Do Theory-Derived Interventions Hold Up in Complex Systems? A Modeling Study of HIV Drug Resistance

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Abstract:

Background: HIV drug resistance (HIVDR) threatens the long-term effectiveness of antiretroviral therapy (ART) and compromises progress towards HIV epidemic control. While, acquired drug resistance (ADR) arises within patients, it also seeds transmitted drug resistance (TDR) in the population. Although several interventions have been proposed and evaluated to address HIVDR, limited research has examined their potential effects within the complex interactions between clinical, social, behavioral, and health system factors that shape HIVDR dynamics. This study aimed to develop and apply a stakeholder informed system dynamics model to evaluate selected HIVDR reduction strategies in the Dar es Salaam Urban Cohort Study (DUCS) area of Tanzania.

Methods: This study was guided by the Decouttere et al's *Integrated Framework for Health Systems Modeling*. A system dynamics model was developed in Stella Architect 4.2.1 and refined through a stakeholder validation workshops involving people living with HIV(PLHIV), healthcare workers, policymakers, regulators, supply chain organizations, implementation partners, and researchers. The model was calibrated using available demographic and HIV program data from the DUCS area between 2016 and 2025. Three co-designed intervention scenarios were simulated from 2026 to 2030 and compared with a baseline scenario: decentralized ART regimen switching, food and transport support, and a combined intervention scenario. Outcomes assessed included HIV incidence, total PLHIV, viral suppression, overall HIVDR burden, ADR and TDR.

Results: Decentralized regimen switching produced the greatest reductions in overall HIVDR burden, ADR, TDR by 2030, while providing food and transport support generated larger improvements in HIV incidence and viral suppression, and the total PLHIV. The combined intervention scenario achieved the most favorable overall reduction in HIVDR burden, ADR, TDR and HIV incidence.

Conclusion: These findings highlight the potential value of considering clinical, health system, and socioeconomic factors simultaneously when designing HIVDR prevention strategies. This observation reinforces the importance of moving beyond single-intervention approaches and demonstrates the value of system dynamics modelling for integrating complex system interactions to support the design, evaluation, and prioritization of contextually relevant HIVDR prevention strategies.