a very low uptake of the TB preventive therapeutic (isoniazid preventive therapy [IPT]) and low use of cotrimoxazole (CTX) in TB/HIV coinfecting patients.
- Poor access to quality care and follow-up cause excess morbidity and mortality among prisoners (between prisons and post release), drug users, miners, refugees, healthcare workers, and others at risk for TB and HIV infection.
 - There is poor implementation and monitoring of TB infection control activities, in part due to a lack of relevant indicators.
- Separate funding streams and lack of coordination impede integration of HIV and TB programs; PEPFAR may be able to utilize its diplomatic influence to address this longstanding deficiency in global health.
- Inadequate data and limited monitoring and evaluation activities limit assessment of TB/HIV program impacts.

Best practices for preventing TB in persons living with or at risk for HIV infection

- Early ART for all HIV+ with combined IPT/CTX
 - When we talk about Test & START for TB and TB/HIV, we need to think of all three interventions: Treatment for those diagnosed with TB, IPT for preventing infection, and ART for those living with TB/HIV co-infection.
 - We should be able to find out in only a couple of steps who needs what intervention.
- Early diagnosis and treatment of TB in HIV+
- Screening for TB and HIV in infants, children, prisoners, miners, health care workers, and other key populations
- Infection control
- Use of global data, joint TB, and HIV programming, and coordination of laboratory and HIV services

Recommendations

The EWG presented 16 draft recommendations focused on the most effective interventions to prevent TB-associated mortality and morbidity. Mr. Harrington presented the first two recommendations:

Recommendation #1: Provide ART for all HIV+ patients regardless of clinical stage/CD4 cell count. Encourage PEPFAR to implement its new Test & START Strategy.

- If implemented and scaled up, this strategy will reduce morbidity, mortality, and the risk of TB co-infection.
- Although ART reduces risk of TB infection by at least 50%, TB-coinfection rates among PLWH are at least 10 times higher than rates among HIV-uninfected individuals, even after years of ART, suggesting that ART alone will not eliminate the risk of TB among PLWH.
- ART + IPT can reduce the risk of TB more than ART alone in populations with early (demonstrated in the TEMPRANO study, presented last year at IAS) and advanced HIV disease. or
- Cotrimoxazole preventive therapy (CPT) also has been recommended for this population for over a decade; it has a synergistic effect when combined with ART and helps to further reduce mortality. It is also very inexpensive.

Recommendation #2: Provide IPT (isonicotinic acid hydrazide, or INH) in high-burden countries and CPT with ART to reduce the risk of TB and mortality. The EWG favors PEPFAR promoting rapid rollout and scale-up of a single pill containing INH and CTX; it recommends considering the use of shorter-acting rifamycin-containing regimens with ART.

- Other TB preventive interventions have proven effective in developed and developing country settings, including a once-weekly dosing of INH and rifapentine; such a regimen should be explored and could provide more sterilizing activity, but the rifapentine could cause adverse reactions when used with some ARTs.

Dr. Pape presented the remaining recommendations:

Recommendation #3: Provide early diagnosis and treatment of TB, and initiate TB treatment before starting ART.

- Use method(s) available at point-of-care (POC) sites (e.g., simple microscopy) or refer immediately patients to quality TB diagnostic centers.
- Use urine lipoarabinomannan (LAM) as the POC test for all HIV+ sick adults within 24 hours of admission. A positive test is an indication for immediate TB treatment.
 - Research study results demonstrated improved mortality rates in patients diagnosed and treated early.
- Scale-up and evaluate implementation of the POC Cepheid GeneXpert Omni and the new generation highly sensitive Cepheid Xpert MTB/RIF Ultra test, including non-respiratory sampling such as stool in young children.

- The Omni is poised to create a revolution in the way TB is diagnosed; however, it will still use spot sputum smear microscopy, which is not as accurate as early morning sputum smear microscopy.
- Scale-up and evaluate implementation of next generation highly sensitive Cepheid Xpert MTB/RIF Ultra test, including non-respiratory sampling such as stool in young children.
- Chest radiography (used in Haiti since 2001) with clinical findings inform immediate initiation of TB treatment in adults.
 - Good quality chest X-ray (CXR) is useful in children, as part of an approach that includes clinical history data, symptoms, contact evaluation, and purified protein derivative (PPD).
 - Training in the expert use of CXR for pediatric TB diagnosis is essential.
- New, simpler tests are needed for detecting latent TB infection (LTBI).
- All TB centers, regardless of size, should be testing for HIV infection.

Recommendation #4: Implement early diagnosis and treatment of TB in prisoners, miners, health care workers, children, drug users, and pregnant women

- Provide HIV and TB screening and treatment.
- Ensure that national HIV and TB programs interface effectively with prison medical systems and mining health services in order to reduce loss-to-follow up.
- Increase continuity of TB and HIV care during inter-facility transfer between corrections centers and minimize post-release treatment gaps to ensure individual health, prevent the development of drug resistance, and reduce the risk of community transmission of infection.
- For all:
 - Avoid overcrowded conditions.
 - Provide condoms, sexually transmitted infection (STI) care, and adequate nutrition.

Recommendation #5: Enhance TB infection control (TBIC) of healthcare workers and patients

- Establish a formalized monitoring system at each medical facility to ensure implementation of infection control (IC) measures to record and report whether clinicians, nurses, patient attendants, and laboratory technicians are occupationally exposed and infected with TB and HIV, as recommended by the TB Care 1 “Guide on the Monitoring of TB Disease Incidence among Health Care Workers”.
- Implement the WHO 2015 “A guide to monitoring and evaluation for collaborative TB/HIV activities” for global and national TB/HIV indicators for TBIC.
- TBIC measures include:
 - Managerial interventions: a) Quickly identify and separate people with TB symptoms from others; b) Institute cough etiquette and respiratory hygiene; and c) Minimize the time spent in healthcare facilities.
 - Environmental controls: a) Increase ventilation: keep windows open, or add windows; b) Add skylights; and c) Build outdoor waiting areas.

- Personal protection: a) Test health care workers for HIV and TB; b) Ensure HIV+ do not work in high risk environments such as medical in-patient wards or TB clinics; and c) Place HIV+ on ART IPT and CPT.

Recommendation #6:

- Develop and evaluate child- and family-friendly strategies for IPT delivery to infants and children such as home-based IPT delivery and shorter rifapentine-based regimens (e.g., fixed-dose child-friendly drug combinations)
- Conduct research to evaluate the optimal duration of IPT in HIV-infected children in high-burden settings.
- Implement appropriate IPT recording tools to document contact IPT management and delivery to all vulnerable populations, including children.

Recommendation #7:

- Integrate HIV and TB screening and improve linkage to HIV medical treatment for children.
- Implement hospital Directly-Observed Treatment Short course (DOTS) linkage to improve continuity of care, treatment outcomes, and recording and reporting of TB infection (including multi-drug-resistant tuberculosis, or MDR-TB) in children and other vulnerable groups.
- Establish TB treatment registers in every health facility to capture the burden of TB in children and adults.

Recommendation #8: Promote HIV/TB prevention and screening in pregnant women

- Incorporate childhood TB training modules for healthcare workers into all maternal and child health programs.
- Strengthen antenatal and postnatal TB screening of pregnant women in PMTCT services to include the use of broader TB screening, immediate IPT initiation, and enhanced monitoring of outcomes for at-risk infants and pregnant women.
- Ensure a robust supply chain and minimize risk of stock outs for the TB vaccine (viz., bacille Calmette-Guerin [BCG]).

Recommendation #9: Develop strategies to reduce HIV- and TB-associated stigma to encourage better protection and care for vulnerable groups, including healthcare workers living with HIV.

Recommendation #10: Measure impact of the implementation of collaborative TB/HIV activities at a program level to guide the response.

Recommendation #11: Designate a ministry of health position to oversee both HIV and TB programs, facilitate collaboration and communication, and minimize redundancy.

Recommendation #12: Strengthen joint TB/HIV programming with set-up of accountability mechanisms at national/sub-national levels. Promote joint TB/HIV program reviews of TB and HIV high-burden countries.

Recommendation #13: Develop operational guidelines for effective care of patients with TB/HIV at both HIV and TB centers to make sure that both TB and HIV care are provided at one center (one-stop operation); develop guidelines for services expected to be offered for TB/HIV patients at different HIV and TB centers to explicitly guide differentiated care within the host country's national HIV and TB programs.

Recommendation #14: Create monitoring systems to measure the time from diagnosis of HIV in a TB patient to initiation of ART, and from diagnosis to viral suppression (VS).

Recommendation #15: Use PEPFAR service delivery mapping systems to show colocation of HIV and TB service delivery centers (including diagnostic laboratory sites) to enable targeting of services to where the need is greatest and to avoid excessive site differentiation, which would make it harder for clients to access high-quality collaborative TB/HIV services.

Recommendation #16: Establish a TB/HIV dashboard to present the results of the mapping exercise along with other program input, process, and impact data to demonstrate where TB/HIV collaborative services are being delivered effectively and where improvements are needed.

TB/HIV Draft Recommendations Discussion

Prioritization

Dr. del Rio characterized the EWG's draft recommendations as an incredibly comprehensive exercise and list. He urged the group to prioritize its recommendations, as it will be impossible to accomplish them all. He asked the EWG to clarify what PEPFAR should consider the highest priorities and triage accordingly.

Dr. Pape agreed that such a prioritization is necessary. He referred to slide #6 in the EWG's presentation, which distilled the high priority recommendations to:

- Immediate ART for all HIV+ patients with IPT/CTX
- Early diagnosis and treatment of TB in HIV+ patients
- Screening for TB and HIV in infants, children, prisoners, miners, healthcare workers, and other vulnerable populations
- Infection control
- Use of global data, joint TB and HIV programming, and coordination of laboratory and HIV services

Mr. Harrington noted that the working group needs to rearrange the draft recommendations to demonstrate that they fall under the five above overarching recommendations.

IPT

Dr. Celum asked if the coformulated IPT/CPT exists and, if not, whether it could be fast-tracked.

Mr. Harrington explained that the combination medication needs to be fast-tracked, noting that WHO and others have talked about development for more than a decade. His understanding is that sponsors have been identified who have been contracted to do so. Donors could help countries purchase the product.

Dr. Mushavi asked if discussion occurred in the EWG about individuals' reluctance to take IPT due to concerns of possible side effects and adverse events.

Dr. Pape noted that numerous studies have demonstrated that the benefits of IPT dramatically outweigh the minimal risk; this is why WHO recommended it as a cost-effective intervention.

Dr. del Rio added that recommendations for IPT are among the most ignored and implementation is long overdue.

Integration of Services

Dr. Karim asked the EWG to discuss disease management by true integration of services, going beyond colocation, as TB/HIV coinfection can be as high as 70% in some PEPFAR-funded countries.

Dr. Pape asserted that integration should be indicated precisely in the recommendations, as it makes a significant difference. He noted that, in Haiti, HIV and TB services are totally integrated. Dr. del Rio expressed the importance of integration, noting that many persons living with HIV infection gain access to ART through TB centers.

Drug-Resistant TB

Dr. Karim wondered if the EWG discussed drug resistant strains of TB, such as MDR-TB and extensively drug-resistant TB (XTR-TB).

Dr. Pape responded that the working group had not had any major discussion around this important issue. Mr. Harrington suggested that the diagnosis section of the recommendation could include the promotion of universal drug susceptibility testing to guide treatment for MDR-TB. However, he expressed concern about this given the constraints of narrowing the recommendations.

Dr. del Rio suggested ranking the EWG's recommendations by priority.

Order of Treatment Interventions

Dr. Karim asked the EWG to explain the data and recommendation for TB treatment before ART; the data show higher mortality when ART is administered after TB treatment.

Dr. Pape commented that the working group followed the original guidelines that call for initiating TB treatment before ART if the patient's CD4 count is below 350, followed by ART two weeks later. Regardless of CD4 count, the EWG would suggest beginning ART at the two-week mark, or as early as possible.

Mr. Harrington added the importance of recognizing that some people who are already on ART come in for TB testing. In those cases, the timing would be different, and TB treatment would follow ART initiation. He noted that TB meningitis might be a scenario in which waiting to initiate ART may be warranted.

Review Process

Dr. Peters inquired as to whether the EWG had considered processes for regular review and updating of the recommendations, pointing out that diagnostic and therapeutic recommendations can become outdated rapidly. He noted that low-cost mobile technology now exists gene mapping. He noted, for example, the WHO list of essential medicines which is updated every two years.

Working Effectively with Governments

Dr. Peters commented on recommendations pertaining to the integration of HIV and TB service delivery- advocating and advocated for a single position in the ministry of health. From his experience, governments can bristle when they are told specifics about institutional arrangements and could create pushback. Perhaps another recommendation underscores need to acknowledge and offer anticipate sensitivities while promoting service delivery model improvements in a manner that does not create discord.

Dr. Pape remarked that the committee feels that it cannot treat TB/HIV as business as usual and wants to promote a more aggressive approach to the disease, as TB is considered an "old disease" and is still the cause of so many deaths. Aggressive treatment is possible: If the CXR suggests TB, the patient is given a rapid HIV test; if the CXR is negative; the patient still receives an HIV test and is placed on IPT as prevention. There is concern that a patient will not return if the treatment is not same day and will transmit TB to others and avoid HIV treatment altogether. Dr. Pape shared that, since 2001 in Haiti, one third of people who have come in for an HIV test have presented with active TB.

Mr. Harrington added that the EWG is relying on WHO to create recommendations that will guide program. One example is a recent study showing improved survival by beginning TB treatment just one day earlier. WHO is currently in the process of updating those guidelines, and they will be available in approximately one year; countries will be able to apply next year to receive that low-cost test in their hospitals. The EWG is not trying to change those guidelines but instead, speed up their rollout.

Dr. Currier noted the potential impact of PEPFAR emphasizing the existing guidelines and promoting activities countries should already be engaging. She advocated for a streamlining the recommendations so as not to lose focus. One example of a potentially unnecessary recommendation pertains to CD4 testing, which many countries are discontinuing.

Dr. Celum pointed to DREAMS as an example of the importance of ambitious targets; perhaps PEPFAR could create TB targets (e.g., 40% increase of persons on IPT by 2018, as an example) to guide country responses to the epidemic.

Workforce

Ms. Treston commented that the increase in early diagnosis and treatment requires an expanded workforce and task shifting. She suggested promoting in the recommendations the use of proven nurse-led models of care for TB diagnosis and treatment and offered to provide references to studies for the working group's consideration.

IPT Duration

Dr. Celum asked if the EWG had included a specific recommendation for the duration of IPT, noting conflicting recommendations for them in the field. She suggested being pragmatic by proposing a minimum amount of time, so that countries would not use duration as a reason not to adopt the recommended action.

Mr. Harrington explained that the working group did not make a recommendation pertaining to treatment duration. The EWG does not have the expertise to override the WHO guidelines, which may shift based on new research. At present, a minimum of six months of IPT is recommended.

Community-Based Interventions

Knowing that WHO guidelines strongly support the use of community-based interventions, Dr. Nabiryo asked how much they were a part of the EWG's discussion.

Dr. Pape remarked that he uses CHWs in his practice in Haiti, and he noted the importance of that group to overall epidemic management.

Urine LAM Test

Dr. Mushavi asked if the recommendation for using the urine LAM as the POC test for all HIV+ sick adults within 24 hours of admission is most sensible in view of patients with low CD4 counts, suggesting that we should be reaching them before their CD4 counts drop below 100.

Mr. Harrington noted the need to consider that countries will move away from CD4 testing; the LAM test will provide the most benefit to those for whom it was intended – viz., persons with advanced disease.

TB Prevention for HIV-Negative Persons

Dr. del Rio asked about preventive TB therapy for HIV-negative patients infected with the disease in light of increased testing. For example, should IPT screening be done at that level?

Mr. Harrington noted the need to protect persons with HIV from acquisition of TB and mentioned that, therefore, consideration should be given to preventive TB therapy for HIV-negative patients. WHO guidance has not been particularly strong on that issue. He also commented that, due to not having the final text on community screening issues, the EWG did not address concerns around task-shifting, CHWs, and screening for TB as deeply as it should have.

Wrap-Up

Dr. del Rio expressed his appreciation for the recommendations and asked the EWG to streamline and prioritize them, considering what has been mentioned around metrics and indicators. The revised recommendations should be submitted to the SAB within two weeks, and the board can formalize it and provide it to PEPFAR.

AIDS 2016 Program Development Update

Kenneth Mayer

Dr. Mayer, the Scientific Programme Committee (SPC) IAS co-chair, reported that he, Mr. Warren, and Dr. Auerbach were among a group of individuals who recently spent time in Durban, South Africa, organizing the 21st International AIDS Conference (AIDS 2016), which will take place there July 16-22, 2016. Those who had the privilege of attending the conference in 2000 know that it was a world-altering event for many and that led to the genesis of PEPFAR. He expressed hope that the upcoming conference will have similar impact. It will be an opportunity to look at, among many things, the PEPFAR program's great successes.

One of the things that conference organizers heard from numerous colleagues in Africa is that many organizations are constrained, given the current status of the South African rand and limitations of program, in sending staff to attend; this would create a missed opportunity. The event could provide significant amounts of training to staff at different sites, and Dr. Mayer expressed the hope that today's discussion would lead to a sense of whether there could be liberalization of some of the requirements that would enable some of the partners to have their key personnel attend, and whether there are additional resources that could be identified. While the conference will certainly be well attended, the hope is for optimal attendance.

Special Presentations

AMB Bix will provide two major special sessions at the conference, both focusing on young women and girls. Other presenters will include Bill Gates, Prince Harry, and Elton John. South African President Zuma and Deputy President Ramaphosa will attend and give, respectively, opening and closing comments. Archbishop Desmond Tutu will be in attendance as well.

Conference Tracks

More than 7,000 abstracts were submitted for the main body of the conference and approximately one third were selected for inclusion. Dr. Mayer described the conference tracks as follows:

- Track A: Basic and Translational Research
 - This track had the fewest abstract submissions, but some very good basic science was submitted.
- Track B: Clinical Research
 - Some high-quality information was tendered and should prove to be excellent presentations.
 - Several two-day pre-conference meetings will focus on areas relevant to clinicians, such as TB/HIV and viral hepatitis.
- Track C: Epidemiology and Prevention Research
- Track D: Social and Political Research, Law, Policy, and Human Rights
 - Social sciences will be well represented.
- Track E: Implementation Research, Economics, Systems, and Synergies with Other Health and Development Sectors
 - This will likely be the largest implementation science meeting to date around HIV.
 - There will be many opportunities to explore best practices.

Conference Leadership

IAS President Chris Beyrer (USA) is the international co-chair of the conference. Olive Shisana (South Africa), a senior social scientist, is the local/regional co-chair. The SPC co-chairs include Dr. Mayer- former CAPRISA 004 Team Member, Koleka Mlisana (South Africa)- current University of KwaZulu Natal Medical Microbiology Department Head, and Stefan Baral (USA)-associate professor at Johns Hopkins University.

Dr. Mayer noted that the conference is not under the total control of IAS, as one third of the partners are civil society, and another third are representatives of various United Nations (UN) agencies. That is reflected in the makeup of the Community and Leadership Programme Committee co-chairs:

- Chris Collins, UNAIDS, Leadership Co-Chair
- Milly Katana, Uganda, Local/Regional Co-Chair
- Sergio Lopez, Paraguay, International Co-Chair

The leadership provides wide representation geographically and in areas of expertise.

Plenary Speakers and Topics

The plenary sessions and speakers will be as follows:

Tuesday, July 19

- Stefanie Strathdee, USA—*Global Epidemiology: State of the Pandemic*
- Elizabeth Bukusi and Maurine Murenga, Kenya—*Implications of Gender on the Response*

- Alex Coutinho, Uganda—*Universal Access: Systems for Health in the Immediate Treatment Era*

Wednesday, July 20

- Nittaya Phanuphak, Thailand—*Prevention Equity: Uptake of Innovations in Testing, Prevention, and Reducing Incidence*
- Anton Pozniak, United Kingdom—*TB and Co-Infections, Co-Morbidities: The Long Game*
- Larry Corey, USA—*Towards an HIV Vaccine*
- Tariro Makadzange, USA and Zimbabwe, and Micheal Ighodaro, USA (Nigerian national)—*Youth Focus: Adolescents at Risk and in the Lead*

Thursday, July 21

- Cyriaque Ako, Ivory Coast—*Expanding Access for All at Risk and in Need*
- Deborah Persaud, USA—*Barriers to a Cure*
- Alessandra Nilo, Brazil—*HIV in Global Health and the SDGs*
- Nancy Mahon, USA—*What's the Business Plan*

Friday, July 22

- Serge Eholié, Ivory Coast—*Towards a New Treatment Era? Translating Results from START and TEMPRANO to Clinical Practice*
- Dorothy Mbori-Ngacha, UNICEF—*Ending Pediatric HIV and AIDS*
- Malebona Precious Matsoso, South Africa—*Essential Medicines, IP, and Access*
- Carlos del Rio, USA—*What's New, What's Next, What's Ahead?*

Some of each day's plenaries will be represented in the abstract submissions as well.

Special Sessions and Symposia

Special Sessions

As Dr. Mayer mentioned earlier, two sessions focusing on young women and girls will involve AMB Birx. A special session on adolescents and key populations will include Elton John and Prince Harry, and one on HIV prevention will involve Bill Gates. UN Secretary General Ban Ki Moon will officiate at the UN High-Level Meeting, which will include representatives from key UN agencies.

Symposia

Symposia sessions will focus on key populations as well as on social/structural drivers of the epidemic in Africa:

- Transgender Persons and HIV
- HIV in Eastern Europe and Central Asia
- Differentiated Models of ART Delivery
- Women, Violence, and HIV
- Faith-Based Session
- Global Fund Replenishment—The Future of HIV Funding
- New Prevention Technologies
- HIV/AIDS & Cancer

Abstract Selection Outcome

From the 7,616 abstracts submitted, 2,421 were selected. Acceptance rates ranged by track from 34% to 54%. There will be high representation by women (56%), and significant representation from Africa (37%), Canada, and the US (33%). Forty oral abstract sessions will comprise 186 abstracts, 21 poster discussions will include 121 abstracts, and 2114 posters will be exhibited.

Dr. Auerbach remarked that very few oral abstracts are accepted for presentation. She asked that SAB members message to colleagues that the conference is one day shorter than in the past and that some key topics received copious numbers of abstracts. Both of these factors affected the percentage accepted.

Oral Abstract Sessions and Poster Abstract Sessions by Track

Dr. Auerbach commented that each track has a very particular focus, and the organizers have been very mindful to select abstracts closely related to that focus, even if the names of the presentations sound similar across tracks.

Track A: Basic and Translational Research

This track will offer a variety of basic science topics and a cross-track session looking at viral genetics and how one can use molecular epidemiology to better understand the epidemic.

Track A Oral Abstract Sessions

- Drivers of HIV Progression
- Immune Control of HIV
- Targeting Reservoirs for Cure
- Acute HIV Infection: The Battle Begins
- Phylodynamics: Tracking Transmission in Vulnerable Populations (cross track, A/C)

Track A Poster Discussion Sessions

- Intrinsic and Adaptive Immunity
- HIV Persistence and Eradication
- HIV Transmission and Pathogenesis

Track B: Clinical Research

This track will include a number of clinically relevant sessions, including approaches with major benefit to clinicians. Opportunities to share best practices, as well as successes and failures, will abound.

Track B Oral Abstract Sessions

- Bad Bugs: Better Drugs—Advances in Hepatitis and HIV Coinfection Treatment
- Clubs, Cash, and Caregivers: Impact on Adherence and Retention
- Long-term Treatment Success for Adolescents and Young Adults
- Supporting Three Generations of Healthy Mothers and Healthy Babies

- Taking TB from Testing to Treatment
- Treat Early and Stay Suppressed
- Treatment Evolution: New Drugs, New Reality

Track B Poster Discussion Sessions

- HIV Drug Resistance: Is it Time to Worry?
- HIV Exposure: How Does It Affect Children?
- Living with HIV: Long Term Effects
- Optimizing Laboratory Diagnostics

Track C: Epidemiology and Prevention Research

This track's sessions will focus on specific populations, including adolescents and transgender individuals.

Track C Oral Abstract Sessions

- MSM: Diverse Realities Require Nuanced Programmes
- Making PrEP Real for Those Who Need It Most: Optimization Strategies
- Testing Times—Interventions to Improve Rates of HIV Testing
- Adolescent Affairs
- Transforming HIV Prevention and Care Talk
- Alcohol, Substance Use, and HIV
- Can Epidemiology Lead to Action—Who, Where, When?
- PrEP: New Drugs, New Questions

Track C Poster Discussion Sessions

- Prevention for Women: The Need for Multidisciplinary Approaches
- Safer Contraception Choices for HIV-Affected Couples
- Circumcision—Where to, How to, Who to?
- Measuring Progress Towards 90-90-90

Track D: Social and Political Research, Law, Policy, and Human Rights

Intellectual property, behavioral economics, and policy issues will be some of the foci of this track, which will look at identities, relationships, new technologies, and community engagement and ethics, among other things.

Track D Oral Abstract Sessions

- Sex through the Ages
- Sex, Babies, and Life
- It's All In the Family
- Challenging Intellectual Property Regimes in HIV and Hepatitis C (HCV)
- Shame-Less: Stigma Interventions That Work
- Policies, Policing & Public Morality

- Barriers Must Fall: Community-Led Delivery
- Cash and Care: Economic Empowerment for HIV Prevention
- Pathways: Moving from Structural Risks to Responses
- Pulling the Levers: Policy, Advocacy Approaches to Influence
- Reality Check: The Intersections of HIV, Violence, and Trauma

Track D Poster Discussion Sessions

- The New Normal: Sexual Identity, Relationships, and Norms
- What's Up: Mobile Technologies, Multimedia, and Mass Communications
- Translating Tradition in the AIDS Response
- Human Rights, Wrongs, and Realities: Translating Frameworks into Actions
- Community Engagement and Ethics in Cure Research

Track E: Implementation Research, Economics, Systems, and Synergies with Other Health and Development Sectors

This track will look at systems-level implementation science and finances of the epidemic, along with a pathway to eliminating mother-to-child transmission, integration of other health care with HIV care, and incarceration.

Track E Oral Abstract Sessions

- Financing the Response to HIV: Show Us the Money
- Bang for the Buck: Cost-Effectiveness and Modeling
- Prepped for PrEP
- Healthy Mothers, Healthy Babies: The Path to eMTCT
- Differentiated Care: Finding the Best Fit
- Innovations in HIV Testing: The First 90
- Target 90/90/90: The Ups and the Downs
- Going Viral for Viral Load Implementation
- Connecting the Dots

Track E Poster Discussion Sessions

- The Dollars and Sense of HIV Service Delivery
- Filling the Gaps in PMTCT/B+ Programmes
- HIV Services in Prisons: Let's Raise the Bar
- Quality Improvement: Aim High
- It Takes a Community: Leadership, Engagement, and Innovation

Dr. Mayer noted that *The Lancet* will hold a special symposium at the conference focusing on incarcerated populations and HIV.

Organizers worked diligently to ensure that sessions around the same topic would not take place concurrently.

Ms. Treston acknowledged IAS's appreciation of nurses in this year's conference, noting the multiple accepted abstracts on nurse-led models of care.

Scholarships

Over 5,700 scholarship applications were completed, and almost 1,000 individuals will receive funding through IAS to attend the conference.

More Issues To Be Covered

Many issues will be covered that are not noted in the sessions mentioned here. The full list will be on IAS website shortly, and the program will continue to be populated, as the late-breaker abstract deadline is near. IAS staff and conference organizers hope to make the online search tool more user friendly.

Use of Data to Guide Programs for Impact

Irum Zaidi, Director of Country Impact, OGAC

Initiatives Around Data

Ms. Zaidi reiterated AMB Birx's report that PEPFAR is using granular data down to the site level, disaggregated by gender and age. She reported on PEPFAR-supported initiatives, noting that the program is using various data to elucidate which populations are being reached, whether those populations are in areas where PEPFAR can have the greatest impact, and whether PEPFAR is using the right programmatic tools to implement in those areas (integrated approach). PEPFAR works to identify costs associated with the work and confirms ways of reducing costs for all interventions (sustainable, epidemic-control operations).

Planning and Monitoring Process

PEPFAR has redesigned its planning and monitoring process by focusing on impact and effectiveness. It is employing integrated-data analysis for quarterly monitoring and this frequent analysis using different data streams is driving planning and allowing PEPFAR to critically analyze data down to the site level.

All Things Data Steering Committee

As it consolidates efforts and develops a routine, PEPFAR has formed the All Things Data Steering Committee, which brings all types of data, data owners, and data streams together to determine how to make data collection a routine process, as the analysis has become more predictable. The committee is exploring ways of looking at and presenting data in a more digestible format that clarifies what action is needed.

Ms. Zaidi presented a map used in 2016 PEPFAR Country Operational Plans (COPs) planning; it demonstrated coverage of ART by district and disease burden, helping PEPFAR to know if it is getting coverage to areas that have the highest disease burden. She then displayed the same map

showing the ratio of males to females on treatment, thereby showing coverage by gender at the district level. This data can be used to assess what district level interventions are needed to increase diagnoses among men, increase linkage to care, and determine viral suppression and retention. This map is a gender-disaggregated clinical cascade visualized in a highly accessible way.

Data Initiatives Supported by PEPFAR

Global Partnership for Sustainable Development Data

This partnership was launched in 2015 just after the Sustainable Development Summit, with the goal of bringing together public, private, and civil society partners. It is a space in which diverse groups can collaborate on all of the data related to the SDGs and fill critical gaps in sustainable development through existing and new data sources.

Health Data Collaborative

This collaborative is similar to the one above but is specifically focused on health data. Multiple global health partners work alongside countries to improve the quality of their health data for impact and to track progress towards the SDGs. They build upon and network existing efforts for enhancing, not duplicating, health information systems, surveillance, and capacity building; this is to disseminate data in a transparent, improved, and integrated way for all to use.

Partnerships with MCC on the Country Data Collaboratives for Local Impact

PEPFAR works with MCC to actualize the Tanzania Data Lab by looking at health data along with education, employment, and other determinants through gender-disaggregated information. The goal is to determine, in the example of DREAMS, how to bring these data together to design interventions for protecting young women from acquiring HIV.

All of the above collaboratives are key in their intention to go beyond the health systems perspective to drive impact in reducing disease.

Q&A Session

Question 1: Dr. Mushavi

Dr. Mushavi asked how PEPFAR plans to collect private sector data, as this has been a difficult area for the Ministry of Health and Child Welfare in Zimbabwe, despite developing some public-private partnership frameworks. When PEPFAR conducts its Site Improvement through Monitoring System (SIMS) site visits, is there an attempt to reach out to the private sector?

Answer: Ms. Zaidi

The private sector is an important constituency that does not always engage as we hope it would. At this time, when we are seeing acute outbreaks of certain conditions, we need real-time reporting regardless of public entity, private organization, or NGO. The question is how do we set up data governance and reporting structures through ministries of health so that we can detect the next outbreak? The Health Data collaborative would work with ministries on setting up those

structures and systems, determining what comprise the key reportable conditions with public health impact.

SIMS visits are conducted at places where PEPFAR is involved at the site level. A contractual agreement exists between the implementing agency and the implementing partner that determines the activities and conditions associated with receiving the funding.

Question 2: Dr. Nabiryo

Dr. Nabiryo wondered how this aligns with the UN agenda of one monitoring system and how it ties in at the country level and with the global partnership vis á vis organizations already on the ground.

Answer: Ms. Zaidi

All of the initiatives are meant to support that one M&E system. We need to recognize that such a system needs to be rooted in this century, with flexible systems that are real time and that can detect current public health threats. There has been individual support of disease within ministries of health; it is time to determine how to integrate and connect that support toward seeing the full spectrum of data at different levels that lead us to take action.

Question 3: Dr. Celum

Dr. Celum asked how many PEPFAR countries have some version of individual-level electronic medical records (EMR) and whether those would replace these initiatives.

Answer: Ms. Zaidi

Some countries use EMR solely for HIV; in other countries, entire health records are electronic. Examples of the latter are Kenya, Zambia, Tanzania, and Ethiopia; differences lie in scale-up levels and scalability. This involves infrastructure within the ministry of health or institutes in which PEPFAR is working, that allows us to maintain records from an IT, data management, and organization perspective. Where EMR innovations are occurring, we need to leverage those with the greater health arena rather than with just HIV.

Stigma and Discrimination Workshop

A. Cornelius Baker, Acting Deputy Coordinator, Office of Affected Populations and Civil Society Leadership (OAPCSL), OGAC

Mr. Baker reported that, earlier that day, USAID Office of HIV/AIDS Director David Stanton opened a large, two-day meeting convened by USAID and including Project Sword, UNAIDS, and other organizations to review and improve the People Living with HIV (PLHIV) Stigma Index. Presentations involved the various ways 80 countries around the world have introduced and are using the index, as well as a review of the soundness of the instruments and methods being applied. Another area of the meeting's focus was measuring the overall context of stigma and discrimination as it relates to the overall global HIV effort.

The Office of Affected Populations and Civil Society Leadership (OAPCSL) very recently launched a stigma and discrimination taskforce in partnership with USAID and other partner agencies. The task force anticipates that its work will lead up to a workshop in August, at which the participants will create a framework for how PEPFAR approaches stigma and discrimination in a more coherent manner. The framework will then be incorporated into the PEPFAR COPs process, updating the guidelines currently in place, and looking at appropriate funding initiatives to support that.

Update on OAPCSL Activities

Addressing Stigma in Health Care and Beyond

OAPCSL staff participated in a UNAIDS stigma workshop in November 2015; the workshop specifically focused on stigma in the healthcare environment and looked at the hierarchy of needs where stigma occurs. The focus was based on AMB Birx's presentation last year in Jamaica on this subject.

Given PEPFAR's investment portfolio, the office's first focus is addressing stigma as it occurs in the healthcare setting and in the healthcare environment. However, it is clear that the experience of stigma is broader than that for PLHIV who live in populations that are heavily impacted by HIV. A larger challenge exists around measuring—including how to support and utilize the Stigma Index, and how to implement it in a consistent way—and responding to that larger-scale experience. This includes developing an overarching framework for using the data in PEPFAR programs.

Analysis of PEPFAR Funding Around Stigma

OAPCSL is conducting an analysis of what stigma-related programs and activities PEPFAR is currently funding. The office is in the process of receiving presentations from agencies on their stigma-related work; it has heard thus far from USAID and the Health Resources and Services Administration (HRSA), and it plans to hear from the others. These sessions will help OAPCSL develop a global framework of ways PEPFAR is already addressing stigma. It will also allow for quantifying achievement of programs that might include research occurring at NIH or specific stigma projects of USAID.

Finally, every program reports improvements around HIV testing to reduce the stigma associated with that testing; examples of this include night testing and testing in the community. OAPCSL is working to determine whether such projects are to be considered stigma focused and to figure out how to calculate their impact. It is developing a matrix with which to survey federal agencies; this will be in addition to their oral presentations. Mr. Baker remarked that feedback from SAB members on the question of calculating stigma-reduction impact is welcome.

HIV-Focused Stigma vs. Key Population-Focused Stigma

OAPCSL is working to create an understanding for itself about HIV-focused vs. key population-focused stigma, as perhaps there is generalized environmental, cultural, and law-related stigma around groups such as gay people and drug users. The question is, when does stigma that may

reflect broadly in law or culture impact on a program's ability to reach HIV-related goals, and when does it not?

Mr. Baker provided the following example: Simultaneously, there can be broad cultural stigma against people who use drugs and a very effective syringe exchange program which reduces HIV infections among drug users. This demonstrates that it is possible to achieve a result without a change in law. The office is working to develop a prioritization plan for funding and programming, especially if the population wants a broader change in law or in social attitudes. PEPFAR's core policy is to support interventions that stop HIV infections but may or may not be focused on drug use or another issue, and OAPCSL is working to reflect on the lived experience of stigma among certain populations and what a community itself is measuring and believes to be important, and then to determine how PEPFAR will engage in that conversation.

Mr. Baker mentioned the HIV Prevention Trials Network (HPTN) 061 study, which Dr. del Rio had referenced on the previous evening. HPTN 061 is the first large-scale study on black, gay men in the US. One finding was that, while investigators wanted to focus on HIV prevention, many of the young men wanted to talk about their experiences with incarceration or unemployment; those issues were higher on their hierarchy of needs than prevention intervention. The question is- what is PEPFAR's role within the hierarchy of needs identified by a community and that may go beyond its core focus of delivery of prevention and treatment services if it is to engage with a population in a respectful and honest way?

A perception exists that, as we get deeper into the epidemic, the experience of stigma in marginalized populations is greater than it may have been previously; however, it is not clear how to measure that experience. Issues that men in the HPTN study and young girls in DREAMS communities are raising as affecting their lives are beyond the healthcare setting, and those are the things that are creating discriminatory and stigmatizing effects in their lives. The goal, if we believe they are essential to addressing the epidemic, is to establish how PEPFAR can support that work.

Summary

OAPCSL plans to produce a series of recommendations and guidance around addressing stigma and discrimination for PEPFAR based on its determination of where priorities and gaps lie. The office looks forward to bringing those to the SAB at its fall 2016 meeting. Mr. Baker noted that his staff has spoken with Rev. Sanders, who is a member of the committee, and that Carole Treston has supported their efforts and will continue to be involved and relied upon in this process.

Mr. Baker asked the SAB for feedback on the OAPCSL's identified issues, direction, and plans. He also solicited request on how the SAB might be engaged once his office comes back with its recommendations to create movement in this critical area for which we do not have the same level of data structure and clean process as in other areas that PEPFAR is addressing.

Discussion

Importance and Weakness

Dr. del Rio characterized stigma and discrimination as the “Achilles heel of HIV work”, asserting that a single intervention is not enough. Everything PEPFAR does needs to include a stigma-reduction component. If it is not part of the core activity, whether it be testing, ART delivery, or other, stigma is the point at which the clientele start leaving.

Scope and Components of Stigma Assessment and Response

Dr. Celum asked if OAPCSL is focusing only on HIV or, given the DREAMS focus, if it will also study stigma around young women seeking contraceptive services.

Mr. Baker explained that the Stigma Index, which is the core instrument, is specific to people living with HIV and therefore does not capture data for, and experience of, key populations. Also, the legal study has focused narrowly on the framework as it affects access to certain HIV-related services and around discriminatory laws in effect for gay men, drug users, and sex workers. Looking at adolescent girls, a large vulnerable population, how do we think about stigma as it affects their lives? What common language do we need to create for it in this framework?

Dr. Auerbach remarked that stigma is a vast, difficult undertaking that has remained a challenge over the history of the AIDS response. She suggested that, for the matrix it is developing, OAPCSL to think in terms of conceptualization, operationalization, and measurement.

Regarding conceptualization, define stigma and discrimination very clearly. Is stigma a cultural phenomenon and discrimination a legal one? Clearly defined terms help us to know these things when we see them. For operationalization, clarify the multiple elements of stigma and discrimination, such as HIV, gender, age, geography, class, etc. in order to understand what is contributing and what PEPFAR is addressing. Dr. Auerbach recommended being clear even if what is produced cannot encompass everyone’s notion of stigma and discrimination. Finally, the office needs to determine the object of this project: Is it stigma reduction? Stigma elimination? Stigma mitigation?

For the activities, it is important to determine whether mitigation (or reduction, or elimination) must be a primary outcome of HIV interventions, or whether it can be an intermediate product within a larger one of, for example, prevention.

Mr. Baker shared an example from the USAID meeting earlier that day, in which data from Ukraine demonstrated that, even when the healthcare setting was welcoming, a very high level of self-stigmatization existed, based on experiences of being thrown out of the family home because of being gay. Therefore, PEPFAR’s role may not be to significantly reduce stigma in the family unit or home, but its focus may become building resiliency in HIV+ persons.

Dr. Celum asked if questionnaires used to probe stigma include specific questions about the quality of healthcare experiences.

Mr. Baker explained that, at the UNAIDS meeting last year, participants looked at specific instruments that measure the healthcare experience. Its group of recommended instruments includes 80 different methods, and that is too many and offers no common framework to understand trends.

He added that the Stigma Index used every three or four years looks at stigma in the healthcare setting, in families, in the community, and broadly in the environment; it is possible to study the results for progression and trends.

Around reporting and enforcement, as people enter the healthcare system and are retained more, and as we create a framework in which people have the right to voice their experience and to complain when they receive bad service, we may see an increase in such complaints. Systems are needed that function to improve quality of service, and the challenge is to make the environment educational and not punitive.

Dr. Kates mentioned the existence of the US Preventive Services Task Force as part of the National HIV/AIDS Strategy, noting that it had developed a measurement tool for stigma. According to Mr. Baker, NIH has assigned a person to be on the OAPCSL task force, and the office is utilizing the good work the group did for a recent, very thoughtful White House meeting on stigma.

Commitments from Grantees on Stigma-Related Deliverables

Dr. Maxwell asked, as she had during the fall SAB meeting, whether PEPFAR is able to ensure and enforce commitments from its grantees to produce measurable deliverables around stigma.

Mr. Baker explained that OAPCSL is interested in tools such as the HIV 360° study in Jamaica that developed matched sets of clients, care, and providers. Questions include how anti-discrimination laws are being enforced in PEPFAR-funded areas, and what reporting and enforcement mechanisms exist. Last year, as part of its COP guidance, PEPFAR mandated that all sites display a poster that it developed with The Global Fund that advertised a discrimination-reporting mechanism. The Global Fund believes that mechanism is not an effective reporting vehicle, as it has received just 30 reports of people being denied service or having experienced discrimination in service over three years. Mr. Baker agreed that the office needs to consider mechanisms for enforcement and for training. It also needs to determine how to ensure continuous training. This is an ongoing effort and OAPCSL needs to identify ongoing processes.

OAPCSL has been reviewing AMB Birx's Jamaica workshop presentation, the November UNAIDS meeting notes, and the White House summary of its meeting, and Mr. Baker suggested that Ms. Treston and Rev. Sanders reference those documents in developing the workshop agenda.

Stigma and the Healthcare Workforce

Ms. Treston commented that stigma and discrimination—multifaceted, complex, and intersectional—resonates with her as a healthcare provider. She has realized upon reflection how much she may have contributed to stigma (particularly self-stigmatization) in the past with the well-meaning intention of protecting her patients. She noted the importance of considering how PEPFAR can affect healthcare workers in the areas of intentional and unintentional stigma. She provided the example of the posters Mr. Baker described, expressing concern for the potential unintended effect of encouraging someone to call a hotline to report discrimination, and wondering if that is any different than when she used to tell patients, “Only you and I have to know that you have HIV.”

Dr. Mayer added that healthcare workers want to feel like they are doing a competent job. Cultural competency is very important.

Mr. Heywood suggested that what we see with healthcare workers related to HIV stigma is a reflection of the general power imbalance between themselves and healthcare consumers, which appears in interactions beyond HIV, such as around young people’s sexual lives, young girls seeking termination of pregnancies, and more. He questioned how one narrows that power imbalance.

Mr. Heywood noted another issue: The healthcare workforce does not receive training on rights, ethics, or other crucial issues; therefore, healthcare workers reflect the general stigmatizing prejudices of their communities. Ms. Treston added that such prejudices are exacerbated by the imbalance Mr. Heywood mentioned.

Dr. del Rio pointed out that the healthcare workers in the HIV settings he has observed are notably not stigmatizing; he wants to be careful not to group all healthcare workers together. However, he agrees that the education of the healthcare workforce is a priority, as that environment must be free from stigmatization.

Dr. Celum’s experience with family planning providers in Africa has shown them to be stigmatizing, and she sees this as a potential barrier to other healthcare services.

Disclosure

Mr. Milan asked if positive models of disclosure exist that are helping to push the needle toward the reduction of stigma.

Mr. Baker referenced discussion at that morning’s Stigma Index meeting that centered on the meaning of the measurements. Because of the nature of the index, it measures the negative. He noted the syringe exchange example, in which overall views may not have changed, but good environmental support may be resulting in reduced infections in the drug user population, which is living, thriving, and healthier in relationship to HIV. The challenge is how to measure those results in a data framework that is larger than solely stigma.

PLHIV Stigma Index and Beyond

It is important to consider the valuable role the Stigma Index has played in quantifying results. Thailand now has completed two rounds of the Stigma Index and recently adopted stigma reduction and elimination as one of its national plan's three or four core goals. It is working with an advisory group made up of PLHIV to produce action plans. This is a strong example of measurement and program development.

Dr. Mayer asserted that indices beyond the Stigma Index may be needed, as some kinds of stigma are socially embedded in generalized epidemics. Also, a challenge exists in comparing such an issue as young people's sexuality—not necessarily stigmatized, per se—and key population issues. People can have multiple identities, such as sexuality and drug use, and therefore experience a combination of forms of stigma. Using a matrix approach and having more than one outcome may be useful.

Societal Opinion Shift

Dr. Macklin raised the concept of considering success stories that are not data driven, noting the powerful shift in the US around LGBTI issues and gay marriage over the past 30 years; the shift was so forceful that, when North Carolina passed its recent "bathroom law", a major outcry ensued that forced the legislature to somewhat backtrack. Obliterating stigma will not eliminate prejudice, but stigma reduction has enabled significant cultural shifts such as gay pride and gay marriage, among other progress.

Even if not data driven, Dr. Macklin suggested that success stories could be used to show a reduction in stigma.

Mr. Baker agreed that it would be helpful to know ways in which other countries might use various forms of popular opinion, adding that OAPCSL needs to learn how to conduct environmental assessments and scans in order to develop a broader framework for how specific populations may be viewed or accepted.

Mr. Heywood shared his perception that stigma has declined significantly over the last decade in South Africa. He offered what he sees as two critical elements of this:

1. A higher level of HIV literacy has demystified the disease and has calmed fears.
 - a. As an example, within the Treatment Action Campaign (TAC), a movement of predominantly PLHIV who wear HIV+ T-shirts, there is no stigma of HIV within the membership; nor does stigma exist between HIV+ TAC members and the families and communities from which they come.
2. Individual empowerment around HIV has grown through solidarity and community support. In parallel, one does not see stigma on the basis of sexual orientation, because people feel more empowered to be out in those communities.

Mr. Heywood remarked that solidarity combined with knowledge is crucial.

Collaboration Across Sectors

Mr. Warren noted that much of the work around stigma and discrimination does not relate to HIV directly, and he wondered about the existence of partners—a framework or collaborative network outside the “HIV bubble”. Without such collaboration, huge opportunities around broader social issues will be missed.

Mr. Baker believes such partners do exist. He noted that this conversation indicates the existing challenge: Stigma is a vast issue, and there are numerous perspectives. How do we drill it down to develop a framework, particularly in PEPFAR countries, so that our program coordinators and staff can operationalize, some in partnership across sectors?

Mr. Baker feels that, in the area of discrimination, it is clear that PEPFAR has other partners. Some work is already ongoing around the legal environment.

Bringing Countries Along

Dr. Nabiryo expressed the importance of documenting the work that has been accomplished in this area and the progress that has been made. If PEPFAR is disseminating new guidance, countries need help in understanding the ways in which it links with the status of the HIV work. PEPFAR needs to provide information around what has happened and lessons learned.

OAPCSL has spoken with UNAIDS on its Agenda for Zero Discrimination in Health Care with the goal of incorporating information relating to its goals going forward. Within PEPFAR, OAPCSL is working with the Office of Sustainability (a member of the task force) on developing a sustainability index to measure stigma and discrimination and to show progress made.

Update on HIV Cure Research

Judith Currier

Dr. Currier expressed the importance of understanding the current status of HIV cure research. She described the four following reasons to search for a cure to the disease:

1. Currently, patients must be treated with ART for the rest of their lives; issues include:
 - a. Side effects and long-term toxicities
 - b. Burden of lifelong adherence
 - c. Cost
 - d. Sustainability
2. Persistent HIV-1 infection may have adverse effects, such as:
 - a. Inappropriate immune activation
 - b. Cardiovascular disease, central nervous system disorders, and other end-organ damage
3. A potential risk for transmission

4. Ongoing stigma of HIV infection

Latent HIV

Dr. Currier noted that HIV-1 integrates into the host DNA. This latent form of HIV- in long-lived central-memory T-cells, is unrecognizable by the host immune system, presenting a barrier to a cure. The cells are hard to measure and are persistent. On top of this, the undetected disease does not get removed by ART.

Much of the basic science work to understand what causes this latency and how it might be “unlocked” has led to a better understanding of HIV persistence. It has identified novel targets for drug development, and this has led to testable hypotheses.

Barriers to an HIV cure

A latent reservoir of HIV infected cells is established very early after infection, and these cells persist during effective ART. Such a reservoir can include cells in the central nervous system and genital tract and could take more than 70 years to eradicate on ART alone.

Approaches to HIV Cure

Dr. Currier reviewed the following five main approaches to curing HIV:

1. Hematopoietic stem cell transplantation
2. Inducing HIV expression from latently infected cells
3. Immune-based interventions
4. Immediate initiation of ART
5. Gene therapy

Dr. Currier began by explaining that two kinds of cure exist:

Functional Cure: Host-Mediated Control of HIV Replication, in the Absence of ART for a Pre-Defined Period of Time (e.g., 5-10 Years)

In this case, the host immune system keeps HIV in check without ART. People in this category are sometimes referred to as host treatment controllers or elite controllers; the latter of these control HIV without ever having had any treatment and hold the keys to understanding the most important mechanisms for an effective immune response.

Sterilizing Cure: Complete Elimination of Replication Competent Virus

In this case, the disease is completely eliminated from the person.

The ‘Berlin Patient’

The only example of the sterilizing cure to date is the so-called “Berlin Patient”, who underwent myeloablative chemotherapy for leukemia, followed by whole-body irradiation and successful transplantation of haemopoietic stem cells from a CCR5 homozygous donor with acute myelogenous leukemia (otherwise described as a new immune system that was resistant to HIV

infection). Dr. Currier noted that such a routine has yet to be replicated successfully and is obviously not scalable.

Possible Reasons for Non-Detectable HIV in the 'Berlin Patient'

It is not known what cured the Berlin Patient. Possible reasons are:

- Long-term ART had reduced his HIV burden prior to him receiving the stem cell transplant.
- Ablative chemotherapy removed his infected cells on long-term ARV suppression.
- Transplanted cells (a new immune system) protected him from HIV infection due to CCR5 delta 32 mutation.
- Allogeneic cells contributed to a graft-versus-host (GVH)-like reaction, creating further clearance of latently infected cells.
- His body generated protective immunity.
- A combination of the above led to the cure.

Hematopoietic Stem Cell Transplantation

Researchers are working on ways to modify the Berlin Patient's treatment protocol, using situations in which HIV+ patients are diagnosed with cancer or other hematological malignancies to attempt to see what can be done to take advantage of those disease treatments. Thus far, several attempts to replicate the transplantation have proved unsuccessful.

Inducing HIV Expression from Latently Infected Cells

Latency reactivating agents attempt to remove the non-replicating virus from reservoirs. Histone deacetylase inhibitors (HDACi), a classic drug developed for cancer treatment, as well as other medications created for other uses, are being studied to determine whether HIV can replicate in people on ART with a suppressed viral load. Three drugs—Vorinostat, Panobinostat, and Romidepsin— are currently being tested in multiple doses and probably in combinations through very small, intense studies.

Immune-Based Interventions

Immune activation involves synergistic strategies to eliminate reservoirs of latent HIV. Compounds called TLR7 agonists can also stimulate the production of HIV from latent cells. The concept is to "kick" (activating the expression of HIV) the reservoir of latent cells with these agents and then kill the cells expressing HIV proteins with other interventions, such as therapeutic vaccines, anti-Env antibodies, and/or anti-PD-L1. This combination approach is thought to provide benefit.

Transient Plasma Viremia Induced by TLR7 Agonist Treatment of Monkeys on ART

This study was presented at the 2015 Conference on Retroviruses and Opportunistic Infections (CROI); it showed that monkeys who were treated with a TLR7 agonist experienced viral bursts, while those on a placebo did not. This suggests that this approach could be successful.

Early ART Initiation

The most relevant approach according to Dr. Currier is early initiation of ART, especially with the rollout of Test & START and with the deployment of prevention interventions in which people will be tested frequently. Opportunities to initiate treatment at the earliest possible stages may exist; this could reduce the size of the reservoir of latent HIV cells, setting patients up for future cure interventions when those become available. In Thailand, researchers found that the HIV reservoir, as measured through HIV DNA, was significantly lower in those who were treated at the very earliest time points. Some efforts have been made globally to treat babies very early after diagnosis. The goal for early ART initiation is to reduce reservoirs and the risk for HIV transmission.

Gene Therapy

Those who attended CROI this year may have attended a plenary session on progress in gene therapy by Paula Cannon of the University of Southern California's Keck School of Medicine. Dr. Currier recommended that SAB members who missed the provocative presentation listen to it online. This therapy involves changing some aspect of the genetic profile of the host, possibly making the immune system resistant to HIV. There is merit to concerns about scalability and cost-effectiveness; however, there may be things that can be used to some effect.

Anti-HIV-1 gene therapy is a very active field of investigation. Examples include:

- Genetically modified CD4+, CD8+, HSC (autovaccination)
- Recombinant T-cell receptor (CD4 zeta)
- Transdominant proteins (Rev M10, Trev)
- Intracellular antibodies and RNA decoys
- Antisense (tat, RevM10, env ViRxsys)
- Ribozymes (U5 hairpin, Rz2 hammerhead)
- dsRNA (RNAi, siRNA)
- RNA aptamer (small RNA antagonists of protein function)
- Zinc finger nucleases (CCR5 directed, SB-728)

Dr. Currier finished by asserting that ART needs to be a primary focus, as all roads to cure begin with it. It is the hope that scalable and low-cost options will be developed that will turn early ART into a cure. She thanked Dan Kuritzkes for providing the majority of the slides used in her presentation.

Discussion

Dr. del Rio commented that it is valuable for this group to know what is on the horizon. He noted that, much like prevention and treatment, cure and vaccines are closer and closer to becoming one, as they are very similar interventions. Although it is not something PEPFAR is taking on at this time, it is important to be able to relay the message that accomplished scientists are interested in and working diligently on finding a cure, thereby providing hope for the future.

Dr. Auerbach added that people in the field often hear that a cure is so far in the future that it is not relevant to people in lower- and middle-income countries. This is very similar to initial arguments around ART and then around PrEP; people do come around and realize the relevance. Therefore, getting countries engaged in the cure agenda now is important, and PEPFAR could leverage some very robust ongoing activities in this area, including the IAS's cross-disciplinary, cross-sector Toward an HIV Cure initiative; the NIH's very dynamic cure research agenda; and work by the American Foundation for AIDS Research (AMFAR). Dr. Auerbach and Dr. del Rio agreed that proactive groundwork needs to be done around community engagement and cure literacy, as people will need to be interested in participating in trials.

Dr. Currier pointed out that a longitudinal AIDS clinical trials group study soon to be started will look at very early treatment of acute infection in global settings, using newer testing models to identify recent infection and to gather and follow a cohort of people who are starting on treatment very early. The study will be conducted in some PEPFAR countries.

Mr. Warren noted that just before AIDS 2016 in Durban, the fifth annual Toward an HIV Cure Symposium, which will focus on community cure literacy, will occur. Also, IAS will issue its new scientific framework. He shared that, about one year ago, TAG, AVAC, and other organizations created an online portal entitled "The Curriculum." It has 16 modules, each created in partnership with a leading scientist and a community advocate in that area. Feedback on the portal is most welcome.

Finally, Mr. Warren remarked that, in AVAC's work within civil society in the US or anywhere in Africa, the issue that most tantalizes and engages a layperson is the idea of an HIV cure.

Dr. Celum is hopeful that the broadly neutralizing antibodies study will go beyond informing a vaccine but will have additional uses. She purported that we need to use these opportunities to paint a picture that the route to a cure is a circle, not a line.

Dr. Mayer noted that, within the next year, there will be both studies on infusible antibodies in PEPFAR countries. Therefore, scientific literacy and engaging community health providers are extremely important elements that PEPFAR should track. Dr. del Rio added that part of the community literacy is the engagement of the treatment community, as practitioners will need to be on board if patients are asked to go off treatment for a study; in a recent study in which he was involved, the skepticism of the provider, the person people trusted the most, led them to not participate in treatment.

Dr. del Rio thanked Dr. Currier for her accessible, valuable presentation.

Public Q&A Open Line Session

Dr. del Rio reminded the SAB that it is an advisory body chartered under FACA, and therefore its meetings are open to the public. He then solicited comments and questions from any guests at the meeting or on the phone.

Deborah Dortzbach, director of health and social development at World Relief and longtime HIV/AIDS program leader, thanked the SAB for its influential and much-needed work in response to the HIV/AIDS crisis. She remarked that the HIV community has experienced numerous pendulum swings about prevention, and she expressed curiosity whether, given the youth bulge, PEPFAR will seek to learn why some youth are delaying sexual activity and then support that in programs, policies, and funding. She also asked if PEPFAR will work to strengthen marriages in a way that supports more satisfying interactions between husbands and wives, enhances communication, and supports the value of women and girls. Some of that initiative existed early on in PEPFAR's efforts; Ms. Dortzbach wonders how the community can lay the groundwork for discovering more evidence-based responses.

Summary Comments and Closing

Dr. Shaffer

Dr. Shaffer thanked all in attendance—including USG partners and the public, SAB members, the four EWG co-chairs, and AMB Birx—for another productive meeting. He added that colleagues in the field are inspired by listening to the thoughts and the process of the SAB.

He expressed appreciation for the PEPFAR deputy principals' engagement in and input to the agenda and for the assistance of OGAC staff. He thanked the SAB for again meeting in the OGAC offices rather than at a hotel venue, thereby allowing for another 500 children to be placed on first-line therapy in Kenya through the cost savings.

Dr. Shaffer expressed his appreciation to AMB Birx for her continued support of the SAB and made it clear that OGAC welcomes the board's thoughts and feedback about today's meeting in order to maximize the use of members' time. He asked that SAB members email him or others with any further feedback.

OGAC staff will be in touch promptly regarding EWG work, with a similar timeline to last time.

Finally Dr. Shaffer proposed the board consider meeting (reconvening) in six months, as much work remains and some exciting results will exist by then around finance and sustainability, as well as with regard to data.

Dr. del Rio

Dr. del Rio offered his gratitude to EWG members for their time and efforts. He echoed Dr. Shaffer's comment regarding rapid changes, and he sees PEPFAR playing a role in alleviating

partners' fears by communicating what is happening. SAB members are ambassadors to the program and can contribute leading-edge information to make programs more effective.

Some things discussed today could potentially lead to a formal letter of recommendation, and Dr. del Rio and PEPFAR staff will be in touch about what they decide to develop in advance of the next SAB meeting.

AMB Birx

AMB Birx expressed her deep appreciation for the dedicated effort of the SAB, noting that the members think about the issues, come well prepared, and ask tough questions that help PEPFAR staff think about how to do this work better and how to improve dialogues with countries to get them focused on core and critical issues discussed today.

She noted the comments and recommendations around cotrimoxazole and INH and issues about co-packaging, pointing out that, even if they cannot be packaged together, they can be placed in blister packs, thereby simplifying things for clients. PEPFAR believes that packaging is important, and there are ways to create a sense of wellness around HIV in that packaging.

AMB Birx asserted the need for engaging others in a deeper conversation that links to fact-based education, so that young girls have the information that they need without prejudice and can make decisions about their health. Communities also need to address the fact that 40% of these girls are raped.

AMB Birx expressed her concern around messaging to "be faithful" in the face of gender inequity, as women have a habit of being faithful to an individual who may not be acting faithfully to her and may be transmitting disease. That woman ends up feeling guilty that somehow she brought HIV into the family. For the last 15 years, either due to Option B+ or PMTCT, the woman has been the index case of the antenatal clinic (ANC); this has created the deeply incorrect misperception that women are the vector of HIV disease and has led to more stigma and discrimination.

AMB Birx believes that PEPFAR needs to engage communities in dialogue and awareness, and she welcomes the time when fact-based education can be brought into churches and schools, and communities will protect young people. She promoted the importance of finding the place for churches to come back together to address the role of cultural issues and community.

AMB Birx thanked the SAB for its partnership, noting that the board's discussions help her think about things in a novel way and inform PEPFAR's programming. She expressed her hope that the board members feel valued and wished them safe travels. She hopes to see them at IAS or other meetings and here again in six months.

The meeting was adjourned at 4:32 p.m. ET.