Complex Systems: An Innovative Approach to Improve Drug-Resistant Tuberculosis Treatment Adherence

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Abstract
The burden of multidrug-resistant tuberculosis (MDR-TB) poses a serious challenge to global TB control and elimination; MDR-TB is far deadlier and more difficult and expensive to treat than drug-susceptible TB. Among the factors that influence MDR-TB treatment outcomes, adherence plays a very important role. Missing medication doses could result in poor treatment outcomes, further transmission of MDR-TB, and further resistance to drugs. The project investigated the key determinants of MDR-TB treatment adherence and develop specific recommendations to improve it in Lima, Peru. The project's main objective was to develop, test, and apply a model that describes how treatment adherence, and consequently, treatment outcomes, could be improved.

The specific aims of this dissertation were to 1) estimate the effects of the information-motivation-behavioral skills model on MDR-TB treatment adherence; 2) develop an integrated system dynamics (SD) model of the interactions most substantially affecting patient adherence to treatment over time, and based on a structured review of the literature as well as interviews and focused group discussions with key stakeholders; and 3) parameterize, calibrate, and test the SD model built in Aim 2 to simulate the effects of various intervention implementation scenarios on treatment outcomes. Implementation science and SD approaches were combined to inform the design of implementation strategies that improve treatment outcomes most effectively.

The analyses showed that adherence is a complex behavior and we need interventions that are designed to improve the patients' information, motivation, and behavioral skills with implementation strategies that are intentionally chosen and measured. Implementation strategies – *what, when, how, who* – must be evidence-based and have a long-term sustainability plan. Adherence, and LTFU, should be monitored during treatment, while interventions are finetuned to fit the context and maximize its impact prior to scaling-up. Though LTFU is an extension of adherence (LTFU is defined as zero adherence for a month of more), its determinants are not identical and we should consider interventions accordingly. The application of implementation science and SD methodology could facilitate and fast-track the process of improving these strategies, close the gap between knowledge and practice, and inform the allocation of resources to minimizing waste.

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