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Prof. Neil Ferguson & Prof. Dr. Hans Heesterbeek
Editors-in-Chief of *Epidemics*

Re. Submission of a research paper to Epidemics

Dear Editors,

We are pleased to submit the attached manuscript entitled *Contribution of unmet needs of individuals at high risk may be underestimated in epidemic models without risk turnover: a mechanistic modelling analysis* for consideration in *Epidemics*.

Epidemic models of sexually transmitted infections (STI) are increasingly used to quantify the contribution of high risk groups to overall transmission. Contributions are often measured from epidemic models by calculating the transmission population attributable fraction of unmet prevention and treatment needs of specific risk groups. However, movement of individuals between risk groups – i.e. "turnover" – is not often considered, despite epidemiological evidence to suggest that STI risk is dynamic over an individual's sexual life course. Moreover, there exist various implementations of turnover without a unified approach of implementing turnover using epidemiological data.

In this paper, we examined the mechanisms by which turnover could influence modelled estimates of the transmission population attributable fraction of high risk groups. First, we developed a new, unified framework to design and parameterize systems of turnover among risk groups in epidemic models when guided by epidemiological data. We then used the new framework in an illustrative, risk-stratified model of an STI and identified for the first time: (a) that fitted models without turnover underestimate the contribution of high risk groups to overall transmission; and (b) the underestimate stems from inferred risk heterogeneity in the presence/absence of turnover which in turn is mediated by three phenomena that shift with varying turnover rates: herd immunity in the highest risk group, influx of infectious individuals into the low risk group, and changes in number of partnerships where transmission can occur.

To our knowledge, this is the first study to examine and thus generate new insights into the influence of turnover on the transmission population attributable fraction of high risk groups; and the first to detail the mechanisms underlying the relationship. The findings have important implications for projecting not only the contribution of high risk groups to overall transmission but also when projecting the potential transmission impact of interventions priortiized to high risk groups.

While our study is framed around an illustrative STI, risk group turnover is applicable to a wide range of epidemic contexts, infections, and hosts. We therefore believe the new framework for parameterizing turnover, the findings, and the mechanistic insights will be of interest to the broad readership of *Epidemics*,

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

Sincerely,

Sharmistha Mishra and Jesse Knight, on behalf of co-authors