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Dr. Katia Koelle, Professor Steven Riley, Dr. Cecile Viboud
Editors-in-Chief of *Epidemics*

Re. Submission of a Scoping Review Paper

Dear Editors,

We are pleased to submit the attached manuscript entitled *Risk heterogeneity in compartmental HIV transmission models applied to assess ART as prevention in Sub-Saharan Africa: A scoping review* for consideration to publish in *Epidemics*.

Compartmental transmission models have played an important role in projecting the population-level prevention benefits of ART scale-up. However, several recent large-scale community-based trials of universal test and treat have not demonstrated the incidence reductions anticipated from modelling studies. One hypothesis for why model and trial results have differed suggests that representations of risk heterogeneity in transmission models have not sufficiently reflected epidemic contexts.

To explore the evidence for this hypothesis, in this paper we conduct a scoping review on representations of risk heterogeneity in compartmental transmission models used to project the prevention benefits of ART scale-up within Sub-Saharan Africa. First, we develop a conceptual framework to organize key factors of modelled risk heterogeneity, such as if/how model populations, rates, and probabilities are stratified along dimensions like age, sex, and sexual activity. Then, using a set of 94 systematically identified modelling studies, we summarize how these factors have been modelled, alongside information regarding the epidemic context and the projected impact of ART scale-up on new infections.

We find that modelled representations of risk heterogeneity vary widely, with approximately two thirds and two fifths of studies considering heterogeneous sexual activity and at least one key population, respectively. Nearly all studies assumed equal rates of diagnosis, ART initiation, and retention across risk groups. Barriers to treatment initiation and retention that may be experienced by key populations were only considered in 5 studies. We also find preliminary evidence at the ecological level that homogeneous models project a greater proportion of infections averted by ART, but that models with key populations project similar ART prevention impacts when those key populations are prioritized for ART cascade engagement.

Our review summarizes model structures and assumptions underpinning the current body of compartmental modelling literature on projections of ART prevention impacts. We highlight the potential influence of different representations of risk heterogeneity on the projected ART prevention impacts, and identify key areas for future model developments. To our knowledge, ours is the first review to focus specifically on models applied to study ART scale-up, and with detailed examination of model structure. As such, we hope you find our review to be of timely interest to the readership of *Epidemics*.

Thank you for your consideration and we look forward to hearing from you.

Sincerely,

Jesse Knight and Sharmistha Mishra