MEANS TO AN END

Cities, states, and provinces are gearing up to halt their AIDS epidemics—though the definition of success varies

By **Jon Cohen**

After what Shane Ryan calls "a silly, stupid weekend" in late April, he joined the many other men in San Francisco, California, who line up six mornings each week and wait for the doors to open at Magnet. Located in the city's Castro district, Magnet provides sexual health services for gay and bisexual men. Last year, the center diagnosed 37% of the new HIV infections in the city. Ryan, like most of the other men in line, came to find out whether his condomless sex had the consequence he feared. "Usually, I'm very safe, always precautious, but I went a little sidetracked that weekend," Ryan said.

Ryan, who is 24 years old and grew up in Ireland, met with a nurse practitioner, who explained that he could immediately start taking antiretrovirals (ARVs). This so-called postexposure prophylaxis (PEP) might abort an infection if indeed he had been exposed to HIV, the nurse explained. Ryan began taking a pill each day that contains four ARVs.

In June, when Ryan's follow-up test came back negative, another Magnet nurse practitioner, Pierre-Cédric Crouch, asked if he wanted to start on *pre*-exposure prophylaxis, or PrEP. "Having gone on PEP is an indication that PrEP might be a good thing for you to do," Crouch said. He explained that the daily PrEP pill contains only two of the four drugs used in PEP and has far fewer side effects. It

PHOTO: © DREW BIRD

After this test showed Shane Ryan's blood was negative for the AIDS virus, Magnet's nurse practitioner Pierre-Cédric Crouch (background) offered him anti-HIV drugs to prevent infection.

is not a substitute for using condoms, he said, but it provides "that extra layer of protection." Ryan opted to try it and was directed to a PrEP benefits manager who would help him get the drug at low or no cost.

Magnet's aggressive attempt to prevent the spread of HIV to people at high risk is part of a groundbreaking citywide initiative launched this January that aims to make San Francisco the first jurisdiction in the world to get transmission down to such low levels that it effectively will "end" its epidemic. Specifically, San Francisco wants to achieve a 90% drop in new infections and deaths by 2020. "I think we're going to get to the point where HIV diagnoses are very rare," says Steve Gibson, who heads Magnet.

New York state and the Canadian province of British Columbia (BC) are also at the vanguard of the ending AIDS movement. These three locales have different definitions of what it means to end AIDS, as well as different approaches, tailor-made to their distinct demographics and politics. All, however, rely on aggressive use of ARVs and intensive efforts to identify newly infected people and their partners. Those strategies reflect several game-changing findings of the past 5 years.

Researchers now know that if infected people take their ARVS and knock down the virus to undetectable levels in the blood, they rarely transmit it to their sexual partners. The approach, called treatment as prevention, pays special dividends with recently infected people, who account for a disproportionate amount of spread. Studies have also shown that uninfected people who take the drugs pre-exposure—PrEP—can greatly reduce their own risk of infection.

Buoyed by these remarkable advances against a virus that to date has infected 76 million people and shortened the lives of half of them, the Joint United Nations Programme on HIV/AIDS (UNAIDS) in 2014 set an "ambitious treatment target" of 90-90-90 by 2020: 90% of infected people worldwide will know their HIV status, 90% of those will receive ARVs without interruption, and 90% of those will have no detectable virus in their blood. Doing the math, that means 73% of the total infected population will have fully suppressed viral levels. This treatment-as-prevention strategy, even without PrEP, will "end the AIDS epidemic as a major global health threat by 2030," UNAIDS predicts.

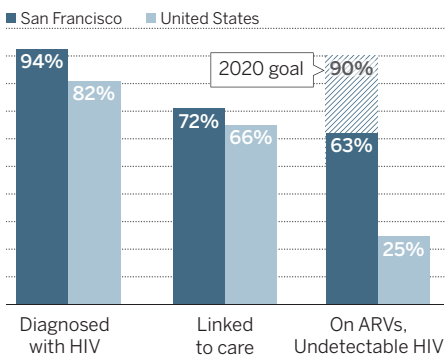
A just-released report, "Defeating AIDS—advancing global health," in the 25 June online issue of *The Lancet*, is less optimistic. "There is an urgent need to do more and to do better now," declares the report, by a commission including heads of state, public health leaders, and even actress Charlize Theron. It notes that too many locales have sluggish responses and little hope of downgrading their epidemics to "low-level endemicity" (see sidebar, p. 230). But BC, New York, and San Francisco aim to pave the way in the ending AIDS movement, which will be a central topic at an international HIV/AIDS meeting in Vancouver 19 to 22 June.

JULIO MONTANER, CO-CHAIR of the Vancouver meeting and the key architect of 90-90-90, took a gamble when he and his colleagues published an editorial in the 5 August 2006 issue of *The Lancet* that argued for making ARVs the backbone of prevention efforts. "We were told by UNAIDS that we were medicalizing prevention, and that this was irresponsible," says Montaner, who is at the BC Centre for Excellence in HIV/AIDS in Vancouver (an offshoot of the University of British Columbia). He acknowledges that he and his colleagues were relying more on mathematical models than hard evidence that treatment as prevention worked. But studies vindicated him. "I'm happy we were right."

Although BC has not declared an explicit goal for "ending AIDS," Montaner says it is committed to reaching the 90-90-90 target by 2020. Nearly seven times the size of New York state, the province has only 4.6 million residents, an estimated 12,000 of whom are infected with HIV, giving it a prevalence rate of 0.3%. The epidemic boomed in the early 1990s in men who have sex with men (MSM). When heroin use surged around 1996 in downtown Vancouver, HIV infections did as well, which led authorities to declare a public health emergency the next year. The government expanded a long-running methadone maintenance program, distributed free needles, and in 2003 opened the first supervised injection site in North America. In 2011, the province began offering ARVs to all infected people, whereas most of the world, concerned about cost and side effects, still recommended withholding treatment until a person's immune system was damaged.

Treatment cascade

For the treatment-as-preventwion strategy to work, people must know their HIV status, receive appropriate medical care, and take ARVs regularly such that their HIV becomes undetectable.



DATA: SAN FRANCISCO DEPARTMENT OF PUBLIC HEALTH

With the widespread use of ARVs, AIDS-related illness and death in BC has plummeted since 1996. New HIV diagnoses have fallen from a high of 681 per year in 1995 to 262 in 2014, with a huge drop among people who inject drugs. But among MSM and heterosexuals, the number of new diagnoses has barely budged for several years. And although Vancouver has been relatively successful, the epidemic is poorly controlled in more remote regions of the province.

In BC as a whole, some 80% of infected people know their HIV status, 61% take ARVs at some point, but only 51% have undetectable viral levels—the cornerstone of the treatment-as-prevention strategy. "Treatment as prevention has not been pushed to the limit," Montaner says. So the BC center and its collaborators have recently stepped up efforts to find infected people and make sure everyone who starts ARVs stays on them so the virus is fully suppressed.

Following a surge in HIV infections from sharing needles, Vancouver opened Insite in 2003 for drug users to inject safely.

As part of its revved-up effort, BC is one of a growing number of places that is exploiting DNA sequencing of the fast-evolving virus to work out how isolates are related. That allows epidemiologists to pinpoint hot spots of transmission, where interventions can then be targeted (*Science*, 12 June, p. 1188). These data have led health authorities to concentrate outreach efforts in the northern, rural part of the province, which is home to many indigenous Canadians.

Some criticize BC's program for not going beyond 90-90-90 and offering PrEP to high-risk but uninfected people like Shane Ryan, a mainstay of efforts in New York and San Francisco. "I don't think we're going to eliminate the epidemic without PrEP," says Susan Buchbinder, who directs HIV prevention at the Department of Public Health in San Francisco. Montaner, who notes that Canada's government-funded health care plan does not reimburse for PrEP, is not convinced PrEP is needed. But he says he is keeping an open mind. If in 5 years the jurisdictions that combine both strategies are ahead of us, he says, "I'll say PrEP is the path to take."

MARK HARRINGTON and Charles King hatched their bold plan for ending the AIDS epidemic in New York in the back of a paddy wagon. In 2012, during an international AIDS conference in Washington, D.C., the prominent activists were arrested outside the White House while protesting the Obama administration's HIV/AIDS policies. Based in New York, Harrington runs Treatment Action Group, an HIV/AIDS think tank, and King is head of Housing Works, which helps find homes for people living with the virus. Convinced that the administration's plan was not aggressive enough, they began brainstorming while en route to their jail cell about how they could do better.

With support from HIV/AIDS researchers at Columbia University and the AIDS Institute at the New York State Department of Health, Harrington and King organized community meetings to explore how New York could drive down new infections to such a low level that the epidemic would peter out. "It brought more gravitas to the whole thing that it was researchers, advocates, and policymakers all working together to push for this," says psychologist Robert Remien, who heads Columbia's HIV Center for Clinical and Behavioral Studies.

The idea received an enormous political boost in June 2014 when New York Governor Andrew Cuomo, a Democrat, announced a three-point plan to end the state's AIDS epidemic by expanding testing, treatment, and access to PrEP. A few months later, Cuomo set up an Ending the Epidemic (ETE) Task Force, which includes Harrington, King, other community advocates, scientists, and government health workers. In April 2015, at a ceremony to unveil the group's blueprint, Cuomo said that when he announced the goal, people thought it was "outrageous." But New York will succeed and set an example, said Cuomo, who budgeted $10 million this year to support the ETE project.

On Gay Pride Day in June 2014, New York Governor Andrew Cuomo (D), shown marching in a Manhattan parade, announced a plan to end AIDS in the state.

The meaning of "ending AIDS" varies from place to place, and the "Defeating AIDS" report urges the international AIDS community to agree on "a precise scientific and epidemiological definition of low-level endemicity." The report defines the end

PHOTOS: (TOP TO BOTTOM) © CHRISTOPHER J. MORRIS/CORBIS; © MICHAEL APPLETON/*THE NEW YORK TIMES*/REDUX

as a reproduction number below one, meaning that each infected person transmits the virus to less than one other person on average. At that rate, the epidemic will gradually fade. No locale has adopted that exact language. Governor Cuomo offered this definition: "The end of the AIDS epidemic in New York state will occur when the total number of new HIV infections has fallen below the number of HIV-related deaths." In 2012, the state had an estimated 3000 new infections and 1653 AIDS deaths (with an ongoing debate about how many of those were HIV related). The ETE blueprint aims to reduce the number of new infections to 750 in 2020.

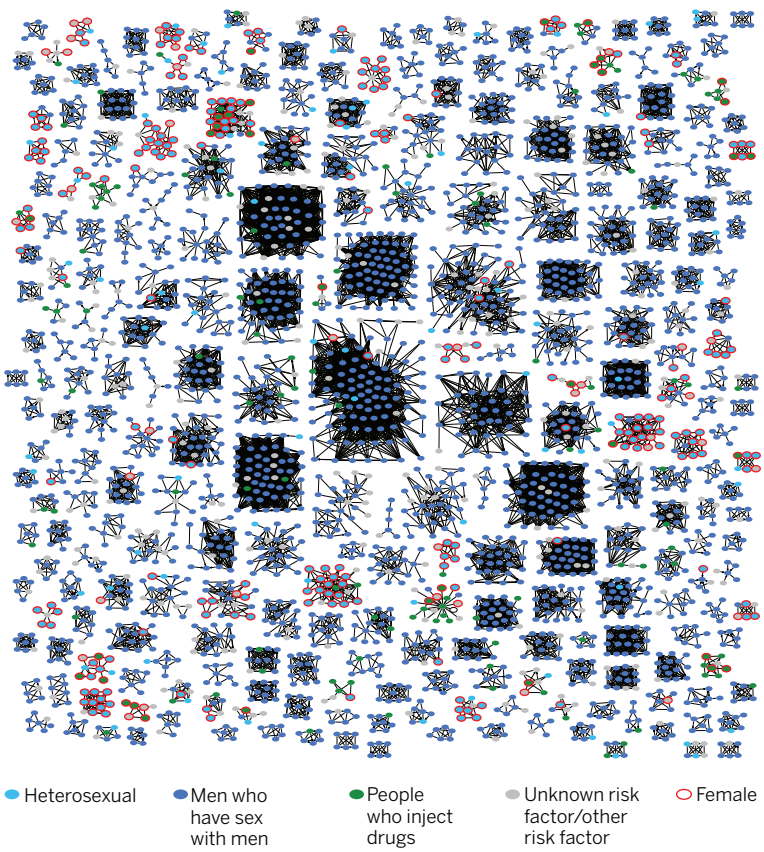
New York has more HIV-infected residents, about half of whom are MSM, than any state. Out of a population of nearly 20 million, an estimated 154,000 people were living with HIV in 2012. Of those, 132,000, or 89%, knew their status, but only 68,000, or 44%, were on treatment and had undetectable levels of virus, far below the UNAIDS target. To decrease the gap between diagnosis and effective treatment, which Harrington refers to as "the Grand Canyon," the blueprint calls for stepping up surveillance to find people who know their status but don't consistently use ARVs and to assist them with nonmedical challenges that might get in the way of treatment, such as finding housing and jobs. It will also provide incentives to both care providers and patients to help people stay on treatment.

Meanwhile, 22,000 New Yorkers don't even know they are infected. To reach them, the state will ramp up routine testing in places like emergency rooms and send out more mobile testing units to high-risk populations, including MSM, transgender people, new immigrants, the homeless, and the mentally ill. ETE is launching a statewide education campaign about PrEP—which has been approved by the U.S. Food and Drug Administration for 3 years but has been slow to catch on, in part because some uninfected people worried that it would brand them as promiscuous and reckless. New York is also creating programs to help people access PrEP drugs. Medical record "autopsies" of people who die from AIDS will try to identify how they slipped through the cracks.

The state's portion of the price tag for putting 68,000 more people on treatment by 2020 is $2.25 billion, according to a recent analysis done by Treatment Action Group and Housing Works. Additional housing support for the 12,000 or so HIV-infected people who are homeless or poor would add as much as $720 million to the bill. But improved care and decreases in new infections would reduce the load on the health care system by enough to save New York nearly $8 billion, the analysis finds.

New York City's hot spots of spread

With genetic sequences of HIV from different people, researchers can identify how the virus moves between individuals (circles). Mapping these transmission clusters can help target treatment and prevention efforts.



GRAPHIC: JOEL O. WERTHEIM/UNIVERSITY OF CALIFORNIA, SAN DIEGO

ON WORLD AIDS DAY in 2013, Diane Havlir of the University of California, San Francisco (UCSF), moderated a forum for the local community entitled "Getting to Zero in San Francisco: How Close Are We?" After experts described their citywide efforts, Havlir, a clinician who heads the HIV/AIDS division at San Francisco General Hospital, invited questions from the audience.

"You guys are all doing great things," a man said. "Are you working together?"

Havlir was taken aback. "At that moment we recognized that we were really *not* working together," she said recently. That discussion sparked the Getting to Zero Coalition, which bands together UCSF, the city's health department, HIV/AIDS advocacy groups, and major hospitals. In January, the coalition released a strategic plan for ending the city's epidemic.

Although San Francisco has just 20% the population of BC, it is home to more HIV-infected people—an estimated 15,901 at the end of 2013, an adult prevalence of about 2%. One of the first cities to be hard-hit by HIV, San Francisco early on developed a strong response by combining the research and clinical resources of UCSF and the local health department. The city's epidemic surveillance is sophisticated and granular, including mapping of viral load levels by neighborhoods, which reveals where people are not controlling their infections. In 2010, San Francisco became the first jurisdiction to recommend immediate treatment for all HIV-infected people. Three years later, San Francisco General Hospital went a step further and launched a RAPID program that starts people on treatment the very day they are diagnosed, if possible. It also sends outreach teams to the streets to search for patients who miss appointments (*Science*, 13 July 2012, p. 175). Researchers at UCSF and the health department pioneered PrEP studies.

Exceptional as San Francisco's response has been, it also has serious shortcomings, which the strategic plan confronts with three "signature initiatives": scale up RAPID citywide, teach people about PrEP and make it easy to get—á la Shane Ryan's visit at Magnet—and work more diligently to keep people taking their ARVs. Testing is a not a big issue, as some 94% of infected people in the city know their status. But whereas 89% of those people see a specialist within 90 days, only 63% start on ARVs and achieve undetectable viral loads for prolonged periods. The Getting to Zero Coalition hopes to end AIDS by bringing that 63% up to 90% by 2020—an even more ambitious goal than the 73% set

Pedro Robles died from AIDS in a Tijuana, Mexico, hospice in 2013 without ever receiving treatment.

No end in sight

By **Jon Cohen**, *in Tijuana, Mexico*

On 6 December 2013, Pedro Robles spent 14 hours in an ambulance being driven up Mexico's Baja California Peninsula. The 51-year-old man was not rushed north for emergency medical care. Time was not of the essence.

Robles had an advanced case of AIDS, and he was being driven 1127 kilometers north from his home in Loreto to Albergue Las Memorias A.C. in Tijuana. A nongovernmental organization (NGO) arranged the trip, because Las Memorias is the only AIDS hospice on the entire Baja California Peninsula, Robles was broke, and Tijuana held out the remote hope that someone there could navigate the medical bureaucracy and maybe save his life. But Las Memorias itself, which also serves as a drug rehabilitation center and is largely run by its residents, has no trained medical staff. And although Las Memorias did what it could to make Robles comfortable, Tijuana ultimately failed him: He died 6 days later without ever having seen a doctor.

As the dream of ending AIDS catches hold in a growing number of locales (see main story, p. 226), Tijuana is hardly anomalous: Many places are still struggling to provide basic treatment and prevention services. Of course, people still die from AIDS in wealthy countries like the United States, which is visible from downtown Tijuana, but appropriate care is so readily available that AIDS hospices shut their doors years ago.

Like Tijuana, too many locales appear to be "running at a standstill" and are saddled by "poor strategy, absence of leadership, or inadequate resources," laments a prominent commission in a report in *The Lancet* last month, "Defeating AIDS–advancing global health."

The drop in HIV infections and AIDS-related deaths worldwide over the past dozen years has been impressive, the report says. But without a "massive and rapid expansion of a comprehensive AIDS response," the global toll—still more than a million new infections and deaths each year—will worsen again over the next 5 years, and the world will fail to reach the United Nations goal of "ending AIDS as a public health threat" by 2030.

Mexico is not particularly hard-hit by HIV. In 2014, UNAIDS estimated the country had 190,000 infected people, which is an adult prevalence of 0.2%—lower than in the United States. The government offers free antiretrovirals (ARVs) and, since

PHOTO: © MALCOLM LINTON

November 2014, has recommended that all HIV-infected people receive them as soon as diagnosed. "When you look back to what we were doing 10 years ago, we are really, really better," says Carlos Magis-Rodríguez of the National Center for HIV/AIDS Prevention and Control in Mexico City. But he acknowledges that Tijuana and other cities in Mexico are struggling.

Tijuana has what is known as a "micro-hyperepidemic." Overall HIV prevalence in Tijuana is 0.6%—the same as the United States. But the rate is soaring in high-risk groups. In women who sell sex, prevalence jumped from 2% in 2003 to 6% by 2012, according to recent studies by researchers from the University of California, San Diego (UCSD), whose team includes Mexico-based colleagues. Clients of these sex workers had a prevalence of 5%, they found. HIV prevalence is also about 5% in the many people in Tijuana who inject drugs. Preliminary studies of men who have sex with men and transgender people suggest about 20% are infected.

In theory, Tijuana should be able to rein in its concentrated epidemic by taking advantage of recent advances. Key among them is the 2011 demonstration that people who fully suppress their HIV levels with ARVs rarely spread the virus to their sexual partners. But this treatment-as-prevention strategy has not gained much traction in Tijuana. UCSD behavioral health scientist Laramie Smith recently pooled data from six studies of nearly 200 HIV-infected people in Tijuana and found that only about half even knew they had the virus. Tijuana offers free HIV testing through NGOs and government-funded clinics, yet no plan is in place to regularly test high-risk people at venues where they hang out, like gay bars or the red light district.

Those who do learn they're infected rarely get treatment. In Smith's study, only 11% received related medical care, and only 3.66% began taking ARVs. The federally sponsored HIV/AIDS clinic, CAPASITS, provides free ARVs, but it is located far from the downtown area and is difficult for many people to reach. Tijuana is also a hub for migrants, including many deportees from the United States, and some do not have the documents required to receive help at CAPASITS. And the services there fall short of those in developed countries: CAPASITS, for example, must ship patient blood samples to Mexico City for measurements of CD4 lymphocyte counts and HIV levels.

José Luis Burgos, a Tijuana-based clinician who works with the UCSD team, says a key problem is that the patient load in Tijuana outstrips the availability of qualified HIV/AIDS doctors. Burgos contends that Tijuana could train primary care physicians to diagnose and treat HIV/AIDS patients. "You need to demystify HIV care," he says. CAPASITS, he notes, has only three doctors and treats some 1000 patients. "What kind of care can you expect from three providers?"

Paradoxically, Mexico's rising economic status is hampering the fight. A 2011 grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria enabled two Tijuana NGOs to launch mobile needle-exchange units. But the grant ended in 2013 when Mexico achieved upper middle income status and became ineligible for Global Fund support. Tijuana's needle-exchange programs shriveled overnight. "Mexico is supposed to be upper middle income, but the border isn't," Burgos says.

The UCSD team soon documented a 40% increase in needle-sharing among a group of users that it has closely followed. That undermines other efforts to reach people with HIV, says UCSD epidemiologist Steffanie Strathdee, who leads the binational research program with her psychologist husband Thomas Patterson. "The sad thing" is when drug users come in for needle exchange, she says, "they have an opportunity to get HIV testing or a referral to a drug treatment program."

Strathdee hopes the group's extensive research will draw attention to the problems and the opportunities in Tijuana. "It's entirely possible to end the AIDS epidemic in Tijuana," she says. And if Tijuana can do it, so can much of the rest of the world. ■

"Mexico is supposed to be upper middle income, but the border isn't."

José Luis Burgos, University of California, San Diego

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by 90-90-90. The city's ending AIDS targets also include reducing new HIV diagnoses from 371 in 2013 to 37 in 2020 and HIV-related deaths from an estimated 91 to eight.

"The biggest challenges are reaching into marginalized populations that are not getting the services they need," says the health department's Buchbinder—transgender people, drug users, African-Americans, and the young. Getting to Zero is massively expanding the use of "navigators" assigned to infected people to help address barriers that interfere with care, such as substance abuse, food insecurity, homelessness, and violence. A new program will better coordinate medical records at different providers to help identify patients who are slipping through the net. And HIV-infected patients deemed at high risk of not taking ARVs will receive extra check-in phone calls and reminders for appointments.

Rigorous evaluation is critical for the campaign to succeed, said Havlir at a coalition meeting in June. Getting to Zero is raising money specifically to track the program's performance, using novel metrics like assessing the impact of PrEP on new infection rates. "This is not just talking, talking, talking," Havlir said. "This is about action."

THE DRIVE TO END AIDS is spreading worldwide, and there is even something of a good-natured race to be first. Washington, D.C., New South Wales in Australia, and Brazil are now in the running as well, and San Francisco has attracted intrigued delegations from Amsterdam, France, and the White House's Office of National AIDS Policy.

From his office at the London School of Hygiene & Tropical Medicine, which he directs, epidemiologist Peter Piot is watching these efforts with interest—and some skepticism. "It's very important that these projects proceed and that we learn from them," says Piot, who chaired the "Defeating AIDS" commission and formerly headed UNAIDS. But he cautions that the intensive efforts in BC, New York state, and San Francisco must continue indefinitely. "These three examples are not North Korean types of islands—there will be constant reintroduction of the virus," he notes.

Ending the global spread of HIV will ultimately take a vaccine, Piot says, stressing that treatment as prevention packs a limited punch. He points to a mathematical model in "Defeating AIDS" that found that even if the world achieves the UNAIDS 90-90-90 goal in 2030, hundreds of thousands of new HIV infections and deaths will still occur each year. "We'll have to see whether these three places can end AIDS as a public health threat," Piot says. "But that doesn't mean one shouldn't try." ■