Methodological concerns regarding a PrEP model

We would like to raise a concern regarding the mathematical modelling study by Brooke Nichols and colleagues,1 which looked at the cost-effectiveness of pre-exposure prophylaxis (PrEP) for HIV-1 prevention in the Netherlands. Specifically, we have found that we are unable to replicate their results using the methodology described in their paper.

In their modelling study the authors divided the population into four risk groups on the basis of sexual behaviour. They used a standard method, Monte Carlo filtering,2–5 for the first stage of their analysis: to calibrate their model. To do the Monte Carlo filtering, the authors assigned ranges to specify the size of the four risk groups, and then sampled each of these four ranges 100 000 times. The ranges the authors used were: 5–15% for the highest risk group, 30–50% for the second highest, 10–35% for the third highest, and 4–46% for the lowest risk group. We have run the authors’ analysis with the same ranges and sampled each of the four ranges 100 000 times. However, we have been unable to replicate their results.

Our results are shown in the figure. We found that none of the 100 000 samples could divide the population into four risk groups. In about 56 000 of our samples (shown in red) the population would have to be divided into at least five risk groups, since the percentage of the population in the four risk groups adds up to less than 100% of the population. In the other approximately 44 000 of our samples (shown in blue) there are too many individuals assigned to at least one of the four risk groups, since the percentage of the population in the four risk groups adds up to more than 100% of the population.

Mathematical modelling studies can be useful for predicting the effect of PrEP on controlling HIV epidemics in both resource-rich1 and resource-constrained6 countries. However, it is important that studies can be replicated to assess their validity. With the methodology described in the study by Nichols and colleagues,1 we have been unable to replicate their findings.

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Authors’ reply

Sally Blower and Laurence Palk state that they cannot reproduce the methodology we described in our paper on the cost-effectiveness of pre-exposure prophylaxis (PrEP) for HIV-1 prevention in the Netherlands.1 However, Blower and Palk tried to reproduce a single aspect of our model calibration (the proportion of individuals engaging in a particular form of sexual behaviour).

Blower and Palk state that they could only reproduce our results when the total percentage of the four risk groups we used to differentiate sexual behaviour did not add up to 100%. In all our simulations, however, the sum of the four risk groups was exactly 100%. To meet this condition, we first randomly selected proportions for the first three risk groups. The proportion of individuals allocated to the last risk group was chosen so that the sum of the four risk groups was equal to 100%.

Model calibration is an important part of mathematical models. Calibration is important since it ensures that a model is able to reconstruct a past, and therefore known, HIV epidemic. Calibration of a model is generally done by comparing simulations with epidemiological data.2,3 For calibration of our model we used the high-quality data available on the well defined HIV epidemic in the Netherlands. The Dutch HIV epidemic is well described since anonymised data about key clinical and demographic parameters of HIV-infected patients are included by the 27 hospitals that provide HIV treatment. These data are then centrally collected.4 Our model calibration therefore not only considered risk behaviour but also important objective parameters such as the annual number of men who have sex with men (MSM) who are newly diagnosed, their CD4 cell count at diagnosis, and the estimated number of MSM living in the Netherlands.4

Figure: Results generated from 100 000 samples

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<th>Percentage sum of all four risk groups</th>
<th>Frequency</th>
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