

# GAFFI POLICY BRIEF



## Minimizing fungal disease deaths in advanced HIV disease and AIDS

### Overview

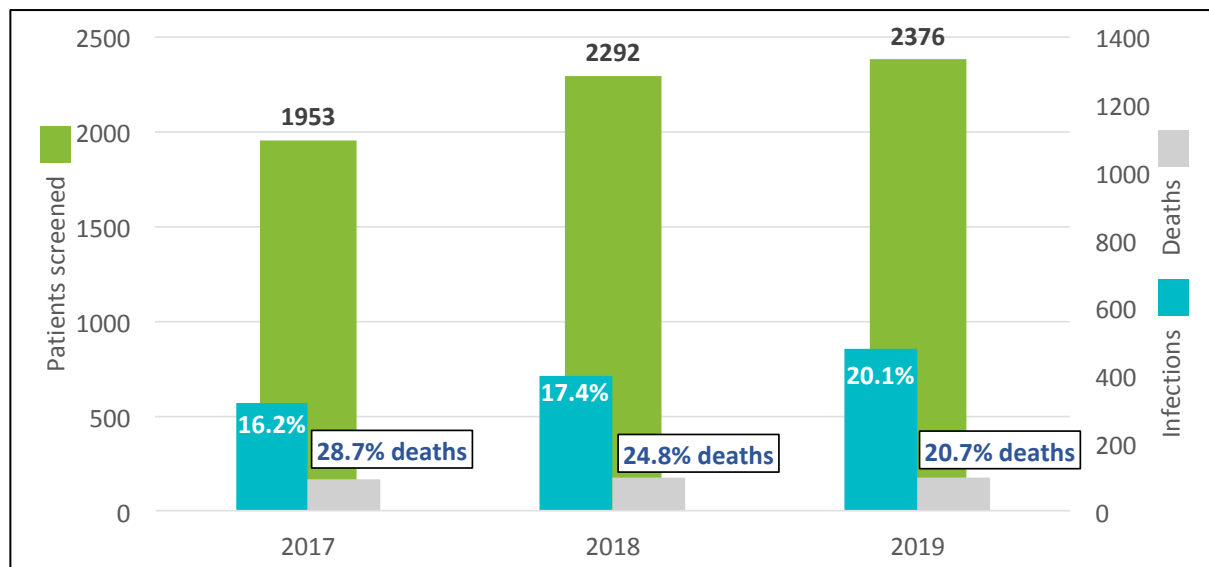
An estimated 38 million people live with HIV infection, of which approximately 4.4 million have advanced HIV disease, and are at high risk of dying. About 680,000 people died of AIDS in 2020, with an average age of 35 years. Nearly 100,000 children die of AIDS annually, and most who are infected in utero don't make it past their second birthday.

AIDS itself is not the cause of death; it is the infections that are lethal as AIDS leaves patients vulnerable as their immune system ceases to function. **Fungal infections<sup>1</sup> cause more AIDS deaths than tuberculosis (TB), but over half of these fungal disease deaths are avoidable.**

### Rapid accurate diagnosis is key to reducing deaths

The recent revolution in diagnostics enables quick and accurate detection of the major fungal infections in AIDS. They are listed on the WHO Essential Diagnostic list.

In Guatemala, GAFFI has demonstrated that rapid diagnosis saves lives. A centralized diagnostic hub received specimens on a daily basis from 13 HIV units around the country. Samples were screened for TB, cryptococcal and *Histoplasma* infections. Results were sent electronically to each centre within 1-2 days. An increasing number of people were diagnosed with life-threatening infections from 2017-2019 (see figure), and there was an 8% fall in deaths over those 3 years<sup>2</sup>. This was not due to changes in therapy as no additional treatments were available in Guatemala over this period.



### Who is most at risk?

In countries with high HIV burdens, 30-45% of people are diagnosed with HIV infection when they come to the hospital, very sick and with poor immune function.

<sup>1</sup> The most common lethal fungal infections in AIDS are *Pneumocystis pneumonia* (~15%), cryptococcal meningitis (~5%, but 15% of deaths), disseminated histoplasmosis (2-8%, depending on locality, with a high mortality), talaromycosis in SE Asia and aspergillosis (~4% of AIDS deaths)

<sup>2</sup> <https://gaffi.org/where/demonstration-site/>

Immunity wanes during HIV infection, reaching critically low levels usually 5-7 years after infection. A proxy measure of poor immune function is a CD4 cell count less than 200, in adults (normal over 800). In the best scenarios, laboratory testing of CD4 counts usually takes one or two days, but a new point of care CD4 test is being deployed which takes 30 minutes to determine if a person has a CD4 count under 200. If low, this triggers an immediate search for lethal infections in the best HIV units.

### Treatment background

Antiretroviral medication (ART) is critical for health in those with HIV, but too many abandon therapy. Some people have antiviral resistance which allows HIV resurgence and a downward trajectory of immune function. UNAIDS notes that only 27.5 million (73%) people are taking ART, and 5% to 23% have resistant virus. Both those who stop ART and those with ART resistance are at similar risk of life-threatening infection as those who have never started ART and have a low CD4 count. Over half those coming to hospital very ill with fungal disease have been prescribed ART previously.

Viral control with ART can be assessed with HIV viral load, but this is a poor indicator of immune system deficiency. Therefore, CD4 counts and HIV viral load tests are complementary, and both need to be used together for maximum impact in reducing deaths.

### Antifungal treatment saves lives

Serious fungal infections in HIV-infected patients are 100% fatal if not treated. All antifungal drugs for treatment in AIDS are listed on the WHO Essential Medicine List and should be available everywhere.

Antifungal therapies generally available	Antifungal therapies not generally available
Cotrimoxazole and fluconazole are widely available and inexpensive	Flucytosine and liposomal amphotericin B are not registered or available in most countries <sup>3</sup>
Main limitation to successful therapy is accurate diagnosis of infection	Flucytosine improves survival by 25% in fungal meningitis.
Both drugs also used for preventative therapy at lower doses, which are ineffective if infection is already established	Liposomal amphotericin reduces mortality by 25-50%, is used for fungal meningitis, histoplasmosis and talaromycosis. It is less toxic to the kidneys than conventional amphotericin and can be given in a shorter intravenous course.

### GAFFI recommends that:

1. Access to fungal disease diagnostics should be as close as possible to the patient, in clinics, local laboratories, or diagnostic hubs – but all need to provide results in a short time frame.
2. CD4 counts are necessary to stratify risk for life-threatening infections at the point of care.
3. Access to cryptococcal antigen testing is provided in every clinical setting caring for patients with HIV.
4. *Pneumocystis* PCR be used to rapidly diagnose pneumonia and be made available as close to patients as possible, primarily to allow for discontinuation of the

<sup>3</sup> <https://gaffi.org/antifungal-drug-maps/>

standard (but toxic) cotrimoxazole medication used for empiric therapy, once the diagnosis is ruled out.

5. *Histoplasma* antigen tests be made available in areas where the disease is endemic.
6. Antigen testing for talaromycosis be made available where the disease is endemic.
7. All antifungals listed in the WHO Essential Medicines List be registered in each country and used for their approved indications.
8. Country guidelines for the management of infections complicating AIDS reflect the updated WHO global guidelines, within a few months of WHO publication.
9. Countries put as much emphasis on reducing deaths associated with AIDS as on ART planning and rollout in their country plans.

#### **How much will these recommendations cost?**

The global cost of screening for fungal meningitis in AIDS is about \$17 million and for treating it ~\$65 million, with the likelihood of saving more than 80,000 lives annually. The costs of diagnosis and management of the other potentially lethal infections in AIDS is usually lower than fungal meningitis as less medication is required.

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