

COMMON SENSE

**Routinely Treating TB Infection Could
Avert More Than 1 Million Cases of TB
Disease In The United States**

COMMON SENSE

ROUTINELY TREATING TB INFECTION COULD AVERT MORE THAN 1 MILLION CASES OF TB DISEASE IN THE UNITED STATES

SUMMARY

Tuberculosis (TB) is an airborne infectious disease that requires long and complex treatment with several antibiotics. People can live with TB infection for years—even decades—without symptoms before developing active TB disease. Millions of Americans are living with TB infection: one in 24 people in the U.S. Recognizing people's right to know their TB status, this paper calls for a more robust national response focusing on diagnosing and treating TB infection in order to prevent future cases of TB and to stop its transmission.

INTRODUCTION

An El Paso, Texas hospital had to screen more than 860 infants and 43 staff for TB after a nursery employee was diagnosed with the disease in August 2013. Public health workers raced to notify parents that their infants were at risk of TB infection, tracing families to at least four other states plus Mexico. It took a year to identify, contact and screen all the people who had potentially been infected as a result of their exposure to TB. Before all final costs were even tallied, the local health department reported preliminary costs of \$263,383 for its efforts.ⁱ

This scenario could have been avoided. According to news reports, while the hospital employee first developed TB symptoms a month prior, she had in fact first tested positive for TB infection—the precursor to TB disease—a *decade* earlier. If that diagnosis had been treated back then, her TB infection would never have developed into TB disease.

TB is preventable, yet virtually every state in the U.S. reports cases of TB each year. In 2013, 9,588 total cases were reported nationwide,ⁱⁱ and 510 people in the U.S. died from TB in 2012 (the last year for which confirmed data are available).ⁱⁱⁱ Moreover, each year about 10 health care workers die of TB in the United States—deaths that could typically be prevented by treating their TB infection before it progresses into disease.^{iv}

To eliminate TB as a public health threat and mitigate the risk of future outbreaks, we need to make screening and treatment more accessible for people living with TB infection before they progress to TB disease. Treating TB infection is the safest, cheapest, and most effective way to prevent this progression.

WHAT IS TUBERCULOSIS?

Tuberculosis (also known as "TB," "TB disease" or "active TB") is an airborne, contagious disease caused by a bacterial infection. Without proper treatment, up to two-thirds of people with TB disease will die.^v A person with TB disease has

symptoms that can include intense coughing, significant weight loss, fatigue, fever, and night sweats. People with advanced stages of the disease can cough up blood and small pieces of lung tissue. When a person with TB disease coughs, the TB bacteria exit the body through the mouth and are expelled into the air. The bacteria can survive suspended in the air for hours, during which time people breathing that air can inhale them and acquire TB infection. Because TB disease is a contagious airborne illness of public health concern, all states require suspected and diagnosed cases of TB disease to be reported to state health departments. These reports are forwarded without identifiers to the U.S. Centers for Disease Control and Prevention (CDC).

WHAT IS THE DIFFERENCE BETWEEN TB INFECTION AND TB DISEASE?

The vast majority of people living with TB infection show no signs or symptoms, and they cannot spread the infection to others. However, people living with TB infection face a risk that the infection will progress and develop into TB disease at some point in their lives.

When a healthy person inhales TB bacteria in the air, the immune system will usually fight the infection by sealing off the invading germs in microscopic locations in the body. The body can then play host to this hidden infection for years—or even decades. During this time the person is not physically sick, does not experience any of the symptoms of TB disease, cannot pass the infection on to other people, and may not even be aware that they have the infection.

However, TB infection can develop into TB disease at any time. This process can be triggered by another illness that weakens immunity, such as diabetes, cancer or HIV or by medications that suppress the immune system. Infants and those with weakened immune systems, such as persons living with HIV infection, are especially susceptible to developing TB disease. However, even young healthy adults are at risk from progression from TB infection to disease, sometimes with fatal outcomes. Overall, between five and 10 percent of people who acquire TB infection develop TB disease at some point in their lives. Once that happens, the person begins experiencing symptoms and can then transmit TB infection to other people, usually through a telltale cough.

According to a study in the *New England Journal of Medicine*, more than 80 percent of cases of TB disease in the U.S. arise from a past TB infection that remained latent or dormant for a time but then “reactivated,” progressing into TB disease.^{vi} Nearly every one of these persons could have been treated with a single course of antibiotics before their TB infection had an opportunity to progress into TB disease.

TB INFECTION AND THE CASCADE OF RISK

When TB infection progresses to TB disease, health risks rapidly multiply. Whereas TB infection can be treated in as few as three months, people with TB disease need to receive treatment for six months or longer with a treatment regimen involving four kinds of antibiotics.¹ If that treatment isn’t administered properly, there is significant risk that drug resistance will develop. Unfortunately, the lack of funding for TB research has left physicians and patients without new, safe and effective drugs to deal with the predictable rise in drug-resistance.

DIFFERENCES IN TB TREATMENT REGIMENS

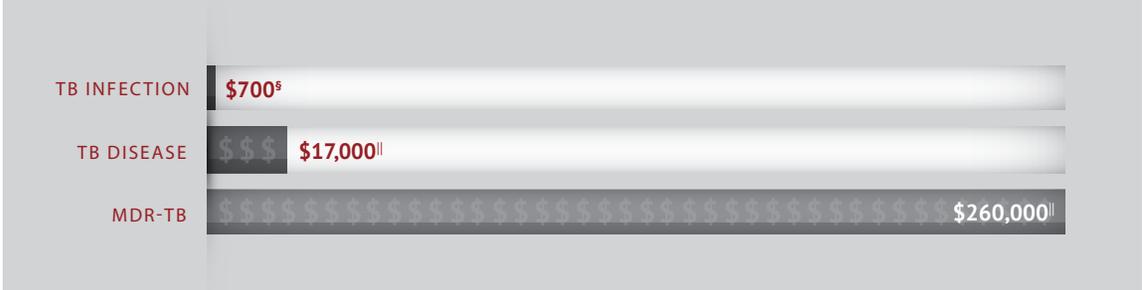
TREATMENT LENGTH



APPROXIMATE TREATMENT REGIMEN



APPROXIMATE COST PER TREATMENT



* CDC: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6048a3.htm?s_cid=mm6048a3_w#Box1
 † New Jersey Medical School Global Tuberculosis Institute: <http://globaltb.njms.rutgers.edu/downloads/products/DrugCardAdult.pdf>
 ‡ Doctors Without Borders: http://www.msfaccess.org/sites/default/files/MSF_assets/TB/Docs/TB_Letter%20to%20MOH%20Latvia%20and%20Health%20%26%20Food%20Safety%20EU%20Commissioner.pdf
 § Shepardson D, Marks SM, Chesson H, et al. 2013. Cost-effectiveness of a 12-dose regimen for treating latent tuberculosis infection in the United States. *International Journal of Tuberculosis and Lung Disease*. 17(2):1531-1537.
 || Marks SM, Flood J, Seaworth B, et al. 2014. Treatment practices, outcomes, and costs of multidrug-resistant and extensively drug-resistant tuberculosis, United States, 2005-2007. *Emerging Infectious Diseases*. 20(5) DOI: 10.3201/eid2005.131037



THE RISE OF DRUG-RESISTANT TB

Multidrug-resistant tuberculosis (MDR-TB) involves resistance to at least two of the antibiotics² used to treat a standard case of TB disease. Treating MDR-TB is highly complex, requiring even more antibiotics—some that are administered via daily injections—and up to two years of grueling treatment. Treatment options are extremely costly and can only be administered by specialists, creating a significant burden on the healthcare system. The “second-line” antibiotics used to treat MDR-TB are less effective and often have severe adverse effects, including liver toxicity and permanent hearing loss. In 2009, more than 20 fourth grade students in Laguna Beach, CA became infected with MDR-TB. Most, but not all, were treated for this infection in a way that prevented the rise of MDR disease.^{vii}

If MDR-TB isn't properly treated, the disease can progress further to extensively drug resistant TB (XDR-TB)—resistance to medicines reserved purely for use against MDR-TB. A diagnosis of even a single case of XDR-TB presents immense public health risks. Costs are exorbitant—often \$600,000 to \$1.5million per case—and patients are typically kept in round-the-clock isolation. Cases of XDR-TB are rising worldwide. Since it was first reported in the medical literature in 2006—after killing 52 of 53 people infected in a South African hospital—100 countries around the world have confirmed cases.^{viii}

Once XDR-TB arises, treatment options become highly limited, and any missteps—either on the part of the clinicians administering treatment or the patient undergoing treatment—can lead to further resistance and a scenario where an individual is suffering from a form of airborne disease for which there is no available cure. Physicians in Mumbai, India, in 2013, reported having patients under hospital care with strains of TB resistant to all antibiotics available at the time.^{ix} South Africa,^x Italy,^{xi} and Iran^{xii} have also reported cases.

*100 countries
have confirmed
cases of extensively
drug-resistant TB
since it was discovered
in 2006.*

EMERGENCE OF TB DRUG RESISTANCE THREATENS NATIONAL AND GLOBAL SECURITY.^{xiii}

Treating infection stops the TB bacteria in its tracks—before it has the chance to develop into TB disease, before it has the chance to spread to other people, before the possibility of developing drug-resistance emerges and before the possibility of death.

¹ Standard treatment for tuberculosis involves two months of treatment with the antibiotics isoniazid, rifampicin, ethambutol, and pyrazinamide, followed by four months of treatment with isoniazid and rifampicin.

² Isoniazid and rifampicin

HOW BIG OF A PROBLEM IS TB INFECTION IN THE UNITED STATES?

According to the U.S. Centers for Disease Control and Prevention, an estimated 11 million people—roughly 1 in 24 people—in the U.S. today are living with TB infection. With each of these individuals having a five to 10 percent chance of developing active, transmissible TB disease at some point in their lives. This equates to between 550,000 and 1.1 million future cases of transmissible TB disease.^{xiv}

Not everyone faces the same relative risk of being infected with TB. A recent study of TB infection among immigrants and refugees cared for by the Baltimore City Department of Health, for example, showed that 53 percent of individuals who reported for post-immigration TB evaluation between 2010 and 2012 were living with TB infection.^{xv}

Groups of people who typically face a higher-than-average risk of TB infection include:

- Adults and children who have had contact with someone who had pulmonary TB (TB disease affecting the lungs)
- Younger individuals, despite normal health, have a greater life-time risk of TB – 6% at age 20 years compared to 3% at age 50 years.^{xvi}
- People living with an illness or health condition that weakens the immune system, including: people living with HIV infection, patients initiating anti-tumor necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ or bone marrow transplantation, patients with silicosis, and diabetics from countries where TB is highly prevalent.
- Health-care workers
- Homeless persons
- Immigrants from countries that have high burdens of TB
- Illicit drug users
- Incarcerated persons^{xvii}

According to the CDC, an estimated 11 million people—roughly 1 in 24 people—in the U.S. today are living with TB infection.

PRIORITIES FOR ADDRESSING TB INFECTION

In the U.S., where, after decades of public health investments, rates of TB disease are relatively low, eliminating TB as a public health threat will require elevating the priority we place on identifying and treating TB infection. In 2000, the Institute of Medicine published a 250-page study of TB in the United States. The report concluded that finding and treating the estimated 10-15 million people living with TB infection in the U.S. is essential to eliminating TB disease. The report found that the U.S. government could better prevent TB disease by improving screening and treatment for TB infection, specifically through efforts targeted toward those most at risk.^{xviii}

INSTITUTE BEST PRACTICES FOR CLINICAL MANAGEMENT OF TB INFECTION

More recently, in November 2014 the World Health Organization issued new guidelines with recommendations for addressing TB infection. These guidelines were the result of a major consultation with physicians and disease control experts across the field, including from the CDC, the U.S. Agency for International Development, Johns Hopkins University, and Boston University. These guidelines issue a conditional recommendation that systematic screening for TB infection should be considered for prisoners, health workers, immigrants from high TB burden countries, homeless persons and illicit drug users, with a strong recommendation to provide systematic screening to additional other specific groups of individuals at high risk.^{3,xix}

HONOR PEOPLE’S RIGHT TO KNOW THEIR TB STATUS

Upon learning they were living with TB infection, 87 percent of the immigrants and refugees screened for TB infection in the Baltimore study cited earlier began treatment. Of those, 91 percent completed treatment, preventing the future development and spread of TB.

It’s important for persons who are either at risk of TB infection or are already living with TB infection to know the risk factors and to seek screening or diagnostic tests in order to prevent disease. Typically led by the Department of Health and Human Services and CDC, the federal government has carried out educational campaigns to raise public awareness of the risks posed by numerous illnesses of public health concern, including Alzheimer’s disease, diabetes, heart disease, HIV infection and lead poisoning, to name but a few.^{xx} We need to do the same for TB.

People have a right to know if they’re living with TB infection that could one day—suddenly and without warning—progress to become active, transmissible TB disease.

People have a right to know if they’re living with TB infection that could one day—suddenly and without warning—progress to become active, transmissible TB disease. Clinicians can even provide patients a personalized assessment of their risks, based on their individual history.^{xxi} With this knowledge, patients can be empowered to prevent illness in their own lives while simultaneously eliminating the potential spread of TB infection to others in their households and in the community.

CONCLUSION

“Even though tuberculosis is in decline, pressure to eliminate the disease needs to be increased or there will be a resurgence as there has been in the past.”

– Institute of Medicine, 2000

There is a well-documented trend in the history of TB in the U.S., called the “U-shaped curve of concern”: when public health efforts are successful in dramatically reducing rates of a disease, those public health efforts are scaled back, allowing the disease to resurge. TB had been steadily declining since 1953, (when the federal government began conducting national surveillance on the disease). With TB declining, and at “all-time lows” in the 1970’s, public health resources for TB activities

³ People living with HIV, adult and child contacts of pulmonary TB cases, patients initiating anti-tumor necrosis factor (TNF) treatment, patients receiving dialysis, patients preparing for organ or bone marrow transplant, patients with silicosis, and diabetics from countries where TB is highly prevalent.

were dramatically reduced at the federal level. But TB infection never went away, and fueled by both HIV and increased international mobility worldwide over the ensuing years, TB roared back and reached epidemic levels in the late 1980s to early 1990s. The costs of reversing this resurgent epidemic were enormous, exceeding \$1 billion in New York City alone.^{xxii}

Although today CDC reports the lowest levels of TB disease ever recorded within our borders, 11 million people in the U.S. are living with TB infection. Without treatment, they will provide a certain source of future cases of TB disease. No location—no city, state or country—in the world has approached TB elimination without a simultaneous approach that treats both TB disease and TB infection.^{xxiii}

Now, while active cases are at all time lows, is the time to mount a vigorous campaign against TB infection.

No location—no city, state or country—in the world has approached TB elimination without a simultaneous approach that treats both TB disease and TB infection.^{xxiii}

RECOMMENDATIONS

1. The CDC should partner with public health organizations to mount a new public educational campaign geared toward high-risk groups that builds awareness of the risks of living with TB infection. The campaign should educate at-risk persons about their right and need to know their TB status, their estimated individual risk of progressing from TB infection to TB disease, and their treatment options.
2. Congress should direct the CDC to work with states and the Advisory Council for the Elimination of Tuberculosis to explore the feasibility of making TB infection a reportable health condition at state level, as TB disease is today. More data will facilitate better targeted testing and will allow us a means of measuring progress in eliminating TB infection.
3. Congress should work with the Department of Health and Human Services to ensure a steady U.S. supply of TB screening tools and treatment regimens.
4. The U.S. government should join other countries in making a three-fold increase in global research and development for new TB tools, including new, better and less toxic drugs for treatment, and an effective vaccine that can prevent TB infection and its progression to TB disease.
5. Congress should assure that sufficient funding is provided to state and local health departments in order to assure that TB infection identification, treatment and clinical follow up is provided.
6. The federal government should articulate a global TB security agenda, which emphasizes providing support to control TB in high-burden areas.

ABOUT STOP TB USA

Our Vision: To eliminate TB as a public health threat in the US

Our Mission: To strengthen TB prevention, care and control in the US

What We Do: Working to create a social movement for public awareness, community empowerment, and policy action by:

- Mobilizing and actively supporting resources for TB elimination
- Serving as a channel of scientific and public health knowledge
- Educating the policy makers and the public about the need for sustaining community public health activities for the elimination of tuberculosis
- Increasing community participation in national TB elimination efforts, with emphasis on building awareness in and participation of persons with or at risk for this disease.



SOURCES

- i El Paso Times. December 30, 2014. Providence Memorial Hospital Pays El Paso Public Health Department \$263,383 For Their Efforts. Online. http://www.elpasotimes.com/latestnews/ci_27229870/providence-memorial-hospital-pays-el-paso-public-health
- ii Centers for Disease Control and Prevention. 2014. Trends in tuberculosis – United States, 2013. *Morbidity and Mortality Weekly Report*. 63(11):229-233. Online. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6311a2.htm>
- iii National Center for Health Statistics. 2014. Deaths: final data for 2012. National Vital Statistics Report Volume 63 Number 9. Online. http://www.cdc.gov/nchs/data/nvsr/nvsr63/nvsr63_09.pdf
- iv Lambert LA, Pratt RH, Armstrong LR, et al. 2012. Tuberculosis among healthcare workers, United States, 1995-2007. *Infection Control and Hospital Epidemiology*. 11(33):1126-1132.
- v World Health Organization. 2015. Tuberculosis. Fact sheet number 104. Online. <http://www.who.int/mediacentre/factsheets/fs104/en/>
- vi Horsburgh CR and Rubin EJ. 2011. Latent tuberculosis infection in the United States. *New England Journal of Medicine*. 364:1441-1448.
- vii American Thoracic Society. 2014. World TB Day 2014. Online. <http://www.thoracic.org/advocacy/world-tb-day/>
- viii WHO. 2014. Multidrug-resistant Tuberculosis (MDR-TB) 2014 Update. Online. http://www.who.int/tb/challenges/mdr/mdr_tb_factsheet.pdf
- ix Udhwadia ZF, Amale RA, Ajbani KK, et al. 2012. Totally drug-resistant tuberculosis in India. *Clinical Infectious Diseases*. 54 (4): 579-581. Online. <http://cid.oxfordjournals.org/content/54/4/579>
- x Klopper M, Warren RM, Hayes C, et al. Emergence and spread of extensively and totally drug-resistant tuberculosis, South Africa. *Emerging Infectious Diseases*. 19(3). Online. <http://dx.doi.org/10.3201/eid1903.120246>
- xi Migliori GB, De Iaco G, Besozzi G, et al. 2007. First tuberculosis cases in Italy resistant to all tested drugs. *Eurosurveillance*. 12(20):pii=3194. Online. <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=3194>
- xii Velayati AA, Masjedi MR, Farnia P, et al. 2009. Emergence of new forms of totally drug-resistant tuberculosis bacilli: super extensively drug-resistant tuberculosis or totally drug-resistant strains in Iran. *Chest*. 136:420–5.
- xiii Feldbaum, H. 2009. *U.S. Global Health and National Security Policy: A Report of the CSIS Global Health Policy Center*. Center for Strategic and International Studies. Online. http://csis.org/files/media/csis/pubs/090420_feldbaum_usglobalhealth.pdf
- xiv CDC. 2013. Latent tuberculosis infection: a guide for primary health care providers. Online. <http://www.cdc.gov/tb/publications/lbti/pdf/TargetedLTBI.pdf>
- xv Nuzzo JB, Golub JE, Chaulk P, et al. 2015. Postarrival tuberculosis screening of high-risk immigrants at a local health department. *American Journal of Public Health*. doi: 10.2105/AJPH.2014.302287. Online. http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2014.302287?url_ver=Z39.88-2003&rftid=ori%3Arid%3Acrossref.org&rft_dat=cr_pub%3Dpubmed&
- xvi www.tstin3d.com
- xvii WHO. 2014. Guidelines on the management of latent tuberculosis infection. WHO/HTM/TB/2015.01 Online. http://apps.who.int/iris/bitstream/10665/136471/1/9789241548908_eng.pdf?ua=1&ua=1
- xviii Geiter, L (Ed.) 2000. *Ending Neglect: The Elimination of Tuberculosis In the United States*. National Academies Press. Online. <http://www.nap.edu/openbook.php?isbn=0309070287>
- xix WHO. 2014. Guidelines on the management of latent tuberculosis infection. http://www.who.int/tb/publications/lbti_document_page/en/
- xx Department of Health and Human Services. 2015. Prevention and Public Health Fund. Online. <http://www.hhs.gov/open/prevention/index.html>
- xxi [tstin3d.com](http://www.tstin3d.com)
- xxii Frieden TR, Fujiwara PI, Washko RM, et al. 1995. Tuberculosis in New York City—turning the tide. *New England Journal of Medicine*. 333:229-233. Online. <http://www.nejm.org/doi/full/10.1056/NEJM199507273330406>
- xxiii Azman AS and Dowdy DW. 2014. Bold thinking for bold results: modeling the elimination of tuberculosis. *International Journal of Tuberculosis and Lung Disease*. 18(8):883. Online. <http://dx.doi.org/10.5588/ijtld.14.0386>