PxWire A Quarterly Update on HIV Prevention Research | Vol. 9 No. 1 | January–March 2016 | AVAC Global Advocacy for HIV Prevention

AVAC's Take

"Big Data." These two words are everywhere we turn these days. PEPFAR uses the phrase to talk about how to be sure that programs are doing the "right things in the right places right now." Major corporations talk about it in terms of using massive information sets to guide decisions. Here at AVAC, we're invoking the term in those ways—and more. We see big as in "a big deal". There are few, if any, quiet years in HIV prevention research and implementation. But this is a year of big [deal] data, whether that's findings from clinical trials, funding levels or readouts from PEPFAR's first year of a geographically focused program plan. What's a big deal for you? Please let us know! *–AVAC*

Ring in the New Year

Anticipation is high for what many expect to be the big news from CROI 2016: results from the ASPIRE and Ring studies of the dapivirine vaginal ring. The two trials of the ARV-based vaginal ring ran for the past three years in Malawi, South Africa, Uganda and Zimbabwe, and collected data on safety, acceptability and its ability to reduce a woman's risk of HIV acquisition. If positive, the data from these trials could form the basis of a regulatory submission, which would help pave the way for manufacturing and future access to a new HIV prevention tool.

PrEP's next generation

Much of the HIV prevention fanfare in 2015 focused on the power of oral PrEP as it took its rightful place as a key prevention option for those at high risk—endorsed by the WHO, a handful of national governments and, most importantly, an increasing number of users.

But, just as scientists didn't stop after the early successes with ART in 1996—when successful treatment required fistfuls of pills on a strict schedule—prevention researchers are looking ahead. One of the "next-generation" PrEP efforts is focused on long-acting injectable (LAI) antiretrovirals. Results from one such study, ÉCLAIR, are expected at CROI. The Phase IIa study looked at the long-acting injectable formulation of GSK1265744 (also known as Cabotegravir), and its safety and acceptability among MSM in the US. This same approach is being evaluated in another study that also includes women and participants outside the US. Results from that trial, HPTN 077, are only expected in 2017, but now is a great time for advocates to watch this space, including reviewing lessons learned from ÉCLAIR that could be relevant for ongoing research.

Announcement of targets heralded but will the money follow?

In late 2015, UNAIDS issued long-awaited HIV prevention targets, including a call for a total of 27 million additional voluntary medical male circumcision (VMMC) procedures by 2020. This works out to more than five million procedures per year on average—two million more than have ever been performed. PEPFAR's peak performance was 2.8 million in a single year. It won't be close to that in 2017. PEPFAR doesn't need to, and indeed shouldn't, pay for the pursuit of global VMMC targets on its own. The Global Fund should ensure that country concept notes fill the space; PEPFAR and UNAIDS should advocate for resource-mobilization in country and global forums; and national governments should step up the pace.

Durban recharge?

Sixteen years after Durban 2000, the first (and only) International AIDS Conference held in Africa, the large international gathering returns to South Africa this July. The context in which this year's conference takes place is an AIDS response that few may have imagined in 2000 when activists were marching for access to treatment, period.

Durban 2000 was a high point of global solidarity. In 2016 will AIDS activism be rekindled and reinvigorated leading to massive mobilization for decisive action on ending the epidemic?

ECHO seeks an answer

Shortly before the New Year, the ECHO trial, which aims to evaluate the impact of various contraceptive methods on women's risk of HIV, got underway. It's a milestone for a study that was several years in the making and underwent several changes along the way. In the final design, the trial will randomly assign women to receive the copper IUD (intrauterine device), DMPA (Depo-Provera) or the Jadelle implant. All participants will receive the same package of counseling and HIV prevention services, and the trial team has said that PrEP will be introduced as standard of prevention in line with evolving national policies. In 2016, advocates can watch trial reports *(http://echo-consortium.com)* for information

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The Years Ahead in Biomedical HIV Prevention Research

Status of select biomedical HIV prevention clinical trials

Trial	2016 Q1	2016 Q2	2016 Q3	2016 Q4	2017 Q1	2017 Q2	2017 Q3	2017 Q4
MTN 017 *	Results expected Q1 2016							
CAPRISA 008	Results expected Q1 2016							
ASPIRE * (MTN 020)	Expected completion Q1 2016							
MTN 025	Anticipated OLE							
The Ring Study * (IPM 027)				Expected completion Q4 2016				
IPM 032				Anticipated OLE				
ÉCLAIR *	Expected completion Q1 2016							
HPTN 076								Expected completion Q4 2017
HPTN 077								Expected completion Q4 2017

* Data presented at CROI, February 22-25, 2016

Daily tenofovir-based oral PrEP is proven and recommended by the WHO for those at substantial risk of HIV infection. Demonstration projects and rollout are ongoing. See more at *www.prepwatch.org*.

NEXT-PrEP *	Results expected Q1 2016							
HVTN 100				Expected completion Q4 2016				
HVTN 702				Anticipated start of South African licensure trial Q4 2016				
HVTN 107	Anticipated start Q1 2016							
HVTN 111	Anticipated start Q1 2016							
HVTN 108		Anticipated start Q2 2016						
HVTN 113					Anticipated start Q1 2017			
HIV-V-A002	Expected completion Q1 2016							
HIV-V-A003	Expected completion Q1 2016						Anticipated start of Ad26 efficacy Q4 2017	
HIV-V-A004								
HVTN 703/HPTN 081	HVTN 104 * Phase I Safety	Anticipated start Q1 2016 Southern Africa. Expected completion Q2 2020.						
HVTN 704/HPTN 085		Anticipated start Q1 2016 the Americas. Expected completion Q2 2020.						
ECHO								Started Q3 2015

Rectal Gel · Vaginal Gel · Vaginal Ring · Long-acting injectable PrEP · Oral PrEP · Preventive HIV vaccines · Antibodies · Hormonal Contraceptives and HIV · Open Label Extension (OLE)/Follow-on

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on enrollment. Are women willing to be randomized? How quickly or slowly are women volunteering? We can also track the trial's responsiveness to PrEP and evolving standards of prevention.

Will 2016 reveal the future for bNAbs?

Broadly neutralizing antibodies, or bNAbs, are potent immune substances that block the activity of many different types of HIV. Isolated from people living with HIV, and then purified and made even more potent in labs, bNAbs are being tested for prevention. "AMP", short for antibody-mediated prevention, is also the name of two Phase IIb studies that will evaluate efficacy of the bNAb known as VRC01 in reducing HIV acquisition. While the passive transfusion of bNAbs is not likely to be a scalable prevention option in itself, these trials might provide important clarity on the bNAbs dosage required to prevent HIV acquisition and inform future vaccine design. In addition to the science of antibodies, this is the first efficacy trial to begin in South Africa since oral PrEP was approved for use there—how will the evolving standards for prevention affect trial conduct?

Decision time for vaccines

Vaccine efficacy trials are rare—too rare, in fact, given that only four vaccine concepts have advanced to this stage in more than 20 years. 2016 could be an exciting year as there may be results from two Phase I/II trials that could spur new efficacy trials. Results from HVTN 100 expected in the first half of the year could result in the go-ahead for a Phase III licensure trial (HVTN 702) testing a new iteration of the RV144 vaccine regimen. At the same time Janssen is testing multiple vaccine candidates in Phase I/II trials to evaluate its Ad26 mosaic vaccine.

Global Fund's fifth replenishment

This year the Global Fund will hold its fifth replenishment meeting seeking pledges for the next three years. The three-year goal of raising US$13 billion for the Global Fund out of a projected US$97 billion global need may not be achievable in light of scaled-back contributions from many countries. But this sum may actually be an underestimate of funds needed to act decisively and with impact. Advocates need to demand replenishment and for country and bilateral investments to begin to meet the full US$97 billion need.

DREAMS and PEPFAR

DREAMS, a PEPFAR program dedicated to lowering HIV incidence by 40 percent among young women and girls in 10 southern African countries by 2017, is now rolling out. To achieve that laudable and very ambitious goal, countries need to start rolling out programs and seeing results in 2016. And PrEP is part of that dream. The PEPFAR Scientific Advisory Group recommended that "100% of DREAMS countries should have PrEP delivery in 2016." 2016 will be a year to watch for signs and progress for DREAMS, as well as an evolving and engaged civil society response and involvement in that work.

ART expansion

The 2015 WHO "treat all" guidelines should result in a major shift in strategy to expand access to ART to achieve UNAIDS' 90-90-90 targets and control the HIV epidemic. As of the middle of last year, 47 percent of lower-middle income countries had yet to adopt the previous WHO guidelines recommending treatment for all with CD4 count below 500. In 2016, will countries adopt the new WHO guidelines to offer ART to everyone living with HIV?

What's next for rectal microbicides?

Results from the first ever Phase II rectal microbicide trial, MTN 017, are expected at CROI. The study looked at a reformulated [reduced glycerin] form of tenofovir gel for rectal application in men and transwomen in Peru, Thailand, South Africa and the US. Final results from this international study are forthcoming but available feedback on acceptability has raised concerns. Trial participants and potential users have said that the applicator, originally designed for vaginal use, is far from ideal for inserting the gel into the rectum. Scientists are exploring the potential for another reformulation with the goal of a more lube-like gel that could be inserted with a finger—no applicator needed. They're also exploring a variety of other potential active ingredients other than tenofovir, such as dapivirine and Griffithsin (which is not ARV-based), as well as best dosing and study design. How do these questions affect the timeline for future studies—including possible efficacy trials? Advocates should watch and weigh in. Which new candidate designs and compounds get the green light is something for advocates to watch in 2016.

About AVAC

AVAC works to accelerate the development and global delivery of HIV prevention tools. To receive regular updates via email sign up at *www.avac.org/signup.*

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