The dawn of novel STI prevention methods: modelling potential unintended effects of changes in cervical cancer screening guidelines on trichomoniasis

Minttu M Rönn,1 Katherine ME Turner2

Trichomonas vaginalis (trichomoniasis (TV)) is a parasite of the urogenital area.1 TV is not a notifiable infection in most countries and, as the majority of infections remain asymptomatic, there is lack of epidemiological data for the infection. In the USA and the UK, screening of TV among asymptomatic individuals in the general population is not recommended by the guidelines.2 3 In Australia, opportunistic testing for asymptomatic TV is done during cervical screening appointments using Pap smear test and wet mount microscopy, which has a sensitivity around 50–60% for TV detection. New guidelines were introduced in 2017 to replace cytology-based testing with PCR testing for high-risk human papillomavirus (HR-HPV) infection, such that cervical cytology is only conducted for those who test positive for HR-HPV.4

Hui et al6 have used mathematical modelling to estimate potential indirect effects of the cervical screening guideline changes on TV prevalence in Australia. In the study, a deterministic compartmental model of TV transmission among heterosexual population was calibrated to low-level (0.4%) TV prevalence reflecting urban Australian population and assuming a steady age-specific cytology-based cervical cancer screening rate among women over 18 years. The authors compare the prevalence in the calibrated model with future estimates of TV population prevalence in the presence of reduced frequency of Pap smear tests. The study suggests that introducing HR-HPV testing could lead to a substantial increase in TV prevalence in the urban population in Australia over a 20-year period.

Mathematical modelling is a useful analytical tool,6 which offers a relatively rapid, low-cost and low-risk method to predict the impact of existing and novel interventions. Models can lead to improved understanding of the ways in which infectious diseases interact and reveal indirect and unintended consequences of interventions. This provides valuable hypotheses for further epidemiological research, which is one of the major contributions of the study by Hui et al. There are few transmission models of TV,7 8 and the study presented in this issue examines a complex research question in the intersection of two STIs.

Where data are scarce, we need to set appropriate expectations to what mathematical modelling can do. With rich data, a model can be calibrated to multiple data sources, validated and then used for forecasting while propagating parameter uncertainty. In the absence of such data resources, a modelling study remains at hypotheses-generating phase. In their study, Hui et al focused on the indirect effects of cervical cancer screening implementation on TV detection. Table 1 describes the broader context of potential interactions between HR-HPV and TV and provides suggestions for future modelling work for TV. A key determinant of STI acquisition risk is differences in (unprotected) sexual activity within the population, with higher number of partners being associated with both HR-HPV and TV acquisition. In the TV model, the transmission dynamics of HR-HPV were not included in the model framework, and the prevalence of TV among those who had HR-HPV infection was assumed to be the same as in the general population. Given the same mode of transmission, we might expect there to be a higher prevalence of TV among those

| Table 1 | Conceptualising how proximate and distal factors for trichomoniasis (TV) can create interactions with high-risk (HR)-HPV and further heterogeneity at the population level |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------|
| **Natural history of TV** | **Sexual risk behaviour** | **More distal sources of heterogeneity (age, ethnicity, urbanicity and region)** |
| **HR-HPV epidemiology and cervical cancer screening interventions** | It is unclear how many TV cases are detected via cervical cytology. Whether there are biological interactions between HR-HPV and TV is not known. | Individuals with more sexual partners are more likely to have HR-HPV. They may also have different test-seeking behaviours. | Variation in cervical screening and vaccine uptake in the population. |
| **TV epidemiology** | There are a number of uncertainties around the natural history and infection duration for TV among women and men. | Individuals with more sexual partners are more likely to have TV. | There is marked variation in TV prevalence in the population and higher prevalence of TV among older populations. |
| **Future considerations for modelling TV** | Sensitivity analyses similar to those done by Hui et al offer a way to explore the uncertainty around natural history parameters. Time series data are needed for TV testing and diagnoses in different settings to improve model estimates. Impact and cost-effectiveness of testing asymptomatic people for TV are not known. | Individuals with HR-HPV infection are more likely to be infected with TV, resulting in greater coinfection prevalence than if the infections were independently distributed. Future modelling studies should account for this if they examine the impact of cervical cancer screening interventions. | The findings from a model calibrated to one setting may not be applicable to other settings in the presence of different epidemiological characteristics. Unexplored heterogeneities may also overestimate the impact of interventions. |

1Department of Global Health and Population, Harvard T H Chan School of Public Health, Boston, Massachusetts, USA
2Faculty of Health Sciences, Bristol Veterinary School, University of Bristol, Bristol, UK

Correspondence to Dr Minttu M Rönn, Department of Global Health and Population, Harvard University T H Chan School of Public Health, Boston, MA 02115, USA; mronn@hsph.harvard.edu
infected with HR-HPV than those not infected with HR-HPV, and this in turn may result in larger number of TV being detected under new guidelines than estimated in the study. Assumptions of the intensity of control strategies at baseline, prior to comparison with counterfactuals, will also impact the magnitude of change seen in the counterfactuals.9

We may also consider the importance of variation within the population; increasing heterogeneity in STI distribution in the population makes it easier to sustain a stable, low population prevalence of infection, but it will make the infection harder to control due to subgroups of the population being exposed to the pathogen at higher rate than others.6 If heterogeneities are epidemiologically important in a given setting, and they have not been included in the model framework, the model estimates of intervention impact can be overestimated. TV prevalence is marked by variation regionally and among minority populations. TV positivity is estimated as 0.4% in Sydney,10 while positivity is 8.4–25% in rural areas and higher among Aboriginal populations.11 TV is also associated with older age.13

In order to take this variation into account in TV modelling, we need further data on number of TV infections diagnosed in different settings, and how these are changing over time. As an example, the model was calibrated to a single clinic-based positivity estimate of TV.10 There are other plausible scenarios that could have given rise to a good model fit, but that would have resulted in lower contribution of cervical cytology to TV control. Furthermore, data are urgently needed now that the field is moving towards point-of-care testing amid considerations of wider implementation of TV testing.14 It is challenging to limit the scope of a modelling study to what is feasible and supported by data. Prior assumptions are also required to create any modelling framework, and the study by Hui et al brings about interesting questions to explore in future.

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