Modeling the effect of HIV/AIDS stigma on HIV infection dynamics in Kenya

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Background

Human immunodeficiency virus infection and acquired immune deficiency syndrome (HIV/AIDS) is a spectrum of conditions

Earliest documented cases were in late 1950s and early 1960s

First outbreak in Africa took place in 1970s

Spread throughout continent in 1980s

Rapid spread throughout Kenya in mid 80s

Declared national disaster in Kenya in 1999

Background

Stigma can be defined as a mark of disgrace associated with a particular circumstance, quality, or person.

Widespread stigma often leads to behavior change

Stigma towards diseases especially problematic

Background

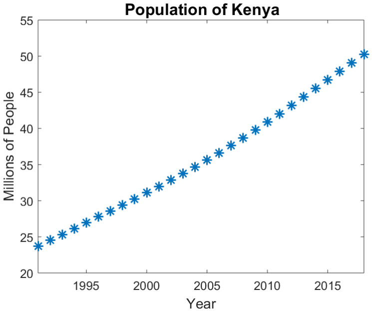
Stigma towards HIV/AIDS is well documented and widespread, especially in sub-Saharan Africa

Resulting behavior change includes

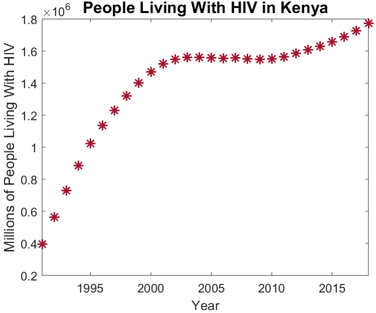
- poor adherence to preventative measures
- avoidance of testing
- delaying or dismissing treatment

These behaviors contribute significantly to persistence of the disease

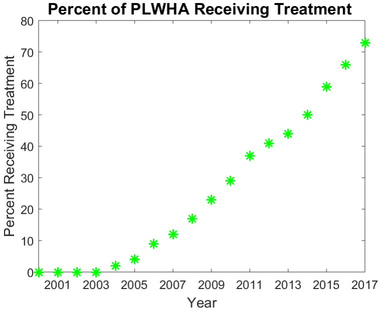
HIV in Kenya



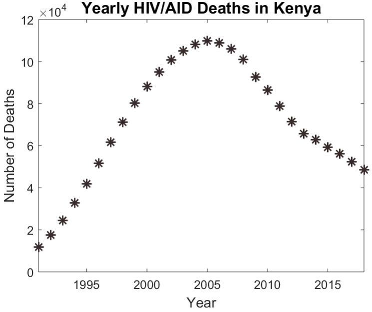
Population of Kenya
Millions of People
Year
55
50
45
40
35
30
25
20
1995
2000
2005
2010
2015



People Living With HIV in Kenya
$\times 10^6$
Millions of People Living With HIV
Year
1.8
1.6
1.4
1.2
1
0.8
0.6
0.4
0.2
1995
2000
2005
2010
2015

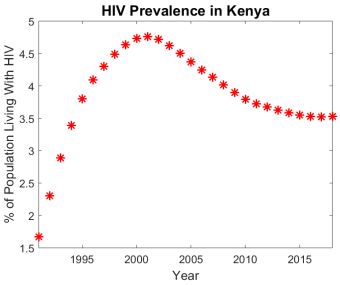


Percent of PLWHA Receiving Treatment
Percent Receiving Treatment
Year
80
70
60
50
40
30
20
10
0
2001
2003
2005
2007
2009
2011
2013
2015
2017



Yearly HIV/AID Deaths in Kenya
$\times 10^4$
Number of Deaths
Year
12
10
8
6
4
2
0
1995
2000
2005
2010
2015

HIV in Kenya



In the early 2000s, the National AIDS Control Council in Kenya...

- Educated population about prevention
- Improved access to testing and treatment
- Reduced stigma towards PLWHA

These factors help Kenya work towards UN Goals of "Getting to Zero" by 2030

Goal

Formulate and analyze a model that considers how stigma towards people living with HIV/AIDS (PLWHA) in Kenya contributes to disease dynamics.

Key Features:

- Stigma is changing over time
- Estimate parameters from available data
- Conduct general analysis of model
- Simulate hypothetical scenarios

Modeling Stigma in Kenya

We focus on two types of stigma:

1. Enacted stigma (societal stigma)
2. Internalized stigma (self-stigma)

Let $\sigma(t)$ denote the fraction of newly infected PLWHA that experience stigma, then

$$\frac{d\sigma}{dt} = \nu(\sigma_b - \sigma),$$

where

ν represents **enacted stigma** $\longrightarrow$ changes due to external drivers

and

σ_b is interpreted as the level of **internalized stigma** $\longrightarrow$ equilibrium value

Modeling Stigma in Kenya

Kenya measured HIV stigma in 2003, 2008, and 2014 via 4 questions:

1. Would you buy fresh vegetables from a shopkeeper or vendor if you knew that this person had HIV?
2. If a member of your family became sick with AIDS, would you be willing to care for her or him in your own household?
3. In your opinion, if a female teacher has the AIDS virus, but is not sick, should she be allowed to continue teaching in the school?
4. If a member of your family got infected with the AIDS virus, would you want it to remain a secret or not?

Modeling Stigma in Kenya

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1. Would you buy fresh vegetables from a shopkeeper or vendor if you knew that this person had HIV?
2. ~~If a member of your family became sick with AIDS, would you be willing to care for her or him in your own household?~~
3. In your opinion, if a female teacher has the AIDS virus, but is not sick, should she be allowed to continue teaching in the school?
4. If a member of your family got infected with the AIDS virus, would you want it to remain a secret or not?

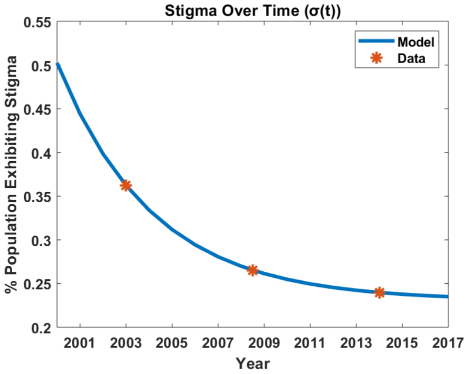
Modeling Stigma in Kenya

We interpret $\sigma(t)$ in Kenya as the percent of adults that answered at least 2 of the following questions in a stigmatizing manner

1. Would you buy fresh vegetables from a shopkeeper or vendor if you knew that this person had HIV?
3. In your opinion, if a female teacher has the AIDS virus, but is not sick, should she be allowed to continue teaching in the school?
4. If a member of your family got infected with the AIDS virus, would you want it to remain a secret or not?

	2003	2008	2014
Stigma Level	36%	27%	24%

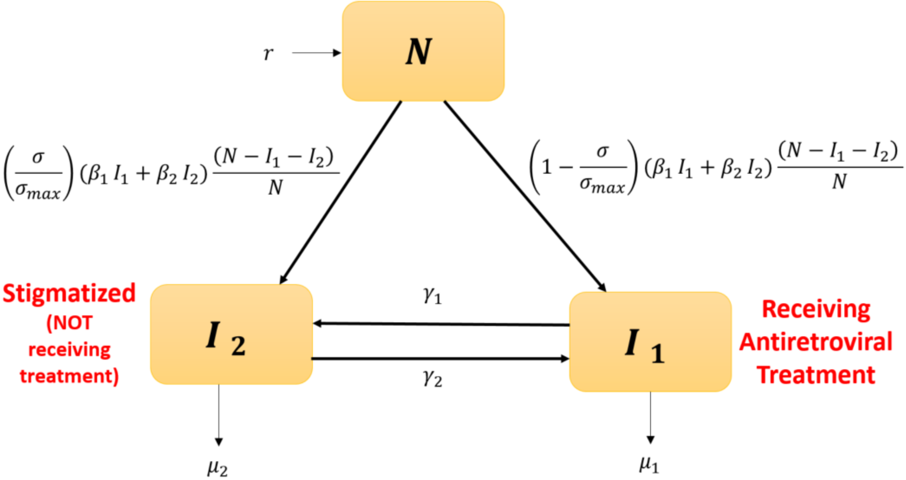
Modeling Stigma in Kenya



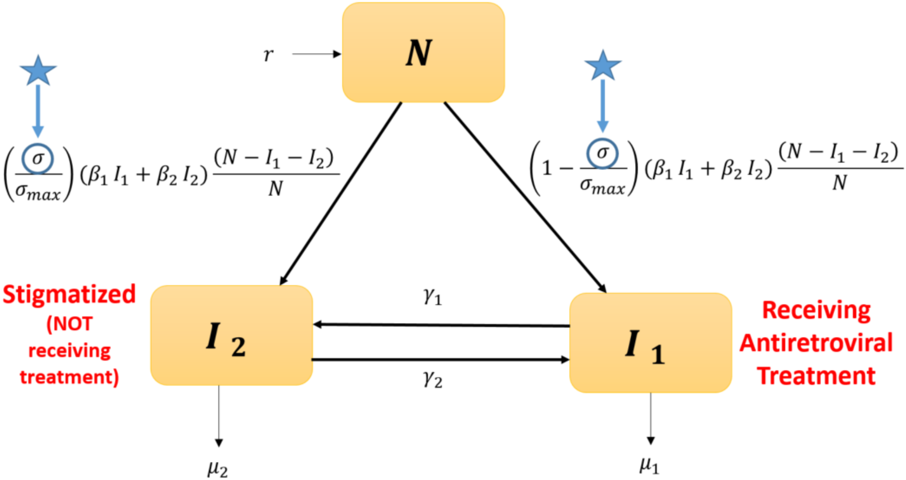
	2003	2008	2014
Stigma Level	36%	27%	24%

$$\sigma(t) = 0.27e^{-0.24t} + 0.23$$
$$\sigma_b = 0.23$$
$$\nu = -0.24$$

Model Formulation

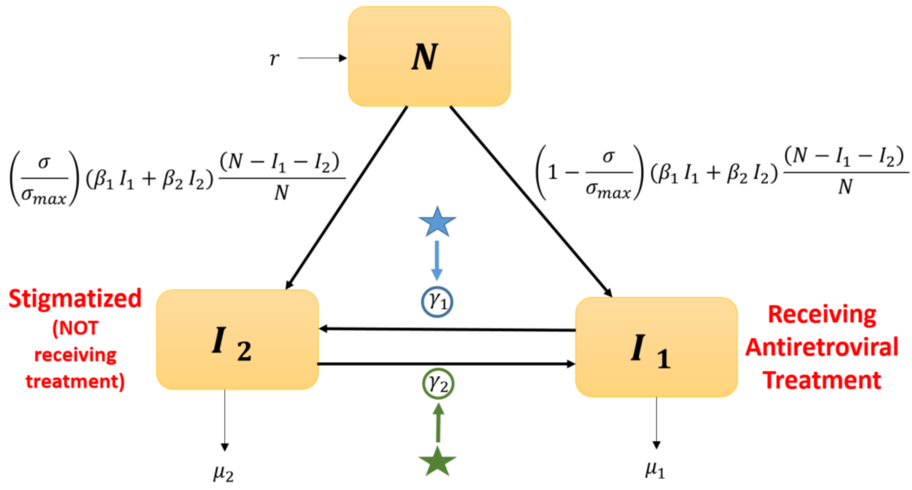


Model Formulation



$$\sigma(t) = 0.27e^{-0.24t} + 0.23$$

Model Formulation



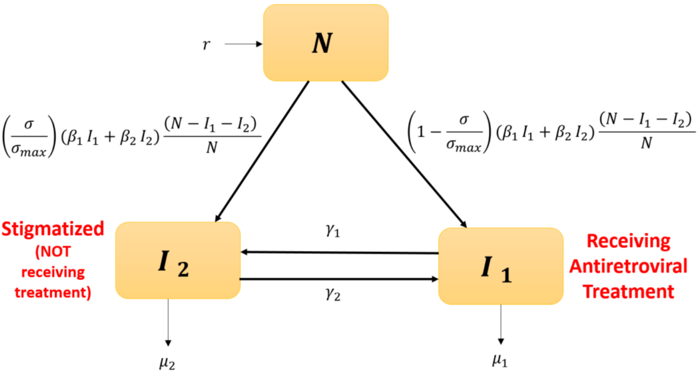
γ_1 is a convex increasing function of σ:

$$\gamma_1 = b\sigma(t)^2$$

γ_2 is a convex decreasing function of σ:

$$\gamma_2 = c(1 - \sqrt{\sigma(t)})$$

Model Formulation



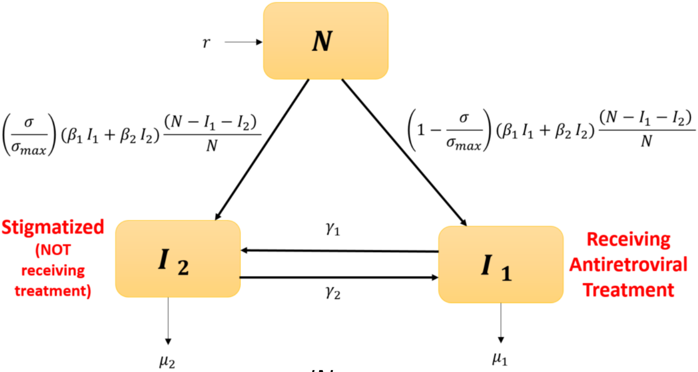
$$\frac{dN}{dt} = rN$$

$$\frac{dI_1}{dt} = \left(1 - \frac{\sigma}{\sigma_{\max}}\right)(\beta_1 I_1 + \beta_2 I_2)\frac{(N - I_1 - I_2)}{N} - \gamma_1(\sigma)I_1 + \gamma_2(\sigma)I_2 - \mu_1 I_1,$$

$$\frac{dI_2}{dt} = \frac{\sigma}{\sigma_{\max}}(\beta_1 I_1 + \beta_2 I_2)\frac{(N - I_1 - I_2)}{N} + \gamma_1(\sigma)I_1 - \gamma_2(\sigma)I_2 - \mu_2 I_2,$$

where $\sigma(t) = 0.27e^{-0.24t} + 0.23$

Reformulate model in terms of Prevalence ($P(t)$) and Percent Treated ($V(t)$)



$$\frac{dN}{dt} = rN$$

Exponentially growing population leads to nontrivial steady state solutions

We reformulate model in terms of Prevalence and Percent Treated

Reformulate model in terms of Prevalence ($P(t)$) and Percent Treated ($V(t)$)

Letting

$$P = \frac{I_1 + I_2}{N} \text{ and } V = \frac{I_1}{I_1 + I_2}$$

Leads to

$$\begin{aligned}
\frac{dP}{dt} &= P[(1-P)(\beta_1 V + \beta_2(1-V)) - \mu_1 V - \mu_2(1-V) - r], \\
\frac{dV}{dP} &= \left(1 - \frac{\sigma}{\sigma_{\text{max}}} - V\right)(\beta_1 V + \beta_2(1-V))(1-P) - \gamma_1 V + \gamma_2(1-V) \\
&\quad + (\mu_2 - \mu_1)V(1-V)
\end{aligned}$$

where $\sigma(t) = 0.27e^{-0.24t} + 0.23$

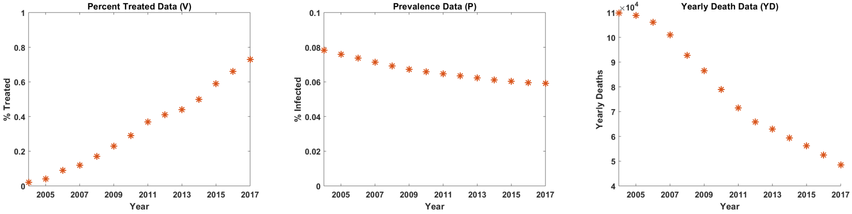
Parameter Estimation Overview

Goal: Find the set of 6 parameters that produce model output that most closely match the data **from 2004-2017**

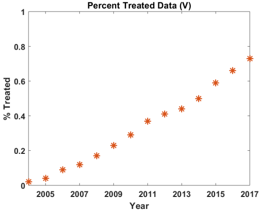
6 Unknown Parameters:

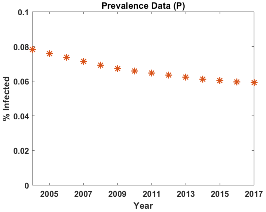
$\beta_1 = 0.1\beta_2$	Transmission rate by I_1 class
β_2	Transmission rate by I_2 class
μ_1	Death rate in PLWHA with low stigma
μ_2	Death rate in PLWHA with high stigma
$1/\sigma_{max}$	Scaling coefficient for $\sigma(t)$
b	Scaling coefficient for γ_1
c	Scaling coefficient for γ_2

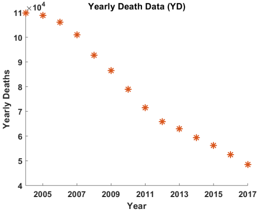
Data:



Optimization Problem







$$\underset{parameters}{\text{Minimize}} \quad \frac{||\vec{V} - \vec{V}*||_2}{||\vec{V}*||_2} + \frac{||\vec{P} - \vec{P}*||_2}{||\vec{P}*||_2} + \frac{||\vec{YD} - \vec{YD}*||_2}{||\vec{YD}*||_2}$$

Subject to:

$\mu_1 \leq 0.5\mu_2 \longrightarrow$ treatment reduces death due to the disease by more than 50% Kasamba (2012), Violari (2008)

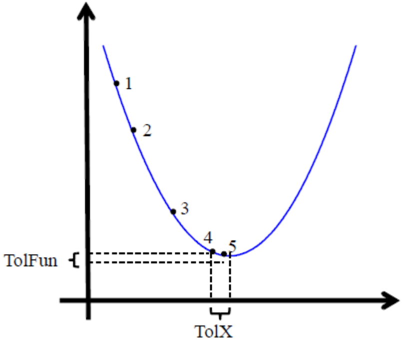
where $\vec{P}$ represents the percent of the population that are a PLWHA
$\vec{V}$ represents the percent of P that are receiving treatment
$\vec{YD}$ represents the number of yearly deaths caused by HIV/AIDS

MATLAB Solver

Global Optimization Toolbox in MATLAB

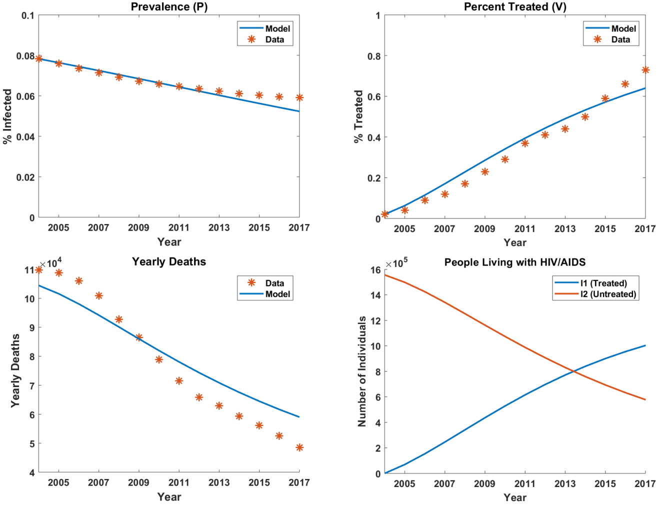
Local Solver: fmincon

- Imposes inequality constraints
- Derivative free
- Objective function inputs parameters and outputs scalar value to be minimized
- Find local minimums only



MultiStart allows us to fully explore parameter space

Parameter Estimation Results



Parameter	Value
r	0.032
β_1	0.0082
β_2	0.082
μ_1	0.021
μ_2	0.068
σ_{max}	0.50
b	0
c	0.133

Sensitivity Analysis

Used Latin Hypercube Sampling and Partial Rank Correlation Coefficients (PRCC) to evaluate the sensitivity of our model with respect to...

1. Total Cases after the 14 year simulation (TC)
2. Yearly Cases in final year of the simulation (YC)
3. Yearly Deaths in final year of the simulation (YD)

	PRCC		
	TC	YC	YD
β_2	0.991*	0.981*	0.956*
μ_1	−0.043	0.044	0.842*
μ_2	−0.880*	−0.893*	0.152
σ_{max}	0.833*	0.809*	0.835*
b	−0.050	−0.053	0.117
c	−0.727*	−0.821*	−0.866*

∗statistically significant values ($p < 0.0001$)

Disease Free Equilibrium

$$0 = P[(1-P)(\beta_1 V + \beta_2(1-V)) - \mu_1 V - \mu_2(1-V) - r],$$

$$0 = \left(1 - \frac{\sigma}{\sigma_{\text{max}}} - V\right)(\beta_1 V + \beta_2(1-V))(1-P) - \gamma_1 V + \gamma_2(1-V) + (\mu_2 - \mu_1)V(1-V),$$

where $\sigma = \lim_{t\to\infty} \sigma(t) = \sigma_b = 0.23$.

Disease free equilibrium is of form $(P^*, V^*) = (0, V^*)$

Disease Free Equilibrium

Letting $P^* = 0$ results in

$$V^*_{1,2} \quad = \quad \frac{-B \pm \sqrt{B^2 - 4AC}}{2A},$$

where

$$\begin{aligned} A &= \beta_2 - \beta_1 + \mu_1 - \mu_2 \\ B &= \beta_1 \left(1 - \tfrac{\sigma_b}{\sigma_{\max}}\right) - \beta_2 \left(2 - \tfrac{\sigma_b}{\sigma_{\max}}\right) + \mu_2 - \mu_1 - \gamma_1 - \gamma_2 \\ C &= \beta_2 \left(1 - \tfrac{\sigma_b}{\sigma_{\max}}\right) + \gamma_2. \end{aligned}$$

For existence of V^* we need $B^2 - 4AC > 0$

Using our estimated parameters, $V^* \approx 0.96$

Disease Free Equilibrium

$$J(0, V^*) = \begin{bmatrix} \frac{\partial P'}{\partial P} & \frac{\partial P'}{\partial V} \\ \frac{\partial V'}{\partial P} & \frac{\partial V'}{\partial V} \end{bmatrix} \Bigg|_{(0,V^*)} = \begin{bmatrix} a_{11} & 0 \\ a_{21} & a_{22} \end{bmatrix} \tag{1}$$

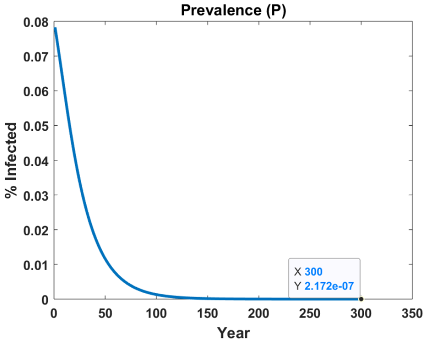
where

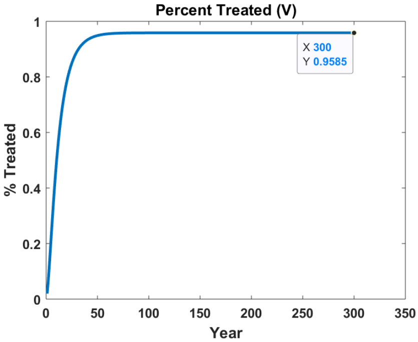
$$\begin{aligned} a_{11} &= \beta_1 V^* + \beta_2(1 - V^*) - \mu_1 V^* - \mu_2(1 - V^*) - r \\ a_{21} &= -\left(1 - \frac{\sigma_b}{\sigma_{max}} - V^*\right)(\beta_1 V^* + \beta_2(1 - V^*)) \\ a_{22} &= -(\beta_1 V^* + \beta_2(1 - V^*)) + \left(1 - \frac{\sigma_b}{\sigma_{max}} - V^*\right)(\beta_1 - \beta_2) \\ &- \gamma_1 - \gamma_2 + (\mu_2 - \mu_1)(1 - 2V^*). \end{aligned}$$

Stability of DFE reduces to $a_{11} < 0$ and $a_{22} < 0$

Using our estimated parameters, the DFE is locally asymptotically stable

Disease Free Equilibrium





Using our estimated parameters,

$V^* \approx 0.96$ & the DFE $(0, V^*)$ is locally asymptotically stable

Simulation Results

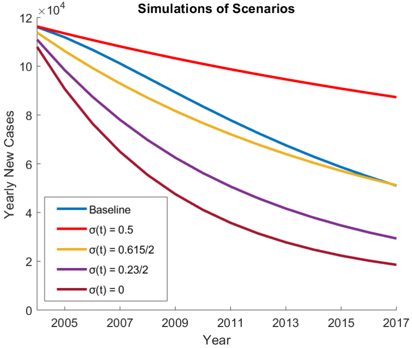
<u>Scenarios 1-4:</u> Constant stigma values

~~$\sigma(t) = 0.27e^{-0.24t} + 0.23$~~

1. $\sigma = \sigma_{max} = 1/2$
2. $\sigma = \sigma_{min} = 0.23/2$
3. $\sigma = 0.615/2$
4. $\sigma = 0$

Simulation Results

Scenarios 1-4: Constant stigma values



Scenario	Switching Month ($I_1 > I_2$)	Total Deaths (millions)	Total Treated (millions)
Baseline	113	1.13	1.04
$\sigma(t) = \sigma_{max} = 1/2$	298	1.31	0.60
$\sigma(t) = 0.615/2$	104	1.09	1.02
$\sigma(t) = \sigma_{min} = 0.23/2$	60	0.91	1.25
$\sigma(t) = 0$	41	0.79	1.34

Simulation Results

Scenarios 5 & 6: Altering enacted and internalized stigma

$$\sigma(t) = ce^{\nu t} + \sigma_b$$
$$= 0.27e^{-0.24t} + 0.23$$

where

ν represents **enacted stigma** $\longrightarrow$ changes due to external drivers

and

σ_b is interpreted as the level of **internalized stigma** $\longrightarrow$ equilibrium value

Simulation Results

<u>Scenarios 5 & 6:</u> Altering enacted and internalized stigma

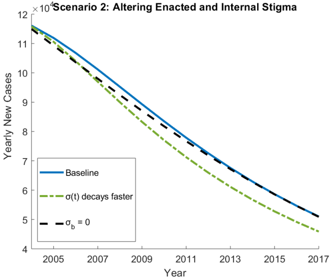
$$\sigma(t) = ce^{\nu t} + \sigma_b$$
$$= 0.27e^{-0.24t} + 0.23$$

5. Double decay rate of enacted stigma of stigma:
   Let $\nu = 2 * -0.24 = -0.48 \longrightarrow \sigma(t) = 0.27e^{-0.48t} + 0.23$

6. No internalized stigma:
   Let $\sigma_b = 0 \longrightarrow \sigma(t) = 0.4e^{-0.04t}$

Simulation Results

Scenarios 5 & 6: Altering enacted and internalized stigma



Scenario	**Switching Month ($I_1 > I_2$)**	**Total Deaths (millions)**	**Total Treated (millions)**
Baseline	113	1.13	1.04
$\sigma(t)$ decays faster ($\nu = 0.48$)	99	1.08	1.09
$\sigma_b = 0$ ($\sigma(t) = .4e^{-.04t}$)	113	1.12	1.04

Simulation Results: Meeting UN Goals

By 2030 the United Nations initiative "Getting to Zero" aims to...

1. Eliminate HIV/AIDS stigma entirely ($\sigma = 0$)
2. 0 new cases
3. 0 deaths

Our model predicts the following in the year 2030:

If we assume $\sigma_b = 0.23$ so that $\sigma(t) = 0.27e^{-.24t} + 0.23$,

Stigma Level	**Yearly New Cases**	**Yearly Deaths**
0.231	24,427	38,448

If we assume $\sigma_b = 0$ so that $\sigma(t) = 0.4e^{-.04t}$,

Stigma Level	**Yearly New Cases**	**Yearly Deaths**
0.120	21,500	36,364

Conclusions

Stigma towards PLWHA in Kenya plays significant role in disease dynamics

Our model meets our qualitative and quantitative goals

The disease free equilibrium (DFE) $(P^*, V^*) = (0, 0.96)$ is locally stable, though UN goals may not be achieved by 2030

Simulations of scenarios highlight importance of treatment and suggest targeting internalized stigma to meet UN goals

Future Directions

Use survey data to further stratify population

- Male vs female
- By age
- Rural vs Urban
- Socioeconomic status
- others...

Apply stigma modeling concept to other diseases

Thank you

Thank you to Academic Affairs for Special Projects Grant.

Open access publication:

Levy, B., Correia,H., Chirove, F., Ronoh, M., Abebe, A., Kgosimore, M., Chimbola, O., Machingauta, H., Lenhart, S., and White, JKA. (2021)

Modeling the Effect of HIV/AIDS Stigma on HIV Infection Dynamics in Kenya.

Bulletin of Mathematical Biology, 83(5), 1-25.

Parameter Estimation: Data

Year	Adult Population	Total Cases	Yearly Deaths	Percent Treated
2004	19,881,691	1,556,539	109,769	2
2005	20,500,063	1,555,886	108,881	4
2006	21,134,459	1,556,425	106,011	9
2007	21,756,530	1,552,905	100,971	12
2008	22,384,120	1,549,630	92,753	17
2009	23,050,075	1,551,573	86,497	23
2010	23,771,983	1,564,451	78,894	29
2011	24,525,795	1,585,198	71,528	37
2012	25,345,229	1,607,145	65,842	41
2013	26,216,858	1,630,997	62,910	44
2014	27,117,617	1,657,895	59,355	50
2015	28,036,000	1,689,424	56,188	59
2016	28,988,590	1,727,026	52,482	66
2017	29,957,102	1,772,350	48,502	73

Goal: Given yearly harvest levels in each region, find the set of 8 parameters that produce harvest values that most closely match the data.