

Nix-TB: Testing a New Potential Treatment for XDR-TB

Tuberculosis has evolved faster than our medicines

Extensively drug-resistant tuberculosis, or XDR-TB, is a strain of tuberculosis, airborne and infectious, that is resistant to four commonly used anti-TB drugs. Essentially, there is no cure and XDR-TB is often considered a death sentence. XDR-TB has been confirmed in more than 100 countries around the world. There are an estimated 40,000 people infected with XDR-TB today—nine percent of all multidrug resistant-TB (MDR-TB) cases—and the problem is growing worse. Without new treatments, XDR-TB is emerging as an extremely deadly and costly global health threat that the world is inadequately equipped to tackle.

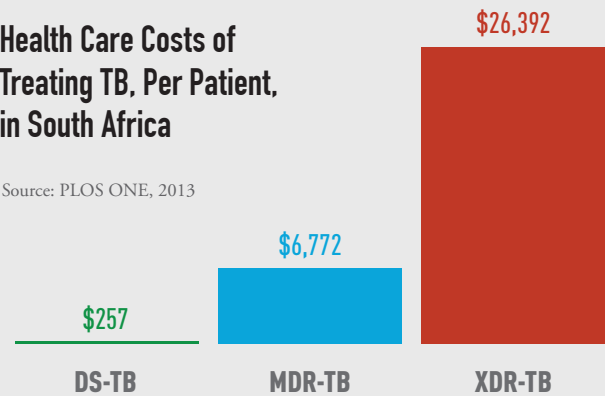
Current care and treatment for XDR-TB

There is no regulatory-approved regimen for curing XDR-TB. Instead, healthcare providers try to individualize treatment, often using antibiotics not normally used for TB, as well as highly toxic medicines not intended to be used for the length of time that TB treatment requires.

Treatment of XDR-TB routinely lasts two years or longer, and consists of thousands of pills plus injections and horrible side effects. It is also extraordinarily costly. In South Africa, for example, the per patient health care cost of XDR-TB is \$26,392, four times

Health Care Costs of Treating TB, Per Patient, in South Africa

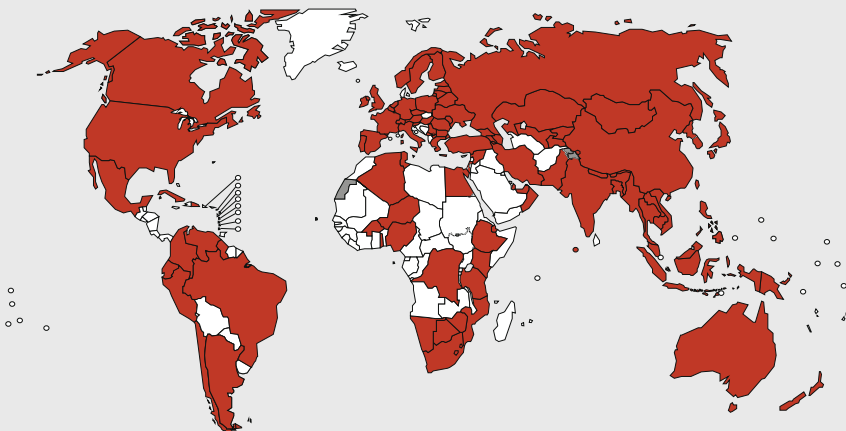
Source: PLOS ONE, 2013



greater than MDR-TB (\$6,772), and 103 times greater than drug-sensitive TB (\$257). Drug-resistant TB comprises only 2.2 percent of South African cases, but it consumes 32 percent of the country's total TB budget.

Despite the length, cost, and intensity of the treatment, outcomes are extremely poor. In one study published in the *Lancet* in 2014, after two years of treatment, only a fraction (16 percent) of people with XDR-TB were cured and nearly half (46 percent) died.

More than 100 countries have reported XDR-TB



Source: World Health Organization, 2013



XDR-TB patients are often isolated or quarantined because of the public health risk of contagion, a measure that is costly for countries and also takes a massive toll on patients and their families. However, this public health measure has failed to contain XDR-TB since patients who fail on treatment—the vast majority—are often discharged back into their communities, where they risk spreading the disease even further.

Worse, most XDR-TB is not treated at all because the cost and complexity of such programs are out of reach for many health systems in TB-endemic countries.

Nix-TB trial: Hope in research

TB Alliance and partners have launched the world's first clinical trial to study an XDR-TB drug regimen with minimal pre-existing resistance. If successful, the injection-free regimen being tested in Nix-TB could transform XDR-TB treatment, with patients being cured by taking a relatively short, simple, and effective regimen. Importantly, the regimen being tested could reduce the complexity and cost of the treatment to a fraction of what it is today, facilitating the global implementation of XDR-TB treatment in resource-poor nations.

Nix-TB tests a three-drug regimen consisting of bedaquiline, which received conditional regulatory approval in several high-TB disease burden countries; the novel antibacterial drug compound pretomanid, which is being tested in multiple clinical trials for TB; and linezolid, an oxazolidinone that has been used off-label to treat

TB. The trial brings hope to those with XDR-TB who have no other treatment options. It includes patients as young as 14 and those who are co-infected with HIV with a CD4 count of 50 or higher.

Nix-TB is an open-label trial that enables patients to be assessed at regular intervals with the aim of being cured in six to nine months. After completing treatment, participants are monitored for two years to ensure they do not relapse. The trial has an adaptive design; if improved treatments become available during the course of the study, they can be incorporated into the trial.

Nix-TB is a partnership between TB Alliance, the sponsor of the trial; Janssen Pharmaceuticals, the discoverer of bedaquiline; and the sites in South Africa where the study is being conducted (Sizwe Hospital, TASK at Brooklyn Chest Hospital, and THINK at Doris Goodwin Hospital.) The study may expand to include other partners and sites.

Pursuing a universal regimen

Nix-TB study is a crucial first step toward establishing a truly “universal” treatment, a regimen to which there is no pre-existing resistance and could therefore treat any type of TB. If the regimen tested in Nix-TB is successful and safe, the study will expand to include people with MDR-TB and then, potentially, people with drug-sensitive TB. Having a regimen that would be usable in such a broad range of TB patients could significantly improve TB control efforts globally.

