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SEXUAL HEALTH

Modelling the potential role of saliva use during masturbation in the transmission of *Neisseria gonorrhoeae* at multiple anatomical sites

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ABSTRACT

Background. *Neisseria gonorrhoeae* can be cultured from saliva in men with pharyngeal gonorrhoea and could theoretically be transmitted from the pharynx to the urethra when saliva is used as a lubricant for masturbation. In this work, we proposed that saliva use during masturbation may be a potential transmission route of gonorrhoea. **Methods.** We analysed the transmission of *Neisseria gonorrhoeae* at the oropharynx, urethra and anorectum with mathematical models among men who have sex with men using data from six different studies. Model 1 included transmission routes (oral sex, anal sex, rimming, kissing, and three sequential sex practices). In Model 2, we added saliva use during solo masturbation and mutual masturbation to model 1. **Results.** Model 2 could replicate single site infection at the oropharynx, urethra and anorectum and multi-site infection across six different datasets. However, the calibration of Model 2 was not significantly different from Model 1 across four datasets. Model 2 generated an incidence of gonorrhoea from masturbation of between 5.2% (95% CI: 3.2–10.1) to 10.6% (95% CI: 5.8–17.3) across six data sets. Model 2 also estimated that about one in four cases of urethral gonorrhoea might arise from solo masturbation and mutual masturbation. **Conclusions.** Our models raise the possibility that saliva use during masturbation may play a role in transmitting gonorrhoea. This is an important area to explore because it contributes to the knowledge base about gonorrhoea transmission.

Keywords: anatomical, mathematical model, men who have sex with men, mutual masturbation, *Neisseria gonorrhoeae*, saliva, sexual behaviour, site-specific, solo masturbation, transmission.

Introduction

Neisseria gonorrhoeae is a common sexually transmitted infection (STI) among men who have sex with men (MSM).[1,2] Emerging evidence suggests that sexual practices involving the oropharynx and saliva may be potential transmission routes of *N. gonorrhoeae*.[3–8] A previous study has explored the site-specific transmission of *N. gonorrhoeae* in MSM and found that sequential sexual practices involving the oropharynx or saliva might explain the relatively high proportion of infections at multiple anatomical sites in MSM.[7] However, the current understanding of the role of the oropharynx and saliva in the transmission of *N. gonorrhoeae* is still unclear.

Masturbation is a common sexual practice,[9] and MSM may use saliva as a lubricant when masturbating. In a study conducted among 446 MSM attending a sexual health service, 33.9% of participants reported they had used saliva as a lubricant for solo masturbation, and 33.6% of participants used their saliva as a lubricant for mutual masturbation.[10] In addition, a cross-sectional study from Australia demonstrated that 48.4–60.8% of 1596 MSM attending a sexual health service reported mutual masturbation using saliva as a lubricant.[11]

The role of using saliva in sexual practice in the transmission of *N. gonorrhoeae* has not been well studied. The proportion of saliva samples positive by culture among men with culture-positive oropharyngeal infection was 8%,[12] 43%[13] and 67%,[14] in previous studies,

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which indicates that viable bacteria are present in saliva. A study reported that *N. gonorrhoeae* bacterial DNA load in the saliva was 446 copies/mL (interquartile ranges (IQR), 204–1390 copies/mL) and was 1.7×10^5 (IQR: 2.8×10^3 to 2.6×10^6) copies/mL in the pharynges.[15] Cumulating evidence suggests that *N. gonorrhoeae* may be transmitted through saliva.[6–8,16] As *N. gonorrhoeae* could be cultured from saliva among MSM with oropharyngeal gonorrhoea, it is possible that infectious *N. gonorrhoeae* could be transmitted via activities involving saliva,[15] such as masturbation; however, there have been no studies or mathematical models examining masturbation as a route of transmission of *N. gonorrhoeae*. We have previously explored saliva's role in *N. gonorrhoeae* transmission among MSM in mathematical models, finding that sexual practices involving saliva (e.g. oral sex, rimming, and kissing) may be important for gonorrhoea transmission;[7,8,16] however, to date, no study has investigated the role of saliva use during masturbation in the transmission of *N. gonorrhoeae*. In this paper, we use these models to test whether adding masturbation involving saliva as a route of transmission of *N. gonorrhoeae* in MSM can improve the model. We then estimate what proportion of gonorrhoea incidence is attributed to masturbation involving saliva.

Methods

Data resource

We identified six available studies using nucleic acid amplification tests with single-site and multi-site infection of *N. gonorrhoeae*: (1) 4873 MSM attending the Melbourne Sexual Health Centre;[17] (2) MSM surveillance data (271, 242 consultations) from all Dutch STI clinics;[18] (3) 1610 community samples of MSM in Thailand;[19] (4) 393 MSM attending STD and HIV care clinics in the USA;[20] (5) 179 MSM with HIV in the USA;[21] and (6) 3049 MSM attending a health centre in the USA[16] (Supplementary Table S1). To ensure the generalisability of our models, we calibrated the model using six site-specific datasets individually.

Transmission framework

We developed population-level, susceptible-infected-susceptible compartmental models based on some published site-specific models.[7,8,16,22,23] According to *N. gonorrhoeae* infection status, the model incorporated eight states, including susceptible, infection at the oropharynx only, infection at the urethra only, infection at the anorectum only, infection at both oropharynx and urethra, infection at both oropharynx and rectum, infection at both urethra and anorectum, and infection at all three anatomical sites (Supplementary Fig. S1).

Simulation of baseline transmission routes for *N. gonorrhoeae* infections

Our model simulated seven baseline *N. gonorrhoeae* transmission routes (Fig. 1). These included four sexual practices: anal sex (urethra to anorectum and anorectum to the urethra), penile–oral sex (oropharynx to urethra and urethra to oropharynx), rimming (oropharynx to anorectum and anorectum to oropharynx), and kissing (oropharynx to oropharynx). These also included three combined sequential sex practices: oral sex followed by anal sex (where the penis acts as a mediator and carries *N. gonorrhoeae* to the oropharynx or anorectum or *vice versa*), using saliva as a lubricant for anal sex (pass *N. gonorrhoeae* from his oropharynx to his urethra) and oral sex followed by oral–anal sex (rimming) or *vice versa* (oropharynx acts as a mediator and carries *N. gonorrhoeae* to the urethra or anorectum.

Simulation of masturbation

Our model included both solo masturbation and mutual masturbation (Fig. 1). The first sexual practice is when a man uses saliva as a lubricant for solo masturbation. An individual's saliva transmits *N. gonorrhoeae* from their oropharynx to their urethra in this route. The second sexual practice is using saliva as a lubricant for mutual masturbation. A man's saliva transmits *N. gonorrhoeae* from his oropharynx to his partner's urethra in this route. Further details are provided in the Supplementary materials.

Model construction

We established three models to examine the effect of masturbation on the transmission of *N. gonorrhoeae* (Fig. 1). We used our published *N. gonorrhoeae* model as the baseline model (Model 1).[7] Model 1 included four sexual practices and three sequential sex practices described in the previous section about baseline transmission routes. In Model 2, we added masturbation to Model 1. To compare the importance of masturbation and sequential sexual practices, we built Model 3. In Model 3, we included only the four sexual practices from Model 1 (oral sex, anal sex, rimming and kissing) and masturbation and excluded the three sequential sex practices. The purpose of this design is to investigate if masturbation alone may explain the multi-site coinfection of *N. gonorrhoeae* without the inclusion of sequential sexual practices.

Model parameterisation and calibration

We used previously published sexual practices and *N. gonorrhoeae infection* progression data for our models' parameters (Supplementary Table S2). In our analysis, we sampled the parameter space using Latin Hypercube Sampling (LHS) on ranges of parameter values. Calibration is performed with LHS as the initial point, and 1000

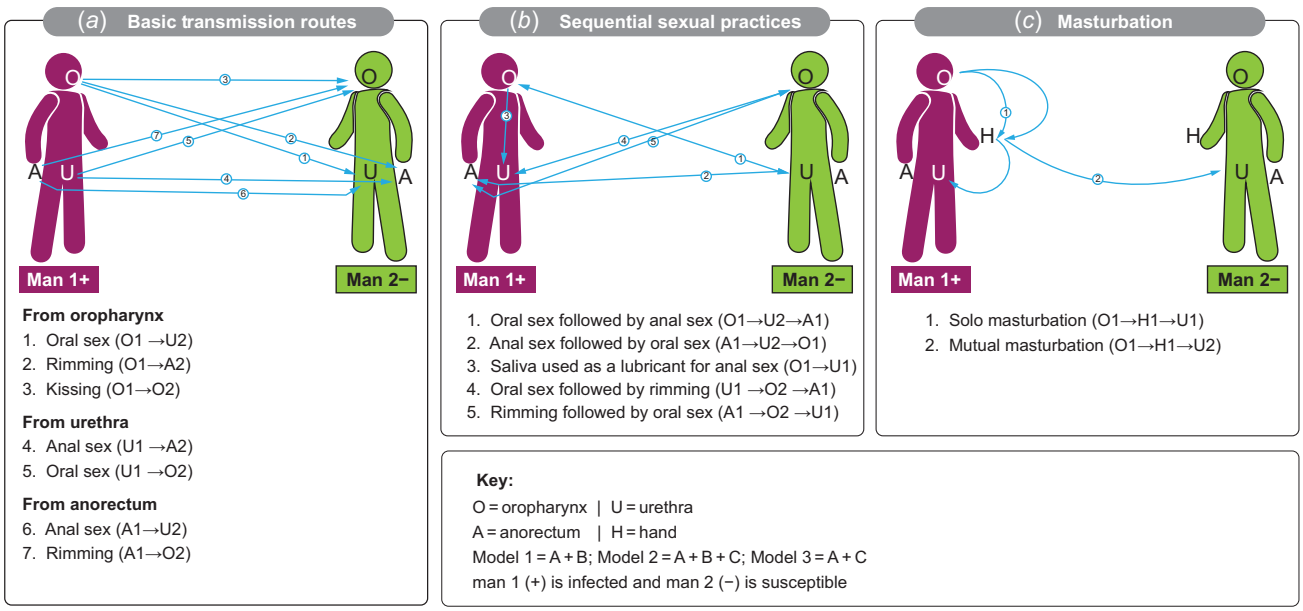

Fig. 1. Transmission routes of *Neisseria gonorrhoeae*. (*a*) Basic transmission routes: oral sex, anal sex, rimming, and kissing. (*b*) Sequential sexual practices including oral sex followed by anal sex (or *vice versa*), saliva used as a lubricant for penile–anal sex and followed by oral–anal sex (rimming) or *vice versa*. (*c*) Masturbation. Saliva uses as a lubricant for solo masturbation, and saliva used as a lubricant for mutual masturbation.

parameter sets are simulated. For each set, we simulated the transmission to obtain the equilibrium prevalence at each anatomical site (i.e. oropharynx, urethra, and anorectum) and multi-site infection (i.e. oropharynx and urethra, oropharynx and anorectum, urethra and anorectum, all three sites). This is compared with the actual data to define the goodness of fit. We use fmincon based on trust-region-reflective to minimise the root mean squared error (RMSE) for each of the 1000 simulations.[24] Out of these simulations, we sorted the simulation outputs in descending order, and 10% of simulations were regarded as the calibrated model estimates to the epidemic trend and used to generate the model outputs with 95% confidence intervals (CIs). Based on our previously reported method,[7,8,22] we estimated the incidence at any given time and calculated the ratio between the number of new infections and the number of susceptible individuals. The model parameters, model calibration process and data sources have been described in detail in our previous publications.[7,8,22]

Statistical analysis

We measured the calibration error by calculating the RMSE and compared models using the minimal RSME between the empirical multi-site infections data and the corresponding calibration results. We also conducted an independent-samples *t*-test to analyse the difference in RSME between the two models. The difference was statistically significant at $P < 0.05$. Additionally, to calculate the effect size, we used Cohen's d to estimate the effect size of RMSE between two models.[25–27] Effect sizes were classified as small (Cohen's $d = 0.2$), medium (Cohen's $d = 0.5$), and large (Cohen's $d \geq 0.8$).[25] When $P < 0.05$ and the difference has a large effect size (Cohen's $d \geq 0.8$), we consider the two models as being significantly different. We used MATLAB R2019a (The MathWorks, Inc.) to solve the system of differential equations and conduct statistical analysis.

Sensitivity analysis

Due to the variations in the duration of sexual practices performed by MSM,[8] we conducted eight univariate sensitivity analyses for the models over the frequency of solo masturbation and mutual masturbation, and the proportion of saliva used for solo masturbation and proportion of saliva use for mutual masturbation. Sensitivity analysis was performed using the LHS method to confirm the model's robustness concerning small parameter perturbations.[28] We performed eight sensitivity analyses for all six datasets (Supplementary Table S3). Details are given in the Supplementary material section.

Ethics approval

This study involved secondary data analysis of datasets obtained from previous publications, and therefore ethical approval was not required.

Results

We constructed Model 2 by adding masturbation as a transmission route to Model 1. Model 2 could replicate single site infection at the oropharynx, urethra and anorectum and multi-site infection in six different datasets. The calibration of Model 2, with regard to the simulated prevalence distribution, is similar to Model 1 across all six datasets (Supplementary Fig. S2). We built a third Model (model 3) by removing sequential sexual practices from Model 1 and then adding masturbation. Model 3 could replicate oropharyngeal, urethral and anorectal prevalence at single anatomical sites, but underestimated the prevalence in men with multi-site infections at both the oropharynx and anorectum across the six datasets.

Our findings demonstrated that the addition of masturbation (Model 2) to the baseline model (Model 1) could replicate both single and multi-site prevalence levels from empirical studies (Fig. 2), but did not improve the calibration. For only two data sets, Model 2 (adding masturbation to Model 1) had a significantly higher RMSE than Model 1, and the effect size of the RMSE was large (Cohen's $d > 0.8$). Taken together, the calibration of Model 2 was not significantly different from Model 1 across four of the six datasets. (Fig. 2; Supplementary Table S4).

Our findings demonstrated that inclusion of masturbation, but removing sequential sexual practices from the model (Model 3), could not replicate the empirical prevalence and incurred large errors during calibration. Model 3 had a significantly higher RMSE than Model 1 (P-value < 0.01 for all six datasets), and the effective size of the RMSE between Model 3 and Model 1 was large (Cohen's $d > 0.8$ for all six datasets). Similarly, Model 3 had a significantly higher RMSE than Model 2 (P-value < 0.01 for all six datasets), and the effective size of the RMSE was also large (Cohen's $d > 0.8$ for all six datasets) (Fig. 2; Supplementary Table S4).

We used calibrated models (Models 2 and 3) to estimate the incidence of gonorrhoea caused by masturbation (Fig. 2). The estimated proportion of the incidence from Model 2 caused by masturbation was between 5.2% (95% CI 3.2–10.1%) and 10.6% (95% CI 5.8–17.3%). Importantly, solo masturbation accounted for the majority of all new cases caused by masturbation (4.9% [95% CI 3.0–9.4%] to 9.7% [95% CI 4.5–17.3%] across six datasets), whereas mutual masturbation accounted only for a small proportion (0.2% [95% CI 0.0–2.0%] to 0.6% [95% CI 0.0–5.4%] across six datasets) (Fig. 3; Supplementary Table S5).

Compared with Model 1, Model 2 included masturbation that did not significantly alter the proportion of gonorrhoea incidence at the oropharynx, urethra or anorectum across the six datasets. However, Model 3 (removal of sequential sexual practices and adding in of masturbation to Model 1) significantly altered the proportion of gonorrhoea incidence at the oropharynx, urethra and anorectum across three datasets. In Model 1, the incidence of gonorrhoea infection varied by anatomic site (oropharyngeal: 33.9–59.8%;

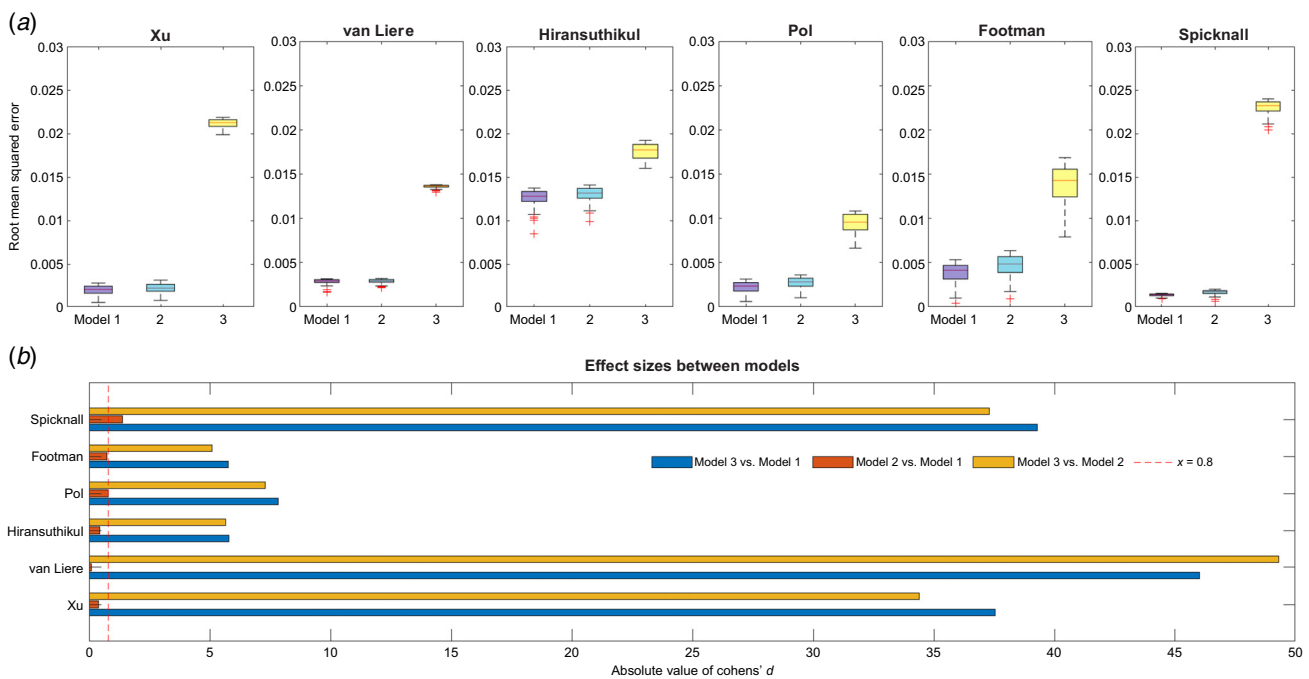

Fig. 2. Root mean squared error and effect size of calibrated models with or without masturbation across six different datasets. (*a*) The boxplots of root mean squared error. (*b*) The effect size of calibrated models. Effect sizes were classified as small (Cohen's $d = 0.2$), medium (Cohen's $d = 0.5$), and large (Cohen's $d \geq 0.8$). Model 1: anal sex, oral sex, rimming, kissing, and sequential sexual practices; Model 2: Model 1 + masturbation; Model 3: sequential sexual practices + masturbation.

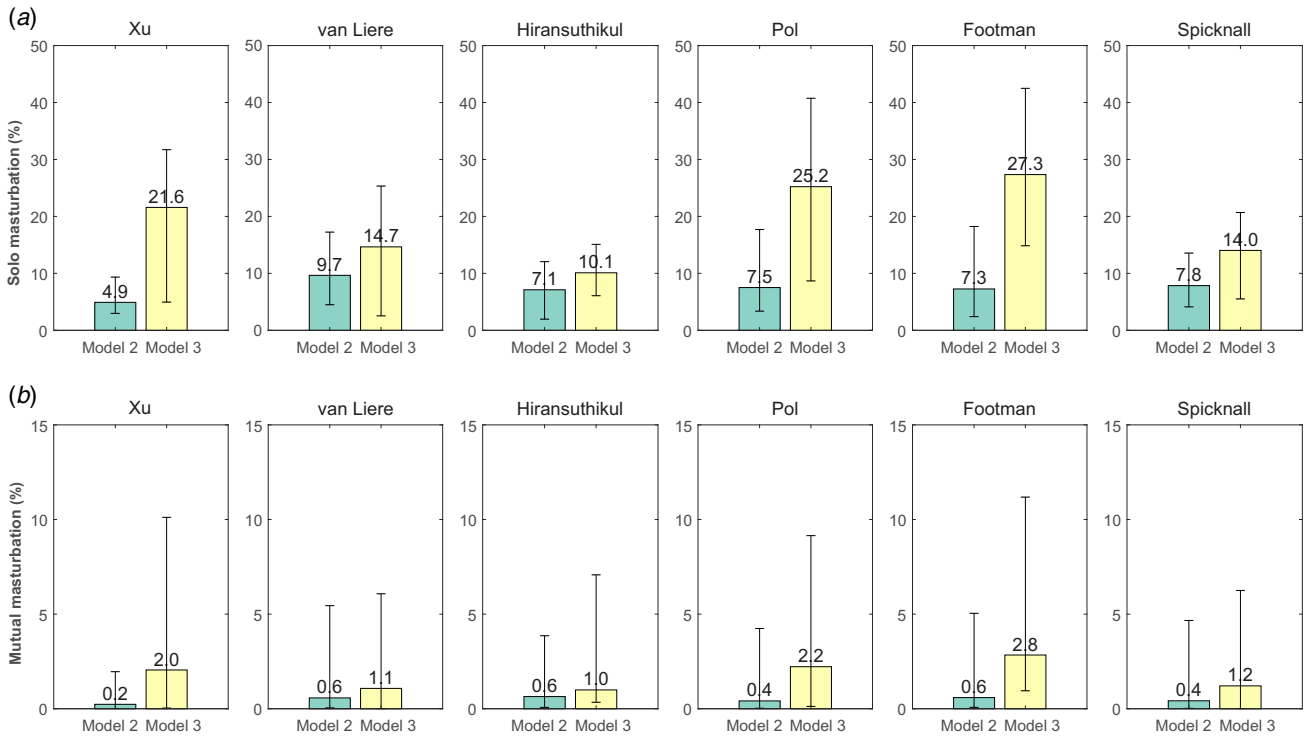

Fig. 3. Mathematical modelling to estimate the proportion of gonorrhoea incidence by masturbation across six different data sets. (*a*) The estimated proportion of gonorrhoea incidence caused by solo masturbation. (*b*) The estimated proportion of gonorrhoea incidence caused by mutual masturbation. Model 1: anal sex, oral sex, rimming, kissing, and sequential sexual practices; Model 2: Model 1 + masturbation; Model 3: sequential sexual practices + masturbation.

anorectal: 18.6–29.9%; urethral: 18.5–36.3%), across six datasets. This was also the case for Model 2, the incidence of gonorrhoea infection varied by anatomic site (oropharyngeal: 32.8–59.0%; anorectal: 17.0–28.4%; urethral: 19.8–29.6%), across six datasets. In Model 3, the incidence of gonorrhoea infection varied by anatomic site (oropharyngeal: 21.3–51.7%; anorectal: 14.0–30.7%; urethral: 28.3–58.8%), across six datasets. The model predicted that about one in four cases of urethral gonorrhoea might arise from masturbation (Fig. 4; Supplementary Table S6).

Sensitivity analysis

The results of sensitivity analysis showed that our findings are robust to the model structure and model parameters. The results also showed that varying frequency of masturbation and the proportion of saliva use for masturbation did not alter our conclusions related to Model 2 calibration (Supplementary Fig. S3). Sensitivity analysis of the RMSE and effect size of calibrated Model 2 across six different datasets showed similar results, and Cohen's d statistic was <0.8 across five datasets. We only found Cohen's $d > 0.8$ in one sensitivity analysis of a dataset (increased the proportion of saliva use for mutual masturbation to double) (Supplementary Fig. S4).

Discussion

This is the first mathematical modelling study to explore the transmission of *N. gonorrhoeae* during masturbation. Our study shows that including saliva as a lubricant for masturbation could replicate the prevalence of *N. gonorrhoeae* at the oropharynx, urethra, and anorectum in MSM, but the calibration was not significantly different from our previously validated models across four of six datasets. When we included masturbation, the proportion of incident infections attributable to masturbation was relatively low compared to other sexual practices. Our model predicted that about one in four cases of urethral gonorrhoea might arise from masturbation, if indeed it transmitted gonorrhoea. To the best of our knowledge, no empirical data have been published to assess the role of masturbation and saliva use for potentially transmitting *N. gonorrhoeae*. This hypothesis was only recently generated following some unexpected findings from a randomised controlled trial.[29] However, it would seem that this potential route of transmission was relatively plausible given that saliva is commonly used for masturbation, and it is relatively easy to culture *N. gonorrhoeae* from saliva. This is an important area to explore because it contributes to the knowledge base about transmission and may lead to further interventions to

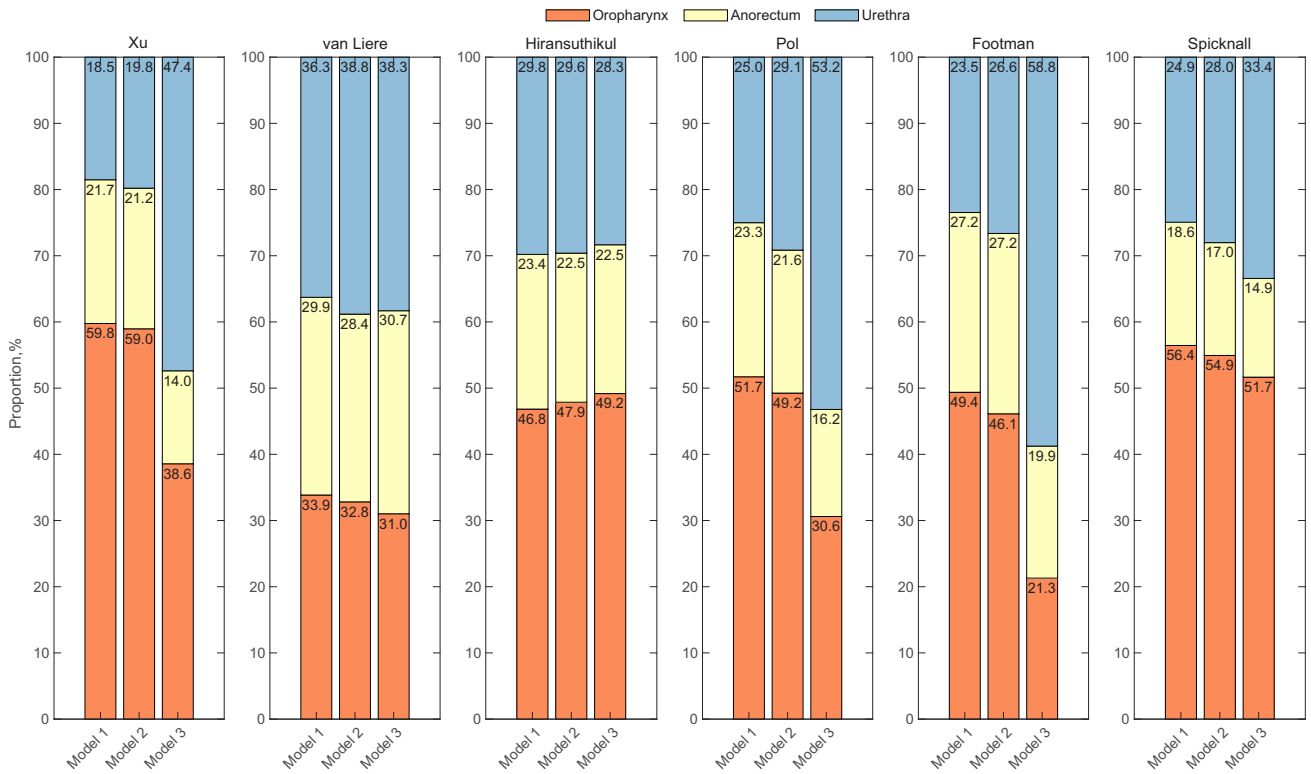

Fig. 4. Mathematical modelling to estimate the proportion of gonorrhoea incidence at the oropharynx, urethra and anorectum using models with or without masturbation across six different datasets. Model 1: Anal sex, oral sex, rimming, kissing, and sequential sexual practices; Model 2: Model 1 + masturbation; Model 3: sequential sexual practices + masturbation.

control *N. gonorrhoeae*. Future empirical studies will be needed to confirm our model findings.

Our models raise the possibility that masturbation may play a role in transmitting *N. gonorrhoeae*, although the models also indicate that it may not necessarily be a transmission route. In our previous model, when saliva was used as a lubricant for anal sex, it improved the model, but unlike masturbation, some empirical studies support transmission when saliva is used as a lubricant for anal sex.[30–32] It would seem probable that if saliva can transit *N. gonorrhoeae* to the anus when used as a lubricant, some transmission may occur when saliva is used for masturbation.

We found that the calibration of Model 2 was similar to Model 1. Although Model 2 had a significantly higher RMSE than Model 1 for five of the six datasets, the Cohen's *d* statistic was >0.8 for only two data sets. However, when considering these, it is important to reflect on how little is known about how saliva is used either as a lubricant for anal sex or masturbation, including the quantity used, exact site on the penis in relation to the urethra and the duration of use. It is premature to be too definite about the likelihood of any transmission from saliva in this context. Future empirical studies will be needed to confirm or refute the findings of our models.

If saliva use during masturbation had a role in the transmission of *N. gonorrhoeae*, its role would likely be relatively minor. Indeed, our results suggest that the inclusion of masturbation would not significantly alter the proportion of incident gonorrhoea occurring at the three anatomical sites; the oropharynx, urethra and anorectum. When we included masturbation, the incidence of urethral infection from any site did not change greatly because the extra number of urethra infections as a result of saliva use during masturbation resulted in a fall in urethral cases acquired from other sites (throat from oral sex or anus from anal sex). Our model estimates that perhaps one-quarter of urethral infection cases were the result of saliva use druing masturbation as compared with other sites; however, these infection cases may have a longer incubation period than urethral cases acquired directly from the partner, presumably because *N. gonorrhoeae* would first need to be acquired in the oropharynx and then transmitted to the urethra.[7] The duration of most oropharyngeal infections is short,[33] and infection is self-limited, so these cases would likely occur within a few weeks after the initial contact and therefore not raise questions for clinicians about transmission.

We also created a third model that excluded sequential sexual practices but included masturbation, and found that

this model worsened the calibration. These results indicated that sequential sexual practices are more important for transmitting *N. gonorrhoeae* than masturbation. The present study revealed that sequential sexual practices might be important for the high proportion of *N. gonorrhoeae* multi-site infections. A previous survey reported that the majority of MSM performed sequential sexual practices in the same sexual encounter.[34] Under this context, we hope our work could encourage further empirical research to explore the role of sequential sexual practices on the transmission of *N. gonorrhoeae*.

The role of using saliva as a medium in the transmission of *N. gonorrhoeae* is a relatively new concept, apart from some case reports >50 years ago that suggested that kissing may transmit *N. gonorrhoeae*.[35,36] Saliva is widely distributed when men have sex together through kissing, using it as a lubricant, and through rimming, and there are varying degrees of evidence to suggest that all of these activities transmit *N. gonorrhoeae*.[35,36] Our work adds the possibility that masturbation involving the saliva may also play a role in the transmission of *N. gonorrhoeae* in MSM.[6,37]

There are some limitations to our study that should be noted. First, there are surprisingly little data about masturbation, including basic issues such as its frequency, duration, and exactly how saliva is used for solo masturbation or mutual masturbation. These uncertainties may affect the estimates that we generated in our models. Second, considerable social desirability bias is likely to be operating when studies try to estimate how commonly men masturbate, so we have taken estimates towards the upper end of published estimates. We have conducted sensitivity analyses for the models over the frequency of masturbation and the proportion of solo masturbation and mutual masturbation to address these uncertainties. Third, we acknowledge that we have built our models despite there being no evidence for (or against) masturbation transmitting *N. gonorrhoeae*, other than that *N. gonorrhoeae* is present in saliva and saliva is commonly used for lubrication during masturbation.[29] We hope that our models will encourage more researchers to undertake some empirical studies to investigate this. Fourth, we acknowledge that there are considerable uncertainties in certain model parameters (e.g. the untreated duration of oropharyngeal and anorectal infections), which may influence estimates of transmission.[16] A publication that is currently available online has reported a shorter duration of rectal gonorrhoea (9 weeks)[38] than we used in our model or what previous studies had reported (49 weeks).[7,8] Fig. 1 in this paper shows that the duration estimate was based on seven cases, of which five lasted between 2 and 3 weeks[38] and, therefore, as the authors mention, may not represent true infection. Therefore, we have not changed our results to include this shorter duration; however, if our model did include a shorter duration of rectal infection, the nett effect would be greater transmissibility of gonorrhoea from the oropharynx and urethra to maintain the infection prevalence. Hence, saliva use during masturbation is likely to play an even more important role for gonorrhoea transmission in MSM. Finally, we used six epidemiology datasets of *N. gonorrhoeae* with single-site infection and multi-site infection in MSM to test our models, which may not fully represent the MSM population.

Conclusion

In conclusion, saliva as a lubricant for masturbation may be a potential transmission route of gonorrhoea. However, considering the finding that men commonly use saliva as a lubricant for masturbation and that viable *N. gonorrhoeae* is often present in saliva among men with oropharyngeal gonorrhoea, it is reasonable to assume it may occur.[35,36] Given the marked paucity of data on masturbation and the increasing incidence of gonorrhoea at the population level, it would seem sensible that investigators explored the transmission of gonorrhoea through saliva and particularly the possibility of transmission when saliva is used as a lubricant for masturbation.

Supplementary material

Supplementary material is available online.

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Data availability. All data analysed during this study are included in this article and its supplementary files.

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