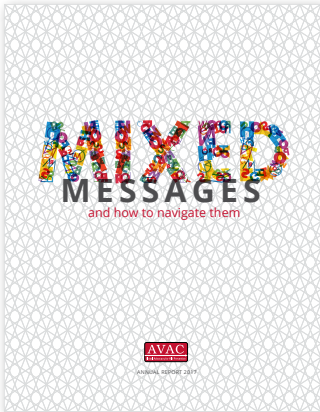


AVAC's Take



This issue of *Px Wire* includes a preview of *AVAC Report*, our annual “state of the field”. Every report has a theme—and this year it’s “Mixed Messages”.

The theme of the Report reflects the ways various messages are playing out in the world of HIV prevention research and implementation.

As readers of the full Report will see, we untangle mixed messages and deliver clear advocacy priorities related to: delivering today’s prevention in the context of a global AIDS funding gap; ensuring that daily oral PrEP has a fighting chance to take hold as a prevention strategy in sub-Saharan Africa; and the monumental task—undertaken every seven years—of reconfiguring the US National Institutes of Health HIV research networks for the future.

This last topic is why we’ve worked to get this preview into your hands before the full Report is published—this content is time-sensitive. We’re sharing our recommendations to the US National Institutes of Health’s Division of AIDS (DAIDS), which is accepting comments on the future of HIV clinical research networks through November 30. Visit <http://bit.ly/2qAj3qh> to submit your comments.

These recommendations are AVAC’s clarion call in the midst of an ever-evolving proposed network structure from DAIDS. During the open-comment period, NIAID and DAIDS leadership have presented a vision for what the 2020-2027 network structure should look like. First, a streamlined two-network vision. Then a three-network vision. And two weeks before the comment period closes, a four-network structure. It’s worth noting that a microbicides-focused network is still off the table.

We hope you’ll engage with DAIDS on these important issues and that you’ll download the full *AVAC Report* when it’s released. And join us in the work of clarifying, loudly and without compromise, what a truly comprehensive, rights-based approach to HIV looks like. —AVAC

Future of DAIDS Trial Networks

Every seven years DAIDS reviews how it structures its funding for HIV treatment and prevention clinical trials. This funding, which comes via NIH, is allocated across different “networks”. The decision about what each network should focus on is a big one. It reflects the priorities and even the philosophy of the largest funder of HIV research worldwide. The current six-network structure will be in place through 2019; the new network structure will be in place from 2020 to 2027, so it must intentionally and explicitly look into the future.

AVAC and partners have engaged in a range of discussions amongst ourselves, with researchers and product developers, and with the DAIDS leadership about what the future network structure should look like. We developed the following principles and priorities in reaction to the plans shared by DAIDS, which proposes a four-part network structure (see centerspread).

What should the DAIDS networks look like—and how should they work?

Simplification of the current prevention trials network structure has been described as a means to reduce inefficiencies in structure and operating procedures. But this move to streamline must not result in oversimplification of the issues and topics that NIH-funded HIV research must address.

Specifically, the new structure must explicitly fund mechanisms that support, cross-cutting research agendas and cross-network coordination. The networks as they currently exist have shown highly variable capacity and interest related to these topics. The existing structure does not have a way to correct for this heterogeneity, which includes different policies with respect to trial conduct and standard of prevention, community and stakeholder engagement at the site and above site level, and how behavioral and social science research is incorporated into trials.

The MTN and IMPAACT are the two networks with an explicit focus on the prevention and treatment needs of cisgender women and adolescent girls. HVTN and HPTN both have significant investments in efficacy trials in

NIH-Funded HIV Trial Networks: A family tree

1991
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1998

The beginning. The Pediatric AIDS Clinical Trials Group (PACTG) and the AIDS Clinical Trial Group (ACTG) were the primary US-funded networks funding research on treatments to block viral replication and treat opportunistic infections in adults and children living with HIV. ACTG 016 was the first trial of the antiretroviral AZT. The drug, which is still used today as part of combination therapy, was tested on its own as “monotherapy”. HIV Network for Prevention Trials (HIVNET) was focused on HIV prevention trials, including vaccine and non-vaccine studies such as HIVNET 016, a landmark trial that found two doses of nevirapine (one to mother and one to newborn) slashed rates of vertical transmission. The AIDS Vaccine Evaluation Group (AVEG) focused on early-phase vaccine research. Established in 1989 and funded through 1997, the Community Programs for Clinical Research on AIDS (CPCRA) was an NIH-funded research enterprise that focused on community-driven and -based treatment research.

1999
-
2005

An era of expansion. Under the network structure launched in 1999, the HIV Vaccine Trials Network (HVTN) was distinct from the HIV Prevention Trials Network (HPTN). In this period, the HPTN launched the pilot phase of HPTN 052, the landmark study that showed that initiating antiretroviral treatment in people living with HIV at CD4 cell counts of 500 or above improved the clinical health of individuals and reduced the risk of onward transmission to primary sexual partners. The same period also saw the launch of the Step and Phambili vaccine trials by the HVTN.

2006
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2012

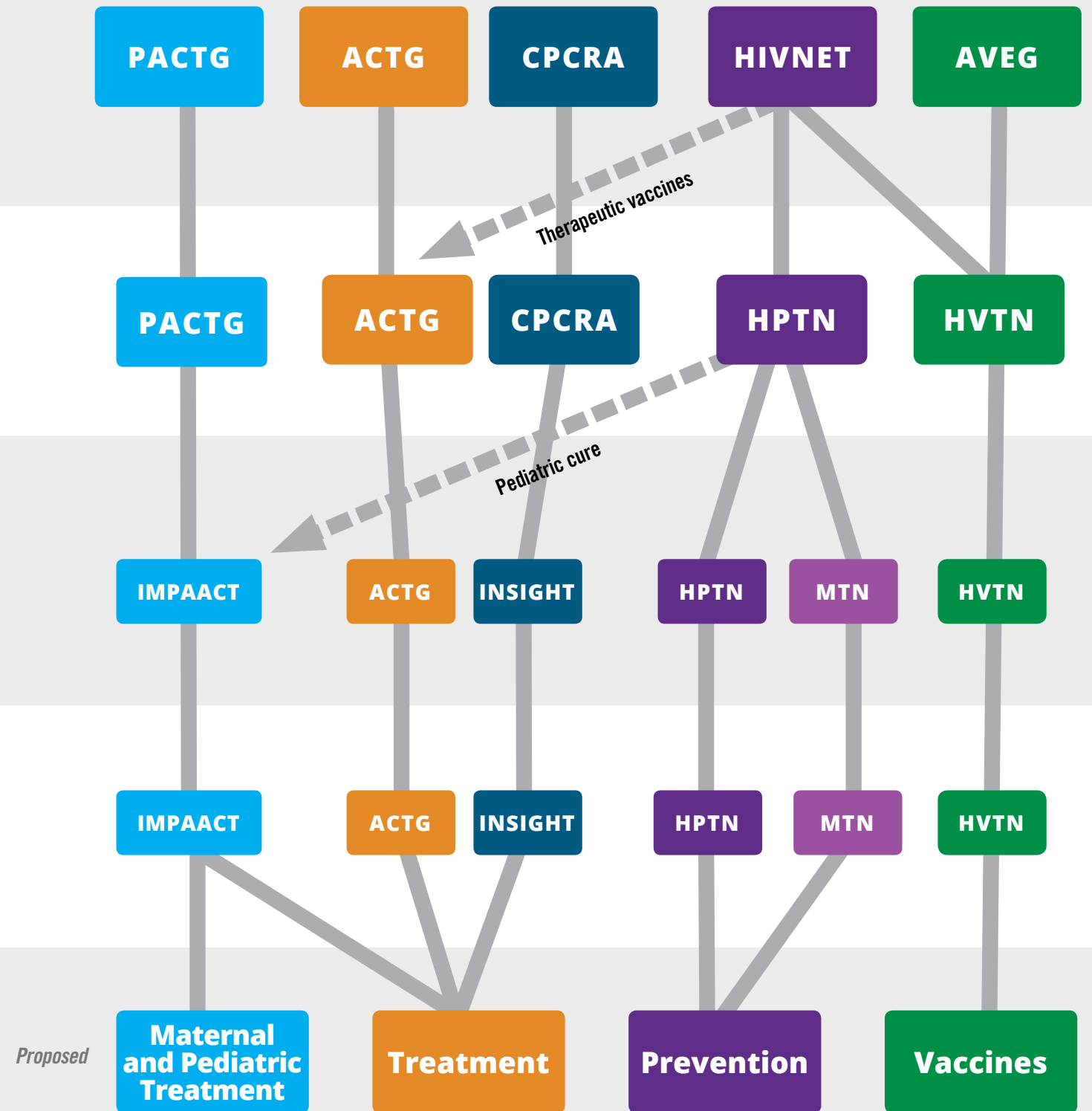
The “women’s prevention” moment. The Microbicide Trials Network (MTN) received funding in 2006 for trials focused on vaginal and rectal topical products (e.g., gels, rings, suppositories etc). In this period, the network launched VOICE—a study of oral PrEP and topical vaginal tenofovir gel—as well as trials of rectal microbicides. The INSIGHT network was created as a merger of two previous treatment-focused groups, and it launched ESPRIT, SMART and START, all trials of treatment in people living with HIV. They were designed to understand when to start ART, whether treatment interruptions were possible and how best to deliver lifelong ART. IMPAACT was launched as a merger of the PACTG and the perinatal science working group of the HPTN. During this time, initial results from HPTN 052 were released, showing benefits of treatment initiation at CD4 count above 500. Additional data were released from non-network PrEP and microbicide trials.

2013
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2020

The era of evidence. By 2013, non-network trials of a vaccine and a microbicide had shown efficacy. Daily oral PrEP was approved by multiple regulators, and in 2015 was recommended by the WHO. Nearly nine million voluntary medical male circumcision procedures had been conducted worldwide, following clinical trial evidence released in 2006. The MTN moved ahead with rectal microbicide research and one of the two efficacy trials of the dapivirine ring, which showed modest efficacy. The HVTN and the HPTN jointly launched two large-scale antibody-mediated prevention (AMP) trials. HPTN also launched two long-acting injectable efficacy trials, and the HVTN began two large-scale vaccine trials.

2021
-
2027

The future? NIH-funded prevention research networks will need to be able to identify and evaluate prevention options that people most at risk of HIV can use safely and consistently—in the context of an array of first-generation strategies like daily oral PrEP, dapivirine ring and possibly even long-acting injectable PrEP. The trials will be more complex to explain and recruit for and the science more sophisticated. Coordination around approaches to product selection, planning for product introduction and research that incorporates the needs and preferences of those most at risk of HIV will be as important as they have ever been.



> *Continued from front*

women, particularly in sub-Saharan Africa, but they have not advanced these trials under an overarching women's prevention agenda or been guided by a set of core principles about how to talk about, implement and act on the findings of trials of products that women can use. If explicit steps are not taken to incorporate the strengths of the existing networks into the new structure, they could be lost or diminished, to the detriment of all.

▶ **Recommendations for network structure and cross-cutting issues:**

- ✓ A comprehensive, cross-network behavioral and social science research agenda that supports consistency in approaches and focus across networks, and that is reviewed on an annual basis and updated as needed.
- ✓ Establishment of either a network core or crosscutting mechanism that guides thinking and investment related to product introduction, from the earliest stages of product development.
- ✓ Institutionalized and consistent research engagement across networks via a funded community and stakeholder engagement division within the core of each network and/or via a cross-network mechanism. This will ensure consistent implementation of the Good Participatory Practice (GPP) Guidelines for stakeholder engagement at site level and, importantly, beyond trial communities.

How DAIDS Should Select Products and Set Its Agenda

DAIDS head Dr. Carl Dieffenbach has been clear that the priority for the next generation of prevention is products that are long-acting and systemic: a shot of antiretrovirals, a vaccine, an infusion of antibodies. The rationale? Many people have multiple vulnerabilities or sites of exposure. People have vaginal and anal sex. They have penetrative sex and do not use the terms “vagina” and “anus”, but prefer “front hole” and “back hole” or other non-gendered anatomical names. People have sex and use drugs. A prevention tool that protects all holes and works in the blood too—and lasts for a long time—has a lot going for it. And that's what Dr. Dieffenbach has argued: “We must develop prevention modalities that are safe, desired and highly effective. These tools should provide systemic protection irrespective of route of exposure.” That's something that topical products can't do.

But it is premature to eliminate user-initiated, on-demand methods—and important not to conflate recent clinical trial results with what people at risk for infection may actually use in their daily lives. As AVAC and many

other stakeholders have said, clinical trials may offer health services, counseling or other benefits that are highly desirable and can serve as motivation for enrolling in a clinical trial. Low adherence in the context of a trial does not mean that products won't be used in real life. Some people can and will take daily oral PrEP. Some can and would use a microbicide. It is inaccurate and potentially dangerous to say otherwise given the evidence currently available.

There is no rationale either in public health or in HIV prevention for an exclusive focus on long-acting systemic products.

And there is no evidence yet from work to date on combination prevention trials, and from the broader landscape of oral PrEP introduction work, to suggest that countries will know what to do with a slew of long-acting products should they become available during the next decade.

▶ **Recommendations for scientific agenda and decision-making**

- ✓ Investment in a product portfolio supported by basic, clinical, behavioral and social science; and market research about clinical efficacy and needs; preferences and priorities of prevention users; providers; and payers.
- ✓ A cross-network strategic collaboration mechanism with budgetary and decision-making authority that guides the overall agenda with transparency and accountability.
- ✓ An explicit fast-track, “hand-off” approach to implementation research on interventions, with an emphasis on efficiency, engagement with national governments and integration into combination prevention packages.

How to Engage (and Learn More)

- Comment today: <http://bit.ly/2qAj3qh>.
- Support microbicide research: <http://bit.ly/2AICnDz>.
- Download our factsheet on the recompetition process at www.avac.org/daids-recompetition.
- Download the recordings of recent webinars with Dr. Dieffenbach at www.avac.org/past-events.

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.