

PREVENTION ● on the Line

AVAC Report 2014/15





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— IN MEMORIAM —

This year's *AVAC Report* is dedicated to all those who perished when Malaysia Airlines Flight 17 was shot out of the sky over Ukraine in July 2014. This was a tragic global loss, but those of us working to end the AIDS epidemic were all particularly affected as the flight included six delegates en route to the International AIDS Conference in Melbourne, Australia: Pim de Kuijer (STOP AIDS NOW!), Joep Lange (HIV Netherlands Australia Research Collaborative), Jacqueline von Tongeren (Amsterdam Institute for Global Health and Development), Lucie van Mens (Female Health Company), Maria Adriana de Schutter (AIDS Action Europe) and Glenn Thomas (World Health Organization).

Each of these individuals brought a profound commitment to their work and—as they were remembered by friends and colleagues—each tackled the challenge of this epidemic with determination and joy. AVAC staff and board members were especially privileged to work with and learn from Joep Lange, a tireless advocate whose kindness

and good humor was outmatched only by his integrity and determination to expand access to high quality AIDS prevention, treatment and care to all who needed it.

These individuals were peaceful warriors and one can imagine that all would also urge remembrance of the many other victims of the conflict in the Ukraine, including casualties of war, individuals living with HIV, and people who inject drugs whose access to treatment, care and harm reduction including opiate substitution therapy has been severely compromised since the conflict started. Last July, former US President Bill Clinton addressed the International AIDS Conference as it mourned together. His words provide "the terms of our interdependence" that we must continue to demand in the name of those we have lost: "The open hand against the clenched fist. The inclusive politics and economics versus division and dominance. Cooperation against control. Life against death."

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Letter from the Executive Director

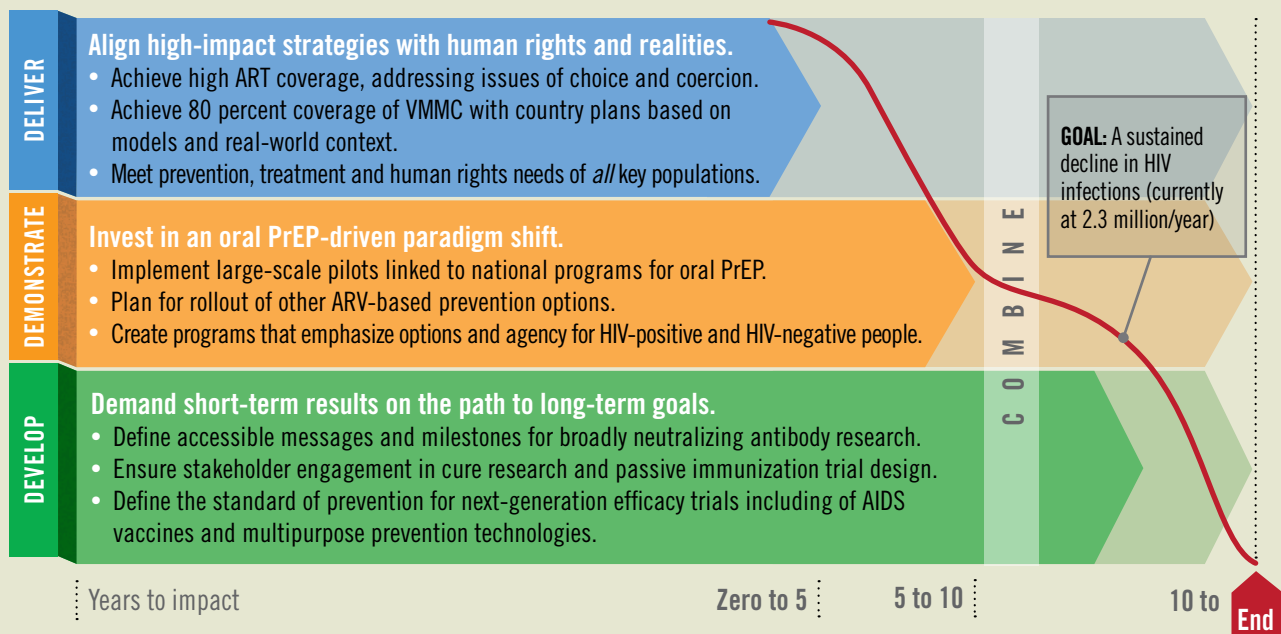
The question AVAC grappled with as we began the work of putting together this year’s Report is: What will this era of the epidemic look like twenty years from now, in 2035? How will it be remembered? What will be included in the official histories, and what will be left out? We’re asking these questions because the present moment is filled with forecasts. In particular, there are predictions about what will happen if various strategies are rolled out and about what the cost of inaction will be.

Such predictions have been a staple of the epidemic response for more than three decades. What is different today are the conversations and the crystal

ball-gazing concerns about whether it will be possible to end the AIDS epidemic. The answer, according to UNAIDS, PEPFAR and many activists and epidemiologists, is a resounding, “Yes ... if ...”—with the “if” focused on the specific steps that need to happen. Some of these steps take the form of targets, such as the UNAIDS “90-90-90” goals of ensuring that 90 percent of people living with HIV know their status, 90 percent of those individuals are on ART and 90 percent of those individuals are virologically suppressed by 2020.

90-90-90 is the latest set of targets advanced by UNAIDS, which also brought us the “Getting to Zero” campaign in 2011

A Three-Part Agenda for Ending AIDS: 2015



AVAC Report 2014/15 At a Glance

PART I *Truth, Lies and Targets* focuses on why targets matter and why they may be going astray.

Key recommendations:

- **Mind the gap** in global and country targets. Set and meet goals for prevention and treatment.
- **Put prevention on the line** with models and messages that reflect all the components of an “ending AIDS strategy”.
- **Set the right targets for the right interventions.** For VMMC and ART, coverage is key. For emerging tools like PrEP, a different approach is needed.

PART II *Advancing a Three-Part Agenda* focuses on key actions across the research-to-rollout continuum. Key recommendations:

- **Align high-impact strategies with human rights and realities.** If science does not get synched up with human rights then there is little hope of bringing the epidemic to a conclusive end.
- **Invest in an oral PrEP-driven paradigm shift.** Now is the time to move from evidence to implementation. Demand is growing, and data are coming in.
- **Demand short-term results on the path to long-term goals.** AIDS vaccine, passive immunization and cure research are years from yielding licensed approaches. But short- and mid-term milestones are a must.

and the “3 by 5” target for antiretroviral treatment coverage before that. UNAIDS has also set an ultimate goal of ending epidemic rates of HIV acquisition and deaths from AIDS by 2030.

In twenty years, we will have ample hindsight as to whether today’s targets have mattered in the quest to end AIDS.

But this year, we’re interested in foresight. We’re concerned about whether the targets that have been set are the right ones; how much targets matter—particularly in the context of a global response running at a disastrous funding deficit; and where prevention targets other than those focused on antiretrovirals in HIV-positive individuals fit in. We’re also cognizant that targets can turn from audacious to absurd in the blink of an eye if financing, political will and community buy-in are missing. AVAC works in coalitions in many of the countries hardest hit by the epidemic. Targets that are developed in Geneva, Washington, D.C.

and other corridors of power can bear little resemblance to the realities of these countries and communities. Where there’s no reality, there’s no relevance. It’s essential that countries have the technical and financial resources to make global targets relevant to national context. Otherwise, the loftiest goals will be ignored.

As we argue in this Report, targets have played a critical role in changing the course of the epidemic (see pages 10-11). Likewise, a poorly thought out target can have no impact at all. Right now, it’s critical that smart targets and tactics are matched to the lofty but achievable goal of bringing an end to AIDS. This is why we’ve devoted Part I of the Report to a look at why targets matter, what targets are missing, and how advocates need to work together to ensure there are strategic targets across the spectrum of prevention options.

A Target That Worked: 3 by 5

The "3 by 5" initiative, launched by UNAIDS and WHO in 2003, set a global target of providing three million people living with HIV/AIDS in low- and middle-income countries with antiretroviral treatment (ART) by the end of 2005. It was positioned as a critical interim step toward universal access to HIV treatment.

The target was audacious, to say the least. By 2003, 30 million people had died of HIV-related illness. Forty million people were living with HIV in low- and middle-income countries, six million people with HIV/AIDS needed immediate

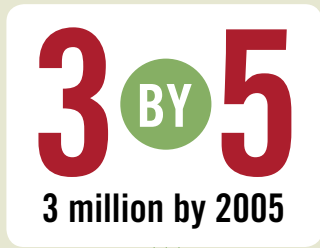
ART based on eligibility criteria at the time. Less than eight percent had access to treatment.

To meet this target, WHO, countries and other partners developed a plan to train 100,000 health workers, strengthen health systems and build the infrastructure needed to provide ART. When the 3 by 5 target was launched, there was an estimated US\$5.5 billion funding gap in the resources needed to meet the goal. But commitments from PEPFAR and the GFATM changed that picture.

Both the funding need gap and treatment target goal were met in 2007.

While the target wasn't met on time, it still changed the course of the epidemic. The number of people on treatment more than doubled between 2003 and 2005, from 400,000 to approximately one million, and by 2007 the number of people on treatment reached three million.

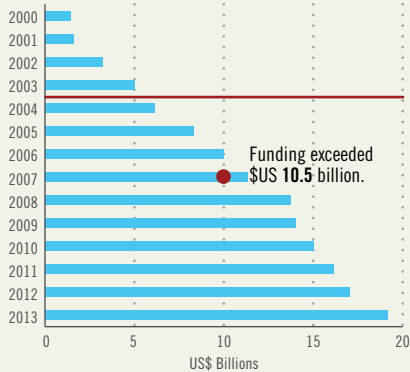
Also by 2005, 14 low- and middle-income countries were providing ART to at least half of the people in need, and several were moving towards universal access.



Evidence of a good target

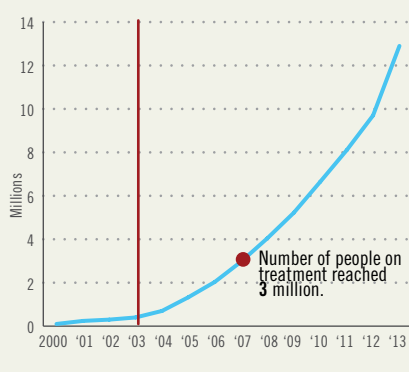
Funding

Global Investment in HIV/AIDS Before and After 2003



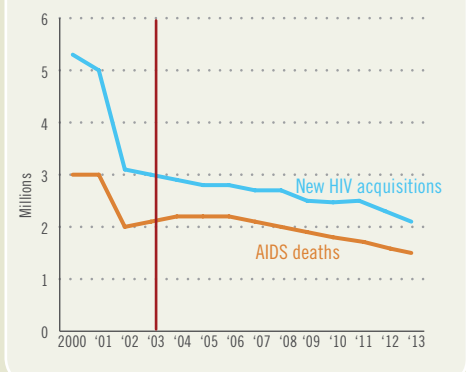
Numbers/Coverage

Number of People on HIV Treatment Before and After 2003



Impact

New HIV Acquisitions and AIDS Deaths Before and After 2003



To learn more:

amfAR and AVAC. Data Watch: Closing a persistent gap in the AIDS response. A new approach to tracking data to guide the AIDS response. August 2014. www.avac.org/sites/default/files/resource-files/DataWatchAugust2014.pdf.

amfAR and AVAC. An Action Agenda to End AIDS: Critical Actions from 2012-2016 to Begin to End the HIV/AIDS Pandemic. July 2012. www.avac.org/sites/default/files/resource-files/AnActionAgendaToEndAIDS2012.pdf

In Part II of the Report, we focus on issues that underpin (and at times undermine) the ability to meet these targets. We identify three specific areas for action:















1 Align high-impact strategies with human rights and realities.

Biomedical advances of the past eight years have made it scientifically plausible to talk about ending the epidemic. But plausible doesn't mean possible. Today some scientists and public health professionals are focused on what can be achieved biomedically—without enough attention to the structural and social contexts in which treatment and prevention are delivered, or to the ways that

biomedical tools require effective behavior-oriented delivery since use is, itself, a behavior. At the same time, some rights-focused partners speak of HIV as being exclusively biomedical, suggesting that there isn't any dynamism or action on the rights-based fronts. These are broad strokes on subtle issues, and there's much work happening in the middle ground. But now is the time to pay close attention to the emergent schism between the science of the AIDS response and a rights-based approach to programs and policies. It need not be a permanent rift; indeed, it cannot be. If science does not get synched up with human rights, there is little hope of bringing the epidemic to a conclusive end.

Anatomy of a Target

Targets get met when all of the elements come together. Effective targets that have impact are:

 <p>Resourced</p>  <p>Targets without sufficient resources are empty promises. Set the price tag, raise the resources and don't ask countries to do more with less.</p>	 <p>Audacious</p>  <p>The best goals redefine possible. There were 50,000 people in low-income countries on ART in 2003. The 3 by 5 target changed the world.</p>	 <p>Achievable</p>  <p>Effective targets reflect evidence and experience. AIDS science is evolving. We can't set a deadline for finding a cure. But we can aim high with research milestones.</p>	 <p>Measurable</p>  <p>Quantification is key. Prevention targets need to be tied to impact, including incidence and other validated, indirect measures.</p>	 <p>Accountable</p>  <p>Setting a target means taking responsibility for mobilizing resources, tracking progress and sharing data.</p>	 <p>Political Support</p>  <p>Country-level support is key. Goals that originate in Geneva won't go anywhere without endorsement by leaders in hard-hit countries.</p>	 <p>Collective Priority</p>  <p>No one, including scientists, can set targets on their own. Civil society, policy makers and politicians all need to buy in.</p>
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2 Invest in an oral PrEP-driven paradigm shift.

The world is failing to deliver the most effective interventions with smart strategy and at scale. Daily oral PrEP for HIV prevention is just one example. WHO now recommends daily oral PrEP as a prevention option for all MSM at risk of HIV. Global targets for PrEP may be released by UNAIDS in the coming months, but there aren't any plans in place to meet them. Demonstration projects are small and disconnected, funding is limited and policy makers aren't heeding the growing demand from men and women, including young women in Africa. Now is the time to spend and act to fill these gaps.

3 Demand short-term results on the path to long-term goals.

It will be years before the world has an AIDS vaccine, cure strategies, long-acting injectable ARVs or multipurpose prevention technologies that reduce the risk of HIV acquisition and provide contraception. But there is plenty of activity in clinical trials and basic science for these long-term goals. This activity needs to be aligned with short-term goals that

can be used to measure progress and manage expectations.

As *AVAC Report* went to press, the United States was grappling with profound questions about the ways that the lives of Black men and women are valued under the law. The world was trying to understand how the West African Ebola epidemics got out of control and whether they were finally coming to an end. There was continued concern and vigilance over anti-homosexuality laws in Nigeria and the Gambia, and over hate-mongering environments and legislation that endanger so many marginalized groups around the world.

These events are not separate from the work that we do to fight AIDS. They embody the issues of racism, inequity, poverty and security that drive the epidemic and must be addressed in order to end it. In addition to the HIV-specific work laid out in these pages, it is essential to work towards fundamental, lasting and positive change in each of these areas. That will be history-making, indeed.



Mitchell Warren

Executive Director

▶ Watch this Space: New trials and data on the horizon

AVAC Report went to press in mid-February 2015. The only sure thing in this field is that it's not possible to predict what will happen next. The next few weeks and months will bring data from a range of ARV-based prevention trials including FACTS 001, IPERGAY and PROUD. It will see the launch of new research and interim reviews of ongoing studies. Our core content and recommendations take aim at critical issues for the coming year, but the specifics will certainly change. Visit www.avac.org for the latest information and our priorities across the field.

Prevention on the Line

PART I Truth, Lies and Targets

Ambitious, actionable targets are essential for an effective AIDS response. But targets can also become irrelevant if they're not developed and pursued with thought, strategy and specificity. In this section, we review why targets matter and why the ones that exist—and the ones that don't—may lead the AIDS response astray.

Watch this Space: Targets, action plans and budgets

As *AVAC Report* went to press in February 2015, UNAIDS had not yet released global targets for prevention or non-discrimination. PEPFAR country teams were working with the Office of the US Global AIDS Coordinator to develop plans for 2015, and the Global Fund to Fight AIDS, Tuberculosis and Malaria was poised to work with countries to turn concept notes into funded plans of action. In the next twelve months, the global AIDS landscape will be affected by developments on these fronts—and by national-level targeting and budgeting decisions. Visit www.avac.org for the latest information, analysis and advocacy plans.

Mind the Gap

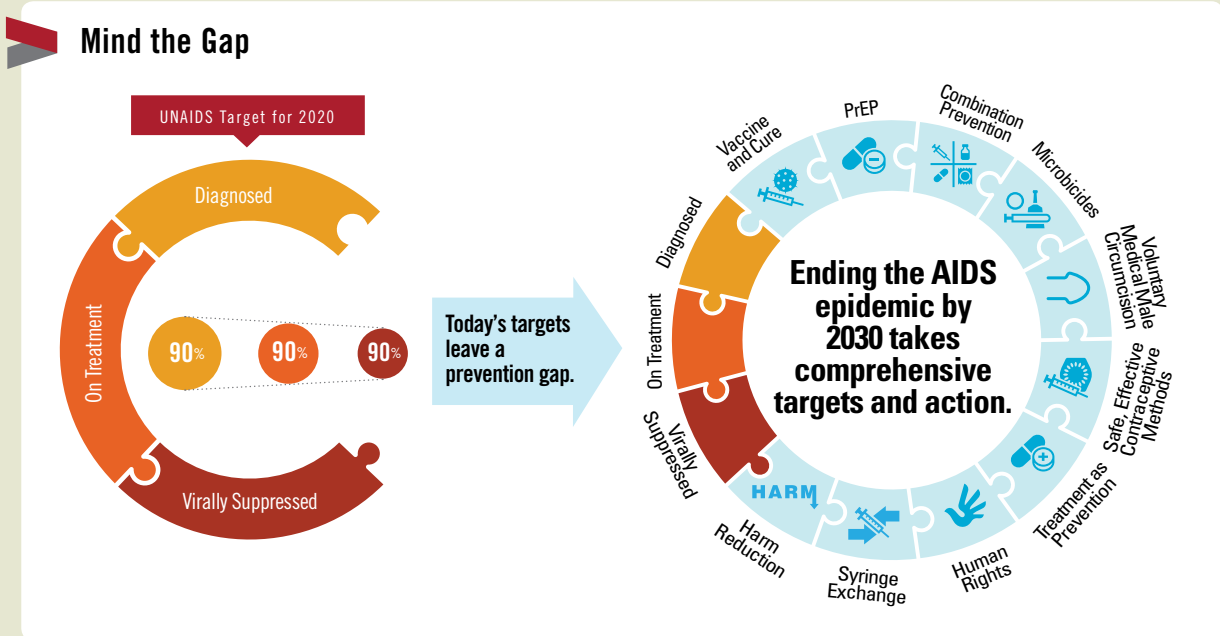
AIDS activism has achieved extraordinary victories for health equity by demanding that global and national leaders and funders set and strive for ambitious targets. The “3 by 5” target for expansion of antiretroviral treatment (ART) access engendered a more robust response than would have happened otherwise.

But another lesson from the history of AIDS is that it is essential to match the tactics to the time. When there is too much of a gap between the targets and the reality, or between the people setting the targets and the people on the front lines, then the audacious runs the risk of becoming the absurd. That’s the direction the HIV/AIDS response is heading in today.

The most clearly defined campaign is centered on “90-90-90”. This is a critical goal and laudable in its emphasis on outcomes that reflect quality of care. But the push towards 90-90-90 has come at

the cost of advancing a more complex, accurate and less pithy framework that encompasses all of the elements needed for an effective end to new HIV acquisitions and deaths from AIDS. This includes newer strategies like PrEP as well as VMMC, male and female condoms and comprehensive harm reduction, which is in crisis in many settings.

It is a fiction that ART for HIV-positive people will, on its own, end the epidemic. Yes, the models suggest that it is possible. And, yes, there are examples of different countries that are close to meeting some of the 90-90-90 coverage goals. And by all means, it is critical to strive for this level of coverage and this type of quality outcome. But comprehensive prevention is also essential. The story that HIV/AIDS can be conquered by ART alone has to change. Programmatic targets for key prevention options must be set by UNAIDS, PEPFAR and national governments.



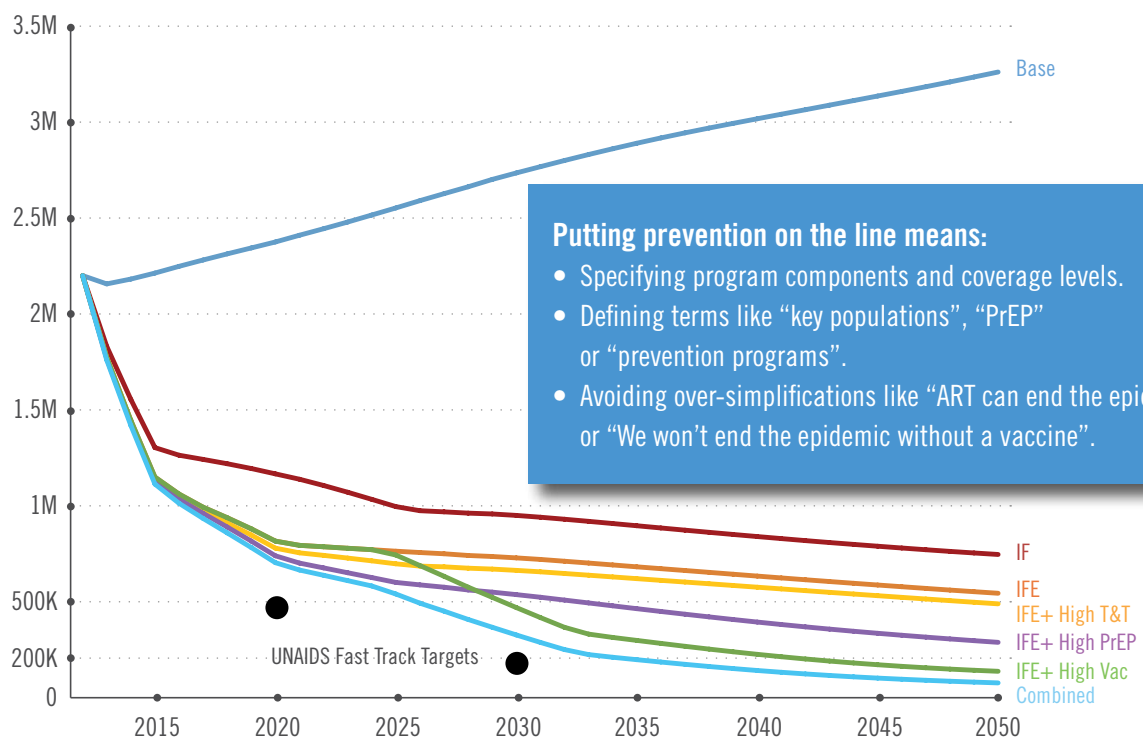
Effective images can oversimplify. The pieces of the puzzle above only fit together into an effective response in the context of behavioral and structural strategies that support individual rights, autonomy and dignity.

Put Prevention on the Line

The signature graphic for “ending AIDS” is the downward sloping line in rates of HIV acquisition and death. The curves illustrate epidemiological models. They are inspiring pictures. But the specific underlying assumptions about prevention can be hard to tease out. Existing models state things like: “constant coverage in prevention programs” or “key population programs

only”. This kind of caption might work for ART, but it doesn’t fly for the other elements of combination prevention, which need to be defined by type of intervention, target population, coverage level and so on. Putting prevention on the (downward-sloping) line to end the epidemic means getting specific, even if it complicates the picture. Here’s an example of what we mean.

New HIV Infections in Low- and Middle-Income Countries by Scenario



The graphic above illustrates how different combinations of interventions affect rates of HIV acquisition. “IF” refers to the Investment Framework 2015 targets scenario. Published in 2011, the Investment Framework called for a strategic alignment of resources and high-impact strategies. “IFE” adds in the 2013 WHO HIV treatment guidelines (increased coverage for CD4 cell counts <500). IFE + T&T and IFE + PrEP and IFE + High Vac model the impact of high coverage and efficacy of “test and treat”, daily oral PrEP, and an 60-80% efficacious vaccine, respectively. Combined is IFE plus all three new strategies.

Source: Stover, John et al., the New Prevention Technology Study Group. “How Can We Get Close to Zero? The Potential Contribution of Biomedical Prevention and the Investment Framework Towards an Effective Response to HIV.” Ed. Julian W. Tang. PLoS ONE 9.11 (2014): e111956. PMC. Web. 11 Feb. 2015.

The point isn’t to choose between one line or the other, it’s that this kind of strategy- and coverage level-specific modeling is needed to give an accurate, actionable picture of how to get to the end of epidemic levels of HIV infections.

Set the Right Targets for the Right Interventions

Different prevention options warrant different types of goals. Right now, there is a tendency to apply the same target-setting approach to a diverse array of tools. One common theme is to set coverage goals for all different kinds of options. This makes sense for some, like ART or VMMC. But it makes far less sense for other programs. As one long-time advocate said of programs targeting injection drug users, “If I fly a plane over a city with a lot of IDUs saying ‘Don’t share needles,’ does that mean I have reached them?” Having implausible or imprecise prevention targets undermines their importance and increases skepticism that real ones can be met.

Therefore we’re looking forward to seeing the final version of the UNAIDS targets—and to seeing targets for specific interventions set by PEPFAR and incorporated into GFATM grants set to be approved later this year.

It’s critical that the right targets get set for the right interventions. That’s not happening at present, hence there’s a risk that prevention tools, particularly newer ones, will be introduced in the context of implausible or confusing targets. How to get to the right targets for the right interventions? See the graphic to the right of approaches that have worked in the past and others that could work in the future.

And consider this more nuanced approach:

- **Set ambitious coverage targets for strategies, like VMMC, ART and harm reduction strategies, that are well-defined in terms of the components of service delivery, impact and populations in need.** Some aspects of

service delivery for these approaches are still being defined and evolving. Even so, these interventions warrant ambitious coverage goals linked to impact.

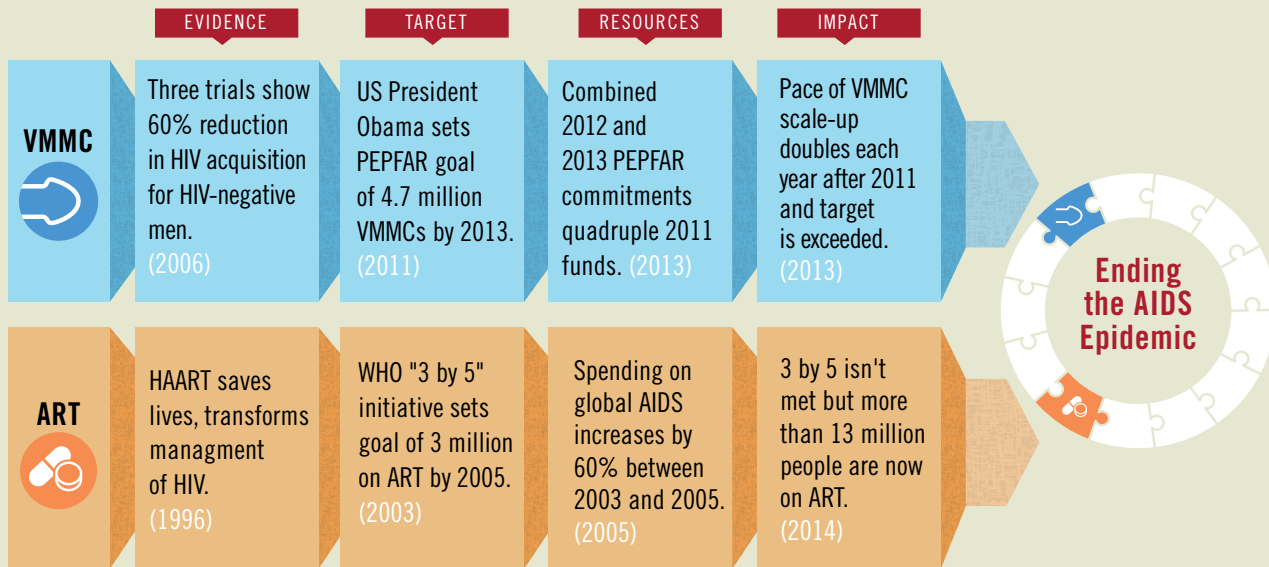
- **Use a combination of process goals and placeholder targets for emerging strategies.**

The draft UNAIDS Prevention Targets highlight daily oral PrEP and cash transfers for adolescents and young women. For these and other strategies, there is great potential but much less clarity about scale-up and delivery. Coverage-based targets (i.e., X percent of a population) can add to confusion when there’s so much that needs to be understood about delivery for impact. Instead, it makes sense to assess and set a deadline for analyzing current operational studies and another deadline for when a coverage target could be in place—e.g., when X percent of current operational studies are completed.

- **Recognize that everything comes with a price**—and that this price can be

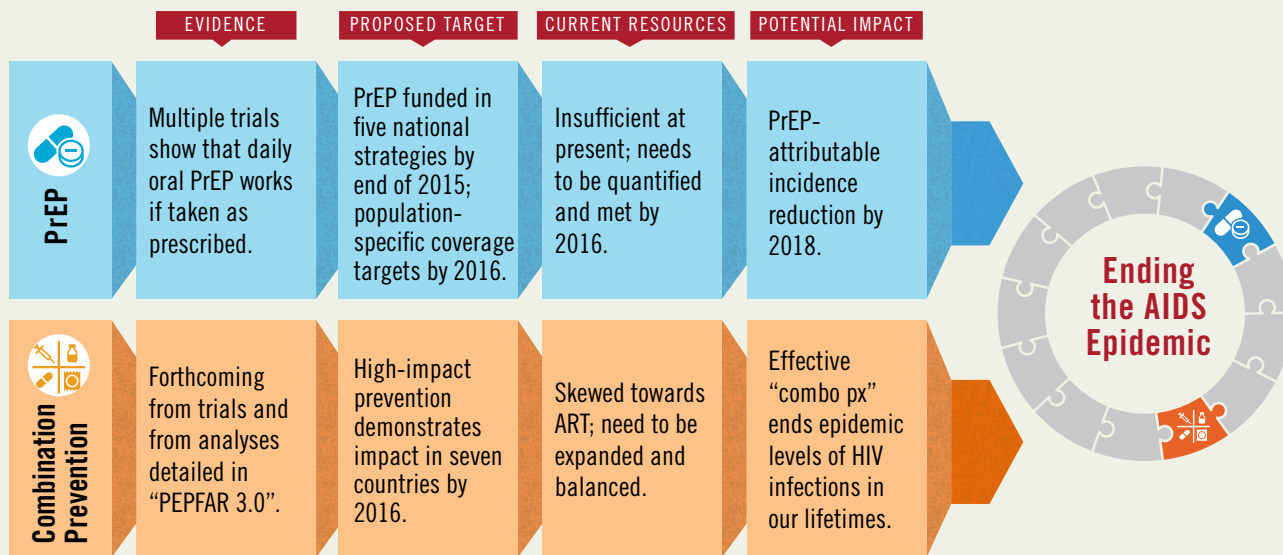
calculated in different ways. There is a global shortfall in AIDS funding at the precise moment that a surge of resources is needed to achieve real change. The GFATM did not meet its target funding level during its last replenishment; advocacy on PEPFAR funding has helped preserve current levels, but additional funds are needed. Targets without price tags have little relevance in the real world. Any discussion of targets needs to include the cost of implementation and the cost-effectiveness in the short-, mid- and long-term.

Targets that Worked: VMMC and ART



Targets that Require Work: PrEP and Combination Prevention

Targets are urgently needed for daily oral PrEP and combination prevention. Here are proposed goals, along with what's in place and what is missing today.



Intervention Update

Voluntary Medical Male Circumcision

Voluntary medical male circumcision (VMMC) is a highly effective HIV prevention strategy that has benefited from ambitious target setting that ticked all the boxes—investment, political will and evidence. In 2011, US President Barack Obama set a target of 4.7 million PEPFAR-supported procedures by World AIDS Day 2013. Nothing about the pace of scale-up to date suggested that such an ambitious goal could be met, but it was. Since 2007, it is estimated that over nine million VMMCs have been performed, with support not only from PEPFAR but also national governments, the GFATM and the Bill & Melinda Gates Foundation. This reflects decisions made by these boys and men, together with their communities—a tremendous, life-saving collective effort.

That’s the good news.

The bad news is that, in 2015, there is no new global target. PEPFAR has not set a new target since 2011. Right now, UNAIDS doesn’t have prevention targets either. That’s a huge omission given the strength of evidence of impact, remarkable progress to date, and feasibility for continued scale-up.

Individual countries including Rwanda, Zimbabwe and many others are setting

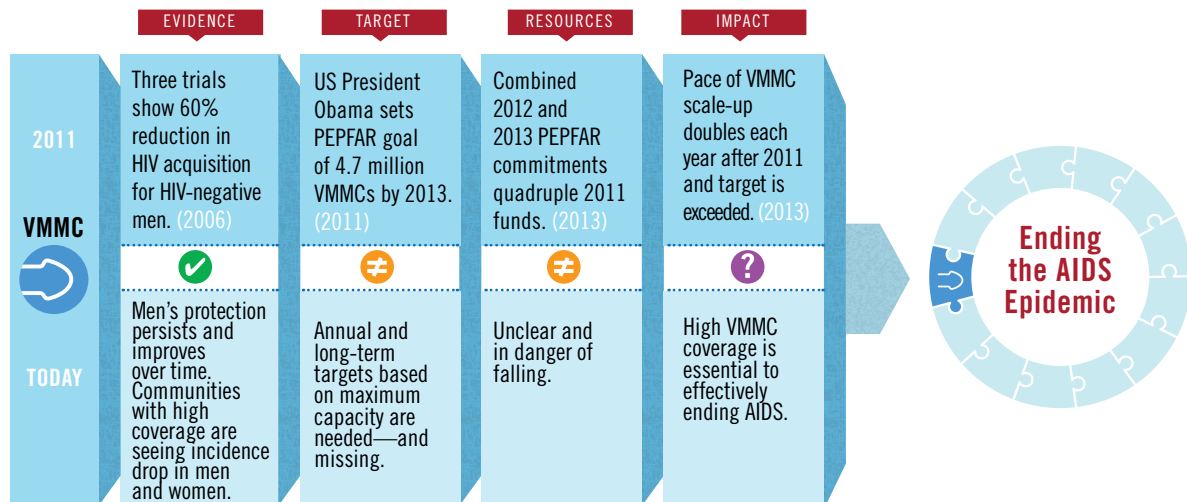
milestones for reaching 80 percent coverage and showing strong political will.

But these country commitments have to be matched by funders, normative agencies and implementers. And it is possible that this might not happen.

Beginning in 2012, PEPFAR almost doubled its annual budgets for VMMC for two years, in support of Obama’s target. This was mainly through use of “central” funds that supplemented countries’ conventional funding. As of today, no 2015 central funding has been identified for VMMC, and unofficial information from countries suggests the 2015 VMMC target is roughly one million less than in 2014. Reports also suggest that countries aren’t seeking funds from GFATM grants to fill the gap left by PEPFAR.

In the next 12 months, VMMC in sub-Saharan Africa will likely experience a contraction. New cases of HIV that might have otherwise been prevented will occur and the infrastructure will be lost. This makes little financial or public health sense. Countries should be resourced to perform at current or even expanded capacity. Advocacy is needed to ensure that this is a brief slow-down, and that 2016 sees programs back on track. Now is the time for a *new* target (see below) with global endorsement.

Past Success, Present Gaps: VMMC targets, 2011 and today



Prevention on the Line

PART II → Advancing a Three-Part Agenda

For the past three years, AVAC has used a “3-D” framework for conceptualizing the work that needs to be done across the HIV prevention research-to-rollout continuum. In the pages that follow, we present our three top-line recommendations for work on the effort to deliver today’s strategies, demonstrate the utility and impact of emerging interventions and develop additional strategies that will someday help to bring the epidemic to a conclusive end.

Watch this Space: ARV-based prevention

AVAC Report went to press in February 2015, weeks before the planned release of much-anticipated data from the PROUD and IPERGAY trials of daily oral PrEP among gay men and other men who have sex with men in Europe, and from the FACTS 001 trial of the 1% tenofovir gel microbicide in South African women. The recommendations and analysis in the pages that follow are urgent, irrespective of the specific data announced. But the detailed findings will have profound implications for national and regional strategies of research and implementation. Visit www.avac.org for the latest information, analysis and advocacy plans.

DELIVER

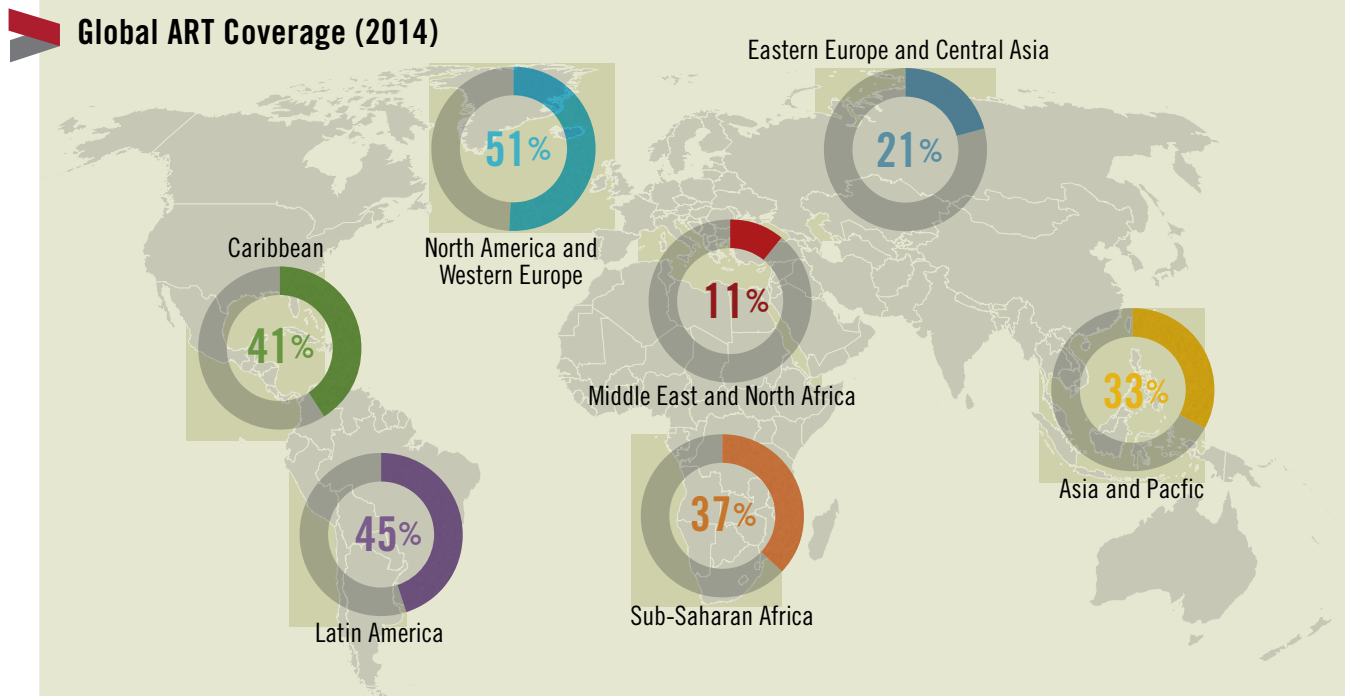
Align high-impact strategies with human rights and realities

Today there is a vast amount of scientific literature about how to treat and prevent HIV effectively, including many articles focused specifically on what it will take to end the epidemic. But the realm of peer-reviewed papers isn't reality. And there is a real danger that some or all of the potential benefits of today's strategies will be lost because of an unbridged gap between the science- and human rights-based agendas for the global AIDS response. That's why one of our top recommendations and priorities for 2015 is: **Align high-impact strategies with human rights and realities.**

More than thirty years ago, AIDS activists redefined the way that people living with a disease related to doctors and researchers. People living with HIV—who insisted on this term, with its dignity and agency, rather than “AIDS victims” or “sufferers”—became experts on the science of the virus. They and their doctors, nurses, friends and allies, including many researchers, mastered pathogenesis, immunology and drug development.

In the absence of drugs—or even, at the outset, a name for the pathogen—human rights and HIV were closely

Global ART Coverage (2014)



Here is the current view of global ART coverage. To close the gaps and have a high impact, it's key to have high-quality services, better, simpler regimens and a comprehensive, rights-based approach that puts informed choice and civil society leadership at the center. This approach isn't in place of or in addition to the scientific evidence. It is evidence-based, with extensive reports showing that ART succeeds with community-based models of delivery and support.

Adapted from: UNAIDS. Fast-Track: Ending the AIDS Epidemic by 2030. www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report.

connected. In the early years of the epidemic in the United States, the government did little to provide accurate information or fund research. The majority of HIV cases were in gay men, and their lives, it seemed, did not matter. In that context, investment in research, acceleration of trials and other forms of scientific work were a human right. At the same time, rampant stigma and mistrust of the government meant that traditional epidemic control measures like routine testing and contact tracing were rejected by many in the LGBT community—contentious decisions whose public health impact is felt to this day.

Today these same issues have been reconfigured again. In many contexts there is a growing gap between scientific and rights-based discourses about the AIDS epidemic. And that's *within* the world of HIV. There is an even bigger gap between the HIV response and the broader agendas put forward by LGBT individuals, women and girls and other “key populations” (see box, at right, about how this term is used and misused today).

There are many reasons for the ways that human rights- and science-based agendas for HIV have parted ways—and why there's a growing focus on bringing these agendas back together. The GFATM now has human rights as one of the pillars of its five-year strategy. As Treatment Action Campaign co-founder Mark Heywood noted in an essay published in 2014, an increased emphasis from UNAIDS on country government leadership—regardless of national policies and politics, and sometimes at the expense of the agendas articulated by

Language Watch: Defining Key Populations

What's in a name? A lot, as it turns out. Right now, the terminology for “key populations” is, well, key to many conversations about effective AIDS programming. But the term isn't used precisely. Sometimes it's a euphemism for gay men and other men who have sex with men (MSM) and transgender women. Sometimes it refers to these groups and sex workers. Sometimes it's used to refer to adolescent girls. Euphemisms don't have a place in effective public health. Fortunately, this fuzziness is a problem that can be addressed by good data collection and forthright discussions of who is actually at risk and/or in need. Key populations are groups that have a disproportionate burden of disease and lack of access to services—in any epidemic and in any context. The determination of key populations is a data-driven question that can be answered by reviewing country-level data, provided that there's an active effort to measure HIV incidence and prevalence in marginalized and criminalized groups. In many situations, women and girls are key populations. Targets and planning documents that tackle “key pops” (meaning gay men, MSM, transwomen and sex workers) on the one hand and women and adolescents on the other needlessly muddy the waters. Clarity is key.

affected communities—is one contributing factor. “Inter-governmental, governmental and donor agencies are now retreating from human rights commitments—and have been doing so since 2010.”¹

This retreat from human rights has come at the same time as a series of groundbreaking scientific advances. With

¹ Heywood, Mark. “The unravelling of the human rights response to HIV and AIDS and why it happened: an activists' perspective.” Extract from: *AIDS Today: Tell no lies, claim no easy victories*. International HIV/AIDS Alliance (International Secretariat). October 2014.

new biomedical tools come new demands for public health programs, which face human-resource shortages, infrastructure challenges and restrictive policy environments. These tools also bring new demands for stakeholders to envision innovative, even radical, new approaches to delivery that dismantle the barriers between the biomedical, behavioral and structural drivers of HIV risk and individual behavior. After all, oral PrEP is a behavioral intervention—it has to be used correctly and consistently to have a benefit, just like ART. Right now, there are big dreams for radical new approaches to HIV prevention using biomedical tools. But with the possible exception of VMMC (see page 12), there's not much of a prevention revolution happening on the ground. Advocates who doubt that biomedical advances will be rolled out with a rights-based approach are entitled to their skepticism, but what's also needed, from all stakeholders, is a commitment to working together over the next few years to ensure that there's funding, innovation and category-busting implementation of truly effective prevention.

The problem, of course, is that many of the activists needed to help make this happen are now struggling to keep themselves and their organizations afloat. Funding for human rights-based work among civil society organizations has faltered (see graphic, at right). HIV-focused civil society is better funded than sectors like women's rights or LGBT—but that prosperity is relative, and all are inadequately supported.

What's needed today is a fundamental shift in the conceptualization and

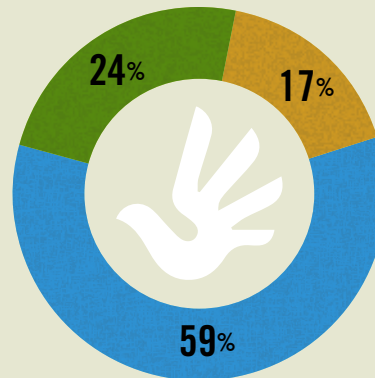
implementation of components of a biomedically oriented approach to ending the epidemic. As the science advances, more money needs to flow to civil society groups—not less. And the programs that deliver these combination packages need to be deeply embedded with, informed and led by people living with and at risk of HIV. Without these close connections, the programs will not reach the people most in need. Shifting funding and program design to include civil society, and particularly people living with and most at risk of HIV, should improve accountability for all involved. Civil society groups need to commit to and deliver on results tied to impact, defined in terms that all agree upon. In addition, here are three more key recommendations:

➤ **Pursue high levels of ART coverage, while addressing issues of choice and coercion.** Having the option to choose to start ART—including at high CD4 cell counts and in order to preserve health and reduce risk of onward transmission—ought to be the reality for every person living with HIV. And in an ideal world, ART expansion would happen in a climate of informed choice. But there are concerns that, as Option B-Plus and other “test and treat” programs that initiate ART regardless of CD4 cell count are introduced, the conditions that allow someone to make an informed choice about whether to start ART and to remain adherent when they do will be overlooked. Will proposed programs that aim to diagnose individuals and initiate ART on the same day be able to provide the type of counseling and peer-to-peer support that will surely

be needed to navigate disclosure, adherence and acceptance of one's diagnosis all at once? They should, but in a climate of scarce resources and diminishing funding for civil society groups there's no guarantee that they will.

- **Revise the “rights versus HIV” rhetoric and reality** that's splitting LGBT groups and other key potential allies from those on the frontlines of the fight against HIV. “Biomedical interventions shift the locus of control towards the medical,” said Chris Beyrer of Johns Hopkins University and the current president of the International AIDS Society, in a plenary at the 2014 HIV Research for Prevention Conference (HIV R4P). He noted that the sites of medical treatment are often closely aligned with repression, abuse and discrimination for people who are persecuted by the state for their sexual orientation, drug use, sex work, migrant status or any other reason. Programs that target individuals who are disproportionately living with and/or at risk of HIV acquisition can only succeed in a rights-based environment. The funders and implementers of biomedically oriented programs must work in solidarity with efforts to roll back repressive legislation. By the same token, rights-focused groups need informed agendas about biomedical tools.
- **Remember that culture and community views often can't be modeled—but they can't be ignored, either.** Whether it is determining the appropriate age range for delivering

Change in Funding for Civil Society Organizations for Human Rights-Related Work



KEY

Percent of civil society groups queried by UNAIDS reporting:

- HIV and human rights funding stayed at the same level
- HIV and human rights funding increased
- HIV and human rights funding decreased

Source: UNAIDS, *Sustaining the Human Rights Response to HIV: An analysis of funding trends*. Geneva (forthcoming).

VMMC or developing efficiency-oriented approaches to treatment delivery, there are models that suggest the right way to proceed. But these models are only as good as the data that go into them. And there are still limited data on a range of key structural and social issues that affect the uptake of services and long-term adherence to strategies, be they PrEP, ART or—someday—a vaginal or rectal microbicide. Stakeholders need to acknowledge that what is modeled isn't necessarily what is possible if cultural, economic and social norms run counter to programmatic goals. Programs won't fail if this complexity is part of the planning; instead, they'll be even more likely to succeed.

Hormonal Contraception and HIV

The past year has seen lots of discussion and some action in the search for answers as to whether hormonal contraceptives, including long-acting methods such as Depo-Provera (DMPA) and other injectable contraceptives and the implant, affect women's risk of acquiring HIV.

In mid-2014, there was uncertainty about the fate of the proposed ECHO trial that would use a randomized design to directly measure rates of HIV acquisition in women using three different methods: DMPA, the Jadelle implant and the copper IUD.

It now appears likely that the trial will move forward. As *AVAC Report* went to press, the trial hadn't officially been funded, but there was reinvigorated community engagement and the signs continued to seem good.

Also, in early 2015, there were two publications of new meta-analyses of existing data on contraceptive use and risk of HIV acquisition among women. The data were all observational. None of these studies randomly assigned women to different methods. This lack of randomization can result in biased results. These meta-analyses used different techniques to crunch the numbers on these data—plus some new information—and came up with largely the same conclusions as the prior systematic reviews.

Both of the new meta-analyses indicate that use of DMPA may potentially increase women's risk of HIV acquisition. Both also found that the magnitude and the statistical significance (e.g., the degree of confidence that the finding was real and not a coincidence) varied by the study quality and/or the population considered.

These findings are not news in and of themselves. However, each time a study or analysis is published on this issue in a zone of such uncertainty—particularly when the results suggest a significant effect—it triggers fresh discussion and debate.

In light of these recent publications, it would be appropriate for the WHO to reconvene an

expert stakeholder group to review recommendations and communication strategies regarding DMPA and similar products with a particular focus on East and Southern Africa where rates of HIV and DMPA use are high.

The new studies add information and questions that need to be conveyed to women living in countries that may host the proposed ECHO trial.

It is critical that the ECHO team engage with civil society stakeholders to explore the meaning of new data as part of trial consultations.

The FP2020 initiative (the global initiative that aims to increase women's access to contraception worldwide) has indicated that it would await the results of the ECHO trial.

It would be invaluable to the field for FP2020 to convene a meeting of family planning policy makers and implementers in potentially affected countries to discuss existing plans, proposed expansion of method mix, and processes for interpreting and acting on these results.

There is a robust civil society constituency following the issues around HC-HIV. Members of this dialogue have diverse views on whether a randomized trial such as ECHO is on the critical path but are united in the need for family planning and HIV programming to:

- Address the uncertainty with clear messages on knowns and unknowns, risks and benefits of all methods;
- Invest in increased method mix today; and
- Sustain investment in developing new contraceptive, HIV prevention and, especially, multipurpose prevention options that could, in the future, reduce HIV risk and prevent unwanted pregnancies.

AVAC will continue to work with partners to ensure that an informed advocacy voice helps guide decisions in this key area.

DEMONSTRATE

Invest in an oral PrEP-driven paradigm shift

AVAC Report has tracked the development of daily oral pre-exposure prophylaxis (PrEP) using tenofovir-based drugs (TDF/FTC and TDF, brand names Truvada and Viread) for a decade now. We have developed information and advocacy from the early days of research controversies through the cascade of research results that led to approval of daily TDF/FTC as PrEP by the US Food and Drug Administration and WHO guidance. We have consistently called for plans to act on evidence of efficacy. We have called for a comprehensive suite of demonstration projects. We have called attention to inaction and to areas of progress. As we have issued our recommendations and worked to make them a reality with partners everywhere from the US to Uganda, Thailand, South Africa and Zimbabwe, we've been frustrated by the slow momentum, lack of coordination and inadequate funding.

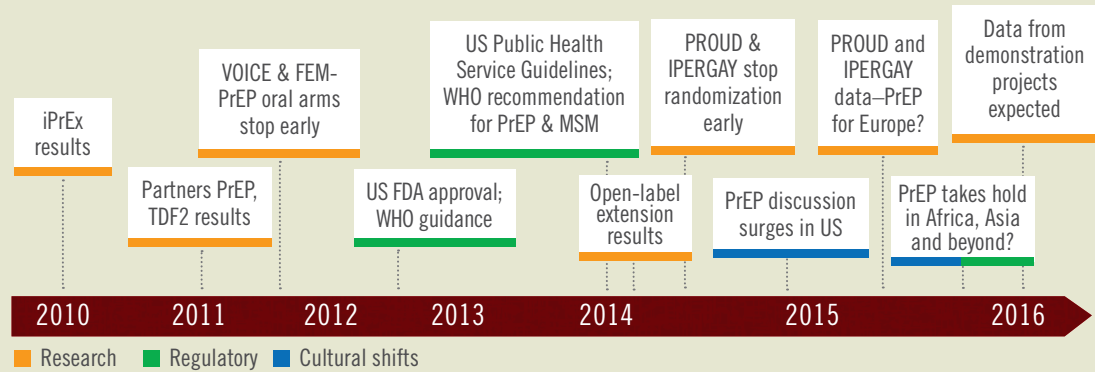
This year, we're still frustrated, but we're also thrilled and excited by the ways that the conversation about this PrEP strategy has changed. Even as funders and governments have been slow to define and implement a comprehensive suite of PrEP demonstration projects, individuals living with HIV and HIV-negative people living in contexts and communities where they feel their

prevention needs are unmet, have begun to demand PrEP. They have initiated a dynamic, even revolutionary dialogue about the right to this life-saving strategy. The discussion has moved far beyond the boundaries of the relatively small HIV prevention advocacy sphere, and the even smaller sphere of biomedical prevention research advocacy. It is part of a wide-ranging conversation about the right to sex without fear or judgment and about ways that HIV-positive and HIV-negative

More Positive PrEP Data in 2014/15

In October 2014, both the UK PROUD study and the French IPERGAY trial of oral PrEP in gay men and other men who have sex with men stopped randomization early after independent data monitoring committees saw evidence of overwhelming benefit. The data from these trials hadn't yet been released as *AVAC Report* went to press, but are forthcoming and will include information on behavior, condom use and adherence. Comparable types of data are expected from the Partners PrEP demo project in East Africa. These data will complement data from iPrEx OLE, the open-label extension trial among gay men, other MSM and transwomen, which found high rates of adherence, particularly in participants who reported higher rates of unprotected anal sex and other high-risk behaviors.

From Proof-of-Concept to Prevention Phenomenon in Five Years



Has the global action on daily oral PrEP been as fast as possible? No. But there has been tremendous activity over the past five years. This timeline can be used to anticipate and speed action on the next generation of ARV-based prevention options.

people can share agency and responsibility as they negotiate their respective options for using ARVs for prevention. In other words, PrEP has become a cause and a rallying cry. But it is not yet a reality for everyone who needs or wants it correctly and consistently. And that is why one key recommendation for 2015 is a call to funders, national governments, implementing agencies and civil society groups working across identities and issues to **invest time and money in an oral PrEP-driven paradigm shift.**

The data all point the same way: daily oral PrEP works if you take it. (It appears that adherence may need to be higher in women whose risk is primarily via vaginal sex compared to individuals whose risk is via anal sex because of differences in how the drug is absorbed in vaginal and rectal tissues.)

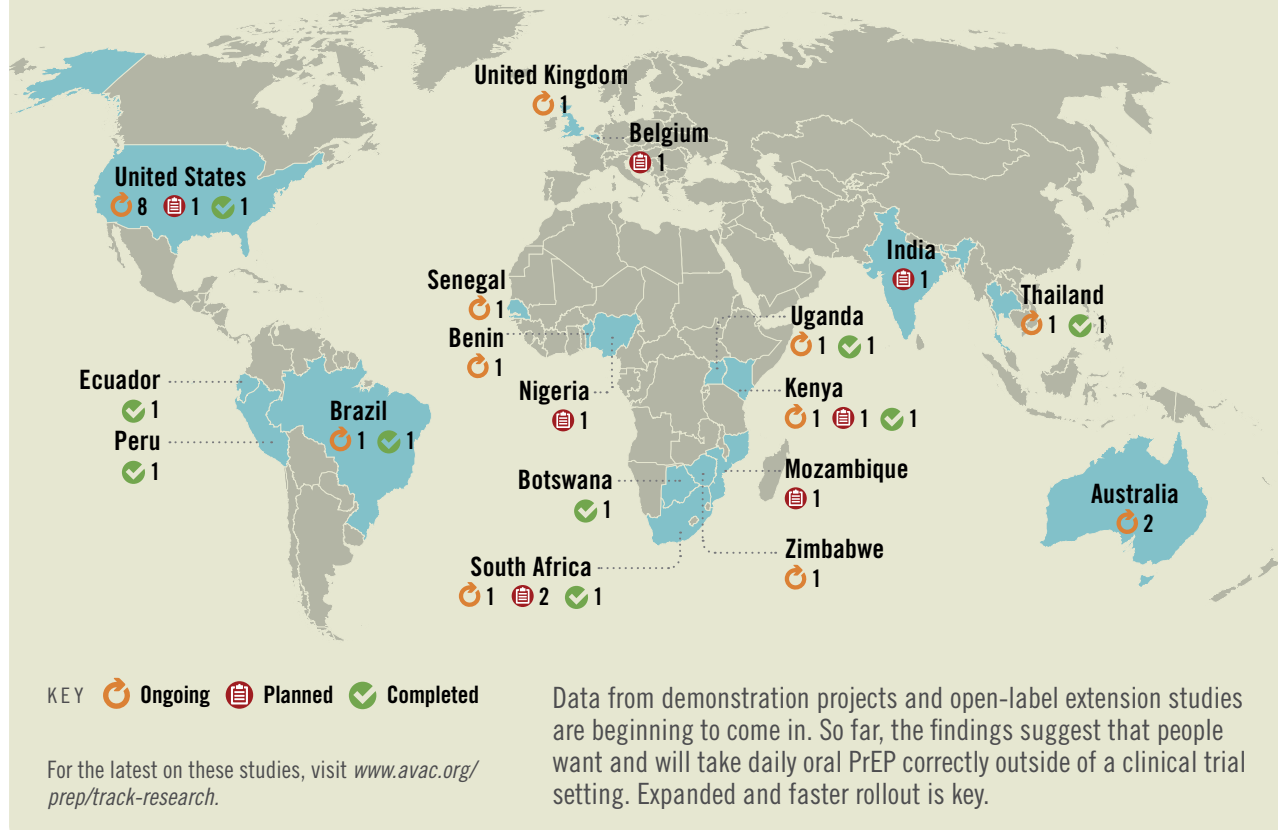
It is time for scale-up to keep up with this demand. This is true both because daily oral PrEP can save lives today and

because learning how to implement this strategy will lay the groundwork for new prevention options, especially ARV-based microbicides, if and when they are demonstrated to be efficacious in clinical trials. The following steps are key to achieving the PrEP-driven paradigm shift:

➤ **Implement large-scale pilots linked to national programs for oral PrEP.**

Daily oral PrEP alone can not address the complex social and structural forces that put individuals at risk (see section starting on page 14). This is why oral PrEP needs to be evaluated in large-scale pilots that provide a range of prevention services and that gather information and trigger action on the factors that help or hinder HIV testing, adherence and disclosure for people who test HIV-positive. Such programs can also serve as platforms for potential introduction of topical microbicides or vaginal rings (see page 23). Countries should initiate activities such as pilots or targeted programs in

Planned, Ongoing and Completed PrEP Evaluation Studies (December 2014)



the context of multi-year national plans to ensure that there is phased expansion, inclusion in national strategic plans and sufficient funding, including via PEPFAR and GFATM.

➤ **Include a PrEP recommendation for women and adolescents in the next revision of the WHO Guidance on ARVs.**

It is quite possible that by mid-2015, the UNAIDS Prevention Targets document will recommend PrEP for women and adolescent girls, while the WHO consolidated guidelines on the use of ARVs will not. Bringing these documents into alignment is essential, especially since the WHO guidance

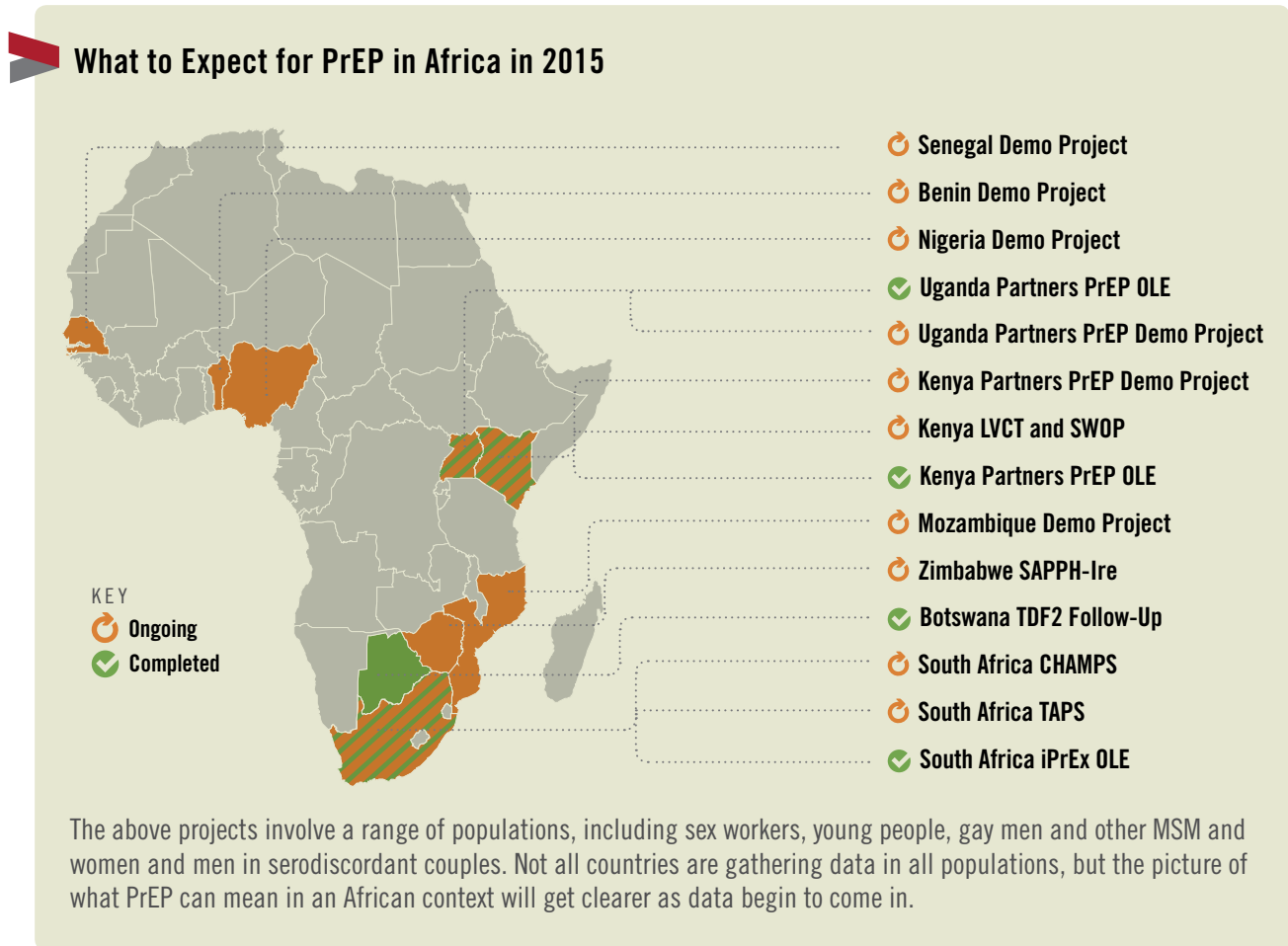
carries far more weight when it comes to national plans and processes. Having clear, consistent guidance on PrEP's utility for women is key.

➤ **Plan and program around rollout of other ARV-based prevention options.**

As we discuss on page 23, the next 18 months will bring results from trials of tenofovir gel and the dapivirine ring. Even if there is evidence of efficacy for either product, there will be a delay between the end of the trial and the launch of pilot projects that make the products available outside of open-label extension trials. But it is possible to project two or three years into the future and envision scaled-up oral PrEP

programs that also serve as a platform for piloting other ARV-based prevention strategies for HIV-negative individuals. That planning should start now and be reflected in coordinated multi-year strategies developed by microbicide and oral PrEP stakeholders. Oral PrEP

rollout should be harmonized with ART for HIV-positive individuals. Linking PrEP and ART provision is one option for creative programming that emphasizes options and agency for HIV-positive and HIV-negative people.



Intervention Update

Anticipating the Results of Microbicide Trials

As *AVAC Report* went to press, the FACTS 001 trial of vaginal 1% tenofovir gel was preparing to release its findings. The trial was designed as a confirmatory study of CAPRISA 004, which found evidence of modest protection in the same product, using a “BAT-24” dosing regimen (two doses: one up to 12 hours before sex and one within 12 hours after). The results will test the field’s coordination and the world’s patience—whatever they are. If the data show evidence of benefit that warrants licensure and introduction, there will still be a period of time when the finite supply of gel is only available to South African trial participants via post-trial access programs. Other countries will need to trigger national processes that could lead to gel availability via open-label studies or pilot projects.

If the data show no evidence of benefit, there will be people who say that it’s time to abandon user-dependent methods in favor of strategies like the vaginal ring or long-acting injectables, and it will be up to the many stakeholders—from social scientists to young women, gay men and other men who have sex with men—to argue otherwise. In *AVAC Report 2013*, we covered this issue in-depth and we’ve reprinted the core recommendations from that document below.

None of the scenarios are simple. But clear, basic explanations and messages are exactly what’s needed. AVAC is working with many partners to develop resources that will help guide advocates, whatever the result is. Visit avac.org and sign up for our Advocates’ Network email list to be part of this discussion as the data emerge.

Don’t abandon vaginal gels and other user-dependent methods for women.

There are competing interpretations of what low adherence in past trials says about the products women will and will not use—and why. Funders and research teams need to use smart research and trial design to move past competing views and generate plans for innovative trials.



Keep searching for methods to improve adherence and measure their effectiveness to determine what works.

Many new adherence measures are being used in trials today. Funders and trial networks need to sustain investment in innovation and evaluation of approaches to identify ones that work—and those that don’t.



Invest in research to better understand why participants—especially women—enroll in trials.

It’s clear that there are many reasons why people enroll in a trial and use (or do not use) a product. If these reasons are not well defined by researchers and communities, products may be discarded unnecessarily.



Plan for success, so that valuable time—and the opportunity to reduce new infections—isn’t wasted after positive trial results.

Delays experienced with the rollout of PrEP and voluntary medical male circumcision (VMMC) should not be repeated in other areas. Researchers need to begin defining a core package of demonstration projects for products that are currently in efficacy trials.



To help ensure clear efficacy findings trials should seek to select participants who are most likely to adhere to a product regimen.

The women who most need new HIV prevention strategies may have difficulty adhering to a product regimen in a clinical trial. Trial designs and follow-up plans should reflect this reality.



Prioritize informed civil society involvement to build a community of champions in support of an eventual product.

For new prevention options to make a difference, community support is essential—even with the most well designed trials and products.



DEVELOP

Demand short-term results on the path to long-term goals

In the preceding pages, we have talked a lot about how to set and meet strategic targets. This is fairly simple for proven strategies like ART for HIV-positive individuals and VMMC. It is more complex, but doable, for emerging strategies like oral PrEP. It is hardest for strategies in development, including AIDS vaccine and multipurpose prevention technologies that would provide contraception and HIV prevention in a single product. Science doesn't run on a schedule, and a breakthrough can come at any time, or not at all. In this context, setting milestones can set false expectations. But while success resists timelines, it is possible to establish mechanisms for accountability and targets related to long-term goals. That's why our recommendation for 2015 is: **Demand short-term results on the path to long-term goals.**

The good news is that the reason the field needs to think this way is because there is more and more clinical activity

related to the "upstream" scientific agenda of immune-based strategies for preventing and/or treating HIV. Broadly-neutralizing antibodies (bNABs) are potent immune responses that can block the activity of many different types of HIV. The science is complex and may be a barrier to advocates following the latest developments. But now is the time to pay attention and ensure that researchers are translating scientific goals into comprehensible concepts since these products are already being evaluated in humans. There are trials of three different bNABs for passive immunization, treatment and/or cure currently underway, as well as plans to test a vector-based strategy designed to generate finite supplies of bNABs. Such strategies would require repeat dosing. This sets them apart from a vaccine regimen that seeks to provide long-term protection after a single series of immunizations. The table at right provides more detail on the differences between these and other strategies currently in development.

Decoding Complex Science; Deepening Stakeholder Engagement

As the science evolves, so do strategies for engagement and education. AVAC is proud to be part of a multi-stakeholder collaborative developing a "CUREicculus" designed to explain cure research concepts from trial design to regulatory issues. Long-time AVAC board member Steve Wakefield from the HVTN is heading up the research literacy effort focused on a planned passive immunization trial using the Vaccine Research Center's VRC01 bNAb candidate. The *Good Participatory Practice Guidelines for Biomedical HIV Prevention Trials* (www.avac.org/gpp) continues to serve as the gold standard for stakeholder engagement across the research life cycle. An online curriculum launched in 2014 provides a new resource for individuals wanting to learn how to use GPP!

Injectable Options and Preventable Confusion: An advocate's guide to the pipeline of antibodies, long-acting ARVs and vaccines

2015 is going to bring lots of activity in early- and mid-phase research on a range of prevention and treatment strategies that have very different dosing schedules, mechanisms of action and potential public health impacts. The one thing these experimental interventions have in common is that they're delivered by an injection or similar strategy.

Does this mean that there's a unified category of "injectable prevention"? Far from it. The similarities are superficial and the differences are key. As many of these trials are moving ahead in similar populations and regions, it is key for advocates to understand the distinctions between these various options.

	What is it?	What could it do?	What's next?
Preventive Vaccines	<p>A preventive vaccine seeks to teach the immune system how to protect itself against infection by a pathogen.</p>	<p>AIDS vaccines have been a key part of the prevention research agenda for nearly three decades. Today's existing preventive vaccines for other diseases involve one or a series of immunizations, and can provide long-term or even lifelong protection. The protection isn't always complete and may wane over time.</p> <p>The one AIDS vaccine strategy to show efficacy to date involved eight immunizations and protection waned after one year. Current research is focused on improving on these results (see the P5 section on page 28) as well as exploring other vaccine candidates entirely.</p>	<p>There is a robust pipeline of AIDS vaccine work, some of which overlaps with the investigations of passive immunization (see below).</p> <p>In Southern Africa, work continues on a suite of trials designed to build on the evidence from the RV144 trial.</p> <p>A range of early-phase trials of other novel candidates to establish the safety and immunogenicity of other novel candidates are getting underway in 2015.</p>
Long-Acting Injectable (LAI) Antiretrovirals	<p>Long-acting injectable antiretrovirals (LAI ARVs) are drugs given via injection that persist in the blood for long periods of time.</p> <p>As they are being tested, LAI ARVs need to be dosed every few months. They are not expected to provide permanent protection (in HIV-negative people) or treatment effects (in HIV-positive people).</p>	<p>In HIV-positive people, LAI ARVs could simplify treatment and change the way ARVs are delivered in some settings.</p> <p>In HIV-negative people, the same ARVs could be long-acting PrEP. This could reduce the burden of adherence and make it easier for some people to take, although issues of regular testing to monitor for HIV infection need to be addressed, as they do for all PrEP strategies (right now PrEP is a daily oral strategy).</p>	<p>Phase II trials of LAI ARVs for treatment and prevention are currently underway.</p> <p>A duo of candidates (TMC-278 and GSK-744) is being tested in combination for treatment in HIV-positive people who are virologically suppressed.</p> <p>The same ARVs are being tested on their own in HIV-negative people as long-acting PrEP, and Phase II trials are just beginning in the US, Africa and Asia.</p> <p>The current suite of trials will provide information that could launch expanded trials designed to lead to licensure for both treatment and prevention purposes by 2016/7.</p>
Passive Immunization	<p>Passive immunization is the transfer of pre-made antibodies to a person. (Vaccines teach a person's immune system to make the antibodies themselves; see above.)</p>	<p>Laboratory-made broadly neutralizing antibodies (bNAb) against HIV could provide protection against infection in HIV-negative people. It might be possible to formulate these bNAb so that a single dose could provide protection for months at a time. Testing bNAb for HIV prevention can also provide proof-of-concept for HIV vaccine trials.</p> <p>In HIV-positive people, bNAb are being tested as part of cure strategies. The bNAb would be given in hopes that they would kill virus released from latent reservoirs.</p>	<p>There are three bNAb (TMB-355, PG121 and VRC01) in human clinical trials in HIV-positive and HIV-negative individuals. Two research groups are testing an adeno-associated virus-based delivery approach that would generate a supply of circulating bNAb.</p> <p>The current trials are testing safety and evaluating optimal doses, among other parameters, and could trigger additional research in both HIV-positive and HIV-negative individuals.</p>

On the vaccine front, HVTN 100 launched in South Africa. This trial is the next in the sequence of studies designed to build on the positive results of the Thai trial known as RV144, which found modest efficacy in 2009. HVTN 100 follows HVTN 097, which found that the Thai RV144 regimen was safe and immunogenic in South African men and women. HVTN 100 will test a variation of the RV144 regimen that's been designed for increased immunogenicity and could lead to an efficacy trial as soon as late 2016 (see pages 28-29 for more details). Also in 2015, J&J and other partners will begin a Phase I/II trial of a vaccine strategy that uses an "alternative" adenovirus vector and a mosaic immunogen (e.g., one which contains genetic material from many subtypes of HIV, in hopes of providing cross-clade protection).

Much of this activity is early phase clinical research. But this doesn't mean that there isn't a role for advocacy. Particular attention needs to be paid to the decision-making processes that trigger trials and/or shelve products, and to the product development pathways for each strategy that moves ahead.

One newer challenge is to articulate the decision points and milestones in the pathways for strategies that could be used in both HIV-positive and HIV-negative individuals, such as long-acting injectable antiretrovirals or broadly neutralizing antibodies. These strategies are scientifically distinct. They work in different ways, and they are being tested with different goals. Long-acting injectables, for example, are a new formulation of a familiar product—ARVs—and they are being tested in trials leading to potential licensure. Passive immunization is unfamiliar to many

people, and trials of HIV-specific antibodies won't necessarily lead to a product on the market. It is essential that the differences between these classes of interventions and the related trials are clear to the stakeholders who may be asked to participate in trials and to the broader array of stakeholders engaged in HIV prevention advocacy. Communities asked to comment on and participate in such research will want and need to know the distinctions, potential public health impact of and product-development pathways for these different products. Right now, these conversations are happening by intervention. It's important to explain the distinctions between the products, but it's also key to create opportunities to discuss multiple strategies and approaches at the same time. Trial teams and product developers should help create these forums, and look to the *Good Participatory Practice Guidelines* for a road map on structure and follow-up.

Linked conversations about these complex issues will pave the way for more in-depth, intervention-specific discussions that could emerge in the years to come.

The questions that do emerge are almost certainly going to do so in the context of limited research funding. If there isn't a transparent framework for decision-making and an agenda that looks at pathways in HIV-positive and HIV-negative individuals, then confusion will ensue. Likewise, if research funding isn't sustained—and the most recent figures show a four percent decline in AIDS vaccine funding between 2012 and 2013 (see figure at right)—then decisions will be driven by dollars, pounds and rand, and not by scientific priorities.

Cure research also requires a detailed mapping of timelines, decision points and areas for in-depth stakeholder engagement. In late 2014, the US NIH-funded IMPAACT network launched a trial that seeks to learn more about the impact of immediate treatment in infants born to HIV-positive women diagnosed at eight months of pregnancy or later, up until delivery. This trial was originally designed to attempt to replicate the “cure” seen in the child the media called the “Mississippi Baby.” This child was later found to still have low levels of HIV in her blood. In scientific circles, the term cure has been replaced by “remission”. This nuance is one of many that has to be translated into community understanding.

Here are some key steps to take in 2015:

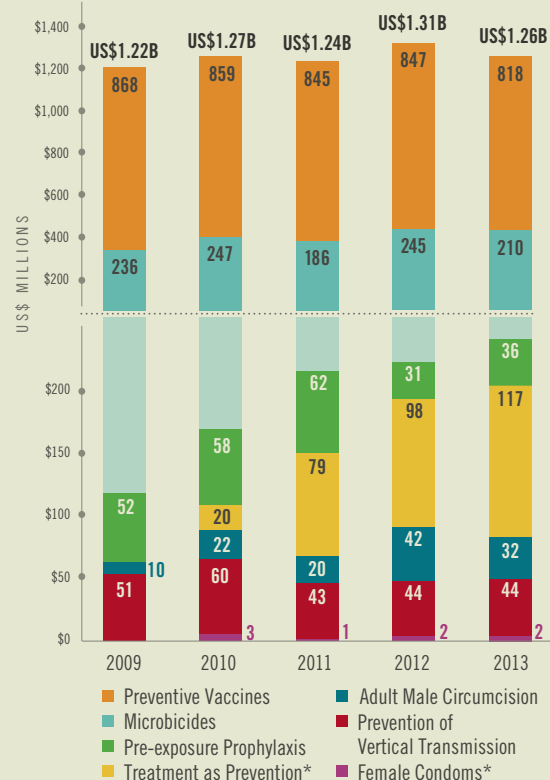
➤ **Define accessible messages and milestones for broadly neutralizing antibody research.**

It is tremendously complex to explain the science, purpose and possible outcomes of these trials. The field needs to ensure that this trial conduct and communications work is well-resourced and that best practices and messages are shared and adapted in real time, for both adults and infants. Answers to key questions should be compiled into a single document that helps stakeholders sort out this complex field.

➤ **Ensure stakeholder engagement in cure research and passive immunization trial design.**

It’s not possible to set a deadline for having an antibody-inducing vaccine, but it is possible to have milestones for research literacy tools, documented stakeholder engagement, transparent exploration of the concerns and support for these trials, and a way

➤ **Global HIV Prevention R&D Investment 2009 – 2013 (US\$ millions)**



*The Working Group began tracking funding for female condom and treatment as prevention research in 2010.

Source: HIV Vaccines & Microbicides Resource Tracking Working Group. HIV Prevention Research & Development Investment in 2013: In a changing global development, economic, and human rights landscape. July 2014. www.hivresourcetracking.org.

forward that reflects both good science and good participatory practice.

➤ **Define the standard of prevention for next-generation efficacy trials, including of AIDS vaccines and multi-purpose prevention technologies.**

This is an age-old recommendation that is made, each year, in a brand-new world. As oral PrEP is rolled out, ART guidelines change, and the world prepares for a potential microbicide ring or gel, it is essential to revisit the principles for incorporating emerging strategies into the standard of prevention for trials.

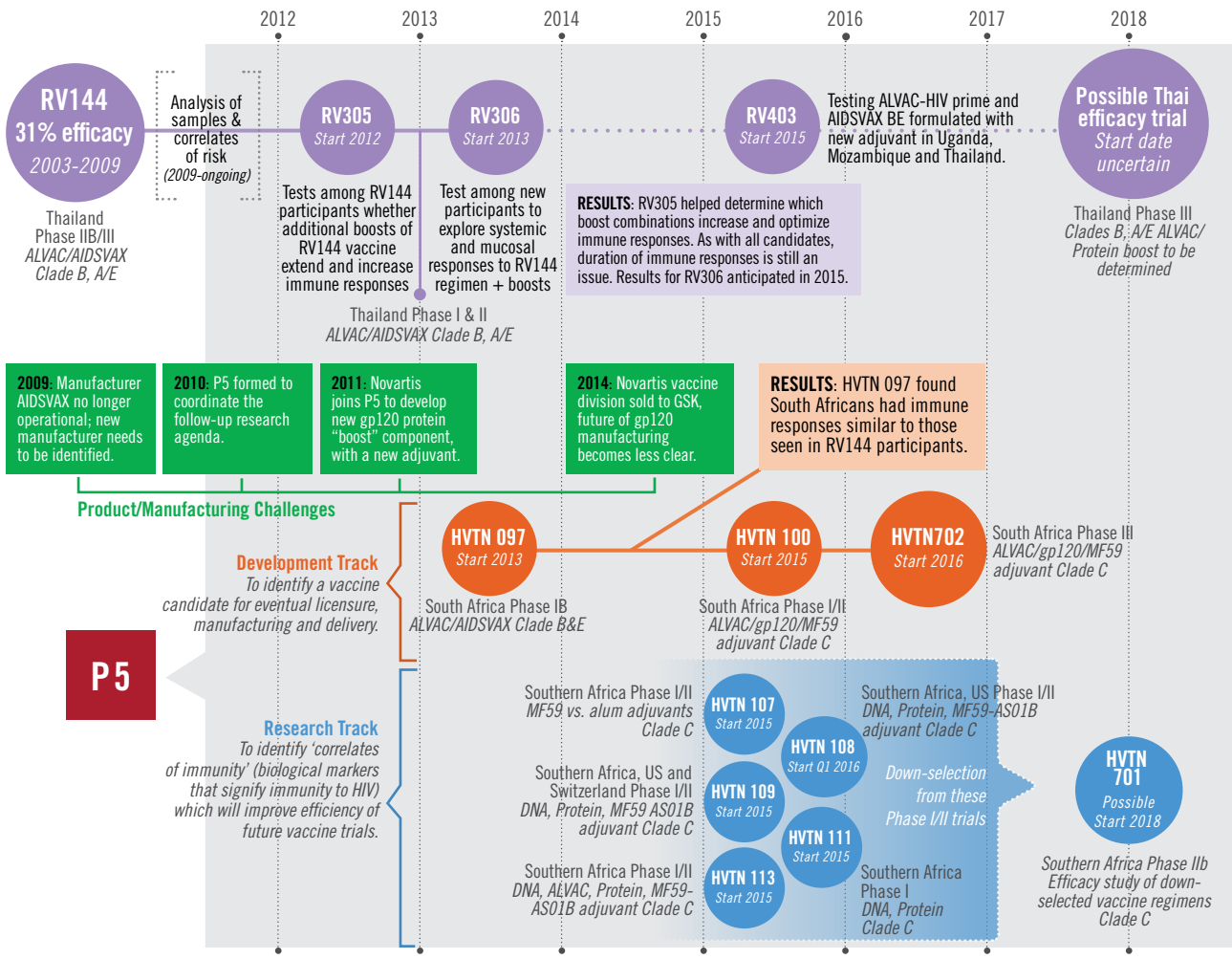
Intervention Update

What's Next for AIDS Vaccines and the Pox-Protein Public-Private Partnership?

It's been more than five years since the news broke that the Thai trial known as RV144 had found evidence of efficacy. RV144 tested a vaccine strategy that used a poxvirus-vectored vaccine to "prime" the immune system and a different, protein vaccine to "boost" it. The overall protection was modest, but the implications were not. RV144 was the first proof-of-concept that an AIDS vaccine could reduce risk of HIV acquisition in

humans. As such, it demanded follow-up. While there has indeed been a lot of work and significant scientific analysis over the past five years, the progress to launch additional trials in humans has been slow (see www.avac.org/vaccines for background). But activity is finally starting to ramp up in Southern Africa. Figuring out what's happening where, when and why isn't easy. These two graphics are designed to help.

What's Next for the Pox-Protein Public-Private Partnership (P5)?

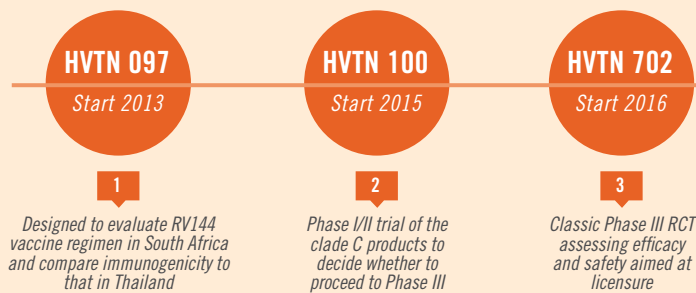


To understand the research that's emerged from RV144, you need to have a two-track mind. Most vaccines and indeed most products are developed via a suite of trials designed to bring a product to licensure. That's one track of

post-RV144 research. The other track has a set of scientific questions that it seeks to answer. Both are going forward in many of the same places, so it's especially important for advocates to begin to track the tracks.

An Advocate's Guide to Tracking the P5 Development Tracks

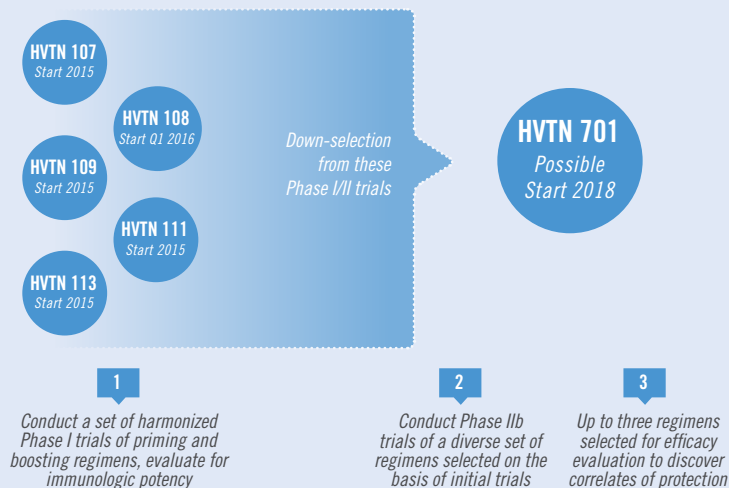
Strategy for the Development Track



What's a development track?

This refers to a series of trials that are designed, as a whole, to lead to a product submitted for regulatory approval and eventual public health introduction. The trial designs—from numbers of participants, to the types of data collected—are set with the ultimate goal of licensure in mind. Of course, licensure depends on evidence of efficacy from the Phase III trial.

Strategy for the Research Track



What's a research track?

The term “research track” is being used to refer to a series of trials designed to add to scientific information about components of an effective vaccine strategy. The trials are designed to identify potent regimens but not to bring any specific regimen to market. An immune correlate is a vaccine-induced immune response such as an antibody or specific type of T cell that is linked to protection from HIV. Finding an immune correlate for an AIDS vaccine could guide strategies to improve this protection. Finding a correlate could also help shorten trials, bring down costs and guide regulatory and policy decisions in the future.

What's the difference?

The P5 development and “research track” trials will take place in many of the same countries and communities. Both tracks will test regimens that might turn out to reduce the risk of HIV infection. The development track trials follow a traditional design. The research track is more flexible or “adaptive”; one regimen might be ruled out sooner than other regimens, and participants may be moved from one trial arm to another. One track is focused on developing a product that could be licensed when the trials are completed. The other aims to advance science—and might have valuable information about how to build an even better vaccine than the one in the licensure track.

There are many questions for advocates to consider as trials on both tracks advance: whether participants in both tracks would get early access to any product that proved effective; how funding will be allocated across the tracks and what will happen if there is a budgetary shortfall; and what this work, based in southern Africa, means for other regions of the continent and the world.

Conclusion

A Field on the Line: A Call to Action at Vancouver 2015 and Durban 2016 AIDS Conferences

In 2015, the International AIDS Society (IAS) will hold a conference in Vancouver, returning to the city for a large-scale meeting the first time since the 1996 AIDS Conference that heralded the beginning of the era of highly active antiretroviral treatment. And in 2016, the IAS will convene the large, biennial International AIDS Conference in Durban, 16 years after the 2000 conference that revolutionized global expectations of AIDS treatment in low-income settings.

The 1996 and 2000 conferences are by many accounts the two most significant global AIDS meetings that have ever taken place. And it is possible, if the right steps are taken, the right funds committed, the right programs implemented and the right partners engaged that the 2015 and 2016 meetings could prove to be watershed moments in the field. These are big “ifs”. The most pressing and fundamental question is one of financial resources. If global investment doesn’t match the price tag for expanded, comprehensive prevention, then all the plans and targets in the world are irrelevant. But if it does, then by 2016, we could begin to see evidence of downward slopes that confirm we’re on track to beginning to end the AIDS epidemic in our lifetime.

Throughout these pages, we’ve talked about target setting and the importance of having specific strategies, clear definitions and strong commitments.

We’ve also talked about the need for short-term action. The world cannot wait until 2020 to find out whether the AIDS response is on track to end the epidemic by 2030. Indicators of progress or problems are already available—and the picture will be even clearer by the time the Vancouver and Durban conferences take place. There is no better use of these large, costly AIDS meetings than to take honest stock of the global response and galvanize action on a global scale.

Both the 1996 and 2000 conferences are remembered as momentous turning points. They’re also remembered for the grief and urgency of the time. People who lived through the early years of the AIDS epidemic remember the dawn of the HAART era as a moment of exhaustion and grief, as well as celebration. And while Durban started a revolution in AIDS drugs for Africa, it took four long years—and an unconscionable number of lives—before that revolution realized its goals.

Today the AIDS response is poised at another moment that could be a revolution, provided that it does not dissipate into rhetoric or dissolve into underfunded documents and plans. Let’s use the memories of those who did not live to return to Vancouver and Durban—as well as our own memories and histories—to fuel the continued fight for lasting change.

AIDS Conferences That Made History—And Must Again

Vancouver 1996 11th International AIDS Conference

Durban 2000 13th International AIDS Conference

“Common sense and experience in infectious diseases dictate that treatment should hit hard and early.” – Joep Lange, 1995



- ✓ Scientific evidence proves that combination antiretroviral medicine can reverse the escalating number of AIDS deaths and save lives.
- ✓ Within one week of the Vancouver AIDS conference, 75,000 patients begin HAART.

- ✓ South Africa is at a boiling point with staggering HIV rates and little government action..
- ✓ Years of fighting inaction on AIDS culminate in massive protests. Durban 2000 becomes a forum for anger about the world’s inaction on AIDS in Africa—and a turning point in the global AIDS response.

Vancouver 2015 8th IAS Conference

Durban 2016 21st International AIDS Conference

“We wouldn’t have the drugs if there hadn’t been enormous activism. If you look at Africa, the situation there with MSM is just horrible. That’s something where I think our voice should have been much stronger.” – Joep Lange, 2014



- > Scientific evidence shows that expanded coverage of ART can benefit individual and public health. But programs are struggling to deliver comprehensive, rights-based services and non-ART prevention is often missing.
- ? Will this be the meeting where science, rights and action get in synch and revolutionize the epidemic—once again?

- > South Africa has more individuals on ART than any other country in the world. It has completed over one million VMMC’s. And it hosts a large share of HIV prevention research trials.
- ? Will Durban 2016 lead to massive mobilization for decisive action on ending the epidemic?
- ? Is the world on track to 90-90-90 and fewer than 500,000 new infections by 2020?

ABOUT AVAC

AVAC works to accelerate the ethical development and global delivery of HIV prevention tools as part of a comprehensive response to the epidemic.

Through advocacy, policy analysis, education and collaboration, we mobilize and support efforts to:

- **Deliver proven HIV prevention tools for immediate impact**, including HIV testing, treatment, voluntary medical male circumcision (VMMC), condoms, prevention of pediatric infections, and syringe exchange programs.
- **Demonstrate and roll out new HIV prevention options**, including daily oral pre-exposure prophylaxis (PrEP), non-surgical devices for VMMC, and vaginal gels.
- **Develop long-term solutions needed to end the epidemic**, including AIDS vaccines, cures and other new solutions for women and men at risk for infection.

While AVAC’s staff is based in New York City, our programs, projects and partnerships operate globally, focusing on countries where HIV prevention research is conducted.



WHAT WE DO

Advocate for Policies and Action

AVAC urges swift and strategic global action to advance HIV prevention.



We call on governments, international agencies, donors and research organizations to:

- Increase financial and political support for HIV prevention research.
- Ensure that research efforts are ethical, scientifically rigorous and focused on the most promising, cost-effective strategies.
- Change laws and policies that harm HIV prevention research and rollout.
- Ensure that new and existing HIV prevention options reach all those in need.

Although AVAC focuses on prevention, our policy work also supports broader access to care and treatment for people living with HIV.

Build Rapid-Response Networks

We help advocates make their voices heard. AVAC supports a global network of HIV prevention advocates through initiatives such as:



- The HIV Prevention Research Advocacy Fellowship Program, which enables advocates in developing countries to monitor, shape and support biomedical research.
- PxROAR (Prevention Research, Outreach, Advocacy and Representation), which provides mentoring and networking

opportunities for advocates in the US and Europe.

- Strategic Initiatives, which enable nimble, strategic, coalition-based responses to emerging and evolving issues, ranging from the development of PEPFAR country operational plans to questions about hormonal contraception and HIV—and much more.

Improve Research Conduct

AVAC puts stakeholder engagement in research into practice.

We are working to ensure that all stakeholders, including research participants, are meaningfully engaged in planning and implementing HIV prevention research. The Good Participatory Practice guidelines for biomedical HIV prevention research—developed by AVAC and UNAIDS—are a foundation for this work. Key activities include:



- Building research literacy to ensure that individuals, civil society organizations and other stakeholders can play a role in shaping prevention research.
- Supporting consultations, trainings and other tools to help trial sites and advocates implement and monitor GPP guidelines.
- Working with national regulatory authorities to adopt GPP at the country level.

Provide Tools for Decision-Making

HIV prevention research is complex. AVAC tries to make it simpler.



To help guide HIV prevention policy, advocacy, and programs, we develop tools such as:

- Annual reports tracking public and private investments in HIV prevention, treatment and cure research
- Educational materials about prevention research, customizable by language and region
- A comprehensive database of HIV prevention clinical trials

Translate and Share the Latest Information

AVAC is the source for global HIV prevention updates and insight.

We work to keep advocates abreast of developments in all areas of HIV prevention through resources such as:



- Advocates' Network, which provides timely updates for individuals and organizations involved in HIV prevention advocacy
- Our blog, *P-Values*, featuring news and perspectives from AVAC staff and partners
- Weekly NewsDigest, a compilation of noteworthy prevention news, research and policy developments from around the world

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