Optimising the implementation of Tuberculosis Diagnostics in high burden countries - an exercise in mathematical modelling and simulation

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Alexandra de Nooy (14581728)
alexandra.de.nooy@student.uva.nl
University of Amsterdam

1 INTRODUCTION

Tuberculosis (TB) is an infectious disease with a notable impact on country health systems. In fact, in 2021 the World Health Organization (W.H.O) estimated that 10.6 million cases and 1.6 million deaths were reported globally, with many of these being recorded in Lower Middle-Income Countries (LMICs) [3, 4]. Further, a review of these numbers over time has shown that while TB-related mortality has reduced over the last two decades (from approximately 2.4 million deaths to 1.6 million deaths), the estimated number of annual cases has remained relatively stable [3, 4]. This highlights that although TB treatment and linkage to treatment has improved overall, there is still significant ongoing community transmission.

A notable challenge to reducing this transmission lies within patients being able to access appropriate diagnostics and results. Frequently, this process is complex with patients having to make many (often expensive) visits to facilities to both provide a sample that can be tested as well as to return to receive their diagnosis [6, 7]. Furthermore, collecting sputum-samples for TB testing can be difficult for both the patient and the healthcare provider [7]. These elements both contribute towards individuals falling out of care or not providing a sample for testing and subsequently not receiving a diagnosis (or treatment) and remaining infectious [7]. As such, this has prompted a global call to develop new TB tests with the potential to reduce the complexity of the current diagnostic pathway, use more appropriate test samples (e.g non-sputum), bring results closer to patients and overall, increase the number of individuals correctly diagnosed [1, 5].

However, as these novel tests begin to be developed according to W.H.O. Target Product Profile guidelines (a document describing the minimum requirements for new TB tests), it becomes necessary to consider how they would be feasibly implemented in countries that have a range of TB diagnostics and infrastructure already in place [2]. This project aims to explore this knowledge gap by simulating, for the high TB-burden country Kenya, a range of novel diagnostic implementation scenarios to determine which would diagnose the greatest number of individuals. This process will require the simulation of the implementation of new diagnostics to different degrees- at an individual level- and for different populations. Scenario results will then be evaluated against the baseline data of an existing TB diagnostic model for Kenya to answer the following research questions (RQ).

Research Question: *In the context of TB diagnosis in Kenya, what combination of new and existing TB diagnostic tests will correctly diagnose the largest number of individuals at different levels of budget availability?*

Further sub-research questions include:

- To what extent does targeting novel diagnostics only at specific population groups, for example HIV positive people, impact the overall number of individuals diagnosed?
- To what extent do different diagnostic implementations impact the number of incorrectly diagnosed individuals (for example false positive or false negative results)?
- Which implementation scenarios have the greatest impact on reducing the diagnostic access gap vs reducing the gap in delivering TB results?
- Which scenarios result in diagnosing the greatest number of individuals under no-budget vs budget constraint scenarios?

2 OBJECTIVES & GOALS

Currently there is limited mathematical modelling research available which considers the impact of new (or still developing) TB diagnostics on Kenya's standard TB diagnostic pathway. In conjunction with supervisors from the Amsterdam UMC, this project aims to fill this gap and provide a framework to guide potential implementation decisions in the future. To achieve this, the following key goals and milestones should be met:

- **Baseline exploration:** Explore and analyse Kenya's baseline diagnostic model data to determine baseline outcome values relevant to the defined research and sub-research questions.
- **Scenario definitions:** Define a set of diagnostic implementation scenarios which consider the impact of different combinations of existing and future diagnostics (as defined by W.H.O) on the number of individuals diagnosed in Kenya as well as on other important outcome variables.
- **Model Adaptation:** Adapt and reparametrize an existing baseline model to fit the defined scenarios and use this model

simulate the results of the new patient pathway.

- **Scenario Analysis:** Aggregate individual level scenario results and determine key outcome variables for each scenario, including scenario cost and number of individuals correctly diagnosed.

- **Evaluation and Scenario Optimisation:** Evaluate key outcome variables against the baseline data. Using the evaluation, optimise for cost and number of individuals correctly diagnosed with TB, so as to identify scenarios which improve on Kenya's baseline and are potentially feasible to implement.

3 PROJECT PLAN

For part-time students, the practical element of the thesis is expected to begin mid-January 2024 following the finalisation of the thesis design. Given that the draft thesis is to be submitted by mid-June, this provides approximately 22 weeks of part-time work on the project. This time frame, in conjunction with the goals and objectives previously described, has been used to develop the planned project timeline below.

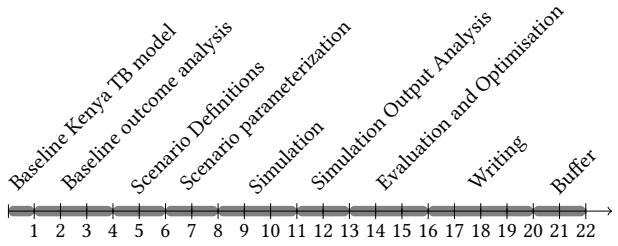

Figure 1: Expected Project Timeline

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