A model of HIV transmission with interacting high risk groups and a bridge population

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Data about HIV transmission in China

Number of persons living with HIV/AIDS (PLWHA)

2013 - **0.81 mil** (nationwide prevalence of 0.06%), of whom **0.174 mil** diagnosed with AIDS, unevenly distributed among provinces, mainly in high-risk groups (Chinese CDC, 2015)
2015 - **1.115 mil** (AEM method), **1.37 mil** (spectrum method), **1.15 mil** (stratification method)
2020 - **1.71 mil** (AEM method), **1.55 mil** (spectrum method), **1.51 mil** (stratification method) (2012 personal communication of Y. Ruan)

Transmission facts

prior to 2006: HIV transmission has been particularly high among injectable drug users (IDUs) and former plasma donors
after 2006: heterosexual sex has become the dominant route of transmission (37.9%:29.4%, assessment of State Council AIDS Working Committee Office, P.R. China, 2008, Huang et al. 2016), a large portion attributable to the role of female sex workers (SWs)

Female sex workers (SWs) as a high risk group

Figures

- No official estimation for the number of SWs in China. **Unofficial estimations:** 4-6 millions in 2000 (Tucker et al. 2010; Wang et al. 2010). Highest estimation: 20 millions (Wei 2000)
- **Status:** 75% are married or have steady relationships (Wei 2000); 27% married or partnered in SW (Ruan et al. 2006)
- 6.9% men aged 18-49 years have bought sex from SWs at least once in their lives (Pan et al. 2011)

High risk factors

- **Behavior:** 18% unprotected sex with primary sex partner(s) and 44% unprotected commercial sex (Ruan et al. 2006). Estimations on consistent condom use with SWs: from 13.9% to 33.7% (Huang et al. 2011)
- High risk of HIV transmission from SWs to long-term partners or to newborns through mother-to-child vertical transmission
- The prevalence of HIV among SWs exceeds 1% at surveillance sites in several regions of China (Huang et al. 2011). The national HIV prevalence among SWs declined from 0.74%) in 2000-2002 to 0.40% in 2009-2011. (Zhang et al. 2015)

Injectable drug users (IDUs) as a high risk group

Estimations

- 15-fold increase in the reported number of illegal drug users (1990–2003) (Xinhua 2007)
- Estimation for the actual number of illegal drug users in 2004: 4–7 millions. Estimation for the number of IDUs: 3.6–6.2 millions (Chinese State Council 2004)

High risk factors

- The first HIV outbreak in China was recorded in 1989 in Yunnan Province, confined to IDUs
- Drug users in China are usually young and are typically poorly educated. As a result, they are usually very sexually active and have a low awareness of the consequences of high-risk behaviors
- 45.5% of IDUs share syringes and 11% of IDUs perform high-risk sexual activities (MOH China 2006)

Biological assumptions

1. Two high risk groups: female sex workers (SWs) and male injectable drug users (IDUs); a non high-risk group: male drug-free clients (DFCs).
2. Only S and I for each group since the AIDS patients are usually hospitalized or inactive, contributing little to HIV transmission.
3. Two HIV transmission routes: needle sharing between male IDUs and commercial sex between SWs and sexually active male clients (including IDUs).
4. The population is assumed to mix homogeneously.
5. All newly recruited individuals to the compartments of male DFCs, female SWs, male IDUs are respectively assumed susceptible.
6. The incidence is mass action.

Notations

Subscripts M, F and D designate male DFCs, female SWs and male IDUs, respectively.

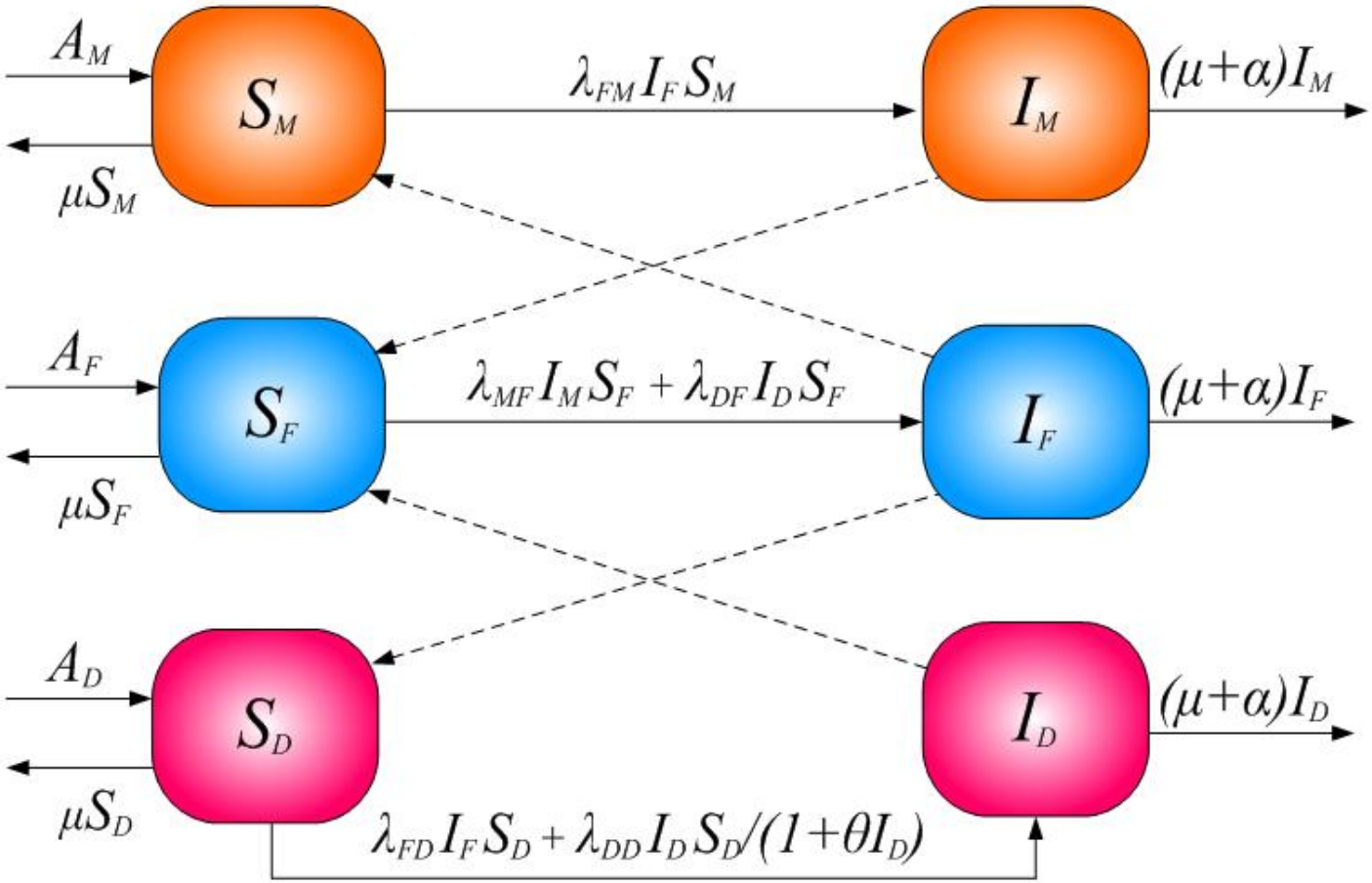
Parameters

Table: Meaning of various parameters

Parameter	Biological meaning
A_M	Constant recruitment into the group of susceptible male DFCs
A_F	Constant recruitment into the group of susceptible female SWs
A_D	Constant recruitment into the group of susceptible male IDUs
λ_{XY}	HIV transmission coefficient from I_X to S_Y
μ	Natural death rate
α	Rate of AIDS development
θ	Inhibition strength of HIV infection among male IDUs

Flowchart

Figure 1. Model flow diagram: solid arrow denotes disease progression, broken arrow denotes disease transmission



The model equations

$$
\begin{aligned}
\frac{dS_M}{dt} &= A_M - \lambda_{FM} I_F S_M - \mu S_M \\
\frac{dI_M}{dt} &= \lambda_{FM} I_F S_M - (\mu + \alpha) I_M \\
\frac{dS_F}{dt} &= A_F - \lambda_{MF} I_M S_F - \lambda_{DF} I_D S_F - \mu S_F \\
\frac{dI_F}{dt} &= \lambda_{MF} I_M S_F + \lambda_{DF} I_D S_F - (\mu + \alpha) I_F \\
\frac{dS_D}{dt} &= A_D - \lambda_{FD} I_F S_D - \frac{\lambda_{DD} I_D S_D}{1 + \theta I_D} - \mu S_D \\
\frac{dI_D}{dt} &= \lambda_{FD} I_F S_D + \frac{\lambda_{DD} I_D S_D}{1 + \theta I_D} - (\mu + \alpha) I_D.
\end{aligned}
\tag{1}
$$

The multigroup SI model

Let us consider the multigroup SI model

$$\begin{cases} \dfrac{dS_i}{dt} = A_i - d_i S_i - \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i g_{ij}(I_j) \\ \dfrac{dI_i}{dt} = \displaystyle\sum_{j=1}^{n} \beta_{ij} S_i g_{ij}(I_j) - (\mu_i + \alpha_i) I_i \end{cases}, \quad 1 \leq i \leq n. \tag{2}$$

Assumptions upon the functions g_{ij}, $1 \leq i, j \leq n$

(i) g_{ij} are locally Lipschitz continuous function on $[0, \infty)$ satisfying $g_{ij}(0) = 0$.

(ii) $0 \leq \lim_{I_j \to 0+} \frac{g_{ij}(I_j)}{I_j} = C_{ij} < \infty$.

(iii) $g_{ij}(I_j) \leq C_{ij} I_j$ for all $I_j \geq 0$.

(iv) The matrix $(\beta_{ij} C_{ij})_{\substack{1 \leq i \leq n \\ 1 \leq j \leq n}}$ is irreducible.

The basic reproduction number

The next generation matrix

$$\mathcal{M}^0 = \left(\frac{\beta_{ij} S_i^0 C_{ij}}{\mu_j + \alpha_j}\right)_{\substack{1\leq i\leq n\\ 1\leq j\leq n}} = FV^{-1}, \quad \widetilde{\mathcal{M}}^0 = \left(\frac{\beta_{ij} S_i^0 C_{ij}}{\mu_i + \alpha_i}\right)_{\substack{1\leq i\leq n\\ 1\leq j\leq n}} = V^{-1}F,$$

where

$$F = \left(\beta_{ij} S_i^0 C_{ij}\right)_{\substack{1\leq i\leq n\\ 1\leq j\leq n}}, \quad V = \operatorname{diag}\left(\mu_i + \alpha_i\right)_{\substack{1\leq i\leq n\\ 1\leq j\leq n}}.$$

The basic reproduction number

$$\mathcal{R}_0 = \rho(\mathcal{M}^0),$$

Since $\rho(FV^{-1}) = \rho(V^{-1}F)$, it also follows that $\mathcal{R}_0 \doteq \rho(\widetilde{\mathcal{M}}^0)$.

The stability of the disease-free equilibrium

Theorem

1. *If $\mathcal{R}_0 \leq 1$, then the disease-free equilibrium $\mathbf{E}_0$ is the unique equilibrium of (2) and it is globally asymptotically stable in Γ.*
2. *If $\mathcal{R}_0 > 1$, then the disease-free equilibrium $\mathbf{E}_0$ is unstable.*

Proof: Lyapunov-LaSalle invariance principle

$$W_1(t) = \sum_{i=1}^{n} \frac{\omega_i}{\mu_i + \alpha_i} I_i.$$

$(\omega_1, \omega_2, \cdots, \omega_n)$ is a strictly positive left eigenvector corresponding to the eigenvalue $\rho(\widetilde{\mathcal{M}}^0)$ of the matrix $\widetilde{\mathcal{M}}^0$

The existence and stability of the endemic equilibrium

Theorem

1. *If* $\mathcal{R}_0 > 1$, *then the system* (2) *is uniformly persistent and has an endemic equilibrium* $\mathbf{E}^*$.
2. *If* $\mathcal{R}_0 > 1$ *and*

$$\left(g_{ij}(I_j) - g_{ij}(I_j^*)\right)\left(\frac{g_{ij}(I_j)}{I_j} - \frac{g_{ij}(I_j^*)}{I_j^*}\right) \leq 0, \quad 1 \leq i, j \leq n,$$

with equality if and only if $I_j = I_j^*$ *for any nonzero* g_{ij}, *then the endemic equilibrium* $\mathbf{E}^*$ *is globally asymptotically stable in* $int(\Gamma)$.

Proof: Lyapunov-LaSalle invariance principle

$$W_2(t) = \sum_{i=1}^{n} c_i V_i(t),$$

with

$$V_i = \left(S_i - S_i^* - S_i^* \ln \frac{S_i}{S_i^*} \right) + \left(I_i - I_i^* - I_i^* \ln \frac{I_i}{I_i^*} \right),$$

$$A = \left(\beta_{ij} S_i^* g_{ij}(I_j^*) \right)_{\substack{1 \le i \le n \\ 1 \le j \le n}}$$

and $c_i = C_{ii}$, the cofactor of the (i, i)-entry of the Laplacian matrix of the directed graph $G(A)$ associated with A.

Applications

$n = 3$, male DFC group$\to_1$, female SW group$\to_2$, male IDU group$\to_3$,
Natural death rates and rates of AIDS development

$$d_1 = d_2 = d_3 = \mu, \quad \alpha_1 = \alpha_2 = \alpha_3 = \alpha$$

Forces of infection

$$\begin{array}{lll} g_{11}(I_1) = 0, & g_{12}(I_2) = I_2, & g_{13}(I_3) = 0, \\ g_{21}(I_1) = I_1, & g_{22}(I_2) = 0, & g_{23}(I_3) = I_3, \\ g_{31}(I_1) = 0, & g_{32}(I_2) = I_2, & g_{33}(I_3) = \frac{I_3}{1+\theta I_3} \end{array}$$

$$\begin{array}{lll} \beta_{11} = 0, & \beta_{12} = \lambda_{FM}, & \beta_{13} = 0, \\ \beta_{21} = \lambda_{MF}, & \beta_{22} = 0, & \beta_{23} = \lambda_{DF}, \\ \beta_{31} = 0, & \beta_{32}(I_2) = \lambda_{FD}, & \beta_{33} = \lambda_{DD}. \end{array}$$

Transmission matrix

$$(\beta_{ij} C_{ij}) = \begin{pmatrix} 0 & \lambda_{FM} & 0 \\ \lambda_{MF} & 0 & \lambda_{DF} \\ 0 & \lambda_{FD} & \lambda_{DD} \end{pmatrix},$$

Applications

Next generation matrix

$$\mathcal{M}^0 = \begin{pmatrix} 0 & \frac{\lambda_{FM}A_M}{d(\mu+\alpha)} & 0 \\ \frac{\lambda_{FM}A_M}{d(\mu+\alpha)} & 0 & \frac{\lambda_{DF}A_F}{d(\mu+\alpha)} \\ 0 & \frac{\lambda_{FD}A_D}{d(\mu+\alpha)} & \frac{\lambda_{DD}A_D}{d(\mu+\alpha)} \end{pmatrix}, \quad \mathcal{R}_0 = \rho(\mathcal{M}^0).$$

Characteristic equation

$$\lambda^3 + a_2\lambda^2 + a_1\lambda + a_0 = 0, \tag{3}$$

$$a_2 = -\frac{\lambda_{DD}A_D}{d(\mu+\alpha)}, \quad a_1 = -\frac{\lambda_{FM}\lambda_{MF}A_MA_F + \lambda_{FD}\lambda_{DF}A_DA_F}{d^2(\mu+\alpha)^2},$$
$$a_0 = \frac{\lambda_{FM}\lambda_{MF}\lambda_{DD}A_MA_FA_D}{d^3(\mu+\alpha)^3}.$$

Let

$$Q = \frac{3a_1 - a_2^2}{9}, \quad R = \frac{9a_1a_2 - 27a_0 - 2a_2^3}{54}, \quad D = Q^3 + R^2.$$

Since the sign of D depends on the concrete values of a_0, a_1, a_2, the nature of the roots of (3) has a similar behavior.

Practical stability conditions

Partial reproduction numbers

$$\mathcal{R}_{MF} = \frac{\sqrt{\lambda_{FM}\lambda_{MF}A_M A_F}}{\mu(\mu+\alpha)} \qquad \mathcal{R}_D = \frac{\lambda_{DD}A_D}{\mu(\mu+\alpha)}$$

$$\mathcal{R}_{FD} = \frac{\lambda_{DD}A_D + \sqrt{(\lambda_{DD}A_D)^2 + 4\lambda_{FD}\lambda_{DF}A_D A_F}}{2\mu(\mu+\alpha)}$$

Theorem

(a) *If* $\mathcal{R}_{MF} < 1$, $\mathcal{R}_D < 1$ *and*

$$(1-\mathcal{R}_D)(1-\mathcal{R}_{MF}^2) > P, \qquad \left(P = \frac{\lambda_{FD}\lambda_{DF}A_D A_F}{\mu^2(\mu+\alpha)^2}\right) \tag{4}$$

then the disease-free equilibrium $\mathbf{E}_0$ *of* (1) *is GAS in* $int(\Gamma)$.

(b) *If* $\mathcal{R}_{MF} > 1$ *and* $\mathcal{R}_D > 1$, *then the unique endemic equilibrium* $\mathbf{E}^*$ *of* (1) *is GAS in* $int(\Gamma)$.

Proof: Jury conditions

Related work and directions for further study

Previous HIV Modeling for Thailand

- Modeling sex industry in Thailand using a two-sex model. (Busenberg, Cooke, and Hsieh, Math Biosci.1995)
- With behavior change and treatment (Hsieh and Cooke, IMA J. of Math. Appl. Biol. Med 2000)
- Modeling SWs and customers with activity levels (Hsieh and Chen, BMB 2004)
- Basic reproduction number for model with SWs and their customers (Hsieh and Wang, BMB 2006)

Thoughts for Future

- **Modeling:** Contact/transmission rate for SWs of different venues; steady partners of SWs; different incidence term for different transmission mode
- **Analysis:** Nicer expression for R0? Reproduction numbers of different risk groups (Hsieh and Chen 2014; Hsieh and Wang 2006)
- **Applications:** Guesstimates of model parameters? Estimating R0?

References (1)

1. M.B. Huang, et al. Characterizing the HIV/AIDS Epidemic in the United States and China, Int. J. Environ. Res. Public Health., 13:30, 2016.
2. J.D. Tucker, et al. Scaling up syphilis testing in China: implementation beyond the clinic, Bull. World Health Organ., 88:452-457, 2010.
3. H. Wang, et al. Mobility, risk behavior and HIV/STI rates among female sex workers in Kaiyuan City, Yunnan Province, China, BMC Infectious Diseases, 10:198, 2010.
4. Z. Wei, A close look at China's Sex Industry, Lianhe Zaobao, October 2, 2000, http://www.usembassy-china.org.cn/sandt/sex-industry.html.
5. Ruan, Y., et al.. Syphilis among female sex workers in southwestern China: potential for HIV transmission. Sexually transmitted diseases, 33(12), 719-723, 2016.
6. S.M. Pan, et al. Clients of female sex workers: a population-based survey of China, J. Infect. Dis., (Suppl.5):S1211-S1217, 2011.

References (2)

1. Busenberg, S., Cooke, K., and Hsieh, Y.-H., A model for HIV in Asia. Math. Biosci., 128(12):185-210, 1995.
2. Hsieh, Y.-H. and Cooke, K., Behavior Change and Treatment of Core Group and Bridge Population: Its Effect on the Spread of HIV/AIDS. IMA J. of Math. Appl. Biol. Med. 17(3): 213-241, 2000.
3. Hsieh, Y.-H. and Chen, C.H., Modeling the social dynamics of the sex industry in Thailand: Its implications for spread of HIV. Bull. Math. Biol. 66(1): 143-166, 2004.
4. Hsieh, Y.-H. and Y.-S. Wang, Basic reproduction number HIV model incorporating commercial sex and behavior change. Bull. Math. Biol. 68(3):551-75, 2006.

Thank you for your attention!