Supplementary Material

Estimating the syphilis epidemic among gay, bisexual and other men who have sex with men in Australia following changes in HIV care and prevention

Anna L. Wilkinson\textsuperscript{A,B,*}, Nick Scott\textsuperscript{A,B,*}, Tom Tidhar\textsuperscript{A}, Phillip Luong\textsuperscript{A}, Carol El-Hayek\textsuperscript{A}, David P. Wilson\textsuperscript{A}, Christopher K. Fairley\textsuperscript{C,D}, Lei Zhang\textsuperscript{C,D}, David Leslie\textsuperscript{E,†}, Norman Roth\textsuperscript{F}, B. K. Tee\textsuperscript{G}, Margaret Hellard\textsuperscript{A,B,H} and Mark Stoové\textsuperscript{A,B,I}

\textsuperscript{A}Disease Elimination Program, Burnet Institute, 85 Commercial Road, Melbourne, Vic. 3004, Australia.
\textsuperscript{B}School of Public Health and Preventive Medicine, Monash University, Alfred Hospital, Commercial Road, Melbourne, Vic. 3004, Australia.
\textsuperscript{C}Melbourne Sexual Health Centre, Alfred Health, 580 Swanston Street, Carlton, Vic. 3053, Australia.
\textsuperscript{D}Central Clinical School, Faculty of Medicine, Nursing and Health Sciences, Monash University, Commercial Road, Melbourne, Vic. 3004, Australia.
\textsuperscript{E}Victorian Infectious Disease Laboratory, 792 Elizabeth Street, Melbourne, Vic. 3000, Australia.
\textsuperscript{F}Prahran Market Clinic, Pran Central, Mezzanine Level, corner Commercial Road and Chapel Street, Prahran, Vic. 3181, Australia.
\textsuperscript{G}The Centre Clinic, 77 Fitzroy Street, St Kilda, Vic. 3182, Australia.
\textsuperscript{H}Infectious Disease Department, Alfred Health, Alfred Hospital, Commercial Road, Melbourne, Vic. 3004, Australia.
\textsuperscript{I}Corresponding author. Email: mark.stoove@burnet.edu.au

* Authors A. L. Wilkinson and N. Scott contributed equally to this manuscript.

† Deceased.
Table S1. Model parameters

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
<th>Symbol</th>
<th>Source/comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIV parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effectiveness of condoms at preventing HIV/syphilis</td>
<td>70%</td>
<td>$\epsilon_c$</td>
<td>(1)</td>
</tr>
<tr>
<td>Effectiveness of PrEP at preventing HIV</td>
<td>86%</td>
<td>$\delta_p$</td>
<td>(2)</td>
</tr>
<tr>
<td>Reduction in HIV infectiousness when virally suppressed</td>
<td>96%</td>
<td>$\delta$</td>
<td>(3)</td>
</tr>
<tr>
<td>Syphilis parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of exposed stage (days)</td>
<td>21</td>
<td>$1/\beta_1$</td>
<td>(4, 5)</td>
</tr>
<tr>
<td>Duration of infectious stage (days)</td>
<td>730.5 (1-3 years)</td>
<td>$1/\beta_2$</td>
<td>(4, 5)</td>
</tr>
<tr>
<td>Duration of treatment from late latent stage</td>
<td>7</td>
<td>$1/\beta_3$</td>
<td>(4)</td>
</tr>
<tr>
<td>Proportion of GBM at high-risk of syphilis</td>
<td>18%</td>
<td>$\gamma$</td>
<td>(6)*</td>
</tr>
<tr>
<td>Increased syphilis risk for high-risk GBM</td>
<td>9.68</td>
<td>$\Gamma$</td>
<td>(6)*</td>
</tr>
<tr>
<td>Proportion who test frequently</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-negative GBM</td>
<td>69%</td>
<td>$\omega^-$</td>
<td>The Burnet Institute*</td>
</tr>
<tr>
<td>HIV-positive GBM</td>
<td>90%</td>
<td>$\omega^+$</td>
<td></td>
</tr>
<tr>
<td>Syphilis testing frequency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-negative GBM</td>
<td>1/224 days</td>
<td>$\tau^-$</td>
<td>VPCNSS</td>
</tr>
<tr>
<td>HIV-positive GBM</td>
<td>1/133 days</td>
<td>$\tau^+$</td>
<td></td>
</tr>
<tr>
<td>Sexual risk parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of serodiscordant sex acts</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV-positive GBM</td>
<td>5%</td>
<td>$\alpha^+$</td>
<td>(7)</td>
</tr>
<tr>
<td>HIV-negative GBM (no PrEP)</td>
<td>5%</td>
<td>$\alpha^-$</td>
<td>(7)</td>
</tr>
<tr>
<td>HIV-negative GBM (PrEP)</td>
<td>5%</td>
<td>$\alpha^-$</td>
<td>Assumed</td>
</tr>
<tr>
<td>Condom use with casual partners</td>
<td>42%</td>
<td>$c$</td>
<td>(8)</td>
</tr>
<tr>
<td>Average time at risk of sexually transmitted infections</td>
<td>50 years</td>
<td>$1/\mu$</td>
<td>Assumed 15-64 year olds</td>
</tr>
</tbody>
</table>

*Syphilis monitoring report, November 2015, Burnet Institute, includes unpublished data from the Victorian Primary Care Network on Sentinel Surveillance (VPCNSS) and the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance projects.

†PrEP trial data in Australia found that 18% of participants accounted for 68% of STI infections. (6) The increased risk was calculated as: ([68/18] infections per person at high risk) / ([32/82] infections per person for low risk) = 9.68.
<table>
<thead>
<tr>
<th>Year</th>
<th>Victorian population size*</th>
<th>Victorian GBM population size†</th>
<th>Victorian HIV+ GBM population size‡</th>
<th>Victorian HIV notifications§</th>
<th>Victorian notified infectious syphilis as of July 2018‖</th>
<th>Among HIV+ GBM Δ</th>
<th>Among HIV- GBM◊</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>5,445,172</td>
<td>49447</td>
<td>3560</td>
<td>178</td>
<td>291</td>
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<td>2011</td>
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<td>3738</td>
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<td>209</td>
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<td>2012</td>
<td>5,611,981</td>
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<td>200</td>
<td>467</td>
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<td>2013</td>
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<td>4121</td>
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<td>654</td>
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<td>2014</td>
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<td>2015</td>
<td>5,924,297</td>
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<td>4544</td>
<td>206</td>
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<td>2016</td>
<td>6,036,731</td>
<td>66263</td>
<td>4771</td>
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<td>2017</td>
<td>6,143,715</td>
<td>69577</td>
<td>5010</td>
<td>194</td>
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<td>2018</td>
<td>6,252,595</td>
<td>73055</td>
<td>5260</td>
<td></td>
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</tbody>
</table>

* Australian Bureau of Statistics 2006–2016 (9)
† Estimated to be 42,000 in Victoria in 2006 (10), assuming annual growth rate of 5%
‡ Calculated based on estimated HIV prevalence among GBM (11)
§ Kirby Institute 2017: annual surveillance report (12)
‖ Victorian Department of Health and Human Services syphilis notification data, by demographic and risk factor (88% of notifications are male; 74% of male notifications were GBM) (13)
Δ Victorian Department of Health and Human Services syphilis notification data: 25% of notifications were among people living with HIV, and 88% of these were GBM (13)
◊ Remaining syphilis notifications among GBM after subtracting HIV-positive GBM syphilis notifications
Figure S1: HIV-model calibration. Panels show the HIV notifications over time (top-left); the number of people living with HIV (top-right); the prevalence of HIV (bottom-left); and the care cascade of HIV (bottom-right).
Model equations

1. Define the following compartments and stratifications

\[ t = \text{time (implemented in monthly time steps)} \]
\[ P(t) = \text{total estimated GBM population size} \]
\[ P^+(t), P^-(t), P^-\_i(t) = \text{total model population size for HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM respectively. Note that these are functions of time due to population growth.} \]
\[ S^+(t), S^-(t), S^-\_i(t) = \text{total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) susceptible for syphilis compartments} \]
\[ E^+(t), E^-(t), E^-\_i(t) = \text{total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) exposed to syphilis compartments} \]
\[ I^+(t), I^-(t), I^-\_i(t) = \text{total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) infectious with syphilis compartments} \]
\[ L^+(t), L^-(t), L^-\_i(t) = \text{total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) late latently syphilis compartments} \]
\[ T^+(t), T^-(t), T^-\_i(t) = \text{total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) treatment compartments} \]

\[ i = \text{subscript to indicate whether or not someone is at low or high risk of syphilis (i=0 for low and i=1 for high).} \]

2. Define the following parameters

\[ \beta_1 = 1/\text{average duration of syphilis exposed period (21 days)} \]
\[ \beta_2 = 1/\text{average duration of syphilis infectious stage (730 days)} \]
\[ \beta_3 = 1/\text{syphilis treatment duration (7 days)} \]
\[ \omega^+, \omega^-, \omega^-\_i = \text{fraction of HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM who test regularly for syphilis} \]
\[ \tau_i^+, \tau_i^-, \tau_i^-\_i = 1/\text{average time between tests for HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM. Note that these are equal to zero for the fraction who do not regularly test for syphilis.} \]
\[ \gamma^+, \gamma^-, \gamma^-\_i = \text{fraction of HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM who are at high risk for syphilis} \]
\[ \delta = \text{relative reduction in the risk of HIV infection for people with viral suppression} \]
\[ \delta_p = \text{relative reduction in the risk of HIV infection for people on PrEP} \]
\[ D(t) = \text{fraction of people with HIV who are virally suppressed} \]
\[ \mu = 1/\text{average time at risk (assumed to be 50 years; 15-64 year olds)} \]
\[ \alpha^+, \alpha^-, \alpha^-\_i = \text{the proportion of sex acts undertaken by HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) populations that are serodiscordant (5%, 5% and 10% respectively)} \]
\[ \Gamma_i = \text{additional risk factor for GBM at high risk of syphilis. Note that } \Gamma_i = 1 \text{ if } i=0 \text{ (low risk is the reference)} \]
\[ c^+, c^-, c^-\_i = \text{average condom use among HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM.} \]
\[ \epsilon_c = \text{effectiveness of condoms} \]

3. Force of infection

Let \( \lambda_{HIV} \) be the proportionality constant (determined in the calibration procedure) for the force of HIV infection. Then the force of infection for HIV among non-PrEP (\( \Theta^- \)) and PrEP (\( \Theta^-\_i \)) users is given by:
\[ \Theta^- = \lambda_{HIV}(1 - \epsilon_c c^-) \left[ \frac{((1 - \delta)D(t) + (1 - D(t)))P^+}{P^+ + P^- + P^0} \right] \]

\[ \Theta^- = \lambda_{HIV}(1 - \epsilon_c c^-) \left[ \frac{((1 - \delta)D(t) + (1 - D(t)))P^+}{P^+ + P^- + P^0} \right] \]

Let \( \lambda^+, \lambda^-, \lambda^- \) be the proportionality constants (determined in the calibration procedure) for the force of syphilis infection among HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM respectively. The force of infection for syphilis among these populations was modelled to account for condom use and mixing between HIV-positive and HIV-negative GBM populations:

\[ \Phi^+_i = \lambda^+ \Gamma_i (1 - \epsilon_c c^+) \left( \frac{I^- + I^+}{P^- + P^+} + (1 - \alpha^+) \frac{I^+}{P^+} \right) \]

\[ \Phi^-_i = \lambda^- \Gamma_i (1 - \epsilon_c c^-) \left( 1 - \alpha^- \right) \left( \frac{I^- + I^+}{P^- + P^+} + \alpha^- \frac{I^+}{P^+} \right) \]

\[ \Phi^-_i = \lambda^- \Gamma_i (1 - \epsilon_c c^-) \left( 1 - \alpha^- \right) \left( \frac{I^- + I^+}{P^- + P^+} + \alpha^- \frac{I^+}{P^+} \right) \]

### 4. HIV-positive GBM differential equations

\[ \frac{dS^+_i}{dt} = \theta^- S^-_i + \theta^-(1 - \delta p)S^-_i - \Phi^+_i S^+_i + \beta_3 T^+_i - \mu S^+_i \]

\[ \frac{dE^+_i}{dt} = \theta^- E^-_i + \theta^- (1 - \delta p)E^-_i + \Phi^+_i S^+_i - \beta_1 E^+_i + \tau^- \omega^+ E^+_i - \mu E^+_i \]

\[ \frac{dI^+_i}{dt} = \theta^- I^-_i + \theta^- (1 - \delta p)I^-_i + \beta_4 E^+_i - \beta_2 I^+_i - \tau^- \omega^+ I^+_i - \mu I^+_i \]

\[ \frac{dL^+_i}{dt} = \theta^- L^-_i + \theta^- (1 - \delta p)L^-_i + \beta_2 I^+_i - \tau^- \omega^+ L^+_i - \mu L^+_i \]

\[ \frac{dT^+_i}{dt} = \theta^- T^-_i + \theta^- (1 - \delta p)T^-_i + \tau^- \omega^+ (E^+_i + I^+_i + L^+_i) - \beta_3 T^+_i - \mu T^+_i \]

### 5. HIV-negative (no PrEP) GBM differential equations

\[ \frac{dS^-_i}{dt} = \frac{dP(t)}{dt} - \theta^- S^-_i - \Phi^-_i S^-_i + \beta_3 T^-_i - \mu S^-_i \]

\[ \frac{dE^-_i}{dt} = -\theta^- E^-_i + \Phi^-_i S^-_i - \beta_4 E^-_i - \tau^- \omega^- E^-_i - \mu E^-_i \]

\[ \frac{dI^-_i}{dt} = -\theta^- I^-_i + \beta_4 E^-_i - \beta_2 I^-_i - \tau^- \omega^- I^-_i - \mu I^-_i \]

\[ \frac{dL^-_i}{dt} = -\theta^- L^-_i + \beta_2 I^-_i - \tau^- \omega^- L^-_i - \mu L^-_i \]

\[ \frac{dT^-_i}{dt} = -\theta^- T^-_i + \tau^- \omega^- (E^-_i + I^-_i + L^-_i) - \beta_3 T^-_i - \mu T^-_i \]
6. HIV-negative (PrEP) GBM differential equations

\[
\frac{dS_i}{dt} = -\Theta(1 - \delta_i)S_i + \Phi_iS_i - \beta_3T_i - \mu S_i
\]

\[
\frac{dE_i}{dt} = -\Theta(1 - \delta_i)E_i + \Phi_iE_i - \beta_1E_i - \omega E_i - \mu E_i
\]

\[
\frac{dT_i}{dt} = -\Theta(1 - \delta_i)T_i + \beta_1E_i - \beta_2T_i - \omega T_i - \mu T_i
\]

\[
\frac{dL_i}{dt} = -\Theta(1 - \delta_i)L_i + \beta_2T_i - \omega L_i - \mu L_i
\]

\[
\frac{dI_i}{dt} = -\Theta(1 - \delta_i)I_i + \beta_1E_i - \beta_2I_i - \omega I_i - \mu I_i
\]

\[
\frac{dT_i}{dt} = -\Theta(1 - \delta_i)T_i - \beta_3T_i - \mu T_i
\]

References


