Mitchell Warren â?? Executive Director, AVAC

We now have the scientific tools to end the HIV epidemic; the challenge lies in delivery

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AVAC is a global advocacy group focused on HIV prevention. It aims to accelerate ethical research and effective deployment of HIV prevention tools while working to ensure their equitable access. In an exclusive PharmaBoardroom interview, AVAC Executive Director Mitchell Warren looks back on the terrific advances that HIV science has made â?? transforming the disease from a death sentence to a manageable chronic illness â?? and why urgent, widespread, and equitable delivery of the solutions it has brought is crucial. Warren also takes aim at the conservative policymakers aiming to hijack HIV prevention efforts for political gain and foregrounds the vital importance of patient choice.

When did you first become aware of HIV/AIDS and how did you come to be involved in the field of HIV advocacy?

I was at university at the beginning of the epidemic in the 1980s. Sitting in the student union, I would regularly see double page spreads in The New York Times and obituaries of young gay men dying of an, at the time, unknown disease.

By the mid-80s a clear connection had been made between HIV infection and what we now know of as AIDS and, professionally speaking, I got involved shortly thereafter. In the waning days of apartheid in the late 80s and early 90s I worked on South African health issues, training black, South African health professionals. Because of apartheid, it was quite a closed country back then and HIV was largely seen â?? as it was in the US â?? as a disease of gay, white men. HIV *was* on the radar but in a minimal way,

I then moved to the country in 1993 to work for a non-profit setting up the first condom social marketing programme. This programme used all the techniques of commercial marketing, but applied them to a social benefit, in this case, condoms for both AIDS prevention and contraception. I spent five years in the country during the entire Mandela presidency at a time when HIV was beginning to reach epidemic proportions. South Africa was, and still is, home to the largest epidemic of HIV globally.

Having previously focused on promoting condoms for prevention, my role has evolved along with biomedical science itself. There are now a much wider range of biomedical prevention options, and I have been at the interface of both product development and product delivery. My work has been focused on accelerating the development of new technologies such as HIV vaccines, pre-exposure prophylaxis (PrEP), and voluntary medical male circumcision, while also ensuring that the fruits of science reach people and that R&D gets delivered.

AVAC has been around since the mid-90s as an HIV prevention and global health equity organisation. How has it grown since then and what are its key activities today?

The organisation was founded 30 years ago as the AIDS Vaccine Advocacy Coalition, but we are now known simply as AVAC to better represent our work beyond vaccines alone. A small group of activists from the AIDS Coalition to Unleash Power (ACT UP) treatment advocacy organisation created AVAC in the late-90s. This was a time when antiretroviral treatment was beginning to be delivered but these activists recognised that the world still needed a HIV vaccine. We know that vaccines are the best and most cost-effective way to end epidemics, so the idea was that if the development of an AIDS vaccine could be accelerated, so could the end of the AIDS epidemic.

Sitting here 30 years later, we still do not have a vaccine, although we do have terrific antiretrovirals for treatment and prevention. HIV is clearly one of the most challenging pathogens in history from a prevention perspective. When I joined AVAC as executive director about 20 years ago, research into what we now know as PrEP â?? a daily pill that can prevent HIV and is today a cornerstone of the AIDS response â?? was just beginning. The early PrEP trials were dogged by controversy but as advocates, we believed that, whether it was a vaccine or PrEP, the idea of doing prevention research with communities at risk of infection was essential.

Over the last decade, science has significantly accelerated the development of new technologies. In 2006 we found that voluntary medical male circumcision was indeed HIV prevention, while in 2010, we saw good results from oral PrEP. Since then, weâ??ve had results for a monthly vaginal ring and an injection given every two months. We have followed the science and as the biomedical pipeline has expanded, we continue to be advocates for R&D.

About ten years ago it became clear that even as the science was generating great discovery, it wasnâ??t being delivered at the scale and with the equity to have impact. That problem is not unique to HIV and can be seen in many other public health areas. We even saw it with COVID, where science was able to deliver a vaccine, but only through policies and programmes could impact be delivered. Therefore, our advocacy work now focuses as much on delivery. Today, AVAC has several programmes that operate as thinktanks, working with product developers to see how we might accelerate product introduction of new technology.

How is AVAC funded?

We are a not-for-profit organisation based in the United States and are dependent on donations. AVAC works with pharma and biotech, given that product development sits with them, but we do not take any funding from them. This allows us to be objective in our advocacy: we can support companies without being said to be in their pocket, while we can also criticise them without risking losing funding.

Our largest funders are the Bill and Melinda Gates Foundation, the US Agency for International Development (USAID), and the UK-based Childrenâ??s Investment Fund Foundation. While we do have individual members who pay small contributions, we rely on philanthropic and governmental donors to accelerate our work around the world.

Many pharma companies have divested or wound down HIV R&D projects over recent decades and HIV prevention R&D is now almost entirely dependent on public sector funders. Given the unique characteristics of HIV/AIDS as a disease and as a market, what role do you hope that pharma can play in working towards the 2030 goals?

We have a long-term perspective on this issue as â?? for the last 20 years â?? AVAC has served as the secretariat of the Resource Tracking for HIV Prevention Research & Development Working Group, along with UNAIDS and IAVI. Looking at R&D into prevention for HIV, TB, malaria, and other neglected tropical diseases, the US National Institutes of Health and the Gates Foundation are by far the most important funders. These two institutions alone account for over 80 percent of investments into all global health R&D, and this is also true of HIV. The NIH is the largest contributor to HIV vaccine and PrEP research (over 70 percent) while the Gates Foundation contributes a much smaller percentage but is rather catalytic.

However, even if most basic science and early development is funded by the NIH or the Gates Foundation, we all recognise that industry has a role to play. Oral PrEP, for example, was first approved in 2012 and was a drug that had previously been developed by Gilead Sciences for antiretroviral treatment. The NIH, the Gates Foundation, the US Centres for Disease Control and Prevention paid for the clinical trials that got us there, but we still rely on Gilead and the generic companies to make the product.

More recently, ViiV Healthcare and Gilead Sciences have developed the two most advanced programmes in PrEP. ViiVâ??s injectable product was developed with support from the Gates Foundation and the NIH, but with ViiV playing an active role and financing a significant chunk of that product development. Interestingly, Gilead is funding its development programme into an every six-month injection by itself. That project is currently in late-stage Phase III efficacy trials which could be huge for patients and a big relief of the burden on health systems. We are, therefore, beginning to see companies step up.

In HIV vaccines, we have seen companies enter and then leave the market. About 15 years ago, Merck (MSD globally) had a major HIV vaccine programme, but their vaccine failed in efficacy trials and Merck is no longer active in HIV vaccine development. They do however have a monthly antiretroviral pill in development.

HIV vaccine science is challenging. Industry players come and go depending on the scientific opportunity, and that is not unique to HIV vaccines. I believe that we will not develop any of these new products without industry involvement but also, if we depend only on industry, we will not get products to market that have an impact. HIV is the best example of where private-public partnerships are critical. The link between public sector funders and both large pharmaceutical and small biotech companies is essential

The UN has set what seem to be extremely ambitious goals around HIV prevention and reduction up to 2030. How realistic are they, how far along the road to achieving them are we, and what will be the most important next steps?

When I took over AVAC, we talked a lot about HIV vaccines and imagining a world without an HIV epidemic. That *did* seem like a pipe dream 20 years ago.

However, things are different today. Over the last decade, we have seen such significant advances in science, that the idea of ending the HIV epidemic has changed from a pipe dream to a possibility. One reason for this was the advent of PrEP in 2010, and the idea that by taking a pill a day, a person can avoid getting HIV. While there are challenges to this delivery model, by demonstrating that it was possible scientifically, we opened up new arenas.

Just one year later, another big breakthrough occurred when antiretroviral therapy was shown not only to suppress the virus in an individual patient but would also cause that patient not to be infectious to others. This is the idea of U=U â?? that an undetectable viral load of HIV means that the virus is untransmittable to others.

If PrEP and U=U could be rolled out to everyone â?? basically testing people, and if they are infected with HIV, getting them on antiretroviral therapy to achieve viral suppression and if they are at risk of HIV getting them on PrEP â?? we could end the epidemic. *We therefore have the scientific tools to end the epidemic*. However, the challenge lies in delivery. Diagnosing everybody, especially with a virus that is so stigmatised, and in some places, even criminalised, is not easy.

This delivery challenge is one of the reasons that, while ending the HIV epidemic with current tools is scientifically plausible, we still need a vaccine. We need to continue striving for a vaccine that, with one or two safe and effective doses administered over the course of a lifetime, could durably prevent HIV. Until that moment comes, we need to roll out U=U and PrEP with scale, urgency, and equity.

The phrasing used by UNAIDS and PEPFAR is *to end HIV as a public health threat*. This epidemic is not going to end in the next six years; we were already behind on some of the targets for 2025 and 2030 even without COVID and the consequent challenges to health systems.

Do I think we are going to reach the 2025 and 2030 goals? I do not. They are hugely ambitious and we need to strive for them but they will not be easily achieved. However, they *are* important guideposts to our work, and signal how to move forward whether we reach them targets or not. At AVAC we advocate that those targets be used to drive political commitments, financial commitments, and product development. If we do miss them, letâ??s be sure we come up with better targets for 2035 and iterate accordingly.

Four years ago, another terrible pandemic hit the world, but stakeholders rallied to develop a vaccine in record time and escape it. Did the speed at which the world tackled COVID frustrate you as a long-time participant in the HIV field?

I found it quite exhilarating. History may not repeat itself, but it rhymes a lot; the success of the COVID vaccines that were developed was entirely because of the decades of investment in HIV vaccines. All the platforms that became COVID vaccines had been developed for HIV vaccines. For example, the very first mRNA investments from the Gates Foundation 20 years ago were for an HIV vaccine and Drew Weissman, who was co-awarded the Nobel Prize for mRNA started out working

on a HIV vaccine. Additionally, other key factors in the successful fight against COVID â?? the clinical trial infrastructure, the investigators, the NIH itself, (now former) NIAID Director Dr Anthony Fauci â?? all came from the HIV world.

It was also exhilarating to watch HIV scientists and activists move against COVID. In March 2020, we created the COVID Advocates Advisory Board, a group of advocates who came out of HIV and TB advocacy, turning their attention to COVID. Through this Board, science, activism, and policymakers were brought together to see what was happening and work accordingly.

However, it was frustrating in that COVID is a comparatively easy pathogen to develop a vaccine against that does not mutate particularly quickly. HIV is the exact opposite. What we have seen in four years of COVID mutations, you can see in one personâ??s body after HIV infection within hours or days. HIV attacks the very cells in our immune systems that are meant to fight off infection.

Additionally, it is hugely frustrating that so much money was galvanised. When wealthy countries risked infection within their own borders, they were suddenly able to unlock billions of dollars. Clearly, for these countries, â??Global Healthâ?? means poor people in other countries. However, HIV *is* a global pandemic that potentially hinders economic development, political development, social development, and security issues around the world. HIV and global health equity do not get policymakersâ?? attention and must fight for scraps. The fact that billions of dollars were unleashed so quickly for COVID tells you a lot about the short-sightedness of policymakers. This remains true today. While COVID should have been a wake-up call on global health, the UN is currently trying to negotiate a new pandemic accord with countries that are reverting to close-minded and short-sighted policymaking. I would have hoped that the COVID experience showed that we are all at risk of infection and that a new pandemic is just around the corner.

On top of that, HIV is being politicised in the US with some conservative think tanks and lawmakers saying that PEPFAR has been hijacked to promote abortion rather than preventing HIV, leading to questions around its funding over the next five years. What is your take on the severity of this issue?

It is an incredibly serious issue. There has been such progress over the past few decades, not only in science, but also organisationally: PEPFAR and the Global Fund to Fight AIDS, TB and Malaria are the two greatest examples of global health and development in the history of the world. They have saved tens of millions of lives by getting people on antiretroviral therapy, saving people from getting infected via PrEP, and bringing all sorts of other benefits. However, we should *never* confuse that progress with success; we have not yet succeeded in the AIDS response and are still off track to reach global targets.

I am deeply worried that for all the progress we have made, we are now at risk of falling backwards. We talk a lot about epidemic control, but if we take our eye off the prize on that aim, HIV will come roaring back. Watching the politicisation of PEPFAR, policymakers lying, and conservative think tanks intentionally misleading is terrifying. This is the quickest way to let HIV resurge, not just in Kenya, South Africa, India, and Brazil, but in the US as well.

We have seen anti homosexuality acts and laws created in countries like Ghana and Uganda, and in various states here in the United States as well, attacking transgender and gay communities. HIV exists as a pandemic because it hits to the heart of peopleâ??s sexuality, or peopleâ??s use of drugs. These are behaviours that are so easily criminalised and stigmatised. For all the progress we have achieved, it will disappear in the blink of an eye if right wing, conservative policymakers around the world get their way

What are your thoughts on how stakeholders can come back together and re-establish common goals?

You do not work in HIV if you are not an optimist at heart! I am hopeful but also nervous because we have seen distrust of science and institutions spread like an epidemic and, sadly, there is not yet a vaccine for misinformation and disinformation. This means that we have our work cut out for us, but we can look at PEPFAR and the Global Fund, national governmental responses, and civil society advocacy successes over recent decades and draw several lessons. The most important of these is that if we stay true to the science, and true to human rights, we can achieve epidemic control for HIV.

It is all about ensuring that our policymaking and our programmatic decision-making are guided by science and human rights. If we do that, we can make treatment and prevention a reality for people and ensure that no one else gets infected. It is a heavy lift but one that I believe is possible.

Do you have any final thoughts?

I would like to finish by thinking about choice. The array of biomedical options that have been created is astounding â?? we now have an injectable, a vaginal ring, and an oral pill â?? but these options need to be actual choices for people. Most importantly, although we must continue to develop products, we must make sure that we are building programmes that deliver choices. None of these products are perfect and all of them have their challenges, side effects or issues.

At the recent Conference on Retroviruses and Opportunistic Infections (CROI 2024) in Denver, Colorado a study showed that when people at risk were provided just PrEP and those who were living with HIV were provided antiretroviral treatment, there was a reduction in new infections. However, when people were offered *choices* in prevention, with the injectable as well as oral PrEP, everyone found something that worked for them. In fact, the group that had just treatment and oral PrEP, still saw a two percent incidence rate, meaning that there were still new infections. For the group that had choices between oral PrEP and injectable PREP, there were no new infections.

Just the idea of adding a choice for people allowed them to find something that worked for them. Back to the issue of targets and the way ahead, If we can give people the options that biomedical science creates, we can help people find something that works for them in their lives. That is huge and something we havenâ??t had until now. Thatâ??s the future, and one that I think is possible.

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