

## State of the Globe: Tracking Tuberculosis is the Test of Time

Thousands of years after tuberculosis (TB) ravaged ancient cultures stretching from Greece to Egypt, more than a century after the *bacillus* responsible for the disease was first identified and decades after the first antibiotic-based treatments appeared, TB continues to thrive.

When the World Health Organization (WHO) was established in 1947, one of its priorities was TB control.<sup>[1]</sup> TB continues to thrive in developing countries and is re-emerging in the industrialized world. Millennium development goals (MDG) target (6.c) states that the prevalence and mortality rates due to TB should be halved by 2015 compared with their level in 1990.<sup>[2]</sup> WHO has developed a new six point Stop TB Strategy to dramatically reduce global burden of TB by 2015 in line with the MDG.<sup>[3]</sup> Stop TB Strategy aims at ensuring that all TB patients, including, those co-infected with HIV and those with drug-resistant TB, benefit from universal access to high-quality diagnosis and patient-centered treatment. The primary vision of the Stop TB Partnership is “*A world free of TB by 2050.*” The mission involves pursuing high quality DOTS expansion and enhancement through six principal components. This strategy builds on the successes of “Directly Observed Therapy, Short-course” (DOTS), goal that at least 70% of new smear-positive cases should be detected and treated with DOTS, and at least 85% of new smear-positive TB cases should be successfully treated.<sup>[3,4]</sup>

While both preventable and curable, TB remains one of the world's major causes of illness and death and is one of the most frequent causes of death in people infected with HIV in resource poor countries.<sup>[5]</sup> Overall, one-third of the world's population is currently infected with the TB *bacillus*. 5-10% of people who are infected with TB bacilli (but who are not infected with HIV) become sick or infectious at some time during their life. People with HIV and TB infection are much more likely to develop TB.<sup>[5]</sup> Someone in the world is newly infected with TB bacilli every second. On average, someone dies from TB every 15 s and over

2 billion people carry strains of *Mycobacterium tuberculosis*.<sup>[6]</sup> TB burden is not evenly spread and TB disproportionately affects people in resource-poor settings, particularly those patients whose immune systems are weakened by HIV particularly those in Asia and Africa.<sup>[7,8]</sup> Twenty-two countries are considered “high-burden countries (HBCs),” which account for approximately 80% of new TB cases each year; most HBCs are in Africa and Asia. India, China, Indonesia, South Africa, and Nigeria have the highest number of new TB cases in the world.<sup>[8]</sup>

Africa, with 3 million new TB cases, accounts for almost a third of the global total and has the highest incidence and prevalence rates of any region. Fourteen of the 15 countries with the highest incidence rates in the world, and 9 of the 22 HBCs, are in Africa. In 2007, Africa's case detection rate was the lowest in the world.<sup>[9]</sup> The developing countries have 90% of the world's TB burden where more than 90% of new TB cases and deaths occur, posing significant challenges to the individual's livelihoods and developing economies as TB primarily affects people during their most productive years.<sup>[9,10]</sup> India is one of the 22 HBCs and has 30% with some 2 million new cases reported there annually. WHO estimates that the largest number of new TB cases in 2008 occurred in the South-East Asia region, where 1.3 million people died in the same year. This region accounted for 34% of incident cases globally.<sup>[11]</sup>

TB and HIV are frequently referred to as co- or dual epidemics due to their high rate of co-infection.<sup>[7,12]</sup> The HIV epidemic has been largely responsible for the resurgence of TB starting in the 1980s, as HIV weakens the immune system, increasing the likelihood that an individual with latent TB will become infected and develop active TB.<sup>[12]</sup> Additionally, TB is harder to diagnose and progresses more rapidly in someone with HIV. As a result, TB is a leading cause of death among people with HIV, especially in developing countries.<sup>[12]</sup> TB is commonly associated with poverty and is prevalent in undernourished individuals. This problem is further exacerbated by the pervasive use of ARV drugs that can damage the immune system of AIDS patients. An estimated 1.4 million of the 9.3 million new TB cases were also HIV positive in 2007.<sup>[9]</sup>

In some parts of Africa, up to 80% of TB patients are estimated to be HIV-positive. TB and HIV both compromise the nutritional status of the infected persons,

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leading to malnutrition, which in turn aggravates the severity of HIV and TB. In fact, the term “triple trouble” was coined to describe the deadly connection between HIV, TB, and malnutrition. HIV infection compromises the host’s immune defenses and can lead to failure to control latent *M. tuberculosis* infection with the subsequent development of active (symptomatic) TB<sup>[12]</sup>. The majority of people who are co-infected with TB and HIV live in sub-Saharan Africa. The “triple trouble” of HIV and TB infection and malnutrition may put those infected at greater risk than those with any of the three conditions alone.<sup>[13]</sup>

Risk factors for developing TB include: being around someone with active TB; having a chronic illness such as diabetes; being immunocompromised either from HIV, chemotherapy for patients with cancer, end-stage kidney disease, prolonged steroid use, working in the health care field; living in a long-term care facility, such as a nursing home, mental institution, or prison. Older people are also at an increased risk of developing TB. People on high dose steroids are immune-deficient in every way. Social factors such as poverty, overcrowding, and homelessness are also risk factors of TB.<sup>[6,14]</sup>

Another social risk factor of TB is alcohol. It has long been evident that there is an association between alcohol use and risk of TB. The risk of active TB is substantially elevated in people who drink more than 40 g alcohol per day and/or have an alcohol use disorder. This may be due to both an increased risk of infection related to specific social mixing patterns associated with alcohol use and influence on the immune system of alcohol itself and of alcohol-related conditions.<sup>[15]</sup>

Most of the TB patients seek healthcare from individuals or private practitioners which are the main source of unreported TB cases. Such patients prefer private health care providers to the public facilities which are either inaccessible or offer poor services as reported in a recent study carried out in India. Private practitioners ask few questions and do not disclose patient’s status. The quality of care offered by public facilities therefore needs improvement. While the proportion of sputum smear-positive cases of TB are globally managed in the private sector remains unclear, limited data from some HBCs suggest that between 60% and 88% of suspect TB cases first approached the private sector for their TB diagnosis and treatment.<sup>[16]</sup> In India, a country that solely accounts for 22% of the world’s estimated TB cases, nearly half of its TB patients are managed in the private sector.<sup>[16]</sup> The deviation from proper control standards allows for increased transmission of TB and increased risk of creating

drug resistance. Poor quality TB treatment not only causes unnecessary suffering and death with a high financial cost to patients and their families, but also damages the reputation of health facilities and health staff.<sup>[17]</sup>

One the most difficult challenges facing TB treatment and management today are the emergence of anti-TB drug-resistance strain. While anti-TB drug resistance is an unavoidable phenomenon, the scale to which resistance emerges can be managed. Although drug resistance can occur because of spontaneous mutations and other random events, the majority of drug resistance can be attributed to human behavior, primarily poor prescribing practices (incorrect dosing or combinations of drugs or both), poor quality drugs, and lack of patient adherence to treatment.<sup>[18]</sup>

Public–private and public–public mix (PPM), is an effective solution to this problem. PPM promotes new approaches and partnerships for delivery of TB care by engaging all health care providers. PPM helps ensure that TB care is in line with International Standards for TB Care. This benefits all the health provider, the sick patient, the TB program, and ultimately the public health of the entire population.<sup>[17]</sup> Collaboration between the public and the private sectors is beneficial and possible. Several countries have proactively engaged the private sector. Such efforts have been met with a moderate amount of success.

The global burden of TB is falling slowly, and at least three of six WHO regions are on track to achieve global targets for reducing the number of cases and deaths that have been set for 2015. However, while increasing numbers of TB cases have access to high-quality anti-TB treatment as well as to related interventions such as ART, an estimated 37% of incident TB cases are not being treated in DOTS programs, up to 96% of incident cases with MDR-TB are not being diagnosed and treated according to international guidelines, the majority of HIV-positive TB cases do not know their HIV status and the majority of HIV-positive TB patients who do know their HIV status do not have access to ART.<sup>[4]</sup>

More than a century after the *bacillus* responsible for the disease was first identified and decades after the first antibiotic-based treatments appeared, TB continues to thrive. It does not have to be this way. TB is an entirely preventable and treatable disease. The drug-resistant strains have emerged in Africa, Russia, China, and India. Unlike HIV, the tubercle *bacillus* succumbs to powerful medications. These drugs are not where they need to be, and when they are, spotty monitoring and poor health infrastructure make it hard to ensure that patients take their daily doses for the 6 months that are needed to eradicate the infection; all of

which encourages drug-resistant strains to survive and keep the disease going.<sup>[19]</sup> Success in eradicating TB depends on early detection and treatment. Co-infection with *M. tuberculosis* and HIV (TB/HIV), especially in the HBCs of Sub-Saharan Africa and South Eastern Asia, multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB in all regions, make control activities more complex and demanding.

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