

The Lancet Infectious Diseases: Drug-resistant tuberculosis set to increase in four high burden countries

- ***By 2040, a third of tuberculosis cases in Russia are predicted to be drug-resistant; compared with one in ten in India and the Philippines, and one in 20 in South Africa.***
- ***Changing nature of disease means that infections with drug-resistant tuberculosis will be increasingly caused by person-to-person infection, rather than non-resistant strains acquiring resistance.***

Cases of drug-resistant tuberculosis are forecasted to increase in the four high burden countries (India, the Philippines, Russia, and South Africa) between 2000 and 2040, with the upturn likely to be a result of increased transmission of drug-resistant tuberculosis between people, rather than by strains acquiring resistance to anti-tuberculosis drugs, according to a study published in *The Lancet Infectious Diseases*.

While better access to treatment programmes will reduce rates of drug-resistant tuberculosis in countries with a high burden, they will not eradicate the problem alone, and current efforts may not be enough to reverse the epidemic.

As a result, research into additional control measures will be needed to prevent drug-resistant tuberculosis spreading between people. To reduce the burden of drug-resistant disease, the researchers recommend that treatment be coupled with ways to prevent spread of the disease, such as early detection, reducing the number of patients who do not complete treatment, and providing tailored treatment depending on which drugs the strain is susceptible to.

“This study uses a complex model bringing together the best available data from multiple sources in four countries hit hard by the drug-resistant tuberculosis epidemic. Our findings show that drug-resistant tuberculosis cases in these countries are expected to rise over the next two decades, and that fewer cases over time will be caused by acquired drug resistance during tuberculosis treatment. These findings suggest that person-to-person transmission will become the engine that drives drug-resistant tuberculosis in these countries,” says Dr Aditya Sharma, US Centers for Disease Control and Prevention, USA. [1]

Latest figures estimate that each year there are 10.4 million new cases of tuberculosis, leading to 1.8 million deaths globally. Nearly 40% of all drug-resistant tuberculosis cases occur in Russia, India, the Philippines, and South Africa – accounting for more than 230000 cases of drug-resistant disease in 2015.

Tuberculosis is a bacterial disease that can be treated with a combination of antibiotic drugs. However, as a result of use and misuse of antibiotics (such as using the wrong drug, or not completing the full course of treatment) bacteria can develop drug resistance (known as acquired drug resistance).

There are two forms of drug-resistant tuberculosis important to public health – multidrug-resistant tuberculosis is resistant to more than one of the first-line drugs for the disease, whereas extensively drug-resistant tuberculosis is additionally resistant to fluoroquinolones and at least one of the second-line injectable tuberculosis drugs. Treating extensively drug-resistant tuberculosis takes up to 2 years with toxic drugs, including daily injections that can have severe long-term side effects (eg, hearing loss, psychosis). Around 40% of people diagnosed with multidrug-resistant tuberculosis die of the disease, compared with 60% of those with extensively drug-resistant tuberculosis.

The study is based on a mathematical model that forecasts how tuberculosis is likely to progress in the four most-affected countries. It uses data from WHO and surveys estimating the number of drug-resistant tuberculosis cases to predict how many cases of multidrug-resistant and extensively drug-resistant tuberculosis would develop during 2000 and 2040. It also estimates how many of these would be a result of non-resistant strains acquiring resistance during treatment.

The model estimates that cases of both forms of drug-resistant disease will increase, suggesting that almost a third of tuberculosis cases in Russia (32.5%) would be multidrug-resistant by 2040, as well as 12.4% of tuberculosis cases in India, 8.9% in the Philippines, and 5.7% in South Africa. This compares to almost a quarter of cases (24.8%) in Russia, 7.9% in India, 6% in the Philippines, and 2.5% in South Africa in 2000.

In addition, almost one in ten cases of multi-drug-resistant tuberculosis in each of the four countries were expected to be extensively drug-resistant by 2040 (9% in Russia and the Philippines, 8.9% in India, and 8.5% in South Africa), compared with around 1% in 2000 (1.3% in Russia, 1.6% in the Philippines, 0.9% in India, and 0.4% in South Africa).

The study predicts that fewer cases of drug-resistant tuberculosis will be caused by strains acquiring resistance – reducing from around 30% of cases of multidrug-resistant tuberculosis in 2000 to 20–25% in 2040, and 80% of cases of extensively drug-resistant disease in 2000, to 50% in 2040.

The study authors propose that increased spread from person to person will be responsible for the growing number of drug-resistant tuberculosis cases.

“We cannot focus solely on curing people with tuberculosis or drug-resistant tuberculosis if we want to halt the epidemic. Even if we prevent new drug-resistant infections, there are enough current cases to keep the epidemic going, and drug-resistant tuberculosis will continue to be an increasingly dangerous threat so long as resistant strains spread through the air from one person to another,” says Dr Sharma. “We need to dramatically step up efforts to break the cycle of transmission – while also maintaining work to rapidly find and treat all people with tuberculosis. We must strengthen infection control measures, focus on households, health centres, and communities to prevent tuberculosis spreading from person to person, and develop more effective diagnostic tests to rapidly and accurately detect drug resistance.” [1]

The authors note that, although their model is based on the best available data, the data for Russia and India was scaled up from regional data and may not represent the true national disease burden. The model does also not take into account population density and migration, which could increase the transmission rates.

Writing in a linked Comment, Professor Andrei Mariandyshv, Northern State Medical University, Russia, said: “WHO’s End TB strategy sets targets to eliminate tuberculosis at a global level. According to this strategy, a 95% reduction in the number of deaths from tuberculosis and a 90% reduction in the incidence of tuberculosis should be achieved by 2035, compared with 2015. An important component of the road map for the elimination of tuberculosis is preventing the spread of drug-resistant tuberculosis, especially in the 30 countries with the highest burden of tuberculosis... The most important measure that might help to prevent the spread of drug-resistant tuberculosis is the implementation of short-course regimens of chemotherapy for patients with multidrug-resistant tuberculosis. Introduction of 9–12 month courses of multidrug-resistant tuberculosis therapy will increase the effectiveness of treatment and reduce the total number of anti-tuberculosis drugs during the course of treatment and save funds that can be used to treat more patients. The use of

new drugs that correspond with WHO recommendations will improve the quality of treatment for adults and children with drug-resistant tuberculosis and will help to eliminate tuberculosis globally.”

NOTES TO EDITORS

The study was funded by the US Agency for International Development and the US Centers for Disease Control and Prevention division of Tuberculosis elimination. The study was conducted by scientists from US Centers for Disease Control and Prevention, South Africa Medical Research Council, University of Maryland Medical Center, Tropical Disease Foundation, Vladimir Oblast Tuberculosis Dispensary, Orel Oblast Tuberculosis Dispensary, Central Tuberculosis Research Institute, Russian Academy of Medical Sciences, Socios en Salud Sucursal, National Institute of Health – Peru, Riga East University Hospital Centre of Tuberculosis and Lung Diseases, Changwon and Yonsei University College of Medicine, Korean Institute of Tuberculosis, Tartu University Hospital, Ministry of Public Health – Thailand, Taiwan Centers for Disease Control.

[1] Quote direct from author and cannot be found in the text of the Article.

For interviews with Article author, Dr Aditya Sharma, US Centers for Disease Control and Prevention, USA, please contact Amy Rowland in the CDC Press Office: E) isc4@cdc.gov T) +1 770 488 5104

For interviews with Comment author, Professor Andrei Mariandyshev, Northern State Medical University, Russia, please contact: E) maryandyshev@mail.ru T) +79 5230 60238

For embargoed access to the Article, please see: <http://press.thelancet.com/resistantTB.pdf>

For embargoed access to the Appendices, please see:

<http://press.thelancet.com/resistantTBAPPX.pdf>

NOTE: THE ABOVE LINK IS FOR JOURNALISTS ONLY; IF YOU WISH TO PROVIDE A LINK FOR YOUR READERS, PLEASE USE THE FOLLOWING, WHICH WILL GO LIVE AT THE TIME THE EMBARGO LIFTS:

[http://www.thelancet.com/journals/laninf/article/PIIS1473-3099\(17\)30247-5/fulltext?elsca1=tlpr](http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(17)30247-5/fulltext?elsca1=tlpr)

Emily Head

Press Officer

The Lancet journals, 125 London Wall, London EC2Y 5AS

T: +44 (0) 207 424 4249

M: +44 (0) 7920 530 997

E: emily.head@lancet.com