Final Project Report on

Examining the effect of contact rate and stability of SIS Epidemic model for N. Gonorrhea and SIT model for HIV transmission

Course Title: Mathematical Modelling in Industry, Government, and Sciences

Course Code: MATH 572

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Abstract

To examine the transmission dynamics of Neisseria Gonorrhea in a heterosexual population along with homosexual males some mathematical models have been formed in the direction of finding equilibrium solutions, stability analysis through phase plane sketches after that determining the normal forward sensitivity analysis. Aiming to improve the modelling by dividing the heterosexual population into two groups of the highly sexually active and the less sexually active population to observe the changes in sexual frequency via direct contact rate. Followed by a mathematical analysis of the SIS epidemic model presented incorporating the computation of its basic reproduction number (R_0) to clarify how fast the gonorrhea disease can be controlled or remain endemic. In particular, for the homosexual core group, the base model extends to the exploration of two interreacting populations which further modifies the HIV transmission model by introducing a new feature (treatment) to develop SIT (Susceptible-Infected-Treated) model. Lastly, advise a few control mechanisms based on the interpretation of mathematical modellings outlined in this project to assist health professionals in order to combat gonorrhea epidemics across the world.

Keywords: Neisseria Gonorrhea, Epidemic, Stability, Reproductive number, HIV transmission.

TABLE OF CONTENT

Introduction

Gonorrhea is caused by the bacterium Neisseria gonorrhoeae and has been nationally notifiable since 1924 [1]. Gonorrhea, or gonococcus a venereal disease involving inflammatory discharge from the urethra or vagina caused by the bacterium Neisseria gonorrhoeae, is the second most commonly reported sexually transmitted infection (STI) in Canada, after chlamydia. N. gonorrhea is not a very disruptive pathogen; however, it can infect warm, moist areas of the human body, including the urethra, eyes, throat, vagina, anus, and female reproductive tract and cannot survive outside the host. Therefore, the transmission of the disease relies on a sexual network to spread the pathogen. [2]

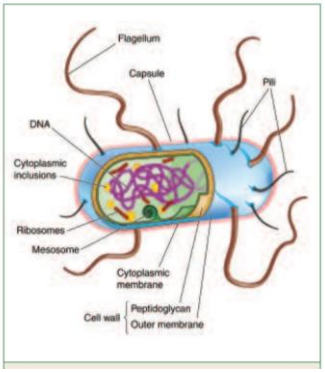
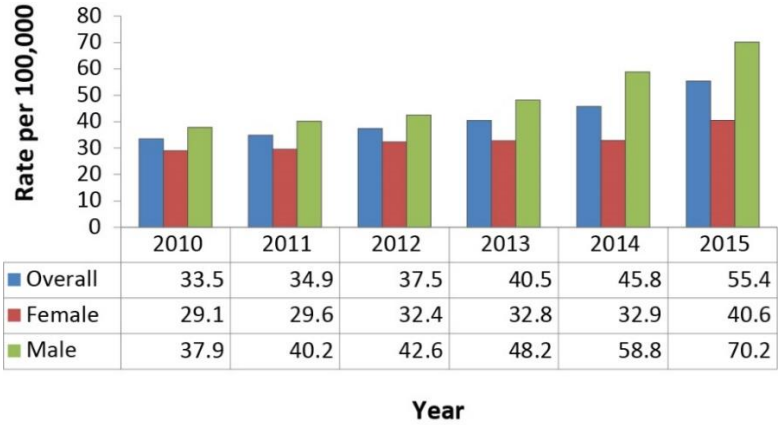


Figure 1:An example of a bacterium with pili helps Neisseria gonorrhea enter a host cell [3]

Transmission dynamics of Gonorrhea

Gonorrhea is a non-seasonal disease. Most infections are genital, Gonococcal infections are usually asymptomatic in females, but symptomatic in males. Due to a short incubation period, it spreads quickly. [4] Gonorrhea rates in Canada rose by 65.4% between 2010 and 2015. Males continue to have a higher ratio than females throughout the times as depicted below in the histogram.



	2010	2011	2012	2013	2014	2015
Overall	33.5	34.9	37.5	40.5	45.8	55.4
Female	29.1	29.6	32.4	32.8	32.9	40.6
Male	37.9	40.2	42.6	48.2	58.8	70.2

Figure 2:Overall sex-specific rates of reported laboratory-confirmed gonorrhea cases, 2010–2015, Canada [36]

Geographic Distribution of N. Gonorrhea

Estimated numbers (in millions) of incident cases of gonorrhea in adults (15–49 years of age) by the WHO region. These data correspond to 20 new gonococcal infections per 1,000 women and 26 per 1,000 men globally. The highest incidence was in the **African region**, with 41 cases per 1,000 women and 50 per 1,000 men, followed by the USA, with 23 cases per 1,000 women and 32 per 1,000 men. The lowest incidence was in the European region, with 7 cases per 1,000 women and 11 per 1,000 men.

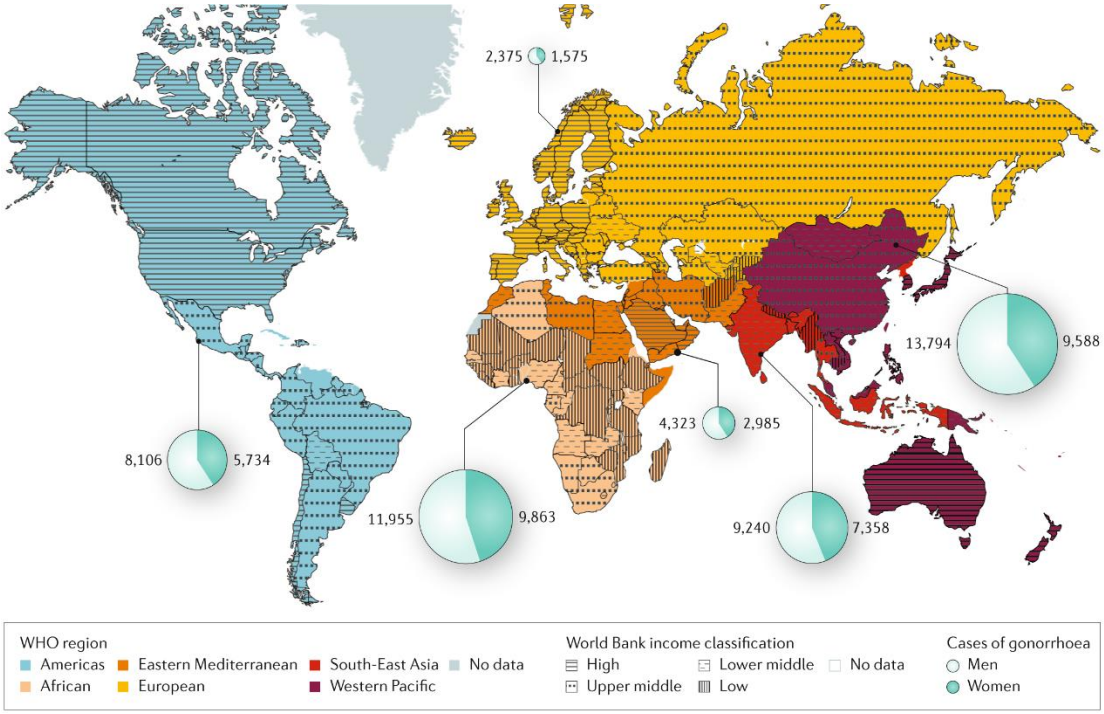


Figure 3:Estimated new global cases of gonorrhea in 2016 [5]

Complications of N. Gonorrhea

The asymptomatic individuals are still contagious. Women are more likely to be asymptomatic than males. Since women are more prone to be asymptomatic, they are at greater risk of long-term complications from untreated infections. [4] In females, symptoms can include vaginal discharge; in males, symptoms often present as painful urination, abnormal urethral discharge, and swollen testicles [6]. Untreated gonorrhea may lead to reactive arthritis, disseminated gonococcal infection and infertility in both sexes (although infertility is rare for men) [7]. Clinical outcomes of untreated gonorrhea include pelvic inflammatory disease, chronic pelvic pain, and ectopic pregnancy in females, [7]. Mother-to-child transmission at birth can result in conjunctivitis in newborns, with a possible progression to blindness if the infection is not detected and treated rapidly [8]. Gonorrhea also increases the infectiousness of HIV.

Provincial Distribution of Gonorrhea cases in Canada

The provinces in Canada with the highest rate increase in the time period were Yukon (237.3%), Newfoundland and Labrador (212.7%), Alberta (159.8%) and British Columbia (143.7%).

Province or territory	Laboratory-confirmed cases by year of diagnosis (rate per 100,000)					
	2010	2011	2012	2013	2014	2015
Alberta	1,182 (31.7)	1,508 (39.8)	2,103 (54.2)	2,017 (50.5)	1,908 (46.4)	3,438 (82.3)
British Columbia	1,365 (30.6)	1,649 (36.7)	1,420 (31.2)	1,841 (40.1)	2,031 (43.7)	3,495 (74.5)
Manitoba	982 (80.4)	1,055 (85.5)	1,349 (107.9)	1,217 (96.2)	1,107 (86.4)	1,085 (83.7)
New Brunswick	64 (8.5)	64 (8.5)	38 (5.0)	47 (6.2)	44 (5.8)	50 (6.6)
Newfoundland and Labrador	12 (2.3)	26 (5.0)	16 (3.0)	41 (7.8)	66 (12.5)	38 (7.2)
Northwest Territories	219 (506.0)	143 (328.7)	192 (440.4)	97 (221.5)	245 (558.2)	361 (815.9)
Nova Scotia	100 (10.6)	102 (10.8)	119 (12.6)	97 (10.3)	114 (12.1)	133 (14.1)
Nunavut	648 (1942.9)	595 (1740.0)	448 (1290.8)	466 (1316.3)	326 (905.0)	306 (837.6)
Ontario	3,966 (30.2)	4,205 (31.7)	4,097 (30.5)	4,540 (33.5)	5,840 (42.7)	5,932 (43.0)
Prince Edward Island	0 (0.0)	11 (7.6)	8 (5.5)	6 (4.1)	7 (4.8)	10 (6.8)
Quebec	2,054 (25.9)	1,864 (23.3)	2,219 (27.4)	2,642 (32.4)	3,312 (40.3)	3,927 (47.5)
Saskatchewan	763 (72.6)	758 (71.1)	1,018 (93.7)	1,213 (109.8)	1,240 (110.6)	957 (84.5)
Yukon	31 (89.6)	6 (16.9)	9 (25.0)	10 (27.5)	49 (132.9)	113 (302.2)
Canada	**11,386 (33.5)**	**11,986 (34.9)**	**13,036 (37.5)**	**14,234 (40.5)**	**16,289 (45.8)**	**19,845 (55.4)**

Table 1,2: Number and rate of reported cases [36]

Centers for Disease Control CDC analysis provides the clearest picture to date of sexually transmitted infections (STIs) in the United States. CDC estimates indicate that about 20 percent of the U.S. population approximately one in five people in the U.S. had an STI on any given day in 2018, and STIs acquired that year cost the American healthcare system nearly $16 billion in healthcare expenses alone. [9] However, in 2020, throughout the pandemic, weekly reported STD cases in the United States fell, but then rise dramatically towards the end of the year compared to 2019 before covid-19, as shown below.

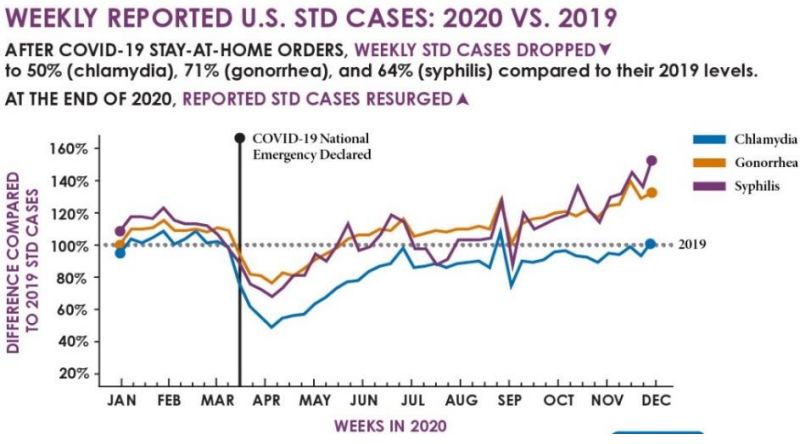


Figure 4: Notifiable Sexually Transmitted Disease Case Reports During the US COVID-19 Pandemic [9]

Research motivation

Analysis of existing data arises quite a few challenges to be addressed which inspire me to proceed with the direction of a mathematical modelling approach to explain logically. Gonorrhea has three striking epidemiology characteristics which must be incorporated into a model. The first is that gonococcus infection does not confer protective immunity. Secondly, individuals who acquire gonorrhea become infectious within a day or two and finally, the seasonal oscillations in gonorrhea incidence are very small (Less than 10%) [10]. In particular, sexually transmitted infections such as gonorrhea, are better described by an SIS (susceptible-infectious-susceptible) framework because once recovered (or following treatment) the host is once again susceptible to infection. In the majority of cases, this renewed susceptibility is due to the vast antigenic variation associated with sexually transmitted diseases [11]. The nature of the disease is very transmittable between sexes, which encourages me to interpret the most important consequences of changing the sexual frequency based on higher and fewer sexual relationships among susceptible individuals with infected men or women. Moreover, concentrating on what conditions the gonorrhea outbreaks can occur or remain endemic afterwards how the population is negatively or positively related to such factors, possibilities of coexistence in each group. Finally, in what circumstances does the homosexual community play a crucial role in the spread of the disease, and what modifications are required to change this MSM model to the HIV transmission model.

Model Interpretation

To begin with, interpreting the constants, and parameters, of the given two-dimensional continuous-time model for the Heterosexual male and female population along with meaningful assumptions for further modification.

$$x' = -ax + b(f - x)y$$
$$y' = -cy + d(g - y)x$$

Considering a, b, c, d are constants (non-negative) > 0 and $x, y, f, g \in [0,1]$

a = Cure rate for men by taking treatment

c = Cure rate for women by taking treatment

x = Fraction of infected men

y = Fraction of infected women

ax = Cure rates for infected men, so the cure rates for infective men are proportion to the infected population with a constant a.

cy = Cure rates for infected women, so the cure rates for infective women are proportion to the infected population with a constant c.

b = Rate of contact by an infected woman (susceptible men)

d = Rate of contact by an infected man (susceptible women)

f = Fraction of sexually active men who are Promiscuous

g = Fraction of sexually active women who are Promiscuous

$b(f-x)y$ = New infected to the men population.

$d(g-y)x$ = New infected to the women population.

Major assumptions

I. This model assumes a well-mixed steady population (no births, deaths, migration, condom uses are modelled) of equally sexually active people (f, g) with exclusively heterosexual relationships.

II. Members of the population interact freely (means equally likely to encounter each other)

III. Model parameters and constants are strictly nonnegative (Population cannot be negative)

IV. The cure rate of infected men and women ($a,\ c$) is proportional to the infected population ($x,\ y$) so recovery is at a constant rate, proportional to the number of infected.

V. Becoming infected depends only on direct contact between Susceptible and Infected

VI. Newly infected men are added to the population at a rate proportional to the number of infected women and susceptible men. likewise, newly infected women are added to the population at a rate proportional to the number of infected men and susceptible women.

VII. Infected men or women are always promiscuous

VIII. All promiscuous is not infected while there is still a high chance of possibility to get infected.

IX. A recovered individual becomes susceptible since recovery from gonorrhea does not confer permanent immunity.

X. No asymptotic scenarios are considered.

Equilibrium and Stability Analysis

Now, obtaining the Equilibrium points of the given models as follows:

$$x' = -ax + b(f - x)y \qquad (1)$$

$$y' = -cy + d(g - y)x \qquad (2)$$

for a Two-dimensional ordinary differential equation, nullclines are

$$0 = -ax + bfy - bxy$$
$$0 = -cy + dgx - dyx$$

1st equilibrium points $(x^*, y^*) = (0,0)$. If $x^* \neq 0 \; and \; y^* = 0$ and $x^* = 0 \; and \; y^* \neq 0$, also get the 1st equilibrium point at $(x^*, y^*) = (0,0)$.

Now solving equation (2)

$$y = \frac{dgx}{c+dx} \qquad (3)$$

The full calculation is attached to appendices (A), at the end of this final project report.

Now, putting the value of y from (3)

$$x = \frac{bfdg-ac}{d(bg+a)} \qquad (4)$$

Now plugging the value of x in equation (3) we get:

$$y = \frac{bfdg-ac}{b(c+fd)} \qquad (5)$$

Therefore, the coexistence equilibrium points we get $(x^*, y^*) = \left(\frac{bfdg-ac}{d(a+bg)}, \frac{bfdg-ac}{b(c+fd)}\right)$

Now checking the stability at the equilibrium point $(x^*, y^*) = (0,0)$ by performing the Jacobian matrix:

$$(J) = \begin{vmatrix} \frac{\partial}{\partial x}(-ax + bfy - bxy) & \frac{\partial}{\partial y}(-ax + bfy - bxy) \\ \frac{\partial}{\partial x}(-cy + dgx - dxy) & \frac{\partial}{\partial y}(-cy + dgx - dxy) \end{vmatrix}$$

$$(J) = \begin{vmatrix} (-a - by) & (bf - bx) \\ (dg - dy) & (-c - dx) \end{vmatrix}$$

at 1st equilibrium point $(x^*, y^*) = (0,0)$ (trivial solution)

$$(J) = \begin{vmatrix} (-a-\lambda_1) & (bf) \\ (dg) & (-c-\lambda_2) \end{vmatrix}$$

So, eigenvalues are $\lambda_1 = -a < 0$ and $\lambda_2 = -c < 0$, which implies that the 1st equilibrium point $(x^*, y^*) = (0,0)$ is a stable node.

Followed by checking the stability for coexistence equilibrium point:

$$(x^*, y^*) = \left(\frac{bfdg-ac}{d(a+bg)}, \frac{bfdg-ac}{b(c+fd)}\right)$$

$$(J) = \begin{vmatrix} \frac{\partial}{\partial x}(-ax + bfy - bxy) & \frac{\partial}{\partial y}(-ax + bfy - bxy) \\ \frac{\partial}{\partial x}(-cy + dgx - dxy) & \frac{\partial}{\partial y}(-cy + dgx - dxy) \end{vmatrix}$$

$$(J) = \begin{vmatrix} \left(-a - b\left(\frac{bfdg-ac}{b(c+fd)}\right)\right) & \left(bf - b\left(\frac{bfdg-ac}{d(bg+a)}\right)\right) \\ (dg - d\left(\frac{bfdg-ac}{b(c+fd)}\right) & (-c - d\left(\frac{bfdg-ac}{d(bg+a)}\right) \end{vmatrix}$$

$$(J) = \begin{vmatrix} \left(-a - \left(\frac{b^2fdg-bac}{b(c+fd)}\right)\right) & \left(bf - b\left(\frac{bfdg-ac}{d(bg+a)}\right)\right) \\ (dg - d\left(\frac{bfdg-ac}{b(c+fd)}\right) & -c - \left(\frac{bfd^2g-dac}{d(bg+a)}\right) \end{vmatrix}$$

From the definition of the characteristic equation, we know that

$\lambda^2 - \text{tr}(J)\lambda + \det(J) = 0,$

where $\text{tr}(J)=J_{11}+J_{22}$ is the trace of the matrix and $\det(J)=J_{11}J_{22} - J_{12}J_{21}$ its determinant.

$$\text{tr}(J) = \left(\frac{-fd(a+bg)}{(c+df)} + \frac{-cbdg-bdfg}{a+bg}\right)$$
$$= \left(\frac{-(a+bg)}{\frac{c}{dg}+1} - \frac{(c+fd)}{\frac{a}{bf}+1}\right)$$

Examining the conditions tr $J(x^*, y^*)$ <1 or >1 and then followed by det $J(x^*, y^*)$. Here I find the

critical point $\frac{a}{bf}$ and $\frac{c}{dg}$ and if both of them are > 1 or <1 then the eigenvalues have negative real parts $(\frac{-(a+bg)}{(\frac{c}{dg}+1)} - \frac{(c+fd)}{\frac{a}{bf}+1}) < 0$, thus, the coexistence equilibrium (x^*, y^*) is stable.

Det (J) = $(\frac{-fd(a+bg)}{(c+fd)} * \frac{-(c+fd)bg}{(a+bg)}) - (\frac{cd(a+bg)}{b(c+fd)} * \frac{ab(c+fd)}{d(a+bg)})$

$= bfdg - ac$

$= \frac{bfdg}{bfdg} - \frac{ac}{bfdg}$

$= 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$

From this critical point, I take into consideration the following cases:

i) $\frac{a}{bf} > 1$ and $\frac{c}{dg} > 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is stable.

ii) $\frac{a}{bf} < 1$ and $\frac{c}{dg} < 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

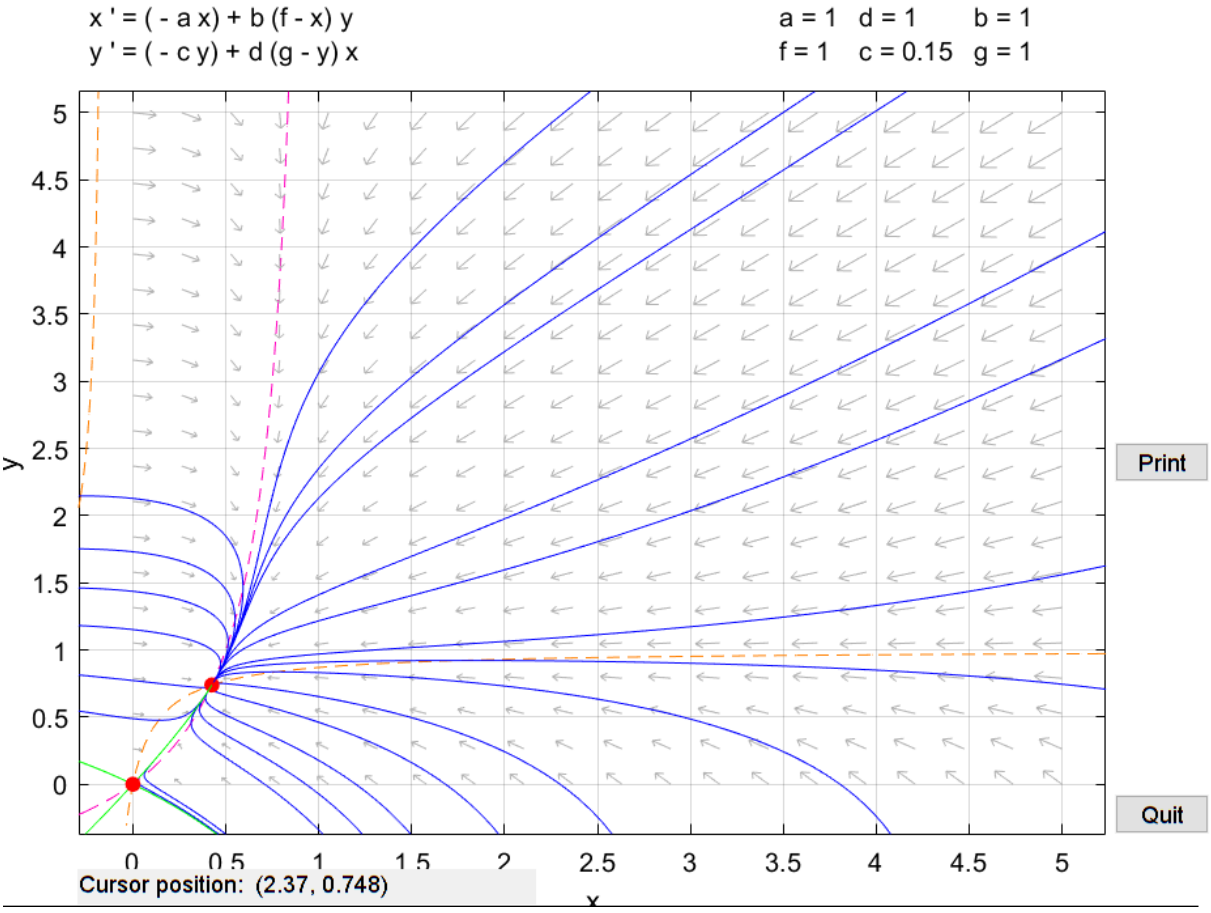
iii) $\frac{a}{bf} > 1$ and $\frac{c}{dg} < 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

iv) $\frac{a}{bf} < 1$ and $\frac{c}{dg} > 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

Since populations x, y is nonnegative, Thus, we need to examine whether x^*, y^* are nonnegative.

Phase Plane Analysis

Demonstrating the Phase plane sketches:



Hence, we can perceive that there will be an epidemic if the presented condition on the parameters remains true:

i) $\frac{a}{bf} < 1$ and $\frac{c}{dg} < 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

ii) $\frac{a}{bf} > 1$ and $\frac{c}{dg} < 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

iii) $\frac{a}{bf} < 1$ and $\frac{c}{dg} > 1 = 1 - \left(\frac{a}{bf}\right)\left(\frac{c}{dg}\right)$, thus the coexistence equilibrium (x^*, y^*) is unstable.

Sensitivity Analysis

After computing the normalized forward sensitivity indices of the heterosexual population at the coexistence equilibrium with respect to each parameter, the equilibrium is positively related to parameters b, d, f, g and negatively related to parameters a, c. In addition, it can be observed that the most important parameters for the heterosexual population at the coexistence equilibrium point are the parameters f, g while the least important parameters are a, c.

$$\gamma_a^{x^*} = \frac{-abg\,(c+fd)}{(a+bg)\,(bdfg-ac)} = -0.676$$

$$\gamma_b^{x^*} = \frac{abg\,(c+fd)}{(a+bg)\,(bdfg-ac)} = 0.676$$

$$\gamma_c^{y^*} = \frac{-cdf\,(a+bg)}{(c+fd)\,(bdfg-ac)} = -0.3$$

$$\gamma_d^{y^*} = \frac{cdf\,(a+bg)}{(c+fd)\,(bdfg-ac)} = 0.3$$

$$\gamma_f^{x^*} = \gamma_g^{y^*} = \frac{bdfg}{(bdfg-ac)} = 1.176$$

Frequency of sexual intercourse

According to Hethcote-Yorke, the gonococcus bacteria that cause gonorrhea grows well only on mucous membranes and dies out in seconds outside the human body. The experimental probability of transmission of gonococcal infection during direct contact between an infected woman to a susceptible man is estimated to be from 0.2 to 0.3 while the experimental probability of transmission from an infected man is approximately 0.5 to 0.7. [12] If the direct contact between the susceptible individual and the infected individual rises, and sexual intercourse occurs with an infected partner several times, then the experimental probability of transmission of infection is increased. [13]

Assumptions:

Assuming a constant population of size N_m and N_w for the men and women correspondingly at risk and the ratio of the population sizes $r = \frac{N_m}{N_w} = 1$.

$\frac{b}{c}$ = Contact rate of infected women, where constant b = rate of contact by an infected woman and constant c = cure rate for women. So, the ratio provides the number of men contacts the average woman has before becoming cured of the disease.

$\frac{d}{a}$ = Contact rate of infected men, where constant d = rate of contact by infected men and constant a = cure rate for men. Similarly, the ratio provides the number of women contacts the average man has before becoming cured of the disease

Strategy to change the contact rate

After applying the mathematical reasoning in my modified assumption model, explained by [12] then the frequency of n sexual intercourse increases as n increases which can be projected to $1 - (0.75)^n$ for infected woman and $1 - (0.4)^n$ for infected man where "n" events are not truly independent due to some contacts involving only one sexual intercourse while others consist of several.

If the frequency of direct contact consisted of exactly one, two or three sexual intercourses, then the contact effectiveness ratio e = $\frac{\frac{b}{c}}{\frac{d}{a}}$ would be approximately 0.42, 0.52, 0.62 proportionally. The value used for effectiveness ratio e is 0.5. As a result, we can observe from the given model that if the contact rate between the constant b = rate of contact by an infected woman and constant d = rate of contact by infected men reduces then the frequency of sexual intercourse can be controlled. On the other hand, if the contact rate between the constant b and d increases then the frequency of sexual intercourse will expand accordingly.

Promiscuous Population

The fraction of the promiscuous population can be divided into two groups of males and females due to the varying practices of human sexuality. The first group is a well-mixed very sexually active population, and the second group is well-mixed but has fewer sexual relations which eventually improves the modelling.

Assumptions:

It is assumed that the contact rates within groups are stronger than the contact rates across groups. This means limited interaction between the groups, but most interactions are within the groups.

Assuming for the very sexually active population f, g = 1, then the fraction of the population that is promiscuous (of either sex male/female) for the given model change to

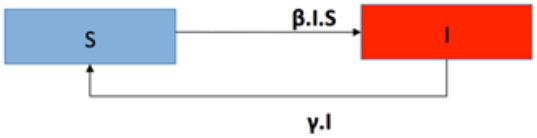
$$x' = -ax_1 + b(1 - x_1)y_1$$
$$y' = -cy_1 + d(1 - y_1)x_1$$

And for the second group who have fewer sexual relations, we assume f, g = e_m, e_w constants for men, and women respectively.

$$\bar{x}' = -ax_2 + b(e_m - x_2)y_2$$
$$\bar{y}' = -cy_2 + d(e_w - y_2)x_2$$

The spread of cure

Gonorrhea has a very short incubation period (3-7 days) and does not confer immunity to those individuals who have recovered from the disease. If recovery does not give immunity, then the model is called an SIS model, since individuals move from the susceptible class to the infective class and then back to the susceptible class upon recovery which means when given treatment the disease leaves the host unprotected, so the infected individuals return to the susceptible population. Infectious diseases, (such as gonorrhea), are better described by an SIS (susceptible-infectious-susceptible) framework.



Assumptions:

i. Assuming that the population considered has a constant size N, $\frac{dN}{dt} = 0$
ii. Only heterosexual contacts transmit infection, and transmission depends on the proportion of infectious individuals in each group and each sex.

Interpretation of model parameters and constants for two interacting populations (men and women):

$\beta =$ contact rate $(\beta_1 + \beta_2)$, where $\beta_1 = \frac{b}{c}$ and $\beta_2 = \frac{d}{a}$ $(\beta > 0,)$

$I(t) =$ Infected individual at time t

$I(t) = (I_m + I_\omega)$ where $I_m = x$, Infected men and $I_\omega = y$, Infected women

S(t) = Susceptible individual at time t

S(t) $= (S_m + S_\omega)$ where $S_m = b$, susceptible men and $S_\omega = d$, susceptible women

$\gamma =$ cure rate $(\gamma_a + \gamma_c)$ where $\gamma_a =$ a; $\gamma_c = c$; cure rate for men and women respectively $(\gamma > 0)$

$\frac{1}{\gamma}$ = the average infectious period of an individual.

The simplest form of this model can be developed by:

$$S' = -\frac{\beta SI}{N} + \gamma I$$

$$I' = \frac{\beta SI}{N} - \gamma I$$

Since $N = (S + I)$, $I = (-S + N)$ so this is a straight line between infected and susceptible.

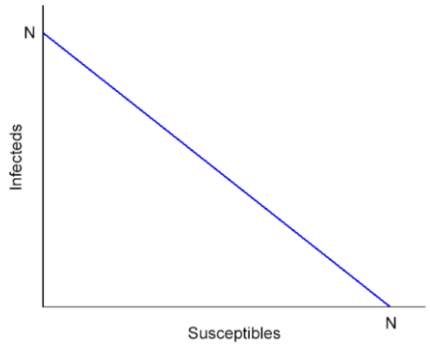


Figure 5: Phase portrait (Time is implicit)

Now, assuming S(t) = N − I(t), and the model above reduces to the first-order differential equation:

$$I' = (\beta - \gamma)I\ (1 - \frac{\beta I}{(\beta - \gamma)N})$$

Discussion on the disappearance of the Gonorrhea epidemic

If $\beta > \gamma$, then asymptotically the susceptible and infected populations go to:

$$\lim_{t\to\infty} \; S(t) = \frac{(\gamma)N}{\beta}, \qquad \lim_{t\to\infty} \; I(t) = \frac{(\beta-\gamma)N}{\beta}$$

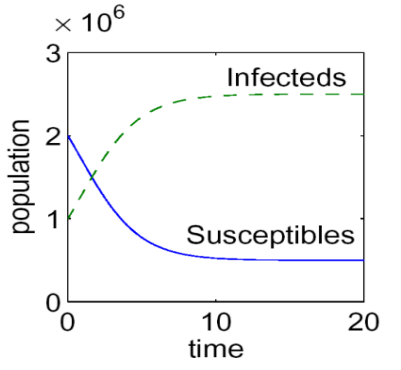
which is a logistic growth equation so, the disease remains endemic. However, if $\beta \leq \gamma$, then the extinction equilibrium becomes stable, and the disease dies out. Here, the basic reproduction number denoted as R_0 for the ratio $\frac{\beta}{\gamma}$. This ratio refers to β = contact rate, γ = cure rate.

The basic reproduction number, sometimes called basic reproductive rate or basic reproductive ratio, is one of the most useful threshold parameters which characterize mathematical problems concerning infections and diseases. This metric is useful because it helps determine whether or not an infectious disease will spread. In many epidemiological models lowering R_0 below the threshold $R_0 = 1$ will eradicate a disease. [14]

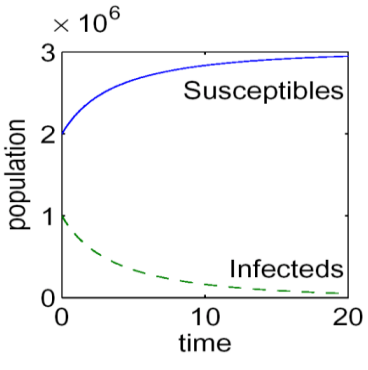
In contrast, we find out that R_0 represents the number of secondary infections caused by β = a single infected individual, $\frac{1}{\gamma}$ = infectious period of individuals. Therefore, In the model above, if the basic reproduction number, $R_0 > 1$ then $\lim_{t\to\infty} \; \big(S(t), I(t)\big) = \left(\frac{N}{R_0}, \frac{N\,(R_0-1)}{R_0}\right)$ the disease is endemic, while if $R_0 \leq 1$, then $\lim_{t\to\infty} \; \big(S(t), I(t)\big) = (N, 0)$ disease-free equilibrium indicates that the disease will go extinct.

Time series solutions

Significantly demonstrate the difference between susceptible and infected populations before and after variations the of cure rate $= \gamma$



When, $\beta = 0.2$, $\gamma = 0.1$, $N = 3x10^6$



When, $\beta = 0.2$, $\gamma = 0.7$, $N = 3x10^6$

Control mechanism for the health official to manage the epidemic

According to the mathematical explanation from the sensitivity analysis section, less risky sexual behaviour is recommended in addition sexually active people should have regular checkups that include STD testing, with the testing of every partner in a sexual relationship to combat the transmission of gonorrhea in our society today. First of all, under certain conditions, the basic reproduction number (R_0) contributes to the control mechanism of the gonorrhea outbreak by achieving endemic and disease-free equilibrium as explained above. As the sexually transmitted infection (STI) of gonorrhea remains a significant global public health concern this requires immediate international attention and resources because the global burden of infection is increasing thus constant monitoring of gonorrhea rates and appropriate treatment of gonorrhea infections are important to cope with changes in antibiotic resistance patterns and to avoid treatment failure. [15]. The three critical elements of STD prevention include:

1. Decreasing the transmissibility of the disease
2. Decreasing the length of time an individual is infected
3. Decreasing the number of sexual contacts.

Sexually Transmitted Infections Treatment Guidelines, 2021 [10] recommend that antibiotic treatment is an essential control measure for gonorrhea. The standard treatment regimen should cure more than 95% of cases. Gonorrhea can be treated with antibiotics such as ciprofloxacin, ofloxacin, ampicillin, azithromycin, cefixime, ceftriaxone, and spectinomycin, ampicillin. Canadian treatment guidelines for gonorrhea have been updated frequently in the past five years to account for new information on antimicrobial resistance to N. gonorrhea [16]. However, new molecular typing reveals that gonorrhea can spread in different sexual contact networks within the same city, with different behavioural characteristics, although individuals act as links between networks [17]. Thus, a combination of wider strategies and increased awareness among microbiologists, epidemiologists, and clinicians and on political levels are essentially significant to tackling the universal burden of gonorrhea and substantially improving the early prevention, diagnosis, contact rate, treatment, and epidemiological surveillance of gonorrhea cases, the latter is especially vital for financing efforts in gonorrhea control.

Preventing Gonorrhea:

Public health officials all agree that preventing gonorrhea is much better than treating the disease [18]. The safest and simplest prevention is to avoid all types of sexual contact. However, this is not always practical. So, healthcare providers suggest that sexual contact be kept with one individual who is at low risk for contracting STDs which also corresponds to the recommendation of my model attained from sensitivity analysis in this project.

The effectiveness ratio of Contact Rate (e) is attained in this project which is also noteworthy in reducing the burden of gonorrhea disease in the heterosexual population so that early identification of infectives by direct contact can shorten their infectious period and, consequently, can reduce the chance of transmitting the infection. Last of all, educational programs, and the use of condoms in clinics or broadcasting media can play a key role to raise awareness and make the sexually active population more concerned about the symptoms and seriousness of this disease so that people can take immediate precautions i.e., treatment or medication [18].

The homosexual core groups

Gonorrhea can persist in Men Sex with Men (MSM) population. Contemplating an example for Norway over the last decade, there had been a steady increase in the reported cases of gonorrhea. The increase is greatest among the heterosexual population in the first line graph, while in the second line graph the level of infections is highest among men compared to women. The situation in Norway follows an international trend where gonorrhea is increasing in several western countries. [19]

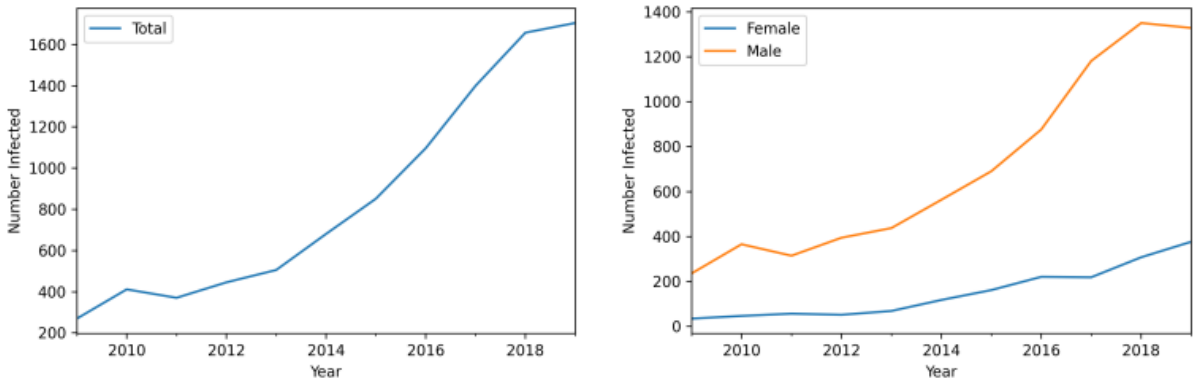


Figure 6: Number of Infected cases and the ratio between male, female

Complications of N. gonorrhea in a Homosexual population

Untreated extragenital infections have an important role in sustaining gonorrhea in an urban population of men who have sex with men (MSM). [18] In my approach, equation (1) from the given model, can be developed to model for homosexual males only model as follows:

$$x' = -ax + b(f - x)x$$

Analysis of the model:

$$0 = -ax + b(f - x)x$$

$$ax = b(f - x)x$$

$$b(f - x) = a$$

$$(f - x) = \frac{a}{b}$$

$$(x) = f - \frac{a}{b}$$

Thus, the equilibrium points are $(x^*) = (f - \frac{a}{b})$. Now determining the stability of equilibria using the stability criterion as follows:

$$f(x) = -ax + b(f - x)x$$

$$= -ax + bfx - bx^2$$

Then the second derivative will be

$$f'(x) = -a + bf - 2bx$$

$$= -a + bf - 2b\left(f - \frac{a}{b}\right)$$

$$= a - bf$$

MSM Model

The given model can be further modified for homosexual males (MSM) homogeneously including (WSW)

$$x' = -ax + b(f - x)x$$

$$y' = -cy + d(g - y)y$$

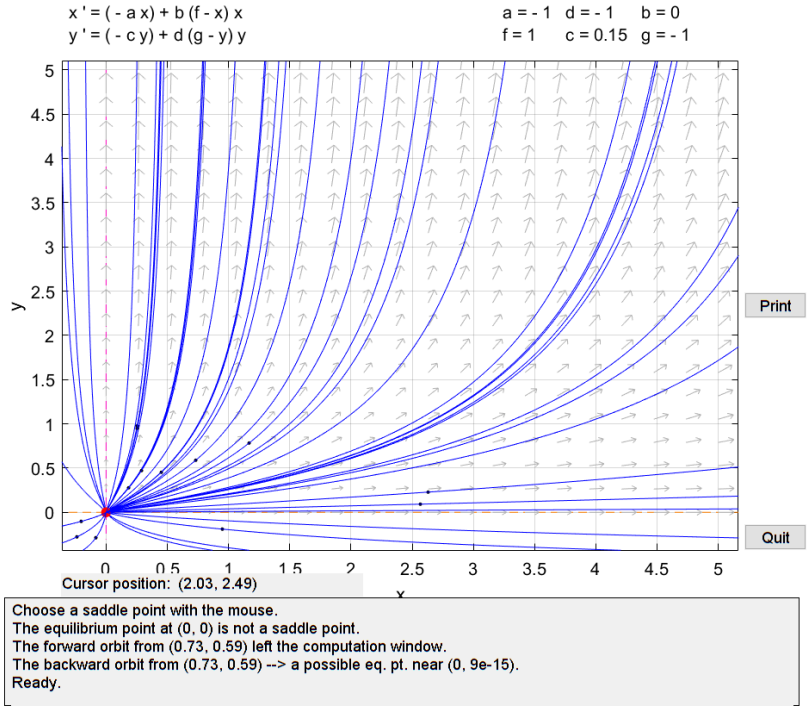
Thus, we get equilibrium points $(x^*, y^*) = (0,0)$ and $(f - {}^{a}/_{b}, g - {}^{c}/_{d})$

$$(J) = \begin{vmatrix} \frac{\partial}{\partial x}(-ax + bfx - bx^2) & \frac{\partial}{\partial y}(-ax + bfx - bx^2) \\ \frac{\partial}{\partial x}(-cy + dgy - dy^2) & \frac{\partial}{\partial y}(-cy + dgy - dy^2) \end{vmatrix}$$

$$(J) = \begin{vmatrix} ((a - bf) - \lambda_1) & 0 \\ 0 & ((c - dg) - \lambda_2) \end{vmatrix}$$

tr (J) = $(a - bf) + (c - dg)$; Det (J) = $(a - bf) * (c - dg)$

As the eigenvalues (λ_1, λ_2) has a positive real part so the equilibrium point (x^*, y^*) is Unstable



Since the modified model for homosexual males homogeneously indicates only sexual contact between men to men and women to women appears to be infeasible so this modelling approach may not be interesting in mathematical biology

$$x' = -ax + b(f - x)x$$
$$y' = -cy + d(g - y)y$$

As a result, by dividing the model into two groups, the given model can be further developed. i) consisting of promiscuous men, women in the heterosexual population and ii) promiscuous men only in the Homosexual male group.

$$x' = -ax + b(f - x)y$$
$$x'_{msm} = -ax_{msm} + b_{msm}(f_{msm} - x_{msm})x_{msm}$$
$$y' = -cy + d(g - y)x$$

The key objective for this modification is to incorporate this modelling approach into the HIV transmission model, which will be detailed in the next section.

Model interpretation

b_{msm} = Infection rate by infected men (susceptible men)

f_{msm} = Fraction of sexually active promiscuous men in MSM population

$b_{msm}(f_{msm} - x_{msm})x_{msm}$ = New infected to the MSM population

Advice to health officials for the homosexual core group

In 1978, Yorke et al. [20] introduced the concept of core groups to model the transmission of N. gonorrhoeae. The concept of core groups suggests that infection can only be maintained in a host population if a highly sexually active group of hosts is responsible for a disproportionate number of transmissions. More recent modelling studies have examined the transmission of antibiotic-resistant N. gonorrhea. Chan et al. [21] mathematical models explained the differential observations of antibiotic-resistant N. gonorrhea in different host populations. Xiridou et al. [22] developed an N. gonorrhea transmission model to determine the impact of different treatment strategies on the prevalence of N. gonorrhea in the Dutch homosexual population and found that increased treatment rates could increase the spread of resistance, whereas re-treatment could slow it down. In my modelling approach no births, deaths, migration, immunity, condom uses, or taking antibiotics are modelled among the MSM population. This implies that separating the population into two categories improves the mathematical model approach and suggest safer sex among heterosexual (non-core group) as well as homosexual male (core group) so a decrease in the sexual contact rate among the non-core population can lead to an increase in predicting the overall incidence of gonorrhea transmission to assist health official.

The transmission dynamics of HIV

HIV is the human immunodeficiency virus, there is indeed no cure for HIV or AIDS (acquired immune deficiency syndrome). Gonorrhea increases the infectiousness of and susceptibility to HIV by increasing the number of HIV target cells in the genital tract and by amplifying HIV shedding (an infected cell releases viral particles, which in turn can infect new cells). [23, 24]. HIV infections weaken the body's ability to fight infection and can cause AIDS the most advanced stage of HIV disease.

Complications

Certain people develop symptoms shortly after being infected. But on average, it takes more than 10 years to develop symptoms. The study published in CDC mortality weekly report from 2010 to 2017 suggested that many people have lived with HIV for more than 20 years. Life expectancy is much shorter for people with AIDS who cannot take the new medications that are now available.

[25] HIV infection and many AIDS-related conditions can be managed to some extent with different treatments.

Model for HIV transmission

Developing a model for HIV transmission, considering no recovery thus the given model becomes:

$$x' = b(f - x)y$$

$$y' = d(g - y)x$$

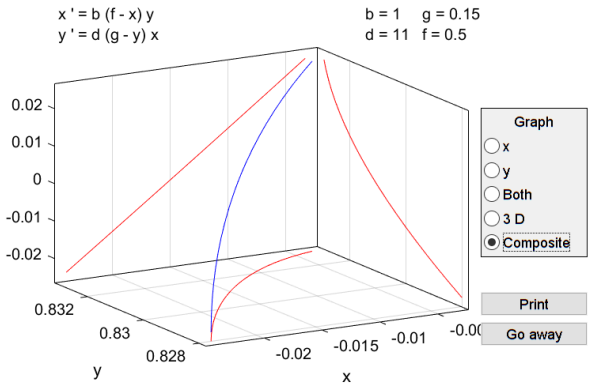


Figure 7:Graph of x vs y without recovery

The model for homosexuals is further modified to model for HIV transmission with homosexual males only.

$$x' = b(f - x)x$$

$$\frac{dx}{dt} = bfx - bx^2 \text{ where } x \geq 0$$

$$x^* = 0,\ x^* = f \text{ are the steady states}$$

Defining $f(x)$ as $\frac{d}{dt} f(x) = bfx - bx^2$. Thus, the derivative is:

$$f'(x) = bf - 2bx$$

Now, evaluating $f'(x^*)$ for each steady-state, which concludes as follows:

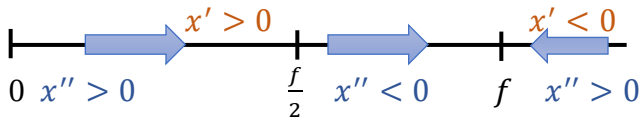
$$f'(0) = bf > 0, \text{therefore is unstable}$$

$$f'(f) = bf - 2bf = -bf < 0, \text{therefore is stable}$$

Computing the second derivative, to know the sign of $\frac{dx}{dt}$, and $\frac{d^2x}{dt^2}$

$$\frac{d^2x}{dt^2} = \frac{d}{dt}\, b(f-x)x$$
$$= \frac{d}{dt}\,(bfx - bx^2)$$
$$= b(f-2x)\frac{\mathrm{d}x}{\mathrm{d}t}$$

So $x^* = 0,\ x^* = f, x^* = \frac{f}{2}$ Therefore, the phase line should be as follows:



Thus, the phase line analysis for the model presented above projected the MSM population growth whenever the density is positive, so the rate of HIV transmission increases as the growth of the MSM population becomes larger. This can also be relatable to the existing data for gonorrhea in England, during the year 2019.

MSM = Gay, bisexual, and other men who have sex with men.* Per 100,000 population

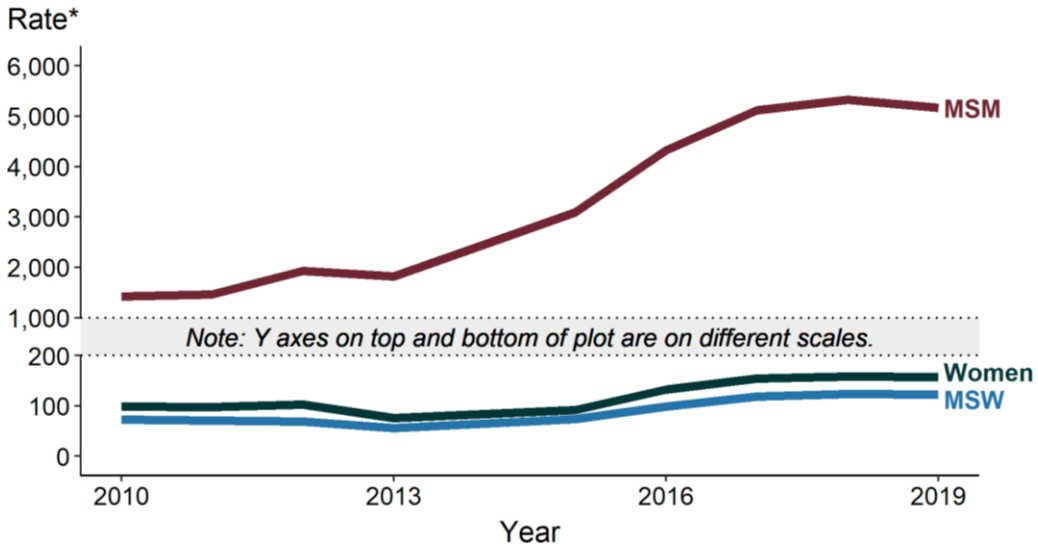


Figure 4: Estimated Rates of Reported Gonorrhea Cases by MSM, MSW, and Women, STD Surveillance Network (SSuN), 2010–2019

To modify other significant terms, the HIV model described above can be further studied and extended to the heterosexual population along with homosexual males, which can be reviewed from the model presented in the previous section for the MSM population.

HIV transmission Model (heterosexual population)

This adjustment includes a simple epidemic model that governs the dynamics of HIV transmission (within and between multiple risk groups). A recent study by Lasry A, Sansom SL, Hicks KA, Uzunangelov V [26] employs linear production functions and a multiple-population SI model to optimize the use of HIV prevention resources in the U.S. but does not consider treatment. Therefore, now taking into consideration treated individuals which implies the model of two interacting populations men and women, where cross-infection can occur due to interactions between susceptible individuals in one population and infected individuals (treated or untreated) in the other population. This occurs in many real-world settings, where risk groups with different behaviours can transmit HIV among themselves and to other risk groups. A typical example is an epidemic driven to transmit HIV to non-IDUs (Injection drug users) via sexual contact. [27]

SIT model for HIV

Constructing a dynamic compartmental model with three disease states, susceptible, infected, and treated (SIT), for two interacting populations, this model defines the epidemic's spread over time as individuals' transition between compartments due to disease transmission and treatment, is specified by the following differential equations:

Men:

$$S' = -\beta_{mm}(I_m + v_m T_m)\frac{s_m}{N_m} - \beta_{wm}(I_w + v_w T_w)\frac{s_m}{N_w}$$

$$I' = \beta_{mm}(I_m + v_m T_m)\frac{s_m}{N_m} - \beta_{wm}(I_w + v_w T_w)\frac{s_m}{N_w} - \gamma_m I_m$$

$$T' = \gamma_m I_m$$

Women:

$$S' = -\beta_{ww}(I_w + v_w T_w)\frac{s_w}{N_w} - \beta_{mw}(I_m + v_m T_m)\frac{s_w}{N_m}$$

$$I' = \beta_{ww}(I_w + v_w T_w)\frac{s_w}{N_w} - \beta_{mw}(I_m + v_m T_m)\frac{s_w}{N_m} - \gamma_w I_w$$

$$T' = \gamma_w I_w$$

Interpreting the meaning of all parameters and terms:

S, I, and T denote the number of susceptible, infected, and treated individuals respectively at time t, $m =$ men, $w =$ women

$\beta =$ contact rate

$\beta = (\beta_m + \beta_w)$, where $\beta_m = \frac{b}{c}$ Contact rate of infected women, where constant b = rate of contact by an infected woman and constant c = cure rate for women. So, the ratio provides the number of men contacts the average woman has before becoming cured of the disease

and $\beta_w = \frac{d}{a} =$ Contact rate of infected men, where constant d = rate of contact by infected men and constant a = cure rate for men. Similarly, the ratio provides the number of women contacts the average man has before becoming cured of the disease

$\beta_{mw} =$ contact rate between an infected individual in men population and a susceptible individual in the women population; similarly, define β_{mm} , β_{ww} and β_{wm}

S(t) = Susceptible individual at time t

$S(\text{t}) = (S_m + S_\omega)$ where $S_m = b$, susceptible men and $S_\omega = d$, susceptible women

$I(t) =$ Infected individual at time t

$I(t) = (I_m + I_\omega)$ where $I_m = x$, Infected men and $I_\omega = y$, Infected women same as in the given model

$\gamma =$ treatment rate

$\gamma = (\gamma_m + \gamma_w)$ where $\gamma_m =$ a = treatment rate for men and $\gamma_w = c =$ treatment rate for women

The relative ratio of both populations, $r = \frac{N_m}{N_\omega}$, $N_m =$ male population $N_w =$ female population

Major Assumption

i. Assuming both infected and treated people can infect the susceptible population, but that treatment decreases infectivity by a factor γ ($0 \leq \gamma \leq 1$)

ii. New infections occur at a rate proportional to the size of the uninfected and infected individual, no disease progression and death are modelled

iii. Individuals in the treated group have a very limited tendency to spread the infection to others.

R_0 has been widely used to evaluate the stability of epidemics specifically estimated for modelling sexually transmitted diseases such as HIV and evaluating the potential for disease-free equilibria [28] a concept that is relevant to the stated goals of international HIV control programs to achieve "zero new HIV infections" [29] and "an AIDS-free generation" [30]

The basic reproduction number is denoted as R_0 for the ratio $\frac{v\beta}{\gamma}$ the average number of secondary infections caused by a typical infected individual in a susceptible population

$$R_0 = \frac{v\beta}{\gamma}$$

This ratio refers to β = contact rate, γ = treatment rate, ν = infection decreases due to treatment. Condition implies that if $R_0 < 1$, the disease-free equilibrium is asymptotically stable and the epidemic dies out, whereas if $R_0 > 1$, the epidemic persists.

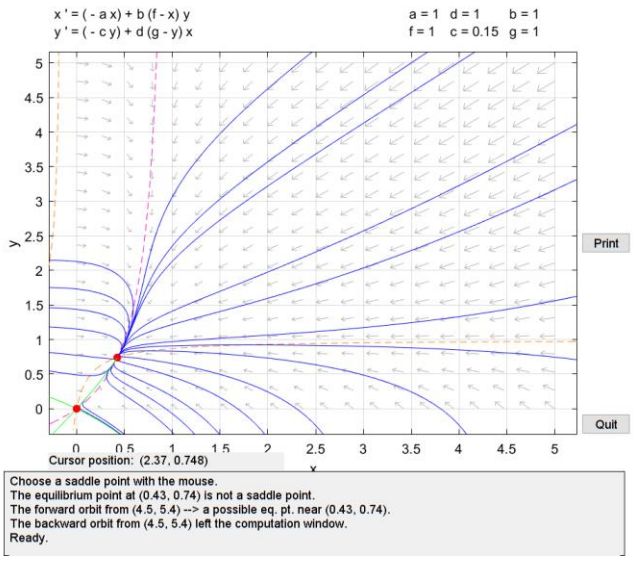
In summary, from the analysis of the basic reproduction number R_0 it can be observed that a framework for analyzing the impact of treatment and prevention programs on HIV transmission can be improved when β = contact rate reduces which incorporates disease prevention whereas γ = treatment rate increases that aimed at expanding access to treatment significantly. Thus, allowing the cross-infection contact rates, β_{mw} and β_{wm} in both populations which implies that HIV transmission reduces from infected persons in the women population to susceptible individuals in the men population (β_{wm}).

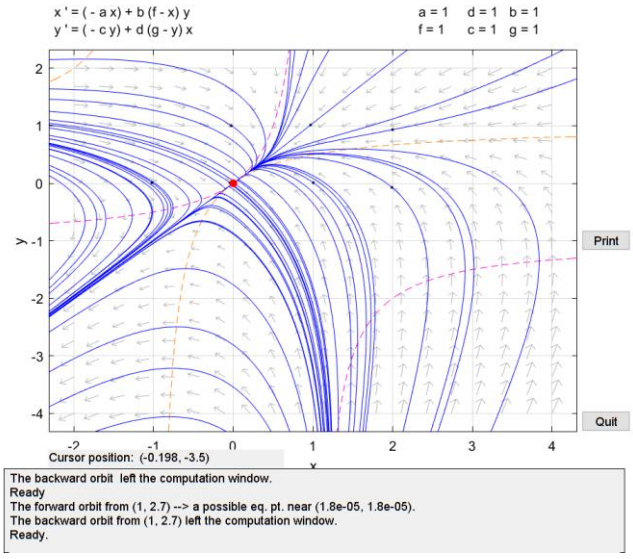
Complications of HIV infection compared to N. gonorrhea

More than 42 million people worldwide are now infected with HIV, despite sustained prevention activities. Although the spread of HIV has been primarily sexual, epidemiological studies have indicated that the efficiency of the spread of HIV is poor, perhaps as infrequently as 1 in every 1,000 episodes of sexual intercourse. However, sexually transmitted diseases (STDs) that cause ulcers or inflammation greatly increase the efficiency of HIV transmission by increasing both the infectiousness of and the susceptibility to HIV infection. STDs might be particularly important in the early stages of a localized HIV epidemic when people with risky sexual behaviour are most likely to become infected. Untreated Neisseria gonorrhoeae (N. gonorrhoeae) infection may lead to the risk of the human immunodeficiency virus (HIV) transmission and acquisition [31]. Men who have sex with men (MSM) are disproportionately affected by sexually transmitted diseases (STDs) and human immunodeficiency virus (HIV) infection. Thus, sexually active MSM should be screened at least annually for gonorrhea at all exposed anatomic sites; some MSM might benefit from more frequent screening. [32] [33].

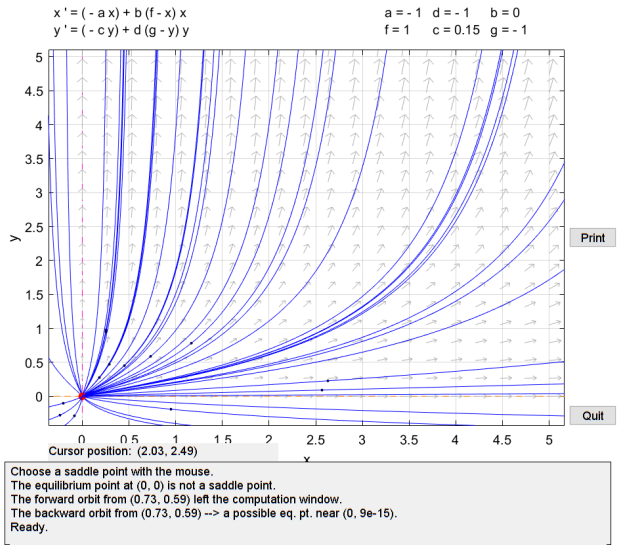
Critique of the models.

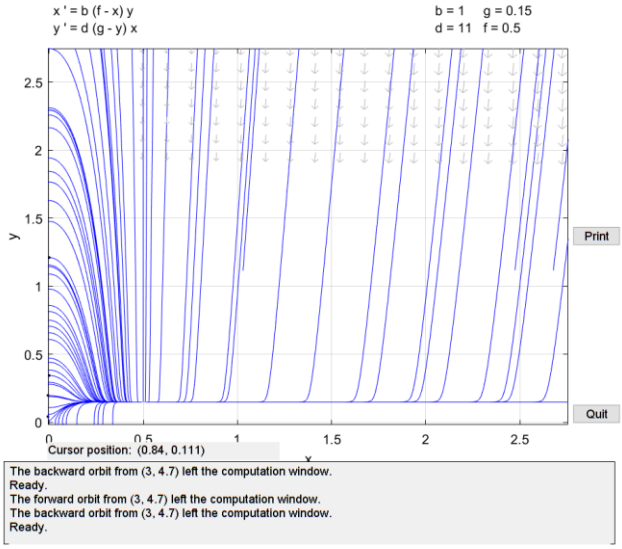
All models have their limitations. In reality, birth and death rate, migration, condom use, screening, medication i.e., antibiotics and other factors will affect the spread of the disease. Therefore, the results are not directly comparable to the real-world data as demonstrated in this project work. In studying (heterosexual, homosexual, and HIV transmission) these three models, I have arrived at





the following conclusions. In my first model, the stability of the heterosexual population shows stable. Side-by-side analysis of first model for heterosexual population demonstrates the variations in phase plane sketches above. However, further research is necessary to carry out by





incorporating age structure, taking antibiotics with other crucial factors to produce the most significant outcome in the infected population. The contrast between the Homosexual male model

and the HIV transmission can be demonstrated by phase plane analysis, which shows that the mathematical model homosexual male population is unstable and thus not a feasible solution, followed by this homosexual model modify to HIV transmission with no recovery rate shows a stable solution presented from the last two phase plane sketches. However, In the case of two interacting population with SIT model, when infected individuals receiving treatment, and their sexual practices among the MSM population change, thus the rate of HIV transmission also minimize; accompanying difficulties and further modification of the model will be considered in the future work involving secondary infections.

Conclusion

The validation of the model defines how well it answers the questions asked, thus this project aimed to create model including complications for a closed population model framework and apply this model to examine the effects of changes in sexual frequency in two different groups, promiscuous men, women along with how fast the disease will go to extinct. One of the major limitations was using a tiny fraction of time Δt continuous-time version of the model, that encounters difficulties to run simulation results while a discrete version can manage with an ODE solver. Modifying the given continuous-time model to probabilistic or stochastic models to deal with population and individuals who are infected at a time, still faces an obstacle to analyze since there is no single function of a single real variable that can completely describe the epidemic which suggests that in terms of numerical analysis stochastic epidemic model will be a more beneficial approach in future work

Future works:

The SIT model demonstrates infected individuals recover with no immunity by taking treatment i.e., medication or antibiotics are very unlikely to spread the transmission of gonorrhea via direct sexual contact. However, individuals who have been treated, continue to spread the infections, still can get infected again (secondary infections) which implies this project will need to conduct additional research to determine the moving equilibrium points and stability of the updated model with the assumption that half of the people change their behaviour (meaning fewer people will become infected again) while the other half never change their behaviour (indicates the disease will remain endemic). Moreover, determine the exact proportion of gonorrhea outbreaks in percentages when infected people are treated with antibiotics vs when they are not. Another future focus will be on gonorrhea prevention in high-risk, frequently transmitting populations (such as MSM), as well as appropriate diagnosis and treatment of pharyngeal gonorrhea, which is harder to eradicate and is an asymptomatic reservoir for gonorrhea-causing bacteria that emergence of antimicrobial resistance (AMR). As a result, due to asymptomatic instances are not taken into account in the mathematical models presented here thus, extending this project work is critical for the dual-infection and multidrug-resistant N. gonorrhea treatment for the joint dynamics of Gonorrhea and HIV transmission.

APPENDICES:

$$x' = -ax + b(f - x)y \qquad (1)$$

$$y' = -cy + d(g - y)x \qquad (2)$$

Mathematical manipulations of coexistence equilibrium point; from equation (2) I calculate:

$-cy + d(g - y)x = 0$

$dgx - dyx = cy$

$dgx = y(c + dx)$

$y = \frac{dgx}{c+dx}$ (3)

$-ax + b(f - x)y = 0$

$b(f - x)\frac{dgx}{c+dx} = ax$ Putting the value of y from (3)

$bfdgx - bdgx^2 = acx + adx^2$

$x(bfdg - bdgx) = x(ac + adx)$

$-bdgx - adx = ac - bfdg$

$x(bdg + ad) = bfdg - ac$

$x = \frac{bfdg - ac}{bdg + ad}$

$x = \frac{bfdg-ac}{d(bg+a)}$ (4)

Now plugging the value of x in equation (3) we get:

$$y = \frac{dg(\frac{bfdg - ac}{d(bg + a)})}{c + d(\frac{bfdg - ac}{d(bg + a)})}$$

$$y = \frac{\frac{bfd^2g^2 - acdg}{(bdg + ad)}}{c + \frac{bfd^2g - acd}{(bdg + ad)}}$$

$$y = \frac{bfd^2g^2 - acdg}{(cbdg + bfd^2g)}$$

$y = \frac{bfdg-ac}{b(c+fd)}$ (5)

MATLAB code

I am using the pplane10.m MATLAB code provided in eclass and modify default system portion according to the model equation each time to get the phase plane sketches and linearization graph of x vs y.

Phase plane code for the Model of Heterosexual population:

```
% Set up for the menu of systems.

system.name = 'default system';
  system.xvar = 'x';
  system.yvar = 'y';
  system.xder = '(-a*x)+b*(f-x)*y';
  system.yder = '(-c*y)+d*(g-y)*x';
  system.pname = {};
  system.pval = {};
  system.fieldtype = 'arrows';
  system.npts = npts;
  system.wind = [0 5 0 5];
```

Phase plane code for homosexual population homogeneously

```
% Set up for the menu of systems.

system.name = 'default system';
  system.xvar = 'x';
  system.yvar = 'y';
  system.xder = '(-a*x)+b*(f-x)*x';
  system.yder = '(-c*y)+d*(g-y)*y';
  system.pname = {};
  system.pval = {};
  system.fieldtype = 'arrows';
  system.npts = npts;
  system.wind = [0 5 0 5];
```

Heterosexual population with no recovery for HIV Transmission

```
% Set up for the menu of systems.

  system.name = 'default system';
  system.xvar = 'x';
  system.yvar = 'y';
  system.xder = ' b*(f-x)*y';
  system.yder = ' d*(g-y)*x ';
  system.pname = {};
  system.pval = {};
  system.fieldtype = 'arrows';
  system.npts = npts;
  system.wind = [0 5 0 5];
```

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