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## Response to Comment from Fontaine and colleagues

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We thank Fontaine and colleagues at UNAIDS for their interest in our work, and the opportunity to correct several misunderstandings (1). In our study we constructed a data-based spatial map of an HIV epidemic in Lesotho, a country in sub-Saharan African (2). The map reveals the geographic dispersion pattern of all HIV-infected individuals. Specifically, it reveals the Density of Infection (DoI): the number of HIV-infected individuals per square kilometer. We found that the epidemic is widely dispersed throughout the country, and the DoI ranges from ~450 HIV-infected individuals/km<sup>2</sup> in the capital city to only one HIV-infected individual/km<sup>2</sup> in small rural communities. Additionally, we show that only ~20% of HIV-infected individuals in Lesotho live in urban centers. We used the DoI map: (i) to determine the feasibility of achieving high levels of treatment coverage, and (ii) to establish how to implement UNAIDS' 90-90-90 strategy in a decentralized health care system. UNAIDS' goals are to diagnose 90% of HIV-infected individuals, treat 90% of the diagnosed, and achieve viral suppression in 90% of treated individuals (3). Achieving these goals will result in ~70% of HIV-infected individuals on treatment and virally suppressed. The strategy is based on using treatment as prevention (TasP) to reduce HIV epidemics: treatment, by reducing an individuals' viral load, can prevent infections. Notably, UNAIDS has not yet determined the feasibility of their 90-90-90 strategy nor have they made any recommendations for implementation.

We are very concerned that Fontaine and colleagues believe that we are suggesting that "denial of life-saving medicines to areas with a low DoI is required to defeat the AIDS epidemic in Lesotho". In fact, we suggest the opposite. We analyze two possible implementation strategies and show that, in order to reach high coverage levels, most of the treatment will need to be provided to HIV-infected individuals living in areas where the DoI is very low. For example, reaching ~70% coverage would require treating many individuals in rural areas where there are as few as five HIV-infected individuals per km<sup>2</sup>. Achieving ~90% coverage would require treating many in areas where the DoI is even lower: two HIV-infected individuals per km<sup>2</sup>. Our results call into question the feasibility of attaining UNAIDS' stated treatment coverage goals, and indicate that the costs of the 90-90-90 strategy will be considerably higher than predicted. Additionally, we show that the two implementation strategies will result in the same level of coverage, but a very different allocation of treatment between urban and rural areas. One will ameliorate, the other

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exacerbate, current urban-rural health disparities. We believe that the implementation strategies that are used should be chosen by the Governments of HIV-afflicted countries.

We would like to correct the misunderstanding that we have predicted the impact of treatment allocation strategies on reducing incidence; our study does not include any predictions. Instead, we have evaluated the feasibility of achieving high levels of treatment coverage and identified (based on different objectives) which communities should use TasP. In previous studies, using geospatial transmission models, we have predicted the epidemiological impact of geographic targeting strategies (4, 5). We have shown that geographic targeting would significantly increase the impact of interventions, such as TasP, on reducing incidence. We are pleased that UNAIDS is now beginning to develop geospatial transmission models and use them to develop geographic targeting strategies. We agree with Fontaine and colleagues that it is essential to include uncertainty in parameter estimation when making predictions. Notably, one of us (SB) introduced the use of uncertainty analysis to the field of predictive transmission modeling (6). Recently we have shown that it is important to conduct more sophisticated analyses that include both uncertainty in parameter estimation and uncertainty in the underlying assumptions of the model (4). These analyses enable a modeler to identify the “best” geographic targeting strategy, and also be able to provide a policymaker with a measure of the certainty (i.e., the probability) that the identified strategy is actually the “best”.

We would like to correct two additional misunderstandings. Coverage in Lesotho is low (only 36%); we did not assume that coverage is zero. We determined the feasibility of reaching high levels of coverage, including that needed for the 90-90-90 strategy to succeed. We also did not propose reducing treatment catchment areas; our results show that - in order to reach high coverage levels - catchment areas in many rural areas will need to be extremely large.

Lesotho has one of the most severe HIV epidemics in the world; ~25% of the general population is infected with HIV. We found that it will be extremely difficult to reach a high level of treatment coverage, because the DoI in many places of the country is extremely low. This occurs because, even though prevalence is high, the majority of HIV-infected individuals in Lesotho live in fairly small widely-dispersed rural communities. We agree with Fontaine and colleagues that it may be possible to achieve the goals of the 90-90-90 strategy in some other countries in sub-Saharan Africa. Our results suggest that the more urbanized the country and/or the lower the prevalence, the easier it will be to reach a high coverage level.

Currently, UNAIDS recommends disproportionately allocating the available resources for HIV treatment (and prevention) to urban centers. The recommendation is based on the results of mathematical modeling studies that show this strategy is the most cost-effective (7). However, our study highlights the critical need for treatment in rural areas. We urge UNAIDS to consider additional criteria, including eliminating urban-rural disparities in healthcare, when developing future policies. Specific criteria can be included as “constraints” and analyzed within a modeling framework. Notably the allocation strategies

that will be identified by using this methodology will be less cost-effective than the currently recommended strategies.

## References

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