HIV 2020

Gazing into the crystal ball at the epidemic's future reveals many exciting advancements. Lower infection rates is just the beginning.

June 26, 2017 By Benjamin Ryan

In the eyes of the mainstream press, the most recent edition of the annual Conference on Retroviruses and Opportunistic Infections (CROI), held in February in Seattle, wasn't a watershed event. This was quite an oversight, however, considering that the findings of one particular study reported at this important HIV-focused scientific gathering were reason for considerable excitement.

According to a recent Centers for Disease Control and Prevention (CDC) analysis presented at CROI, the estimated number of new annual HIV infections, or HIV incidence, in the United States fell 18 percent between 2008 and 2014. This promising downward shift followed two decades of frustrating stagnation.

"That's really tremendous progress," John T. Brooks, MD, a senior medical adviser with the CDC's Division of HIV/AIDS Prevention, tells POZ. Anticipating that the drop is the beginning of a long-term trend, he continues: "We may actually have HIV be a disease that we're controlling rather than reacting to over the next decade."

The dawning of the 2020s will bring HIV into its fifth decade—the first reports of what became the AIDS crisis emerged in 1981. Crystal balls are by their nature hazy, and the current political climate raises many worrisome questions about how shifting federal priorities may affect people living with and at risk for HIV. Nevertheless, thanks to recent promising strides in HIV research and public health efforts to tackle the virus from all sides, leaders in the field are increasingly optimistic about what the next decade of the epidemic will look like.

Anthony S. Fauci, MD, the director of the National Institute of Allergy and Infectious Diseases (NIAID), embraces cautious optimism, saying the 2020s will see "substantial advances, over and above where we are now." He foresees "a great improvement in the ability to manage people who are HIV-infected—either by 1) having them take less toxic and more user-friendly drugs; or 2) getting a proportion of them off therapy" and in a state of what scientists often call viral remission.

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Two key concepts have dominated the public health discourse about HIV during the 2010s. The first is biomedical prevention. This refers to the awesome power of antiretrovirals (ARVs) to prevent transmission, either as treatment as prevention (TasP), whereby HIV is fully suppressed, rendering it virtually impossible to transmit, or in the form of Truvada (tenofovir disoproxil fumarate/emtricitabine) as pre-exposure prophylaxis (PrEP), which grants protection to those at risk for HIV in case of exposure to the virus. The second major concept is the HIV care continuum, which refers to the series of steps required for an HIV-positive person to achieve an undetectable viral load: diagnosis, being linked to and retained in medical care for the virus, receiving ARVs and, finally, full viral suppression.

Gloom and doom has been the name of the game where U.S. care continuum statistics have been concerned, with a mere 30 percent of the national HIV population virally suppressed. However, recent evidence suggests not only that this figure, which was based on 2011 data, was an underestimate to begin with but also that concerted efforts around the country to improve measures of the continuum are beginning to bear fruit. In fact, the CDC pointed to a rising viral suppression rate as a likely driver of the recent decline in new HIV infections. In addition, the CDC says that PrEP, which began gaining popularity in late 2013, may have contributed to the decline in HIV incidence seen in 2014.

Crucial for continued progress in care continuum statistics and PrEP use alike is health care access. On both fronts, the Affordable Care Act (ACA, or Obamacare) has apparently provided a pivotal boost. A recent Kaiser Family Foundation analysis found that between 2012 and 2014, the first year that Obamacare's key provisions were implemented, the uninsured rate among people in medical care for HIV fell from 13 percent to 7 percent in states that expanded their Medicaid programs under the legislation.

Jennifer Kates, PhD, the director of global health and HIV policy at Kaiser, believes that "in almost every way," overall indicators of progress in combatting the U.S. epidemic are "moving in the right direction." However, she says, "This progress could be at risk if current proposals to replace the ACA are enacted and if there are any funding cuts to key federal HIV programs."

Specifically, future federal budget cuts could compromise efforts of the CDC, the Ryan White CARE Act and the National Institutes of Health (NIH) to prevent, treat and research HIV. And after the U.S. House of Representatives passed the American Health Care Act in May—the Republicans' first salvo in the party's ongoing efforts to repeal and replace the ACA—all eyes are now on the Republican-dominated Senate, which is tasked with adapting the bill to its own tastes.

Given the swirl of scandal increasingly consuming the White House, the future of the entire Republican legislative agenda lies in question, including the health care bill. Ideally for the fight against HIV, any legislation that does ultimately pass will preserve support for Medicaid, as well as Obamacare's protections ensuring that individuals with preexisting conditions, like HIV, can access

affordable, quality health care.

Reassuringly, at the end of the day, all public health is local—or so the saying goes. While the CDC may contribute vital federal funds to local efforts, the true fire behind the most impressive recent battles against the epidemic have come at the municipal level. New York City, San Francisco and Seattle are the standard bearers on this front, having masterminded their own highly tailored, full-on assaults against HIV, with increasing indications of success.

According to Kates, these cities "show that it's possible—through collective public, private and community action—to actually implement the right tools at the right scale to the right people and to drive down new infections, increase access to care and reduce disparities."

The question remains, though, whether other cities will follow suit, especially those in the hard-hit South, where local public health responses to HIV tend to remain woefully inadequate. Demetre Daskalakis, MD, MPH, the energetic acting deputy commissioner of New York City's Division of Disease Control, is hopeful for such a sea change and notes that his counterparts in other cities are "looking at what we're doing and sampling our menu."

PrEP, which has seen soaring rates of new users during the past four years, is a key factor in the strategies of the three lead cities and will likely play an increasingly pivotal role in driving down U.S. HIV rates during the 2020s. However, thus far, PrEP's use has largely been limited to white men who have sex with men (MSM) over the age of 25 in major urban areas. This lopsided uptake has raised concerns that Truvada may lead to a collapse in HIV rates among a population that has long enjoyed a declining infection rate, while leaving behind the demographic hardest hit by the epidemic: African-American MSM.

"A world with PrEP is better than a world without PrEP," stresses Eli Rosenberg, PhD, an assistant professor of public health at Emory University, whose research led to the shocking estimate that 11 percent of 18- to 24-year-old Black MSM in Atlanta contract HIV annually. "But racial disparities in infection rates may grow, as the access is uneven."

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In the current one-pill-once-a-day era of HIV treatment, there are so many highly effective and tolerable ARV regimens that future progress in developing first-line therapies (those offered to people with HIV who haven't taken ARVs before) will probably focus more narrowly on simplifying treatments, as with ViiV Healthcare's recent efforts to develop a two-drug regimen.

Tim Horn, deputy executive director of HIV and hepatitis C programs at Treatment Action Group, predicts that Gilead Sciences' investigational integrase inhibitor bictegravir, which recently showed promise in a head-to-head with Tivicay (dolutegravir), will likely bring to an end efforts to improve the effectiveness of triple-drug first-line treatments.

On the other hand, those who have failed multiple ARV regimens will probably more broadly benefit from the expansion of treatment options going forward. In a recent trial of the long-acting

antibody treatment ibalizumab, which was given in biweekly infusions as an adjunct to daily ARVs, the treatment helped suppress the virus among those with multidrug resistance who were on otherwise failing HIV regimens. Ibalizumab is now up for FDA approval.

Long-acting injectable ARVs are also poised to give people with HIV the option of ditching daily drugs, with the regimen of long-acting cabotegravir and Edurant (rilpivirine) given every eight weeks currently in a Phase III trial.

Researchers are also fast at work identifying what are known as broadly neutralizing antibodies that, especially when used in combination, appear highly effective at suppressing HIV. Daily oral ARVs may become a thing of the past for at least some people with HIV as scientists figure out how to treat—as well as prevent—the virus with intermittent infusions of such antibodies.

Fauci is enthusiastic about the possibility that the interval between such infusions could become quite wide and says, “If you could get it to six months and have somebody come in twice a year for an injection—wow!”

In the meantime, the particulars of intellectual property law will likely instigate a considerable shift in what people with HIV keep in their medicine cabinets. In the coming years, an increasing number of ARVs will lose patent protection, including those used as first-line therapies, such as the all-important Viread (tenofovir disoproxil fumarate), a component of numerous combination-ARV tablets.

Horn anticipates that insurers, seeking to cut the high costs of HIV treatment, will likely begin to pressure people with HIV to take cheaper generic equivalents of brand-name drugs. This may mean pushing people off single-tablet regimens and toward multi-tablet equivalents, especially if research doesn’t demonstrate a clear safety advantage to the brand-name alternative.

“That’s where the showdown is,” Horn says.

The prospects for PrEP, meanwhile, likely include an array of choices that will better fit the needs and lifestyles of at-risk individuals. Two major trials in this field are under way: One is examining a long-acting injectable form of PrEP given every eight weeks, and the other is testing daily oral Descovy (emtricitabine/tenofovir alafenamide), which research has shown is safer for bones and kidneys than Truvada, currently the only approved form of PrEP. Much further back in the PrEP research pipeline are a subdermal implant that could last for six months, a microbicidal enema and long-lasting antibody infusions.

And then there are the efforts to find a cure for HIV. Given the byzantine complexity of attacking the HIV reservoir—the amorphous collection of cells in which the virus hides even in the face of successful ARV treatment—experts typically believe that the 2020s won’t see a widely replicable so-called sterilizing cure that would totally rid the body of the virus.

However, recent research advances are raising hopes for what scientists call a functional cure, or a state of extended viral remission, meaning that although a treatment wouldn’t totally eliminate

HIV from the body, the virus wouldn't replicate significantly. We've already seen a handful of cases with this type of remission, including the famous Mississippi Baby, who was aggressively treated for HIV starting at birth and later spent 28 months off ARVs before her virus rebounded at age 4.

"We're going to have a certain percentage of people who are going to go prolonged periods of time without requiring therapy," Fauci says of the next decade.

Recent research suggests that the smaller the viral reservoir, the greater the likelihood individuals may achieve such extended viral remission. Consequently, treating HIV as early and as consistently as possible—both efforts likely yield smaller and more unstable reservoirs—is probably a fundamental prerequisite to increasing the chances of such an outcome.

In the near future, efforts used to shrink the reservoir—researchers are investigating numerous avenues, including genetic treatments—may not fully cure the virus. But as scientists reach for that ultimate goal, they may succeed in finding ways to diminish the harmful chronic inflammatory state to which even well treated HIV gives rise and which is believed to raise the risk of many aging-related health problems.

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"The future of HIV is gray hair," predicts New York City's Daskalakis.

Indeed, with an overall life expectancy approaching normal and new membership to their club falling, the HIV population is steadily marching toward its senior years. At the beginning of the 2010s, only a bit more than one third of HIV-positive U.S. residents were 50 or older. That proportion is projected to reach one half by 2020. By 2030, more than a fifth will likely be older than 65.

Unfortunately, living longer with HIV comes with a higher risk of various aging-related conditions, such as diabetes, high cholesterol, cardiovascular disease, high blood pressure, cognitive decline and bone loss.

But there's no need to push the panic button just yet. Bear in mind that these are largely manageable conditions. Eleanor E. Friedman, PhD, a fellow at the Oak Ridge Institute for Science and Education who conducted one of the first studies to look at the health challenges of seniors living with HIV, stresses that this group is largely well poised to weather such additional challenges, owing to these individuals' wealth of experience in managing HIV itself.

"If you have spent so many years practicing good self-care," Friedman says, "I mean emotional self-care, and dietary self-care, and medication self-care, then this shouldn't throw you off your

stride.”

It may be that a simple way to allay various age-related conditions in older people with HIV is already readily available. A major, highly important trial called REPRIEVE is currently looking at whether cholesterol-lowering statins may improve the health of people with HIV on numerous fronts, including the risk of heart disease and death, possibly by lessening chronic inflammation (see sidebar below).

At present, liver disease poses a major threat to the overall HIV population, largely because approximately one fifth of those living with HIV are coinfected with hepatitis C virus (HCV), which attacks the organ. HIV itself accelerates such HCV-related liver damage. But for those with HIV and HCV, cirrhosis and liver cancer are hardly inevitable, considering how easily hep C can be cured now, thanks to new, highly effective medications. And while the sky-high cost of these drugs has led insurers to limit who can receive coverage for them, current hep C treatment guidelines move HIV/HCV-coinfected individuals toward the front of the line.

“We have the opportunity to really eliminate this disease in HIV infection,” says the CDC’s John Brooks of the benefits of modern HCV treatment. “The value in terms of the illness and death that’s averted by getting rid of this coinfection could be enormous.”

In the end, the holy grail in the quest to end the HIV pandemic is a vaccine. Fauci says the world is unlikely to see a highly effective vaccine this side of 2030. However, he remains cautiously optimistic about the advanced vaccine trial launched in sub-Saharan Africa in late 2016. The study is testing a retooled version of the vaccine that showed moderate success in a previous trial in Thailand. According to Fauci, it may yield a vaccine that cuts HIV risk by 50 to 60 percent.

If the vaccine proves that powerful, Fauci says it would be a go. In fact, a recent paper projected that a vaccine that cut HIV risk in half could eliminate more than 6 million cases worldwide by 2035.

Just imagine what decade six of the epidemic might look like.

The Heart of the Matter

First, the worrisome news. Even when taking successful antiretroviral (ARV) treatment, people living with HIV face up to double the risk of heart disease of HIV-negative individuals. And as the HIV population ages, the virus’s apparent contribution to health events such as heart attack and stroke looms ever larger.

And now for the promising news. A simple solution to this increased health risk may already be at hand. Research suggests that cholesterol-lowering statins reduce harmful chronic inflammation, which even well-treated HIV may fuel and which scientists believe contributes to increased rates of aging-related diseases, including heart disease.

Seeking gold-standard proof that statins lower the risk of heart disease as well as death among

people with HIV, in April 2015, the National Institute of Allergy and Infectious Diseases and the National Heart, Lung, and Blood Institute launched a mammoth global trial called REPRIEVE. The study is geared to enroll 6,500 HIV-positive participants at 100 research sites around the world, including in the United States, who will be randomized to receive a placebo or the statin Livalo (pitavastatin) in addition to their standard ARVs.

The first results from REPRIEVE are expected in 2020 but may come earlier if a clear benefit to taking a statin emerges particularly quickly.

The study's investigators are hoping to gain a wealth of knowledge from the trial, including information about the complex mechanisms involved in HIV's contribution to heart disease and whether statins lower rates of other health conditions, such as kidney disease and cancer. They've also set their sights on developing a heart-disease risk calculator that is specific to people living with HIV.

REPRIEVE's ultimate goal is to maintain the more than two decades of scientific progress that have steadily found effective ways to make HIV a more manageable and less harmful infection.

In short, success in the trial would be great news for the next decade of the epidemic.

For more information on REPRIEVE, including how to participate, visit reprievetrial.org. Women, who are strongly encouraged to join the trial, can check out followyourheart.reprievetrial.org.

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