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**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

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**Table S1.** Model parameters

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

[*]Syphilis monitoring report, November 2015, Burnet Institute, includes unpublished data from the Victorian Primary Care Network on Sentinel Surveillance (VPCNSS) and the Australian Collaboration for Coordinated Enhanced Sentinel Surveillance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 S2.** Population size, notifications and prevalence

| Year | Victorian population size[*] | Victorian GBM population size[†] | Victorian HIV+ GBM population size[‡] | Victorian HIV notifications[#] | Victorian syphilis notifications as of July 2018[ǀ] | Victorian notified infectious syphilis among GBM[ǀ] | Among HIV+ GBM[Δ] | Among HIV- GBM[◊] |
|---|---|---|---|---|---|---|---|---|
| 2010 | 5,445,172 | 49447 | 3560 | 178 | 291 | 189 | 42 | 148 |
| 2011 | 5,520,378 | 51919 | 3738 | 218 | 322 | 209 | 46 | 163 |
| 2012 | 5,611,981 | 54515 | 3925 | 200 | 467 | 304 | 67 | 237 |
| 2013 | 5,710,847 | 57241 | 4121 | 218 | 654 | 467 | 103 | 364 |
| 2014 | 5,817,241 | 60103 | 4327 | 219 | 632 | 411 | 90 | 321 |
| 2015 | 5,924,297 | 63108 | 4544 | 206 | 949 | 617 | 136 | 482 |
| 2016 | 6,036,731 | 66263 | 4771 | 233 | | | | |
| 2017 | 6,143,715 | 69577 | 5010 | 194 | | | | |
| 2018 | 6,252,595 | 73055 | 5260 | | | | | |

[*] 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)

[ǀ] 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

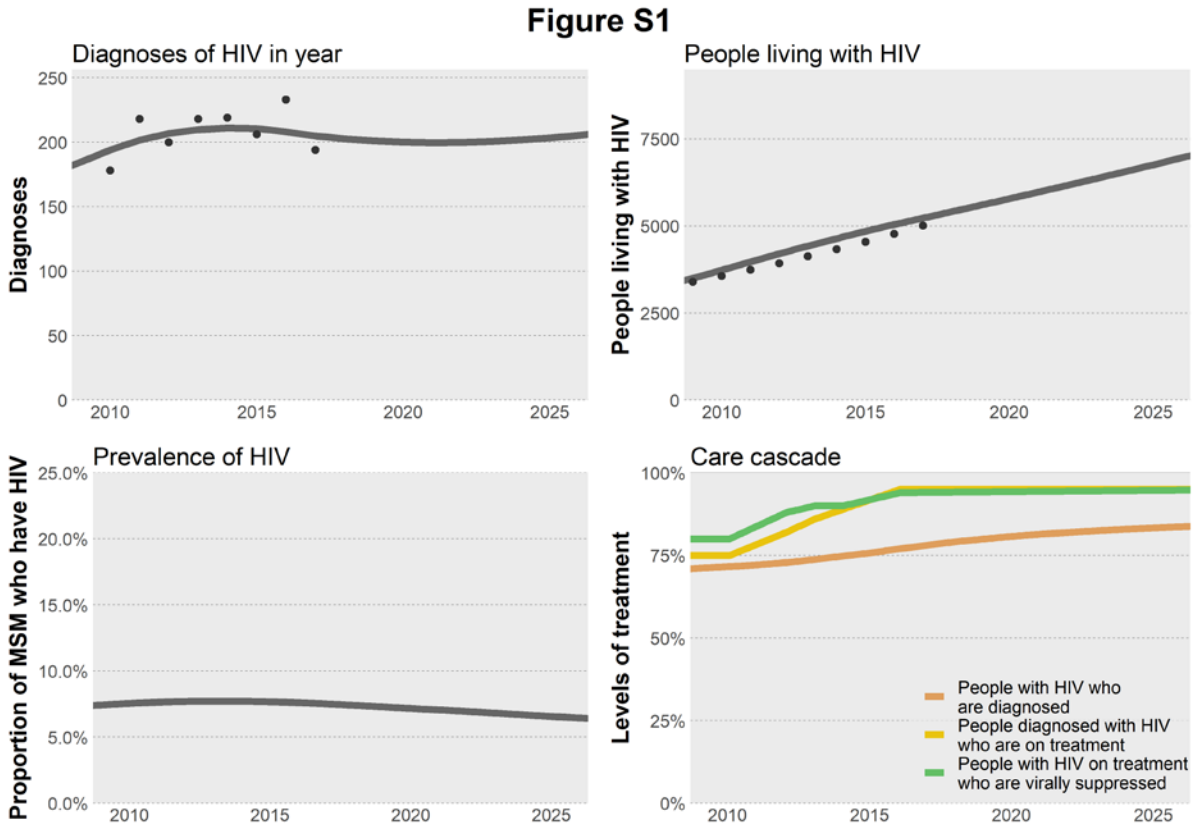


**Figure S1: HIV-model calibration**. Panels show the HIV notifications over time (top-left); the number of people living with HIV (top-right); the prevalence of HIV (bottom-left); and the care cascade of HIV (bottom-right).

**Model equations**

**1. Define the following compartments and stratifications**

$t =$ time (implemented in monthly time steps)
$P(t) =$ total estimated GBM population size
$P^+(t), P^-(t), \widehat{P^-}(t) =$ 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.
$S^+(t), S^-(t), \widehat{S^-}(t) =$ total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) susceptible for syphilis compartments
$E^+(t), E^-(t), \widehat{E^-}(t) =$ total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) exposed to syphilis compartments
$I^+(t), I^-(t), \widehat{I^-}(t) =$ total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) infectious with syphilis compartments
$L^+(t), L^-(t), \widehat{L^-}(t) =$ total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) late latently syphilis compartments
$T^+(t), T^-(t), \widehat{T^-}(t) =$ total size of the HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) treatment compartments

i = 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**

$\beta_1 = 1/$ average duration of syphilis exposed period (21 days)
$\beta_2 = 1/$ average duration of syphilis infectious stage (730 days)
$\beta_3 = 1/$ syphilis treatment duration (7 days)
$\omega^+, \omega^-, \widehat{\omega^-} =$fraction of HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM who test regularly for syphilis
$\tau_i^+, \tau_i^-, \widehat{\tau_i^-} =$1/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.
$\gamma^+, \gamma^-, \widehat{\gamma^-} =$fraction of HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM who are at high risk for syphilis
$\delta =$relative reduction in the risk of HIV infection for people with viral suppression
$\delta_P =$relative reduction in the risk of HIV infection for people on PrEP
D(t) = fraction of people with HIV who are virally supressed
$\mu =$ 1/average time at risk (assumed to be 50 years; 15-64 year olds)
$\alpha^+, \alpha^-, \widehat{\alpha^-} =$ 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)

$\Gamma_i =$ additional risk factor for GBM at high risk of syphilis. Note that $\Gamma_i = 1$ if i=0 (low risk is the reference)
$c^+, c^-, \widehat{c^-} =$ average condom use among HIV-positive, HIV-negative (no PrEP) and HIV-negative (PrEP) GBM.
$\epsilon_c =$ 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 ($\widehat{\Theta^-}$) users is given by:

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

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

Let $\lambda^+, \lambda^-, \widehat{\lambda^-}$ 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:

$$\Phi_{\mathrm{i}}^+ = \lambda^+\Gamma_i(1-\epsilon_c c^+)\left(\alpha^+\frac{I^- + \widehat{I^-}}{P^- + \widehat{P^-}} + (1-\alpha^+)\frac{I^+}{P^+}\right)$$

$$\Phi_{\mathrm{i}}^- = \lambda^-\Gamma_i(1-\epsilon_c c^-)\left((1-\alpha^-)\frac{I^- + \widehat{I^-}}{P^- + \widehat{P^-}} + \alpha^-\frac{I^+}{P^+}\right)$$

$$\widehat{\Phi_{\mathrm{i}}^-} = \widehat{\lambda^-}\Gamma_i(1-\epsilon_c \widehat{c^-})\left((1-\widehat{\alpha^-})\frac{I^- + \widehat{I^-}}{P^- + \widehat{P^-}} + \widehat{\alpha^-}\frac{I^+}{P^+}\right)$$

**4. HIV-positive GBM differential equations**

$$\frac{dS_i^+}{dt} = \Theta^- S_i^- + \widehat{\Theta^-}(1-\delta_P)\widehat{S_i^-} - \Phi_{\mathrm{i}}^+ S_i^+ + \beta_3 T_i^+ - \mu S_i^+$$

$$\frac{dE_i^+}{dt} = \Theta^- E_i^- + \widehat{\Theta^-}(1-\delta_P)\widehat{E_i^-} + \Phi_{\mathrm{i}}^+ S_i^+ - \beta_1 E_i^+ - \tau_i^+\omega^+ E_i^+ - \mu E_i^+$$

$$\frac{dI_i^+}{dt} = \Theta^- I_i^- + \widehat{\Theta^-}(1-\delta_P)\widehat{I_i^-} + \beta_1 E_i^+ - \beta_2 I_i^+ - \tau_i^+\omega^+ I_i^+ - \mu I_i^+$$

$$\frac{dL_i^+}{dt} = \Theta^- L_i^- + \widehat{\Theta^-}(1-\delta_P)\widehat{L_i^-} + \beta_2 I_i^+ - \tau_i^+\omega^+ L_i^+ - \mu L_i^+$$

$$\frac{dT_i^+}{dt} = \Theta^- T_i^- + \widehat{\Theta^-}(1-\delta_P)\widehat{T_i^-} + \tau_i^+\omega^+(E_i^+ + I_i^+ + L_i^+) - \beta_3 T_i^+ - \mu T_i^+$$

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

$$\frac{dS_i^-}{dt} = \frac{dP(t)}{dt} - \Theta^- S_i^- - \Phi_{\mathrm{i}}^- S_i^- + \beta_3 T_i^- - \mu S_i^-$$

$$\frac{dE_i^-}{dt} = -\Theta^- E_i^- + \Phi_{\mathrm{i}}^- S_i^- - \beta_1 E_i^- - \tau_i^-\omega^- E_i^- - \mu E_i^-$$

$$\frac{dI_i^-}{dt} = -\Theta^- I_i^- + \beta_1 E_i^- - \beta_2 I_i^- - \tau_i^-\omega^- I_i^- - \mu I_i^-$$

$$\frac{dL_i^-}{dt} = -\Theta^- L_i^- + \beta_2 I_i^- - \tau_i^-\omega^- L_i^- - \mu L_i^-$$

$$\frac{dT_i^-}{dt} = -\Theta^- T_i^- + \tau_i^-\omega^-(E_i^- + I_i^- + L_i^-) - \beta_3 T_i^- - \mu T_i^-$$

**6. HIV-negative (PrEP) GBM differential equations**

$$\frac{d\widehat{S_i^-}}{dt} = -\widehat{\Theta^-}(1-\delta_P)\widehat{S_i^-} - \Phi_i^-\widehat{S_i^-} + \beta_3\widehat{T_i^-} - \mu\widehat{S_i^-}$$

$$\frac{d\widehat{E_i^-}}{dt} = -\widehat{\Theta^-}(1-\delta_P)\widehat{E_i^-} + \Phi_i^-\widehat{S_i^-} - \beta_1\widehat{E_i^-} - \widehat{\tau_i^-}\widehat{\omega^-}\widehat{E_i^-} - \mu\widehat{E_i^-}$$

$$\frac{d\widehat{I_i^-}}{dt} = -\widehat{\Theta^-}(1-\delta_P)\widehat{I_i^-} + \beta_1\widehat{E_i^-} - \beta_2\widehat{I_i^-} - \widehat{\tau_i^-}\widehat{\omega^-}\widehat{I_i^-} - \mu\widehat{I_i^-}$$

$$\frac{d\widehat{L_i^-}}{dt} = -\widehat{\Theta^-}(1-\delta_P)\widehat{L_i^-} + \beta_2\widehat{I_i^-} - \widehat{\tau_i^-}\widehat{\omega^-}\widehat{L_i^-} - \mu\widehat{L_i^-}$$

$$\frac{d\widehat{T_i^-}}{dt} = -\widehat{\Theta^-}(1-\delta_P)\widehat{T_i^-} + \widehat{\tau_i^-}\widehat{\omega^-}(\widehat{E_i^-} + \widehat{I_i^-} + \widehat{L_i^-}) - \beta_3\widehat{T_i^-} - \mu\widehat{T_i^-}$$

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