

Treatment

Living with HIV, Dying of Tuberculosis

By Matthew M. Kavanagh

HIV does not kill people. People living with HIV/AIDS die of opportunistic infections. This is a basic medical principle that anyone on anti-retroviral (ARV) therapy can tell you—but 25 years into the HIV/AIDS pandemic global leaders seem to not to have gotten the message.

In the global south—Africa, Asia, and Latin America—tuberculosis (or TB) is the leading killer of people living with HIV and AIDS. Yet to look at the global response to HIV/AIDS, one could be excused for think-

Less than 1% of PLWHA have been screened for TB.

ing scientists had just discovered that keeping people alive requires more than ARVs.

According to the best available data from the World Health Organization (WHO), as few as 1% of people living with HIV/AIDS around the world are even screened for tuberculosis.¹ Of those who were screened for TB, more than one in four had active tuberculosis (Figure 2).

TB is killing hundreds of thousands of people living with HIV/AIDS every year worldwide, yet the response has been a near-complete failure. Where's the outrage? Where's the action?

Tuberculosis in the early days of the AIDS pandemic

Tuberculosis has been around for thousands of years. Yet in an era in which we can clone sheep and send information across the earth in the blink of an eye, TB continues

to kill two million people each year. Over nine million people develop active TB each year and an overwhelming 95% of these cases occur in the global South—yet we continue to use drugs and diagnostic tools developed over half a century ago and a vaccine we know is ineffective.²

The TB and HIV link is far from a new story. Indeed, in the US doctors and activists were panicked in the late 1980s and early 1990s as TB rates skyrocketed with the HIV pandemic and they struggled to get the twin

diseases under control. New York City, for example, saw a four-fold increase in TB rates between 1985 and 1988.³ AIDS groups filed lawsuits and ActUp New York staged a major demonstration at city hall—demanding that people living with HIV/AIDS (PLWHA) be given safe housing away from the TB wards and over-crowded shelters where they were placed at such risk.

A *New York Times* piece from the time captured well the fear in its title, “AIDS Patients, Facing TB, Now Fear Even the Hospital.” And the advice was clear: “Doctors advise that anyone infected with H.I.V. be tested for tuberculosis and, if positive, start taking the drugs that would help them avoid developing active disease.”⁴ That advice has changed little in the last 15 years.

New York has improved dramatically since then. The number of TB cases report-

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ed among PLWHA has dropped 90% since the early 1990s. Few of these people dying compared to the hundreds of deaths each year at the height of the city's TB-HIV co-epidemic.⁵ But those living in more impoverished cities across the world continue to face a high risk of getting TB.

A global crisis

In sub-Saharan Africa, which has the highest rates of both diseases, TB is the leading killer of people living with HIV/AIDS. HIV/AIDS has caused TB incidence to triple since 1990.⁶ Autopsy studies from across Africa have shown undiagnosed TB in 14–54% of people with HIV infection.⁷

In Southern Africa the estimates are even more overwhelming. In Swaziland, for example, almost 80% of those with TB tested for HIV are found to be positive. The Ministry of Health estimates that TB kills 50% of HIV infected patients and accounts for more than 25% of all hospital admissions.⁸

The emergence of drug-resistant TB is a growing threat to people living with HIV/AIDS. In one now infamous case in Tugela Ferry, South Africa, extensively drug-resistant TB spread through an HIV support group—killing 52 of the 53 people, most within weeks.

Living with HIV, but dying of TB: Where is the global action?

Ten years after the ActUp demonstrations, officials from WHO's Stop TB Department moved to clarify the need for TB testing for PLWHA, stating that "...those found to be both HIV-positive and with active TB need referral for TB treatment; those without active TB should be offered TB preventive treatment with isoniazid."⁹ The WHO and UNAIDS unveiled plans in early 2004 to expand collaboration between national TB and HIV/AIDS programs, promising that "TB case-finding will be intensified in high HIV prevalence settings by introducing screening and testing for tuberculosis into HIV/AIDS service delivery points."¹⁰

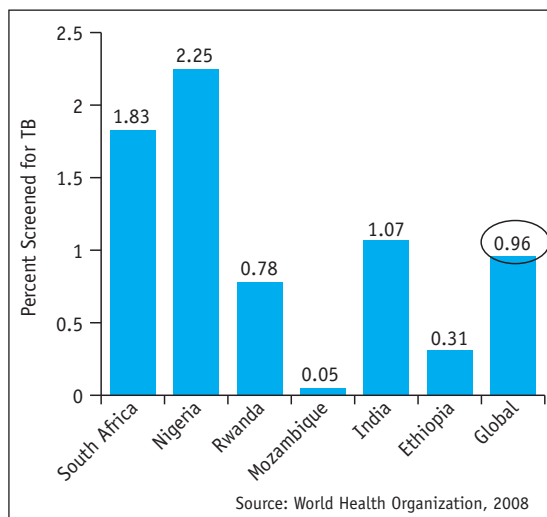
Nearly five years later, the evidence shows the response to be anemic at best.

A failing global response

One of the most logical indicators of whether AIDS programs are, in fact, taking seriously the threat of TB to people living with HIV/AIDS is the extent to which PLWHA are being screened

for TB. It is but one of the key interventions needed—in addition to providing preventive therapy and scaling up infection control. But it is perhaps the most measurable starting point.

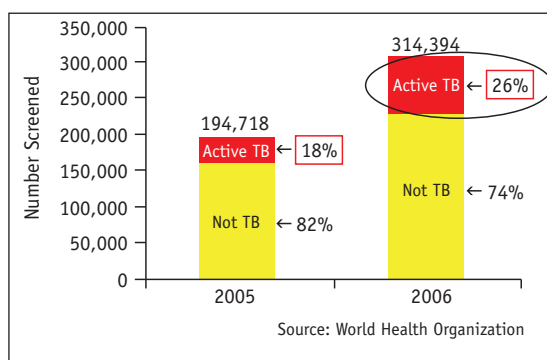
Figure 1. Percent of PLWHA screened for TB in select high TB burden countries and globally



The most recent WHO data show that a total of 314,394 HIV-positive people attending HIV care services were screened for TB. This is a total of 0.96% (less than 1%) of the total 33 million estimated PLWHA. In South Africa in 2006 only 1.83% of PLWHA were screened for TB; in Nigeria in 2007 2.25% of the estimated number of people living with HIV had been screened for TB.

One in four of the PLWHA who were screened had active TB (Figure 2). Without proper treatment, approximately 90% of PLWHA die within months of developing TB.¹¹ The standard of care is clearly to screen every person receiving HIV services for TB—so why are we so behind?

Figure 2. Global outcomes of screening PLWHA for tuberculosis



A second disturbing reality is that most countries and programs do not even know how many PLWHAs are being screened for TB. Researchers with the RESULTS Educational Fund and the ACTION Project spoke or corresponded with dozens of officials at WHO, UNAIDS, PEPFAR, the Global Fund, and the World Bank, as well as ministry or program officials in South Africa, Kenya, Botswana, Swaziland, and Lesotho. The answer across the board was the same: TB testing of PLWHAs is not currently being tracked and is universally understood to be quite low.

In Swaziland—whose TB-HIV rates are so striking—the health system was set to roll out a “pilot program” in August 2008.

Over 25 years into the pandemic—decades after knowledge of the TB-HIV link—how can we still be at the stage of pilot programs? How can we still be failing to even screen 99% of PLWHAs for the disease most likely to kill them?

Where do we go from here?

We must demand universal TB screening and care. Every HIV program in a high co-infection region should be regularly screening every PLWHA it serves for TB. It is important to recognize that TB screening is especially difficult for PLWHA—who often come up “negative” using the century-old TB diagnostic that involves technicians looking at sputum through a microscope. Nonetheless, a combination of laboratory and clinical screenings can be used to identify TB—and must be used to ensure PLWHA are not living with HIV and dying of TB.

Those with TB must have immediate access to treatment, and those who have not developed TB must be put on preventive therapy to protect against it. All too often the TB programs and the HIV programs are simply not coordinated—so people accessing free anti-retrovirals (ARVs) that may cost thousands of dollars are still dying because they cannot access the \$20 course of TB treatment.

PLWHA in the global south deserve infection control measures that work. Increasingly, as ARV treatment has been scaled up across the world, reports are coming that these treatment centers are becoming breeding grounds for TB as people wait for hours in small, unventilated spaces. Simple measures like fans and windows can help stop TB from spreading.

Those of us in wealthy countries must hold the big AIDS donors accountable for providing good public health to people around the world. None of the three biggest—the Global Fund to Fight AIDS, TB, and Malaria, the Presidents Emergency Plan for AIDS Relief (PEPFAR), or the World Bank—has a concrete plan to ensure that all the people being reached by advanced AIDS treatment are being screened for the disease that’s most likely to kill them.

And we must also value impoverished people at least as much as we value male baldness, erectile dysfunction, and other conditions that can be solved by a little blue pill. Research and development are badly needed for a truly effective TB vaccine as well as new treatment and diagnostics. It is outrageous in our scientific era that the chief way people are diagnosed with TB is through a single person’s looking through a microscope hoping to spy bacilli. In southern Africa we hear of labs with backlogs so long that the weight of racks of petri dishes awaiting attention is actually cracking the floor. It’s time for a 21st century response to this centuries-old disease.

And finally, what is most needed is a global activist response. Amazing groups like ActUp in the US and the Treatment Action Campaign in South Africa having taken on TB-HIV in a serious way, but they cannot do it alone. Activism was key to pressuring companies and regulatory agencies to research and develop the drugs that are keeping so many alive and the push to ensure universal access to them. Likewise, it is through activism that we will see the end of the TB crisis.

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Food insecurity, malnutrition and HIV/AIDS treatment: A global perspective

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Malnutrition is a general term describing improper nutrition, either in excess or deficiency. Some examples include protein and/or calorie deficiency, micronutrient deficiency and over-nutrition resulting in obesity.¹ Manifestations of malnutrition vary globally. In resource-poor areas described in this paper, it manifests as kwashiorkor (protein malnutrition), and marasmus (protein and calorie malnutrition), or the deficiency of specific nutrients. In New York City, a resource-adequate setting, the majority of malnutrition takes the form of obesity, with possible deficits in micronutrients due to consumption of food available in low-income communities.

While malnutrition is exhibited differently depending on location, food insecurity is present everywhere. We define food insecurity as the lack of regular access to ample quantity and quality of safe, nutritious food that meets dietary needs as well as food preferences of individuals and communities.

This article examines the effects of malnutrition and food insecurity in the global HIV/AIDS community, and proposes possible solutions to decreasing global malnutrition and food insecurity.

There is a large body of evidence that supports that inappropriate food intake negatively impacts immune function.^{2,3} Deficits in certain micronutrients such as vitamin A,⁴ vitamin C,⁵ vitamin D,^{6,7,8,9} zinc,¹⁰ selenium,^{11,12} copper,^{13,14} and iron^{15,16} impair immune function. A high content of dietary fatty acids, specifically saturated fat, plays a role in immune suppression.¹⁷ Protein deprivation decreases many body functions including the production of inflammatory mediators that are needed to fight infection.^{18,19}

Studies completed before and after the advent of Highly Active Antiretroviral Therapy (HAART)²⁰ show that wasting (a form of malnutrition) is a predictor of death for HIV-positive individuals.^{21,22,23,24} A groundbreaking 2006 study done in 2006 found that moderate to severely malnourished people starting HAART experienced a six-fold higher hazard ratio for death. Those starting Antiretroviral Therapy (ART)²⁵ who were moderately to severely malnourished were twice as likely to die as those who were not malnourished. Malnutrition decreases survival in patients starting ART and HAART for several possible reasons: impairment of immune reconstitution and in turn a prolonged period of opportunistic infection risk; adverse effects on drug absorption; lower threshold for drug toxicity; and/or decreased physical function.²⁶

Food insecurity plays a major role in the development of malnutrition in resource-poor and resource-adequate settings. In resource-poor settings, there is decreased or no adult labor in HIV/AIDS affected households. These households have less capacity to produce or purchase foods and have higher medical costs. In addition, children often stop their schooling to work, or simply because the family affected by HIV can no longer afford the education. Research in Tanzania showed that food consumption decreased 15 percent per capita when an adult died. Funeral costs deplete monies that could be used for food. The agricultural knowledge base of families and communities decreases as individuals with farming and science knowledge die from HIV/AIDS.²⁷

Women are especially vulnerable in HIV/AIDS-affected households. Usually, they care for the sick and dying in addition to maintaining heavy workloads related to gathering food and feeding the household. If the mother dies of HIV, often the family goes hungry because of

decreased means of food gathering and preparation. One study showed that food insecurity and malnutrition were the most immediate problems faced by female-headed households affected by HIV/AIDS in Uganda.²⁸

Our work with hundreds of clients in New York City has demonstrated many similarities among our food insecure population. Food assistance programs are not geared towards people living with HIV/AIDS who have increased nutritional needs. In addition, there are few supermarkets or places that offer fresh, whole foods in low-income neighborhoods. Markets that do carry these types of foods tend to be very expensive. This makes it difficult for HIV-positive individuals to obtain nutritious foods through food stamps and other supplemental subsidies.

Due to the lack of nutritious foods accessible to low-income HIV-positive individuals, many eat foods that contain a high amount of refined carbohydrates, saturated and trans-fats, and calories with little micronutrient value. Because of this we see many obese clients with diseases characteristic of the general obese population.

Food insecurity in itself is a risk factor for HIV/AIDS transmission. Malnutrition has been shown to increase transmission of HIV from a pregnant woman to her fetus, which remains a major issue in the developing world.²⁹ In addition, because of food insecurity and decreased access to safe water supplies, HIV-positive mothers are forced to breastfeed their children, which further increases the risk of HIV transmission.³⁰

In addition to mother to child transmission, food insufficiency is associated with increased HIV risk-taking behavior and sex exchange. A recent study of food security and HIV risk behaviors interviewed 2,051 adults in Botswana and Swaziland. The individuals were asked information about their food intake over the previous 12 months. Condom use, sex exchange, and other HIV risk-taking behaviors were examined. For women, sex exchange was defined as exchanging sex for food, money or other resources; for men, sex exchange was defined by paying for or providing resources for sex. HIV risk behaviors included inconsistent condom use, intergenerational sex and lack of control over sexual relationships. Of all study participants, 32% of women and 22% of men experienced food insufficiency in the previous 12 months. This study sends a clear message

that without adequate food, individuals may surrender long-term health and safety to survive in the present.³¹

A program in the Democratic Republic of Congo (DRC) demonstrates that when multiple institutions work together, societies can successfully diminish malnutrition and food insecurity. Bukavu, like other cities in the DRC and around the globe, suffers continual conflict and humanitarian crises. Many structures—including society, economy, and health care system—are near collapse. Because of the lack of infrastructure, and security, deploying effective social programs is difficult. However, in 2003, Médecins Sans Frontières (Doctors Without Borders) worked with the Food and Agriculture Organization of the United Nations and the World Food Programme of the UN to create a food security program for HIV-positive individuals in Bukavu. This included distribution of seeds, tools and agricultural support, as well as a nutrition support system which distributed food rations and nutrition education to over 200 families. This program improved the medical management of HIV, as demonstrated by overall weight gain. If many more medical and nutrition agencies collaborated together, using Bukavu as an example, there would be more success in overcoming the challenges of food insecurity, malnutrition and HIV.³²

Clearly there is overwhelming evidence that confronting malnutrition and food security in the HIV/AIDS community is necessary to successfully treat the disease. It is imperative that in addition to increasing access to HIV medications, organizations must also provide nutritious, safe and sustainable food assistance.

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Transgender people, hormonal therapy, and HIV treatment interaction

Darby Hickey

"More than 25 years after the first report of AIDS, the disease continues to affect the [men who have sex with men] population more than any other in the United States," according to the Center for Disease Control and Prevention's (CDC) *Morbidity and Mortality Weekly Report* of September 12, 2008.¹ New data released by CDC in August showed that annual estimates of new HIV infections are 40% higher than previously thought—about 56,000 people a year. The communities hit hardest are African American men and women, Latinos, and gay and bisexual men of all races.² Within these carefully drawn categories, some based on behavioral risk factor and others on racial, gender and sexual classifications, one community heavily affected by the epidemic remains invisible in the eyes of officialdom a quarter century since the first reports of the disease: transgender people.

Studies of female transgender individuals have reported HIV positivity rates ranging anywhere from 19 to 47%.³ A San Francisco study found that while 35% of transgender women were HIV+, only 2% of male transgender individuals were HIV+.^{4,5}

Several factors place transgender women at elevated risk. Melendez and Pinto describe a need among female transgender individuals to feel safe and loved by a male companion, which can lead to risky behavior and elevated risk of HIV acquisition. Stigma and discrimination also correlate with high risk behavior. One study of transgender individuals reported that over half of the participants reported some form of harassment or violence in their lives, and over 25% reported experiencing a violent incident.⁶

Although not all transgender people take hormones as part of their gender transition, a great many do. For those who are also HIV positive and taking anti-retrovirals, there is "so much that is unknown," says Chloe Dzubilo, a long term HIV

survivor and activist on AIDS and trans issues in New York. Dzubilo, who learned of her diagnosis in 1982, says she is shocked at how little is known not only about the interactions of hormones and HIV medications, but also about the long term effects of HIV medications in general. “Knowledge about hormones is a missing piece,” says Dzubilo. “It’s multi-layered,” she continues, noting additional factors, such as Hepatitis C co-infection, lack of access to hormones accompanied by medical supervision, and changing self-perceptions about one’s own desires for transition. For so many transgender people who are only able to get hormones off the “street” (often through social networks), the implications of taking hormones without medical supervision presents a giant question mark. “Nobody knew what we were taking,” said Dzubilo, “so how do they know what’s happening with HIV meds and hormones?”

For Dr. Robert Garofalo of Northwest University in Chicago, “interactions between hormones and HIV therapies are not always the most important consideration.” Garofalo runs an adolescent HIV program through Childrens’ Hospital and the Howard Brown center, and has worked with transgender health in the youth and adolescent context for over a decade. He describes overall lifestyle challenges to HIV treatment adherence. Some are no different from those of other patients, while some are unique to trans youth—the difference between remembering to take specific medications at certain times each

GlaxoSmithKline warns of a “significant decrease” in potency of amprenavir when co-administered with estrogen.

day as opposed to getting a hormone injection every two weeks, for example. Garofalo states what many others say—“there is no official contraindication between HIV medications and hormone therapy.” When asked how that is the official medical perspective when so little information exists about the combination of the two, he admits “that’s a great question.” JoAnne Keatley, Director of the Center for Excellence for Transgender HIV Prevention at the Pacific AIDS

Education and Training Center in San Francisco, agrees that “hormones are not contraindicated” for people taking HIV medications.

“There needs to be a paradigm shift,” says Dr. B.W. Furness, cofounder of the transgender health clinic at Whitman Walker Clinic, in Washington, DC. “Once that shift happens and there are grant [funding] streams, you will get more data.” That criticism is voiced by transgender activists as well as other doctors and researchers. “There needs to be money for research,” Furness says, a point Dr. Garofalo of Chicago echoes, noting additional barriers. “It’s something National Institutes of Health, clinical trials networks, pharmaceutical companies should get interested in,” yet being on “hormone treatment might make a trans person excluded from a trial. Even if they’re not [explicitly] excluded, they’re probably underrepresented similar to adolescents, so for trans adolescents, it’s a double whammy.”

Despite the shortage of clinical data, experts in the field who have published on the subject have come to similar conclusions about what they know about ARV and hormone therapies. Drs. Lynn E. Connolly and Lori Kohler, in a 2006 article for University of Washington’s HIV Web Study, write that the metabolism of hormones differs from the metabolism of nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs and NtRTIs).^{7,8} There have been no documented interactions between hormones and NRTIs/NtRTIs, according to Connolly and Kohler. It’s a different story with non-nucleoside reverse transcriptase inhibitors (NNRTIs) and protease inhibitors (PIs). Those classes of HIV drugs mainly affect hormone levels in a patient’s blood, while hormones usually have not been documented to alter ARV potency, with some exceptions. “Although numerous antiretroviral medications can alter estrogen levels,” write Connolly and Kohler, “the effect of estrogen compounds on antiretroviral medication levels appears to be limited to a few antiretroviral medications, namely amprenavir (Agenerase) and the amprenavir pro-drug fosamprenavir (Lexiva).” GlaxoKlineSmith prescribing information quoted by Connolly and Kohler showed a “significant decrease” in potency of amprenavir when co-administered with estrogen for a month in ten patients, “suggesting that

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this drug combination may lead to a loss of virologic control and possible amprenavir resistance.” A number of NNTRIs and PIs can increase or decrease levels of hormones, which can cause problems if not properly monitored by a doctor a few times a year.

The sources of clinical information on the interaction between hormones and HIV medications are not studies involving trans people but women taking contraceptives simultaneous with HIV drugs. A February 2007 presentation by Drs. Barry Zevin and Linette Martinez asserts that there has actually never been such a study specifically of transgender people on both hormone therapy and ARV.⁹ Zevin and Martinez are affiliated with the Tom Waddell Clinic in San Francisco (under the city's Department of Health), which published “Protocols for Hormonal Reassignment of Gender” originally in 1998. They directly address concerns about interactions between testosterone and ARV taken by HIV positive transgender men, which obviously cannot draw parallels from research on contraceptives which contain estrogen.¹⁰ The Tom Waddell Clinic protocols highlight the particular impor-

tance of monitoring liver function, for both trans men and trans women. This is not a reason to deny hormone therapy but an incentive for working to keep transgender patients with HIV or infection with Hepatitis C in care, and feeling positive about themselves and their transition. Specifically referencing HIV, the protocols state “HIV is not a contra-indication or precaution for any of our protocols. While drug-drug interactions may occur we know of no specific dangerous interactions or likely causes of drug failure. Treatment with hormones is frequently an incentive for patients to address their HIV disease.”

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