

# An Economic Modelling Approach for Antimicrobial Stewardship Programs in Low-Middle Income Settings

Determining the cost-effectiveness of digital antimicrobial stewardship programs for addressing antimicrobial resistance at a district hospital level in South Africa

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## Objective

To develop a framework for determining the cost-effectiveness of antimicrobial stewardship programs in low-middle income settings, through building a cost-effectiveness model for implementing digital antimicrobial stewardship programs at district hospitals in South Africa.

## Introduction

Antimicrobial resistance (AMR) is a **global threat**

- To health: 4.95 million deaths associated with bacterial AMR a year<sup>1</sup>
- To economy: US\$28.9 billion/year to treat complications caused by AMR<sup>2</sup>

Low- and middle-income countries (LMICs) are particularly vulnerable

- Difficulty quantifying burden due to lack of surveillance infrastructure<sup>3</sup>
- In South Africa, 50% **rise in antimicrobial consumption** from 2019 to 2022<sup>4</sup>

Antimicrobial stewardship programs (ASPs) are key to reduce the burden<sup>5</sup>

- Existing 2017-2024 Guidelines in South Africa, however still rising AMR<sup>6</sup>
- **Innovation in digital/mobile ASPs** – facilitates clinical practice and collection of surveillance data, time and (potentially) cost-saving as compared to current ward-based programs

Research gap: cost-effectiveness analysis of digital ASPs

- Key for **resource allocation**, particularly in resource-limited LMICs.

## Methods

Quantifying the costs and benefits of ASPs, using the following outline:

<b>Population</b>	Patients attending district hospitals in the chosen LMIC (e.g., South Africa) with suspected infectious disease
<b>Intervention</b>	Mobile ASP application for healthcare workers
<b>Comparators</b>	(1) Current standard-of-care (2) Ward-based ASPs
<b>Outcomes</b>	Incorrect prescriptions averted Disability adjusted life years (DALYs) averted

## Approach 1: Decision Tree Model

Clinical ASPs aim to reduce AMR through **improving prescribing practices**.

Use of a simple decision-tree model to determine the costs of the ASP (treatment and program costs) and associated benefits (percentage of incorrect prescriptions averted)

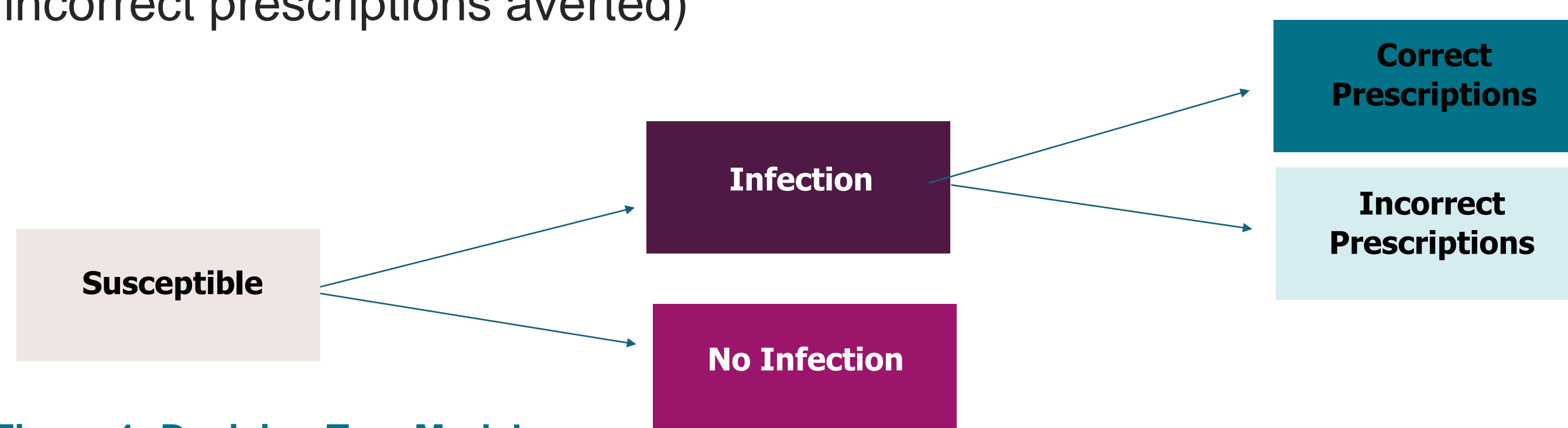


Figure 1: Decision Tree Model

### Evaluation of Decision Tree Modelling Approach:

- ✓ Good data availability, Minimizes assumptions: more reliable outputs
- ✗ Outcome of incorrect prescriptions averted is less comparable for decision-makers, does not consider time (an important factor in the development of resistance)

## Approach 2: Markov Model

Antimicrobial resistance **increases patients' health burden** (more severe disease with higher fatality) compared to antimicrobial sensitive infections. Through improving prescribing practices, ASPs reduce the development of resistance **over time**.

Thus, Markov model allows evaluation of the impact of ASPs on antimicrobial resistance burden over time.

**Model Characteristics:** Provider perspective with life-time horizon; 3-month cycle length, based on the average number of infectious diseases per person per year and the length of infectious disease.

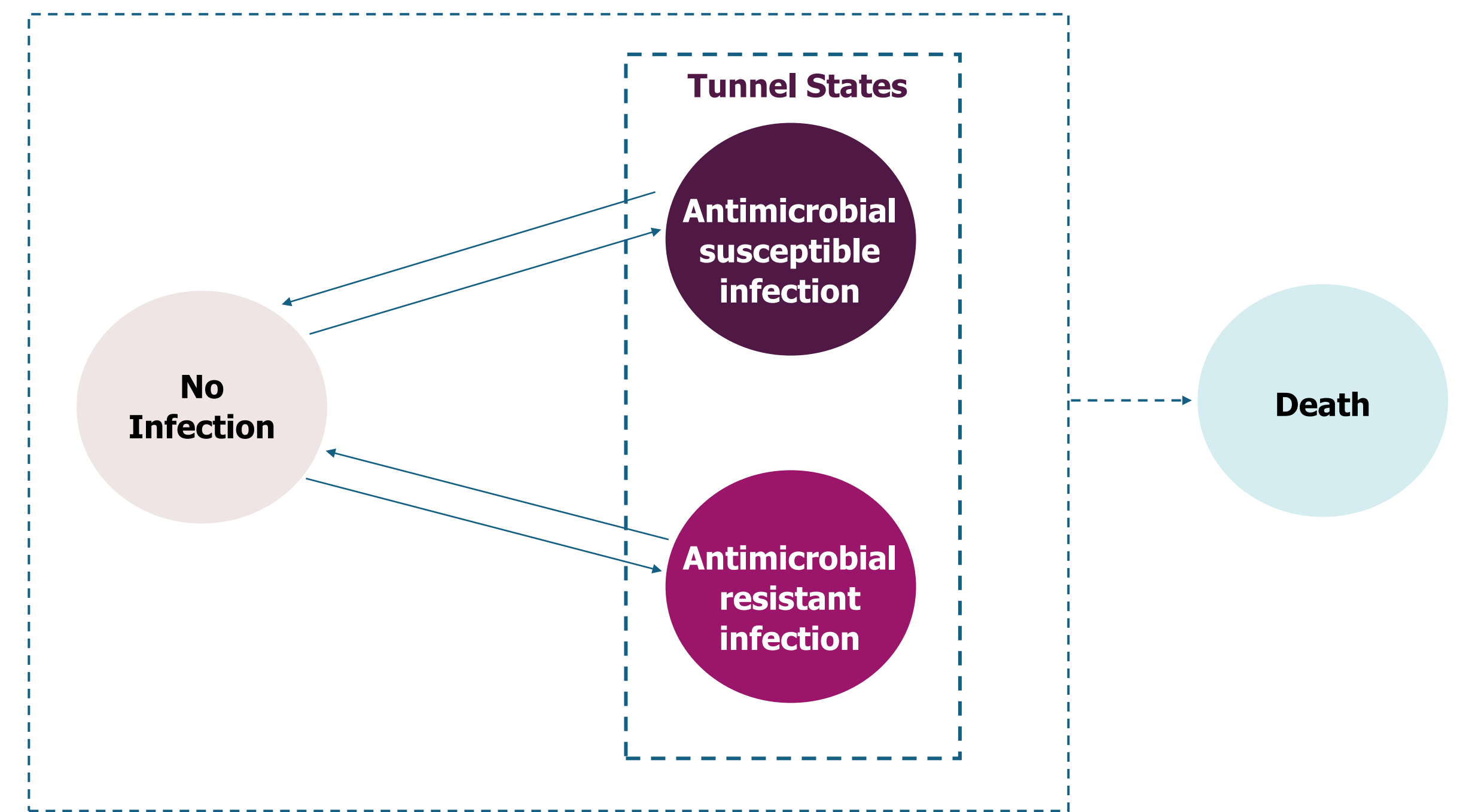


Figure 2: Markov Model

### Model Dynamics:

- Four health states: 'no infection'; 'antimicrobial susceptible infection (AMS)'; 'antimicrobial resistant infection (AMR)' and 'death'
- All patients begin in 'no infection' state
- Patients may remain in 'no infection', or transition to 'AMS' or 'AMR' states
- After one cycle in 'AMS' or 'AMR' state (tunnel states), patients return to 'no infection' state
- Patients can move from 'no infection', 'AMS' or 'AMR' states to 'death' (absorption) state

### Transition Probabilities:

- Sourced from Global Burden of Disease study<sup>1,7</sup> and relevant literature from the chosen LMIC (e.g., National Surveillance Guidelines South Africa)<sup>8</sup>
- In the intervention arm, probabilities change annually due to the effect of ASPs in reducing AMR burden over time<sup>9</sup>

**Utilities:** Country-specific AMS and AMR DALYs from Global Burden of Disease Study<sup>7,10</sup>

### Costs:

- Treatment Costs: Antimicrobials per disease episode; Hospital admissions
- Program Costs: Specific to the interventions under evaluation
  - Ward-based ASP: Program development; ward rounds; audits
  - Digital ASP: Mobile application development and maintenance; healthcare worker online-consultations; audits

### Model Outputs:

- Incremental cost-effective ratio (ICER) in DALYs averted for digital ASP compared to ward-based ASP and standard-of-care
- Compare ICER to chosen country's willingness-to-pay threshold

### Evaluation of Markov Modelling Approach:

- ✓ Shows impact of ASPs over time; comparable outcome measure
- ✗ Challenges in data availability; requires several assumptions (e.g., extrapolations of program efficacy from other countries and from other similar interventions)

## Intended Impact

- In the reference case for digital ASPs in South Africa, both the decision-tree and Markov models provide useful output measures to decision-makers to determine cost-effectiveness of the intervention.
- Provided sufficient data is available to limit assumptions, the Markov model is preferred, as it produces a more comparable outcome measure.
- The frameworks proposed can be applied to evaluating ASPs in other LMIC settings

**References:** 1. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet 2022;399:629-655. 2. OECD. Embracing a One Health Framework to Fight Antimicrobial Resistance, 2023. 3. Sulis G, Sayood S, Gandra S. Antimicrobial resistance in low- and middle-income countries: current status and future directions. Expert Review of Anti-infective Therapy 2022;20:147-160. 4. National Department of Health. Surveillance for Antimicrobial Resistance and Consumption of Antibiotics in South Africa 2018-2022, 2024. 5. World Health Assembly. Global action plan on antimicrobial resistance WHA 68.7, In 68th World Health Assembly, Geneva, 26 May 2015, 2015. 6. Essential Drug List Committee. South African Antimicrobial Resistance National Strategy Framework: A One Health Approach 2017 - 2024: National Department of Health 7. Ferrari AJ, Santomauro DF, Aali A, et al. Global incidence, prevalence, years lived with disability (YLDs), disability-adjusted life-years (DALYs), and healthy life expectancy (HALE) for 371 diseases and injuries in 204 countries and territories and 811 subnational locations, 1990-2013;2021: a systematic analysis for the Global Burden of Disease Study 2021. The Lancet 2024;403:2133-2161. 8. National Department of Health. Surveillance for Antimicrobial Resistance and Consumption of Antibiotics in South Africa 2018-2022, 2024. 9. Tuon FF, Gasparetto J, Wollmann LC, et al. Mobile health application to assist doctors in antibiotic prescription - an approach for antibiotic stewardship. Braz J Infect Dis 2017;21:660-664. 10. Naghavi M, Vollset SE, Ikuta KS, et al. Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. The Lancet 2024;404:1199-1226.