


# The “Human Factor” in the Control of Tuberculosis: Non-Adherence to Treatment and How to Prevent it

*El “factor humano” en el control de la tuberculosis: La no adherencia al tratamiento y cómo prevenirla*

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The “End TB Strategy”, published by the World Health Organization (WHO) in 2015, aims to reduce the number of deaths from tuberculosis (TB) by 95 %, the incidence by 90 %, and catastrophic expenses related to the disease to 0 % by 2035.<sup>1</sup> 2035 being 11 years from now, we don’t see great optimism in the achievement of these objectives. One of the reasons why TB is still a global pandemic is its prolonged treatment and the challenges to achieving proper adherence to it. Adherence to prolonged treatments, including TB, is a complex and dynamic phenomenon in which a wide range of factors influences the behavior of treatment acceptance. The WHO defines adherence as: “the degree to which a patient’s behavior, in terms of medicine-taking, following a diet, or making lifestyle changes, corresponds with the recommendations of the healthcare provider.”<sup>2</sup>

Adherence encompasses various behaviors, including: 1) spreading and maintaining a treatment program; 2) attending follow-up appointments; 3) using prescribed medication properly; 4) making appropriate changes in lifestyle; 5) avoiding contraindicated behaviors. According to the WHO, there are five interacting factors that influence treatment adherence: 1) Socioeconomic factors (poverty, access to healthcare and medications, illiteracy, the presence of effective social support networks, and cultural adaptation to health

practices); 2) Treatment-related factors (complexity and duration of the prescribed regimen, past therapeutic failures, and adverse effects); 3) Patient-related factors (lack of resources, religious beliefs, educational level, lack of perception of improvement regarding the disease, trust in the physician, desire to feel in control, self-efficacy, and mental health); 4) Disease-related factors, such as its severity and impact on the patient’s mental state; and 5) Factors related to the healthcare system and team (health facilities with inadequate infrastructure and deficient resources, underpaid and overworked healthcare personnel that provide brief, low-quality consultations, inadequately trained healthcare staff, limited system capacity to educate patients and provide follow-up in chronic diseases, and lack of knowledge about adherence and how to improve it).<sup>3,4</sup>

In Argentina, Arrossi et al conducted a cross-sectional study where they identified poverty and the fact of receiving healthcare in hospitals instead of nearby health centers as factors that are significantly related to non-adherence.<sup>5</sup>

A case-control study in Peru described male gender, adverse reactions, history of non-compliance with treatment, poverty, and the use of illicit drugs as adverse factors for adherence. Conversely, adequate TB knowledge and easy access to a healthcare center during regular hours were factors that improved adherence.<sup>6</sup>

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In this issue of the American Review of Respiratory Medicine (RAMR), Jajati et al<sup>7</sup> published an original study for Argentina on the direct costs of the treatment of pulmonary tuberculosis in adherent and non-adherent patients at a public hospital of the city of Buenos Aires. In their study, they compare the costs associated with a) an adherent outpatient with b) adherent inpatients, and c) non-adherent inpatients. The costs in USD were: 257.79; 4,015.26, and 8,165.87, respectively. In other words, the direct costs of treating an outpatient were approximately 15 times lower than those of hospitalized patients. Furthermore, a non-adherent inpatient incurred double the cost of an adherent inpatient. They mention smoking, homelessness (extreme poverty), malnutrition, alcoholism, substance abuse, and HIV as statistically significant factors for non-adherence.

Several international studies cited by Jajati et al reach to the same conclusion: non-adherence has both economic and health costs. This is because patients who remain infectious due to incomplete treatment become sources of disease spread. Moreover, there is a risk of selecting drug-resistant mutants and creating and spreading drug-resistant strains of *Mycobacterium tuberculosis*.

Management and control strategies for TB have shown to be vulnerable and insufficient during the COVID-19 pandemic. Isolation, social distancing, and the collapse of the healthcare system have limited patient access to healthcare facilities, worsening the TB situation in the countries and hindering proper adherence.<sup>8</sup>

Particularly in Argentina and especially in the AMBA (Buenos Aires Metropolitan Area), the worsening of socio-economic conditions is another significant factor negatively impacting patient adherence to treatment. At the hospital level there are patients with very low incomes, overwhelmed by the daily challenges of securing food, having shelter, transportation, dealing with crime, and coping with addictions, among other unfortunate factors. Within the bleak environment in which these individuals live, chronic cough seems like a minor concern, and they often seek healthcare with extremely critical TB. Unfortunately, under these circumstances, we witness the death of young individuals from TB, a disease that can be prevented, easily diagnosed and treated effectively. If they manage to recover, once they are discharged, they return to their complex life situations, and

regrettably, it is common for them to discontinue their treatment.

Is there any possibility of improving adherence? Yes. Directly Observed Therapy (DOT) is a tool that has been applied for several years with varying levels of success. An important aspect is that it should be carried out in the vicinity of the patient's residence or shelter (in the case of the homeless). Digital technology helps. The Video Observed Therapy (VOT) and its variants, through a mobile phone, have shown to be more effective than DOT.<sup>9,10</sup>

Well, let's assume an ideal scenario where we have an efficient healthcare system that is also concerned about TB. Would we be able to achieve near 100 % adherence, so that TB would have to decrease until it disappears?

Let's look at the example of a bacterial disease that can be easily diagnosed, needs short treatment, and has no drug resistance: syphilis.

With such a promising picture, has it disappeared? NO. In the United States, syphilis rates are at their highest point in 70 years. The Centers for Disease Control and Prevention (CDC) in the United States indicated that 207,255 cases were reported in 2022, which represent a significant increase in five years.<sup>11</sup>

So, what are we missing in our analysis?: the human factor, both from the healthcare system and the patients. Could we modify the healthcare system to make it more "friendly" towards those who need its services? Quick, warm, efficient, understanding care, without extremely long wait times or bureaucracy that can be incomprehensible to many patients. Maybe we could, but it will take a long time, considerable efforts, and, above all, interest in making this transformation.

And with regard to the patients, could we make them understand the illness they are experiencing and the need for treatment? We could achieve that with an educational effort, in most patients, but there will always be a difficult-to-reach remainder with seemingly insurmountable barriers, that will unfortunately carry their TB to the ultimate consequences (for them and the surrounding society).

I don't want to conclude this editorial with such a pessimistic view of the future of TB. Let's remember the "golden" 80 % (for example, in vaccination). If we can ensure that a similar or higher percentage of TB patients can be integrated into a comprehensive and sustainable healthcare system,

providing them with adequate social and economic support, perhaps we will see a significant decrease in the incidence and prevalence of TB over time. Hopefully!

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