

# Who Still Dies of AIDS, and Why

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*In the age of HAART, the virus can still outwit modern medicine.*

By Gary Taubes

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**The Departed** From left: top row, Glenn Williams, Thomas Morgan III, Bill Harmon; second row: Bob Hattoy, Vilma Santiago, George Drayton; third row, Mark Hayes, Stephanie Williams, Willi Ninja.

(Photo: Clockwise from top left: Courtesy of the AIDS Action Committee; courtesy of Tom Ciano; courtesy of Ocean Morisset; courtesy of Claudia Drayton; courtesy of Andrew Der; courtesy of Housing Works; courtesy of Bill Keyes; courtesy of Adrianna Shea; courtesy of Iris House/IrisHouse.org)

In the video, filmed last November, Mel Cheren appears understandably dismayed. He's being interviewed by a reporter for CBS News on *Logo*, a gay-themed news program; he's sitting in a wheelchair, and he's talking about the indignity and the irony of dying from AIDS at a time when AIDS should be a chronic disease, not a fatal one. Cheren, a music producer and founder of West End Records, had been an AIDS activist since the earliest days of the epidemic. It was Cheren, in 1982, who gave the Gay Men's Health Crisis its first home, providing a floor of his brownstone on West 22nd Street. In the interview, Cheren talks about what it's like to lose more than 300 friends to the AIDS epidemic, outlive them all, and then get diagnosed yourself at age 74.

Indeed, the fact that Cheren had plenty of sex through the height of the epidemic, had been tested regularly, and had apparently emerged uninfected had led him to believe that testing was no longer necessary, or at least so one doctor had told him half a dozen years earlier. He'd only learned the truth after he began losing weight, had trouble walking, and was finally referred to a specialist who didn't consider AIDS an unreasonable diagnosis for a man of Cheren's experience and advanced years and so ordered up the requisite blood test. "There was one guy," Cheren says in the interview, explaining how he might have been infected. A male escort. "We really hit it off, sexually ..."

By the time Cheren learned he had AIDS, he was already suffering from a rare, drug-resistant pneumonia, what infectious-disease specialists refer to as an opportunistic infection, and he had lymphoma, an AIDS-related cancer

that had spread to his bones.

Within a month of his diagnosis, Cheren was dead. The official cause was pneumonia, although, as his cousin Mark Cheren points out, cause of death in these cases is a moot point. “Infection from pneumonia was probably the culprit,” he says, “but only because that acts quickest when you don’t stop it.”

Dying from AIDS, or dying with an HIV infection, which may not be the same thing, is a significantly less common event than it was a decade ago, but it’s not nearly as uncommon as anyone would like. Bob Hattoy, for instance, died last year as well. Hattoy, 56, was “the first gay man with AIDS many Americans had knowingly laid eyes on,” as the *New York Times* described him after Hattoy announced his condition to the world in a speech at the 1992 Democratic National Convention. Hattoy went on to work in the Clinton White House as an advocate for gay and lesbian issues. In the summer of 1993, he told the *New York Times*, “I don’t make real long-term plans.” But the advent of an anti-retroviral drug known as a protease inhibitor, in 1995, and then, a year later, the multidrug cocktails called HAART—for highly active anti-retroviral therapy—gave Hattoy and a few hundred thousand HIV-infected Americans like him the opportunity to do just that.

If the pharmaceutical industry ever needed an icon for evidence of its good works, HAART would be it. Between 1995 and 1997, annual AIDS deaths in New York City dropped from 8,309 to 3,426, and that number has continued to decline ever since. The success of HAART has been so remarkable that it now tends to take us by surprise when anybody does succumb, although 2,076 New Yorkers died in 2006 (2007 figures are not yet available). Though many of the most prominent deaths, like Cheren’s and Hattoy’s, tend to be of gay men, the percentage of the dead who contracted the disease through gay sex is now reportedly as low as 15 percent (with a large proportion still reported as unknown). Intravenous-drug users make up the biggest group, 38.5 percent, and women account for almost one in three of total AIDS deaths.

One of the ironies of the success of HAART is that it has fostered the myth that the AIDS epidemic has come to an end, and that living with HIV is only marginally more problematic than living with herpes or genital warts. This is one obvious explanation for why HIV infection is once again on the rise among young men—specifically, MSMs, as they’re now known in the public-health jargon, for men who have sex with men—increasing by a third between 2001 and 2006. Among those 30 and over, the infection rate is still decreasing, notes Thomas Frieden, commissioner of the city’s Department of Health and Mental Hygiene, suggesting that the increased rate of infection among men under 30 is due in part to decreased awareness of the disease or the toll it can take.



From left to right: William “Violet” Silver, Sylvia Ocasio, and Mel Cheren.

(Photo: Courtesy of Matthew Rosenblum; courtesy of Iris House/IrisHouse.org; courtesy of Bryan Raughton)

“If you do the mathematics,” Frieden says, “HAART became available in 1996. If you were of age before then, sexually active, and you saw a lot of people dying or sick or disfigured from AIDS, maybe you’re more careful than if you came of age after 1996 and didn’t see that. When we’ve done focus groups, what young men have told us is that the only thing they hear about HIV these days is that if you get it, you can climb mountains, like Magic Johnson. Certainly it’s true that the treatment for HIV is very effective and it’s possible to live a long and productive life with an HIV infection. It’s also true that it remains an incurable infection. That the treatment is very arduous and sometimes unsuccessful. It remains a disease often fatal, and frequently disabling.”

At the moment, some 100,000 New Yorkers are infected with the HIV virus, and AIDS remains the third leading cause of death in men under 65, exceeded only by heart disease and cancer. The question of who will die from AIDS in the HAART era—or who dies with an HIV infection but not technically from AIDS—and what kills them is worth asking now that such deaths have become relatively infrequent.

**F**rieden’s Department of Health and Mental Hygiene tried to answer this question with a study it published in the summer of 2006. The newsworthy conclusions were that deaths among New Yorkers with AIDS were still dropping, thanks to HAART, and that one in four of these individuals was now living long enough to die of the same chronic diseases that are likely to kill the uninfected—particularly cancer or heart disease—although most of these non-HIV-related deaths were from the side effects of drug abuse. HIV-related illnesses were still responsible for the remaining three out of four deaths. Or at least “HIV disease,” in these cases, was recorded as a cause of death on the death certificates.

What the Health Department study couldn’t do is say precisely what these HIV-related deaths were. For the answer to this question, you have to go to physicians who specialize in treating HIV-infected patients. Michael Mullen, clinical director of infectious diseases at Mount Sinai School of Medicine, for instance, says the best way to think about AIDS deaths is to divide HIV-infected individuals into three groups.

*“If it’s 1988, 1989,” says one doctor, “and I have a patient with HIV disease and hypertension, he’s not going to live long enough to die of hypertension. I want to treat the disease.”*

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The bulk of these deaths occur within the first group, those who either never started HAART to begin with or didn’t stay on it once they did. For these patients, “it might as well still be the eighties,” says Mullen, and they die from the same AIDS-defining illnesses that were the common causes of death twenty years ago—pneumocystis pneumonia, central-nervous-system opportunistic infections (such as toxoplasmosis), lymphoma, Kaposi’s sarcoma, etc.

A large proportion of these victims are indigent; many are intravenous-drug users—IVDUs, as they’re known in the official jargon, accounted for 21 percent of HIV-positive New Yorkers in 2006, but, as noted above, 38.5 percent of the city’s AIDS deaths. The virus is no more aggressive or virulent in these cases. Rather, these are the people who either don’t or can’t do what it takes to fight it. “These individuals are repeatedly admitted to the hospital,” says Mullen, “sometimes for opportunistic infections, sometimes for drug-related issues, often for HIV-related lymphomas and malignancies. They will not take the medication, nine times out of ten, because of drug use.” Often these individuals are co-infected with hepatitis, which increases the risk that the more toxic side effects of the anti-retroviral drugs will lead to permanent liver or kidney damage.

By far the highest death rates in this group are in what the authorities now refer to as concurrent HIV/AIDS diagnoses. These patients never get diagnosed with HIV infection until they already have active AIDS. (Cheren, because of his age and his AIDS awareness, is an extreme case.) These constituted more than a quarter of the 3,745 new cases of HIV infections diagnosed in New York in 2006. “Those people have never been tested before,” says Mullen. “Believe it or not, people like this still exist.” Typically, they’ve had the infection for ten years—the average time between HIV infection and the emergence of AIDS—but won’t know it or acknowledge it until admitted to the emergency room with pneumonia or some other opportunistic infection. These individuals are twice as likely to die in the three to four years after their diagnosis as someone who was just diagnosed with HIV alone. Half of these deaths will occur in the first four months after diagnosis, often from whatever AIDS-related ailment led them to the emergency room in the first place.

It’s because of these concurrent HIV/AIDS diagnoses that the Centers for Disease Control and Prevention and the city’s Department of Health and Mental Hygiene have been lobbying for HIV tests to be given routinely to anyone who visits an emergency room for any reason. In one recent study from South Carolina, almost three out of four of those people with concurrent HIV/AIDS diagnoses had visited a medical facility after their infection and prior to getting their blood tested for the virus—averaging six visits each before they were finally tested and diagnosed. “By remaining untested during their routine contacts with the health-care system,” said Frieden, in testimony to the New York State Assembly Committee on Health, “they have missed the high-quality treatment that could improve their health and extend their lives. Many may have unknowingly infected their partners—and these partners may not learn that they are infected until they too are sick with AIDS. And so this cycle of death continues.”

The second group of HIV-infected patients consists of those at the other extreme, the ones who are least likely to die from AIDS or its complications. These individuals were diagnosed with HIV after the advent of HAART and have taken their medications religiously ever since. In these cases, HAART is likely to suppress their virus for decades, and they're now significantly more likely to die of heart disease or cancer than of anything related to AIDS. To get an idea of the mortality rate among these patients, consider Alexander McMeeking's practice, on East 40th Street. McMeeking ran the HIV clinic at Bellevue from 1987 to 1989 and then left to start a private practice. To the best of his knowledge, only three of his 300-odd Bellevue patients survived long enough to get on HAART. They are still alive today. "Fortunately, thank God, all three are doing great," says McMeeking. "I tell them they will essentially die of old age."

McMeeking's practice now includes 600 HIV-infected patients, and last year he lost only two of those—one to lung cancer, another to liver cancer.

Now the question is whether these patients doing well with HAART are actually more susceptible to the kind of chronic diseases that kill the uninfected. Are they more likely to die from heart disease, cancers, liver and kidney failure, and other chronic diseases either because of the HIV itself or the anti-retroviral regimen keeping it under control? One observation made repeatedly in studies—including the 2006 report from the Department of Health and Mental Hygiene—is that these HIV-infected individuals appear to have higher rates of several different cancers, in particular lung cancer among smokers, non-Hodgkins lymphoma, and cancers of the rectal area. These cancers appear both more precocious and more aggressive in HIV-infected patients—they strike earlier and kill quicker. The reason is not yet clear, although a likely explanation is that the ability of the immune system to search out and destroy incipient malignancies is sufficiently compromised from either the anti-retroviral drugs, the virus, or the co-existence of several viruses—squamous-cell cancers of the rectal area are caused by the same human papilloma virus that causes cervical cancer in woman—that the cancers get a foothold they don't get in non-HIV-infected individuals.

*"I still expect most of my patients to live a normal life expectancy," says an AIDS doctor, "but they may do so with a bit more nips and scrapes."*

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One finding that's considered indisputable is that HAART, and particularly the protease inhibitors that are a critical part of the anti-retroviral cocktail, can play havoc with risk factors for heart disease. They raise cholesterol and triglyceride levels; they lower HDL, and they can cause increased resistance to the hormone insulin. These changes often accompany a condition known as HIV-related lipodystrophy, which afflicts maybe half of all individuals who go on HAART. Subcutaneous fat is lost on the face, arms, legs, and buttocks, while fat accumulates in the gut, upper back (a condition known as a buffalo hump), and breasts. The question is whether these metabolic disturbances actually increase the likelihood of having a heart attack. It's certainly reasonable to think they would, but it's remarkably difficult to demonstrate that the drugs or the virus itself is responsible: The fact that a relatively young man or woman with AIDS has a heart attack does not mean that the heart attack was caused by HIV or the disturbance in cholesterol and lipid levels induced by the therapy.

Any difference in disease incidence between HIV-infected and uninfected individuals, explains John Brooks, leader of the clinical-epidemiology team within the CDC's Division of HIV/AIDS Prevention, can be due to the infection itself, to the therapy—HAART—or to “the host, the person who has HIV infection, both physiologically and socioculturally.” It's the last factor—the host—that complicates the science. Until recently, for instance, physicians saw little reason to worry about heart-disease risk factors in their HIV-infected patients and so didn't bother to aggressively treat risk factors in those patients, as they did the HIV-negative. “Think about it,” says Brooks, “if it's 1988, 1989, and I have a patient with HIV disease and hypertension, he's not going to live long enough to die of hypertension. I want to treat the disease.”

The rate of cigarette smoking among HIV-infected individuals is also twice as high as the national average. The rate of intravenous drug use is far higher, as is the rate of infection with hepatitis B or C, because intravenous drug use is a common route to getting both HIV and hepatitis. So the fact that an HIV-infected patient may seem to be suffering premature heart disease, diabetes, or liver or kidney disease earlier than seems normal for the population as a whole—or the fact that a study reports such a finding about a population of HIV-infected individuals—only raises the issue of whether the population as a whole is the relevant comparison group. “Since one of the major risk factors for HIV is intravenous drug use,” says Brooks, “you have to ask, what's the contribution of heroin to somebody's kidney disease versus the HIV versus untreated high blood pressure versus smoking?”

From his own clinical experience, McMeeking agrees that heart disease, certain cancers, and liver and kidney disease do seem to pose a greater threat to his HIV-infected patients than might otherwise be expected in a comparable uninfected population. “I still expect most of my patients to live a normal life expectancy,” he says, “but they may do so with a bit more nips and scrapes.”

The third group of HIV-infected individuals consists of those in the middle of the two extremes. HAART, in these cases, has literally been a life saver, but has not guaranteed a normal life expectancy. These are the patients, like Bob Hattoy, who were diagnosed with AIDS in the late eighties or early nineties, before the advent of HAART. They began on one drug (AZT, for instance) and then stayed alive long enough to get on protease inhibitors and the HAART cocktails. These patients were on the cusp of the HIV transformation from a deadly to a chronic-disease epidemic; they were infected late enough to survive but too early to derive all the benefits from HAART.

The anti-retroviral drugs of HAART work by attacking the life cycle of the virus. The earliest generation of HAART drugs attacked the enzymes that the virus uses to reproduce in the cells. (Protease inhibitors, for instance, go after an enzyme called HIV-1 protease, which the virus uses to assemble itself during reproduction.) The latest drugs go after the methods that the virus uses to enter cells in which it will replicate. The key to the effectiveness of HAART, as researchers discovered in the mid-nineties, was to include at least three drugs in the cocktail to which the patient's specific virus had no resistance. This would suppress viral replication sufficiently so that the virus wouldn't be able to mutate fast enough to evolve resistance to any of the drugs. But patients who began on one or two anti-AIDS drugs and only then moved to HAART already had time to evolve resistance to a few of the drugs in the cocktail. This

made the entire package less effective and increased the likelihood that they would evolve resistance to the other drugs as well.

“We call it ‘sins of the past,’ ” says Mullen. “We gave these patients sequential monotherapy; it was state-of-the-art at the time, and a lot of those people are alive today because of that. It got them through until HAART came along, but their HAART is not highly active, only fairly active. Their virus has baseline mutations that interfere with the response.” This group of patients also includes those who were infected initially with a strain of HIV already resistant to one or several of the components of HAART, or those patients who were less than 99 percent faithful in taking the regimen of pills that constitute HAART. Anything less than that and the virus has the opportunity to evolve resistance.

Perhaps a quarter of all new cases, says Mullen, are infected with a strain of the virus resistant to one or more drugs in the HAART cocktail. “You can’t use the frontline regimen, because the virus has already seen those drugs,” he says. “You have to go to more complicated regimens. This is why we do resistance testing before we start a person on medication. We see what drugs the virus has seen or is resistant to and can take that into account.”

Sins-of-the-past patients have to have faith that the pharmaceutical industry can stay one step ahead of their disease. The prognosis, at the moment, is promising. There are several entirely new classes of AIDS drugs, including one by Merck, called an integrase inhibitor, that was just approved by the FDA last October. A recent report of the discovery of 270 new human proteins employed by the AIDS virus to hijack cells and start replicating—the definition of a successful infection—means the pharmaceutical industry will not run out of new targets to block the infection in the near future.

Still, some sins-of-the-past patients simply do worse than others, and the occasional patient will lose the battle before new drugs come along or simply give up. “I had a friend who died last week,” one sins-of-the-past patient told me recently. “He just lost faith. He would get sick a lot, would get better, then sick again. Finally he decided to try Eastern medicine, and stopped taking his [HAART] medications entirely. It killed him. It’s not a good example, other than to show that people can reach their breaking point.”