

Want to end TB? Diagnose and treat all forms of the disease

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A Somali woman from the town of Biyoqobobey in Ethiopia, holding a bottle of unpasteurized camel's milk. Credit: Author provided

Tuberculosis should be a specter of the past, something only our greatgrandparents feared and died of. Alas, although almost all cases of TB today are both preventable and treatable, several different strains and manifestations of the disease still sicken and kill <u>millions of people</u> <u>every year</u>.

Global <u>tuberculosis</u> interventions are usually tied to <u>larger HIV/AIDS</u> <u>programs</u>. As such, <u>billions of dollars</u> are spent every year improving medical care for people living with HIV and fighting the opportunistic infections – foremost, tuberculosis – that continue to kill so many AIDS patients.

And yet, a growing proportion of new TB cases occur in people without HIV. According to the <u>World Health Organization</u>, every year, over nine million people around the world who do not also have HIV are sickened and die from several different forms of tuberculosis.

Tuberculosis is much more than simply a complication of HIV/AIDS, and it is definitely not a disease of the past. As we observe World Tuberculosis Day, it's worth looking at some of the most threatening and yet neglected forms of TB, as well as the struggles many people still face getting the right diagnosis and medical care.

TB from animals a growing concern worldwide

A <u>majority of TB patients</u> around the world suffer from strains of the contagious pathogen *Mycobacterium tuberculosis* in their lungs. *Mycobacterium tuberculosis* (or *M. tuberculosis*, for short) usually causes



painful and long-lasting coughs, weakness, weight loss and fevers.

But as I detail in a recent article in <u>The Lancet</u>, there are several additional pathogens that cause TB disease. These additional mycobacteria species are a rising threat as the number of new *M*. *tuberculosis* cases around the world declines.

The most concerning of these mycobacteria are "zoonotic" – or transmitted to humans from animals. Human Mycobacterium bovis infection, for example, was <u>once very common around the world</u> but has been almost completely eliminated in North America and Europe, thanks to regulation of the dairy industry and introduction of pasteurized milk. But *M. bovis* is still a <u>major public health problem</u> in rural communities that lack adequate health services and agricultural regulations.

In addition to *M. bovis*, several other species of zoonotic mycobacteria can cause TB in livestock and wildlife, but we do not know much about the risk these pathogens pose to humans. Because people are often infected by consuming unpasteurized milk, *M. bovis* and other zoonotic mycobacteria are thought to cause <u>more "extrapulmonary" tuberculosis</u> in humans – or TB infections outside the lungs. These patients experience different symptoms, and their disease is more likely to be misdiagnosed or missed altogether.

The neglect and invisibility of these lesser-known mycobacteria, zoonotic forms of tuberculosis and extrapulmonary TB cases result, paradoxically, from the incredible success of global TB control efforts focused on the elimination and treatment of pulmonary cases of *Mycobacterium tuberculosis* and on TB in populations with a high HIV/AIDS burden.

Difficult to diagnose



One of the biggest challenges to broader TB control is, in many places, the lack of adequate diagnostic tests.

After a person is diagnosed with TB, molecular typing of the pathogen can determine exactly what kind of mycobacteria the patient has, determine if there is resistance to any medications, and optimize their treatment regimen. But this level of testing <u>is unavailable</u> in many lowincome countries and in most of Africa. In other words, most people with zoonotic tuberculosis live in communities that lack the kinds of diagnostic tests required to determine that's what they have.

There is also little disease surveillance or research on zoonotic TB, even in the pastoralist African populations thought to be at highest risk. The lack of knowledge about the existence and spread of zoonotic mycobacteria is largely due to the fact that they remain some of the most difficult pathogens to detect. Testing technologies are prohibitively expensive and unreliable without state-of-the-art laboratories, and there is still no way to easily detect mycobacteria in milk. Also, only expensive blood tests can tell if someone has an active tuberculosis infection or if they have merely been exposed to a tuberculosis-causing agent, such as the bacille Calmette-Guérin (BCG) vaccine.

Zoonotic TB also requires different treatment regimens: <u>*M. bovis* is</u> <u>intrinsically resistant to pyrazinamide</u>, a key, first-line anti-tuberculosis drug, so patients need some alternative medications and a longer treatment duration. Plus, <u>many extrapulmonary infections</u> are now resistant to one or more first-line TB drugs, which may contribute to its higher mortality rates.

Zoonotic TB threatens global TB control

Drug-resistant TB is itself a <u>growing problem</u>, and may be a result of substandard diagnostic tests and treatments for people, as well as the



overuse of antibiotics in livestock husbandry. Rising rates of drugresistant TB strains portend serious future challenges in TB treatment and control.

Zoonotic TB is a global problem. A few people infected with zoonotic TB in Africa have presented with active tuberculosis in the United States and Europe, and as refugee and migrant flows continue, these cases will undoubtedly increase. But it remains to be seen if the global health community will act now on zoonotic tuberculosis, or if investments will be made only once the disease more seriously threatens populations outside the African continent.

As a first step, rapid and affordable diagnostic tests and disease surveillance are desperately needed in communities at highest risk of the disease.

Beyond this, we need new investments in research on a range of pathogenic mycobacteria–not just *M. tuberculosis*–as well as new investments toward the development of field-ready and inexpensive diagnostic and drug-resistance tests. In addition, we need creative ideas about how to design and implement health care and food safety interventions that are responsive to the lives, economies, and diets of pastoralists and other rural livestock holders.

The donor community's focus on *M. tuberculosis* and on TB among AIDSaffected populations has unintentionally resulted in the invisibility and neglect of other forms of TB disease. The number of people contracting and suffering from zoonotic tuberculosis is probably much higher than we think.

Broadening our global health attention to include investments in developing better diagnostics and offering better clinical recognition and treatment for zoonotic TB not only would help those who suffer, but is



necessary to end the scourge of tuberculosis once and for all.

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