**BIOS27816: Population biology of infectious diseases of global health concern**

# Pathogens with Complex Transmission Mechanisms: Case Study in HIV

UChicago Center in Paris

Paris, France

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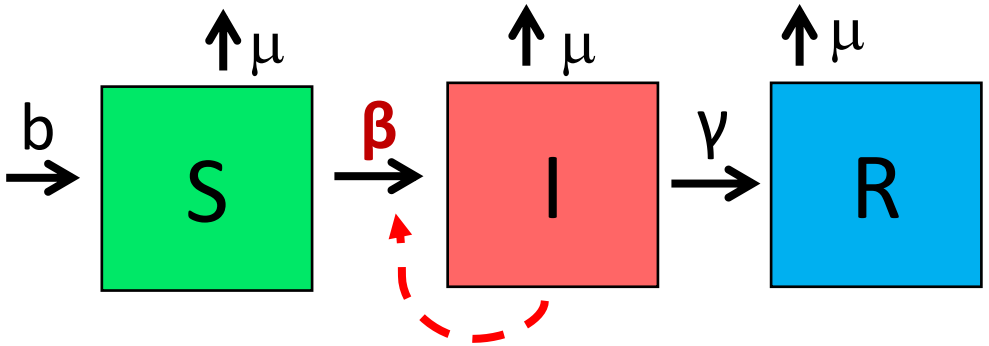
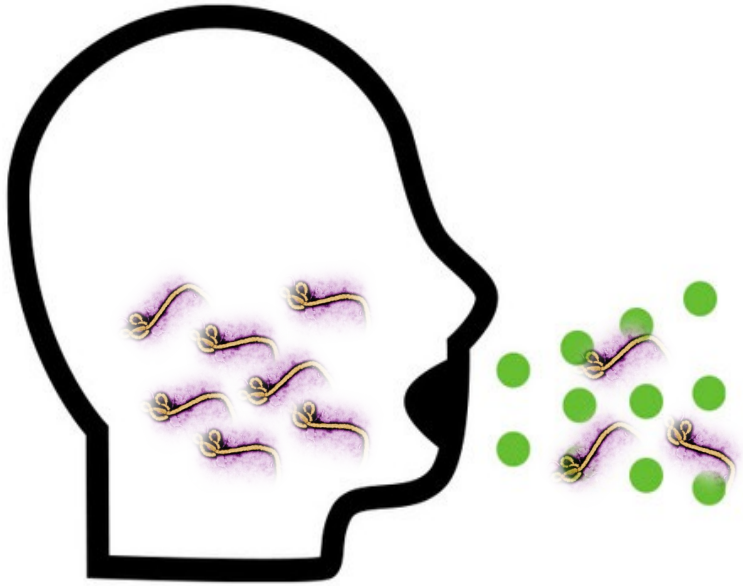
# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Directly-transmitted** diseases are transmitted via exchange of bodily fluids
  - Droplet (> 5 microns ) spread or direct contact
  - Includes sexually-transmitted pathogens, though often modeled with a more complex contact network
  - Smallpox *(Variola* spp.), HIV, Mononucleosis (*Epstein Barr virus*)
- **Indirectly-transmitted** diseases are transmitted via droplets retained in air
  - Droplets < 5 microns in diameter
  - Measles, COVID (*SARS-CoV-2*)

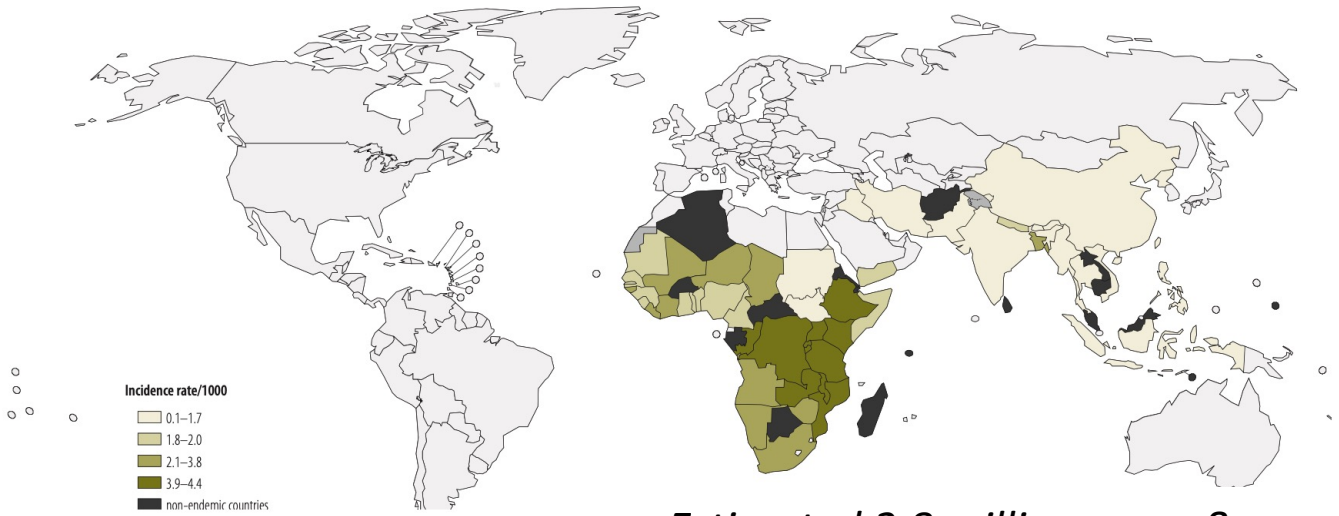


# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Environmentally-transmitted** pathogens are transmitted outside of the host (e.g. water-borne, food-borne)
  - Examples: Cholera (*Vibrio cholerae*), Salmonellosis (*Salmonella* spp. bacteria), White-Nosed Syndrome (*Pseudogymnoascus destructans*)

Global Burden of Cholera, 2012




*Estimated 2.8 million cases & 95,000 deaths annually*

Ali et al. 2012. *WHO Bulletin.*

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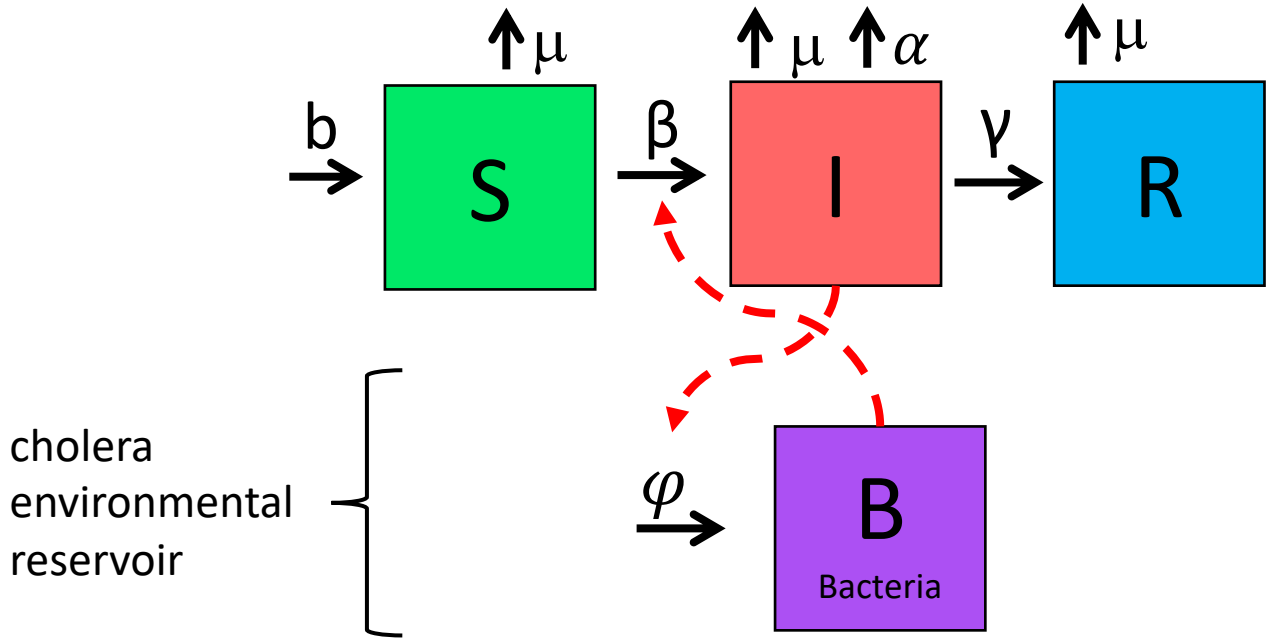
  - Examples: Cholera *(Vibrio cholerae)*, Salmonellosis (*Salmonella* spp. bacteria), White-Nosed Syndrome (*Pseudogymnoascus destructans*)
  - Here, the **environmental reservoir** is often modeled as its own population

$$\frac{dB}{dt} = \varphi IB$$

$$\frac{dS}{dt} = b(S + I + R) - \beta SB - \mu S$$

$$\frac{dI}{dt} = \beta SB - \gamma I - \mu I - \alpha I$$

$$\frac{dR}{dt} = \gamma I - \mu R$$




Codeço 2001. *BMC Infectious Diseases.*

# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vertically-transmitted** pathogens are transmitted mother-to-child *in utero*
  - Examples: HIV, *Herpes simplex virus*, *Cytomegalovirus*, Rubella, Zika

# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

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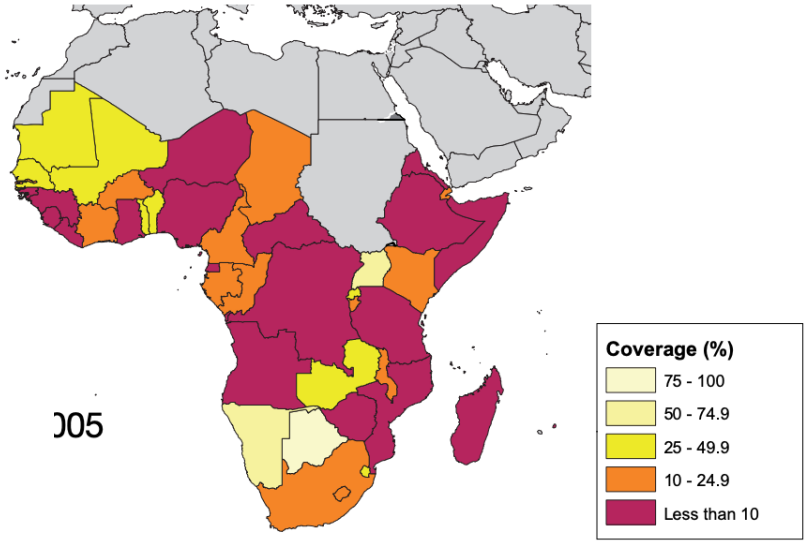
  - Examples: **HIV**, *Herpes simplex virus*, *Cytomegalovirus*, Rubella, Zika

- In untreated HIV+ mothers, rate of vertical transmission for HIV = 15-45%
- Reduced to <1% for those on ART, though global access to ART is geographically heterogenous

ART coverage for those in need, from WHO



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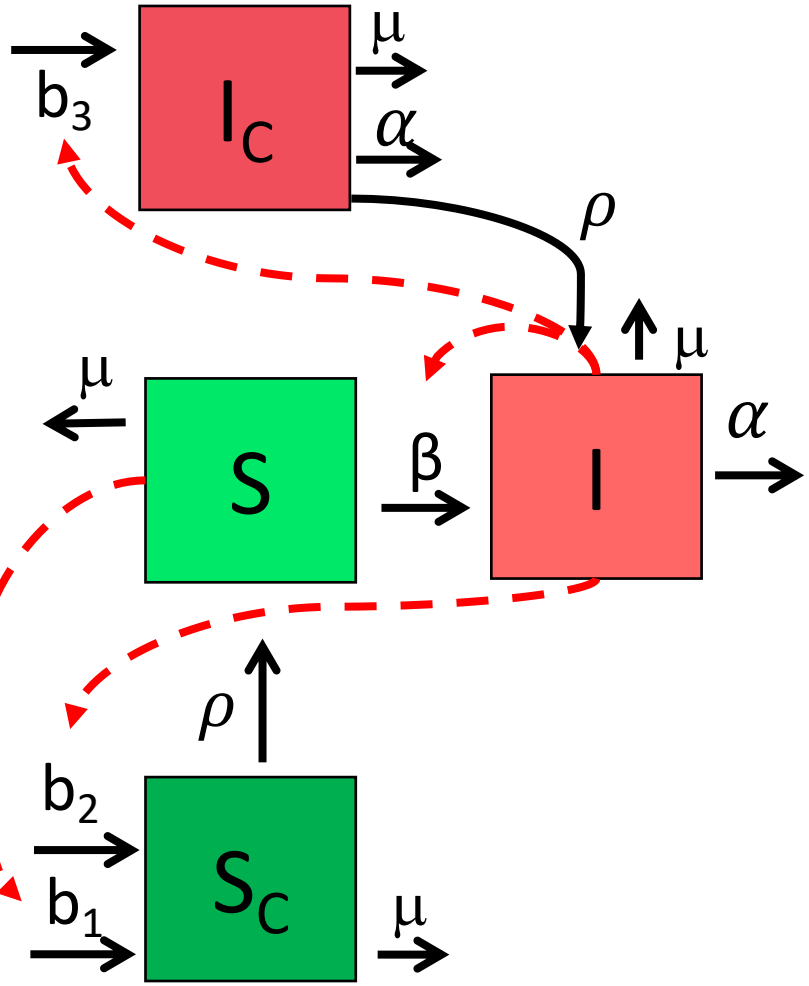


$$\frac{dS}{dt} = \rho S_C - \beta S(I_C + I) - \mu S$$

$$\frac{dI}{dt} = \beta S(I_C + I) + \rho I_C - \mu I - \alpha I$$

$$\frac{dS_C}{dt} = b_1 S + b_2 I - S_C(\rho + \mu)$$

$$\frac{dI_C}{dt} = b_3 I - I_C(\rho + \mu + \alpha)$$

Yusuf et al. 2021. *Chaos and Fractals.*

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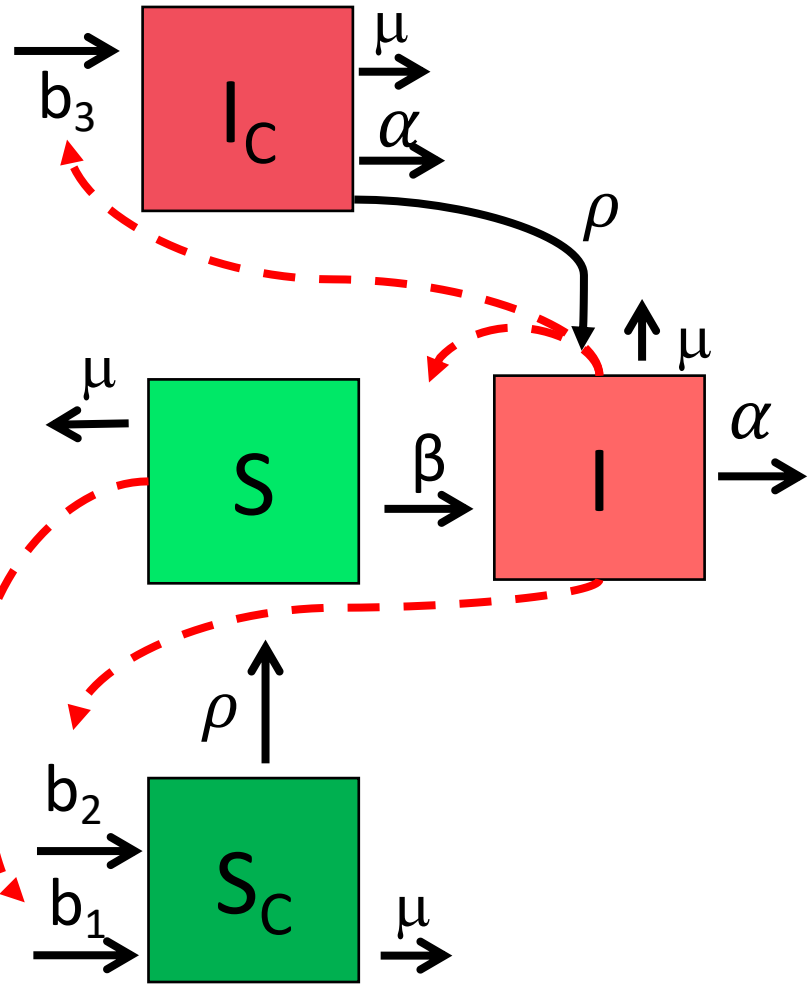


$$\frac{dS}{dt} = \rho S_C - \beta S(I_C + I) - \mu S$$

**Vertical AND horizontal transmission!**

$$\frac{dI}{dt} = \beta S(I_C + I) + \rho I_C - \mu I - \alpha I$$

$$\frac{dS_C}{dt} = b_1 S + b_2 I - S_C(\rho + \mu)$$

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Yusuf et al. 2021. *Chaos and Fractals.*

# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Euclidean **vector**: a quantity with a magnitude and direction

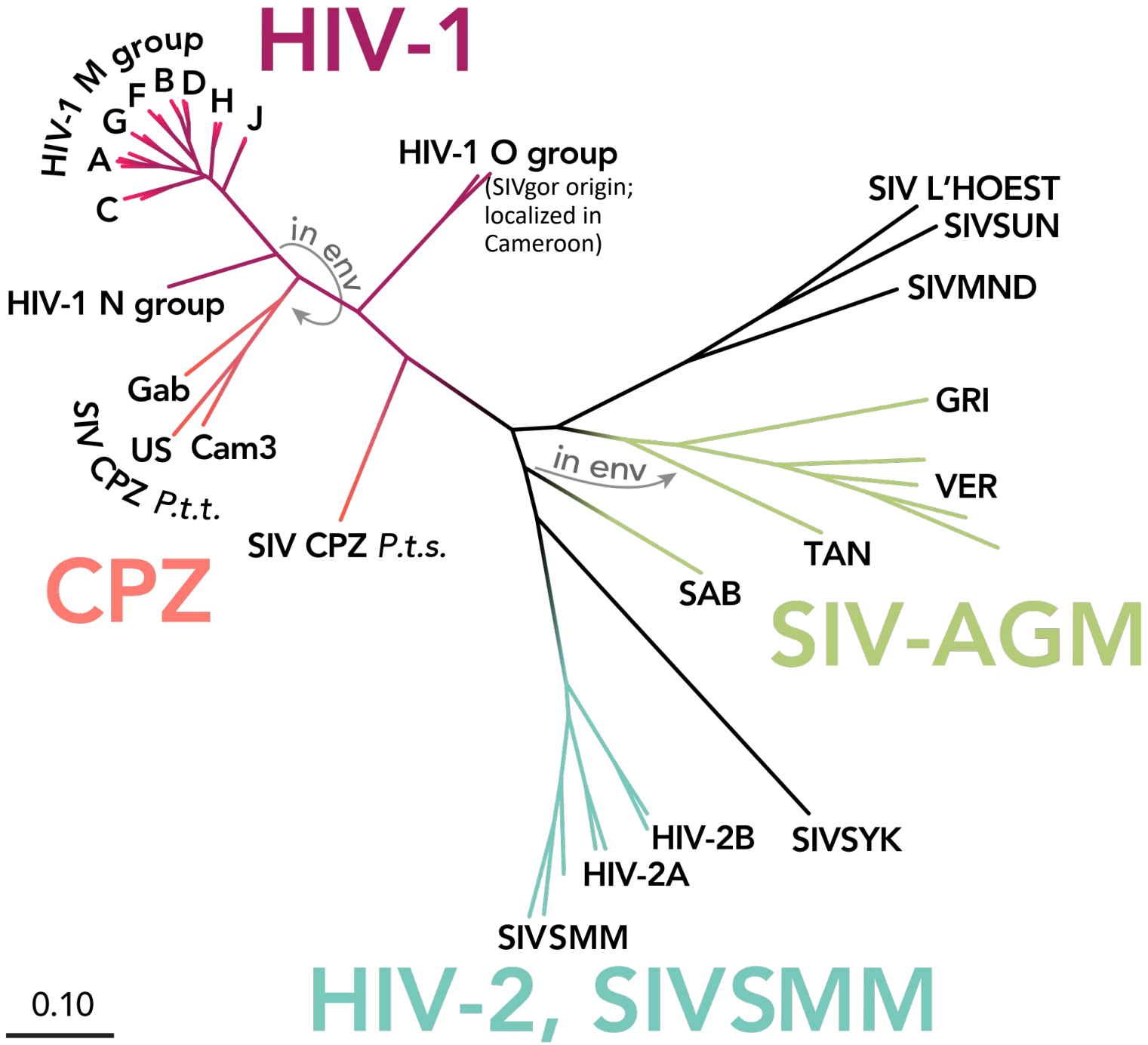
  - Epidemiological **vector**: an agent that carries and transmits an infectious patient into another living organism

# Pathogens exhibit **diverse transmission mechanisms** that require tailored modeling structures

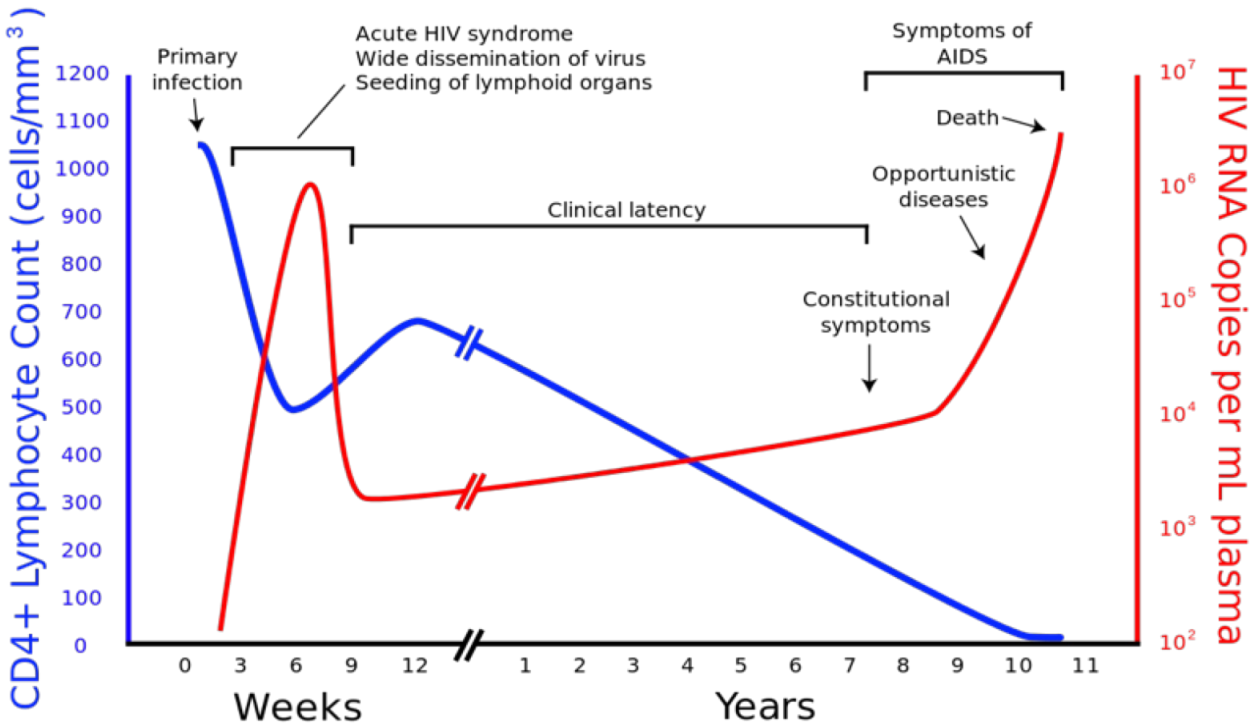
- **Vector-borne** diseases (a type of indirect transmission) are transmitted via blood-feeding arthropod (mosquitoes, ticks, fleas)
  - Malaria: Mosquito-borne protozoan *Plasmodium spp.*
  - "Arboviruses": Mosquito-borne viruses, including Dengue, Zika, Yellow fever virus, West Nile virus, Chikungunya virus
  - Sleeping sickness, also known as African trypanosomiasis: tsetse fly vector and protozoan pathogen (trypanosome)
  - Chagas disease: kissing bug vector and trypanosome pathogen
  - Plague: flea vector and bacterial pathogen (*Yersinia pestis)*

# Learning about HIV

- Human immunodeficiency virus = 2 species of lentivirus (a type of retrovirus) that infect humans and over time cause AIDS (acquired immunodeficiency syndrome)
- HIV-1 and HIV-2 believed to have diverse zoonotic origins in Africa
- Estimates of HIV spillover date ~late 19th/early 20th century.
- Earliest human viral sequences from a patient in Kinshasa in 1960

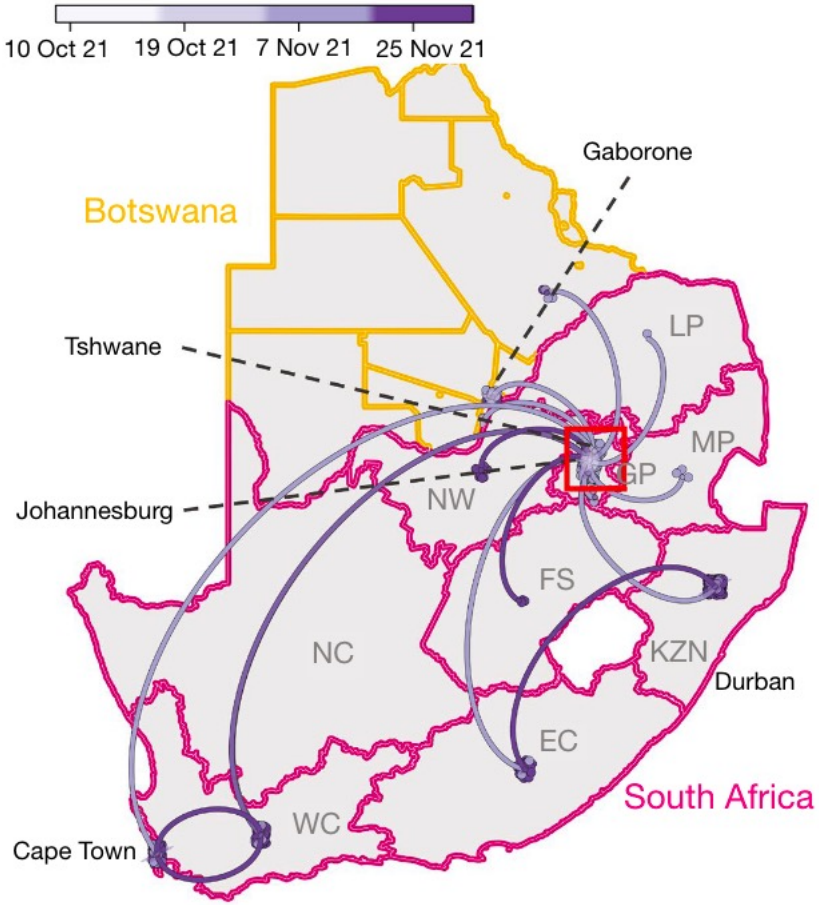


# First global recognition of HIV



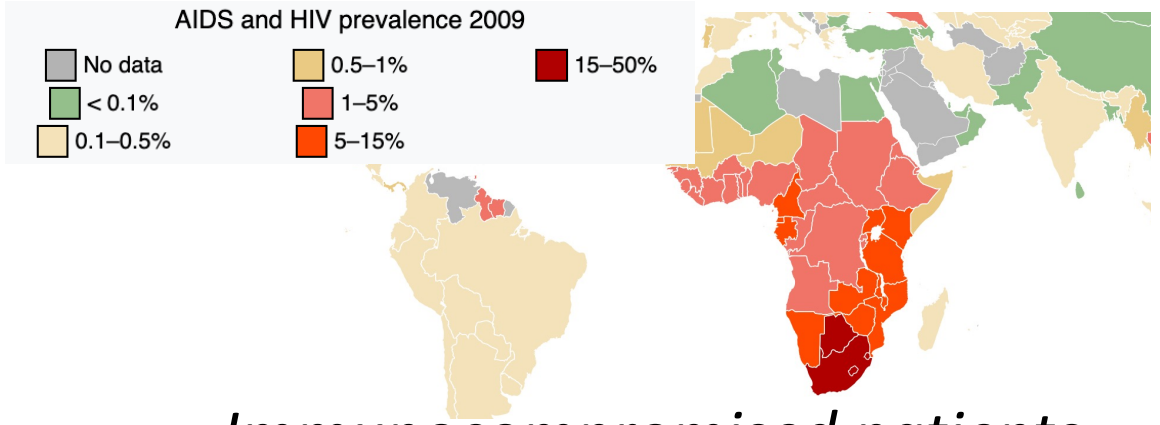

- First recognized by newspapers in 1981 as gay men and injecting drug users in the US began reporting to hospitals with rare pneumonias and skin cancers
- Widespread fear and intense stigma attributed to ‘gay cancer’
- Virus co-discovered in 1983 by American Robert Gallo and Insitut Pasteur team, Françoise Barree-Sinoussi and Luc Montagnier
- Early cases concentrated in gay men, injecting drug users, and hemophiliacs. Later understood that everyone was at risk
- *Immunocompromised patients pose risk for virus evolution.*

# *Immunocompromised patients pose risk for virus evolution.*



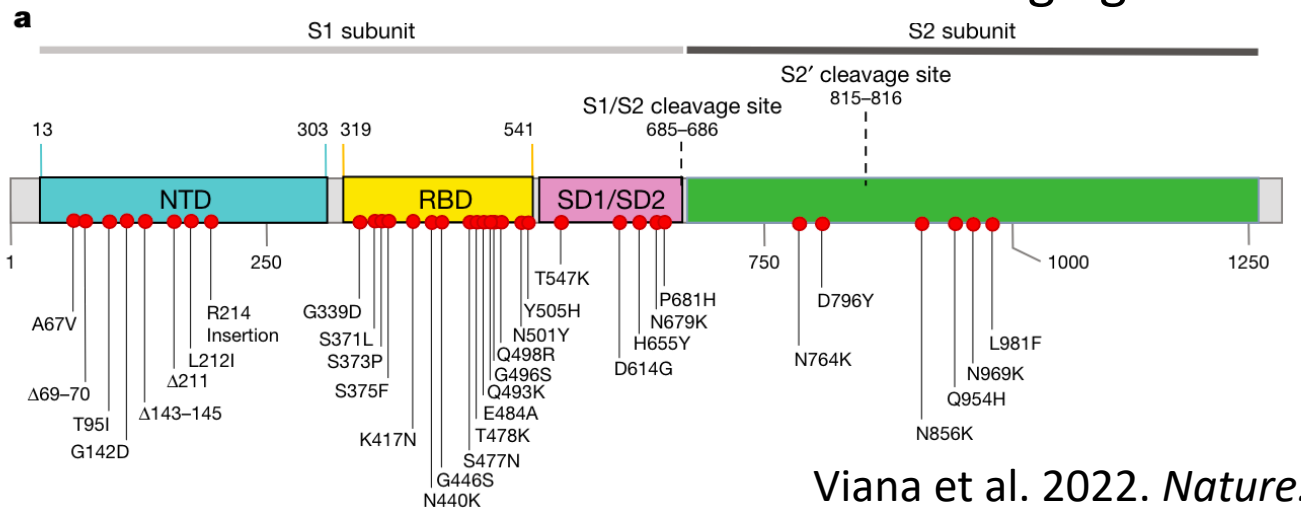

Botswana HIV prevalence = 24.8%

South Africa HIV prevalence = 19%



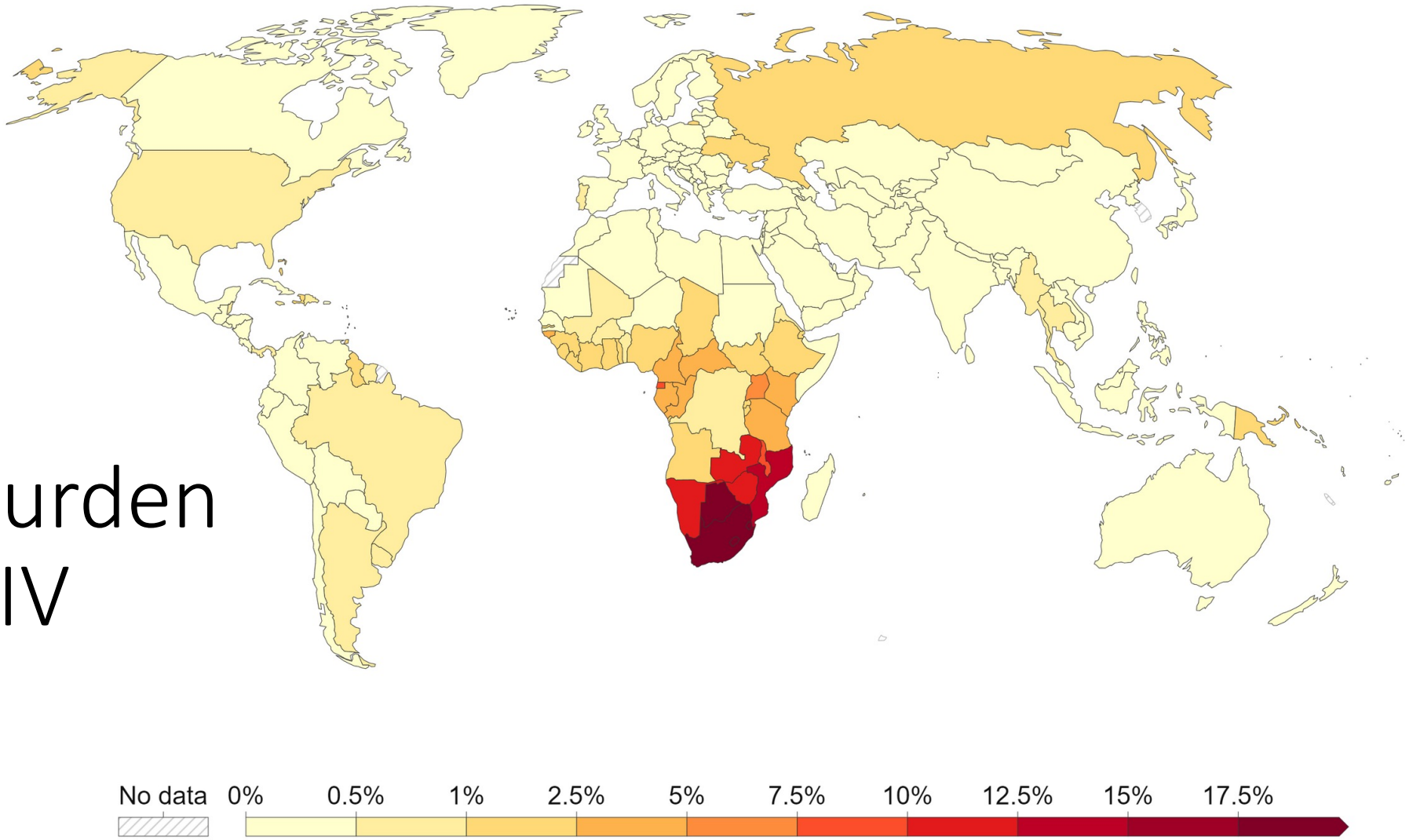

*Immunocompromised patients pose risk for virus evolution.*

>30 spike protein mutations in emerging Omicron

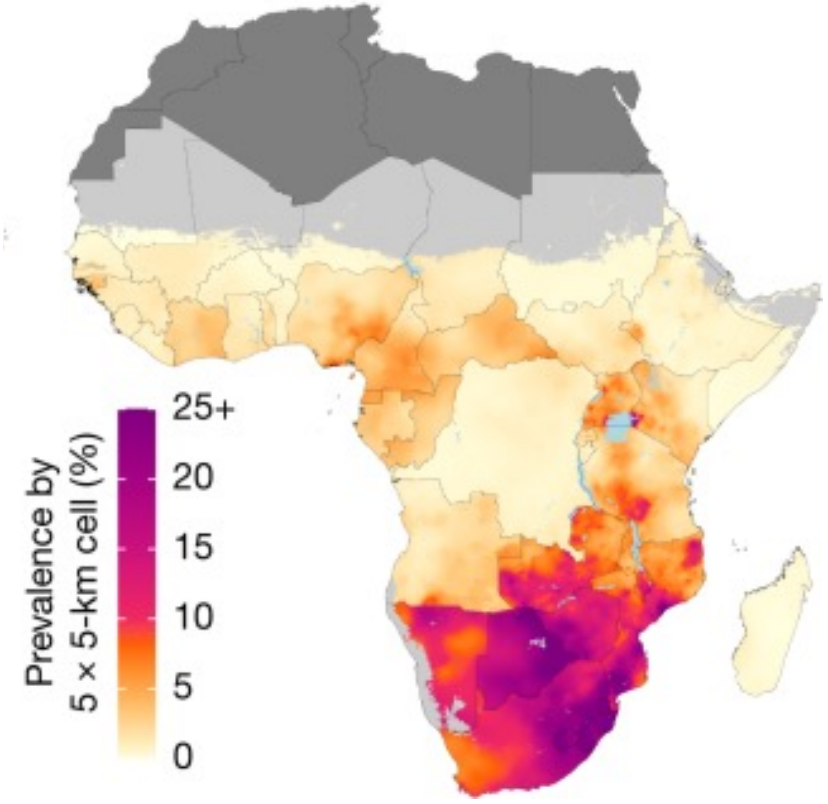


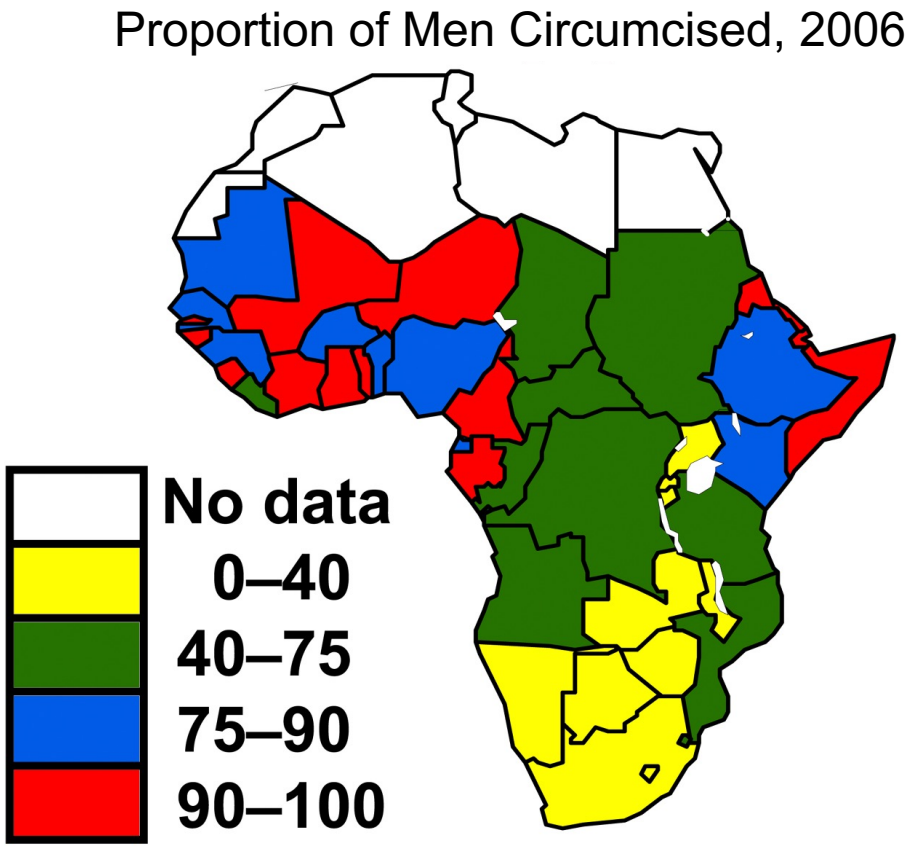

Viana et al. 2022. *Nature.*

# Global burden of HIV



# HIV epidemic in African appears to be largely driven by heterosexual transmission, often related to sex work



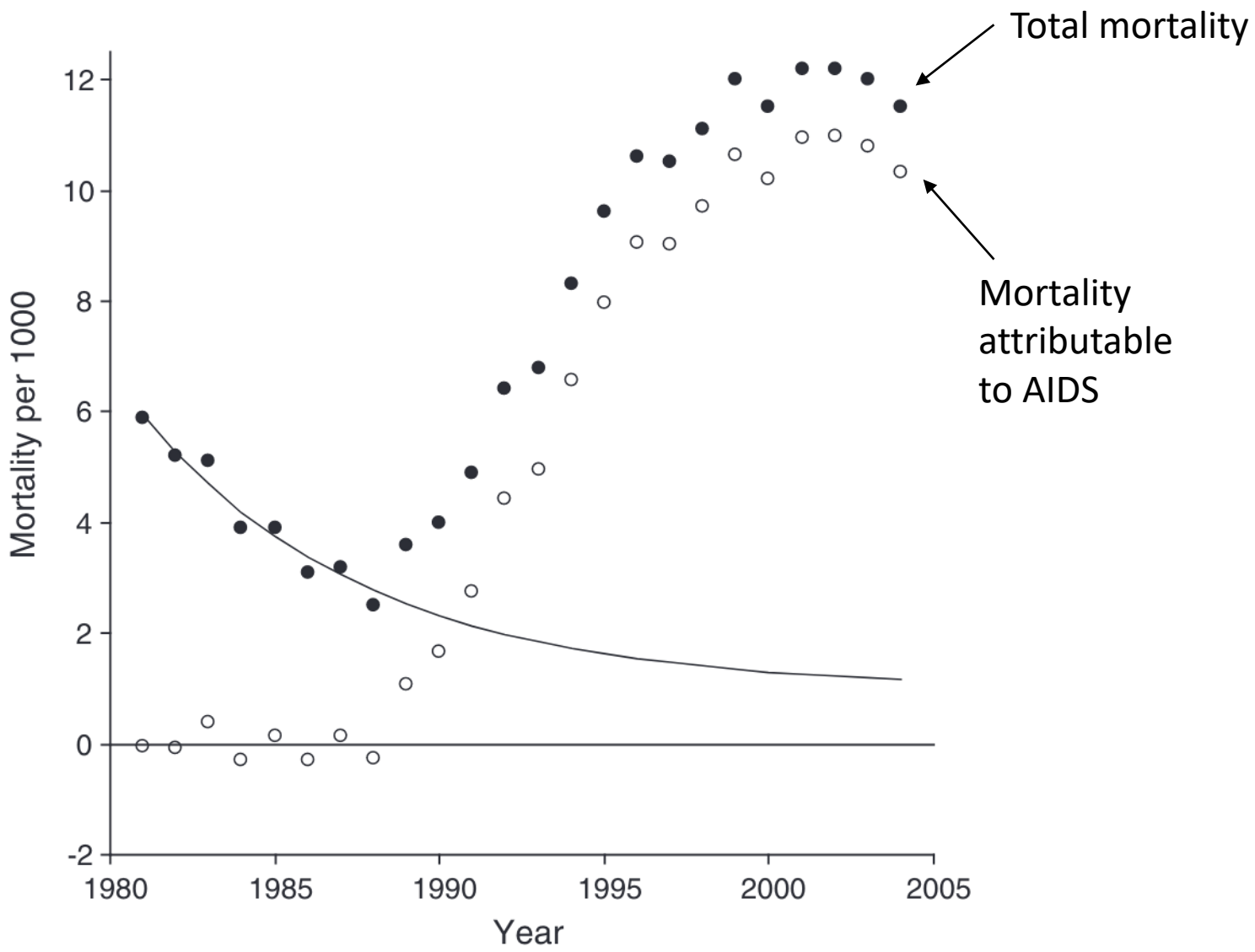

Male circumcision reduces transmission of HIV from women to men in heterosexual intercourse by 60%.

Williams et al. 2006. *PLoS Medicine.*
Auvert et al. 2005. *PLoS Medicine.*
Dwyer-Lindgren et al. 2019. *Nature.*

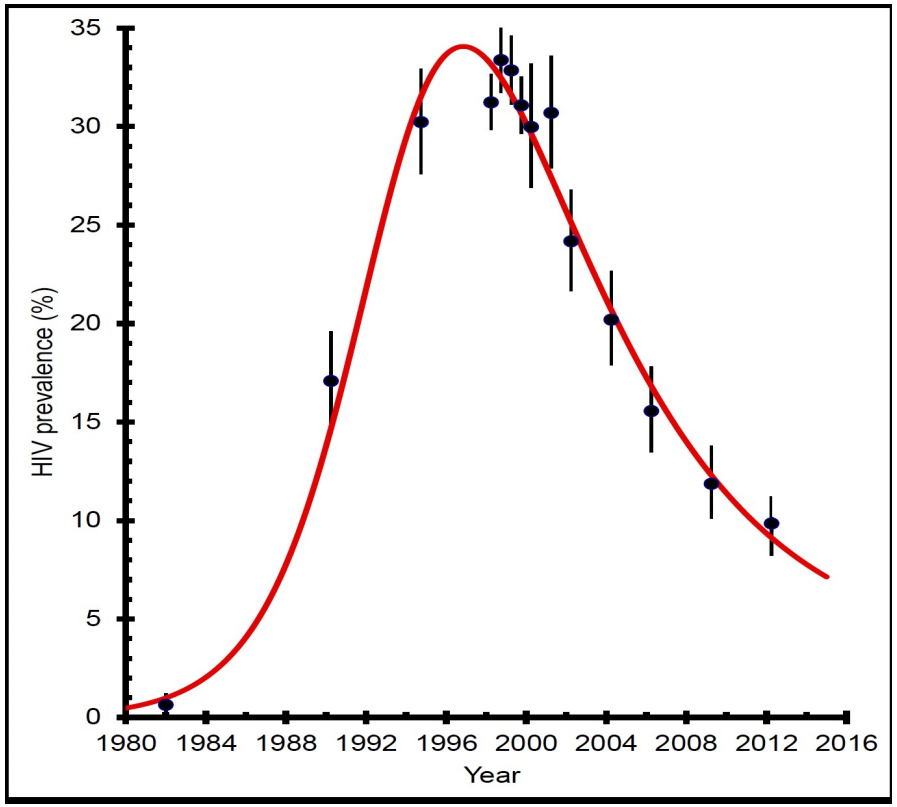
# HIV in Harare

- 1890-1980: modern-day Zimbabwe under British colonial rule as ‘Rhodesia’
  - Named after British diamond magnate Cecil Rhodes who first directed it
  - Same person who founded De Beers Diamond Cosortium and Rhodes scholarship
- Separate governance of Northern Rhodesia (contemporary Zambia) and Southern Rhodesia (contemporary Zimbabwe) and Nyasaland (contemporary Malawi). Forced together in 1953 despite heavy African opposition.
- Secession and eventual independence of Northern Rhodesia and Nyasaland
- 1970 white-colonialist government declared itself the independent nation of Rhodesia; violent civil war ensued until modern-day Zimbabwe was achieved independence in 1980
  - This was around the same time that the western world became aware of HIV

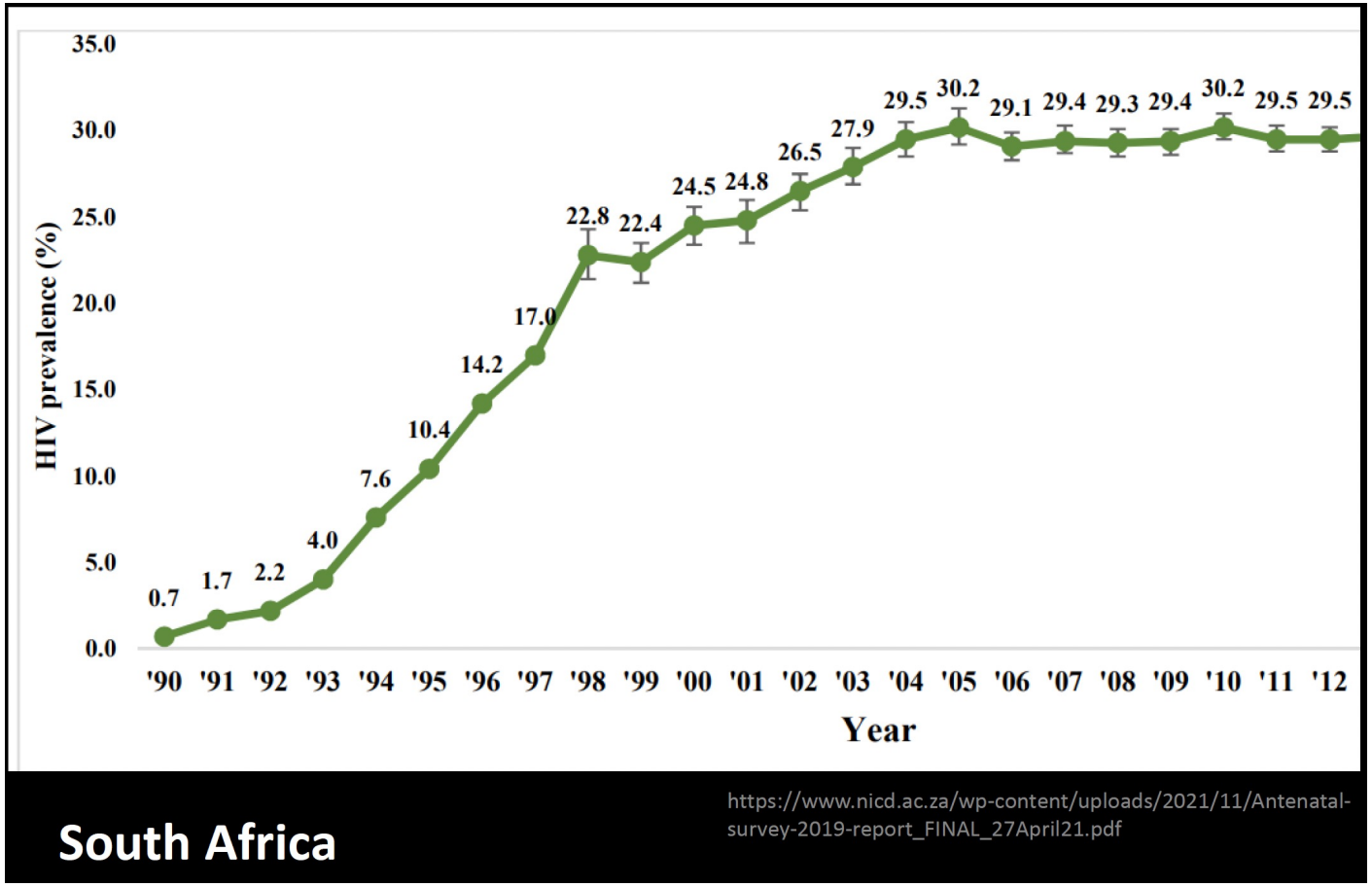
# Mortality in Harare



# HIV in Harare



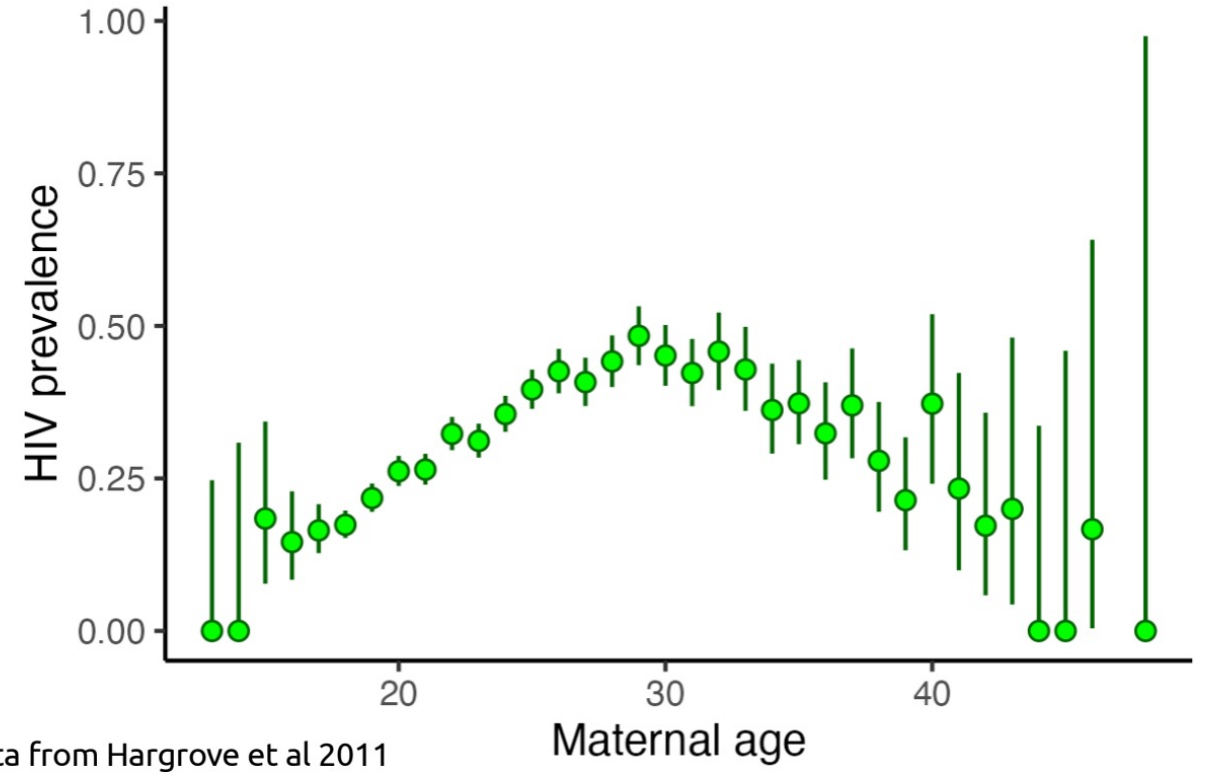

# HIV in South Africa



# HIV in Harare

the ZVITAMBO study – carried out between 1997 and 2000

## ZVITAMBO: Age vs prevalence

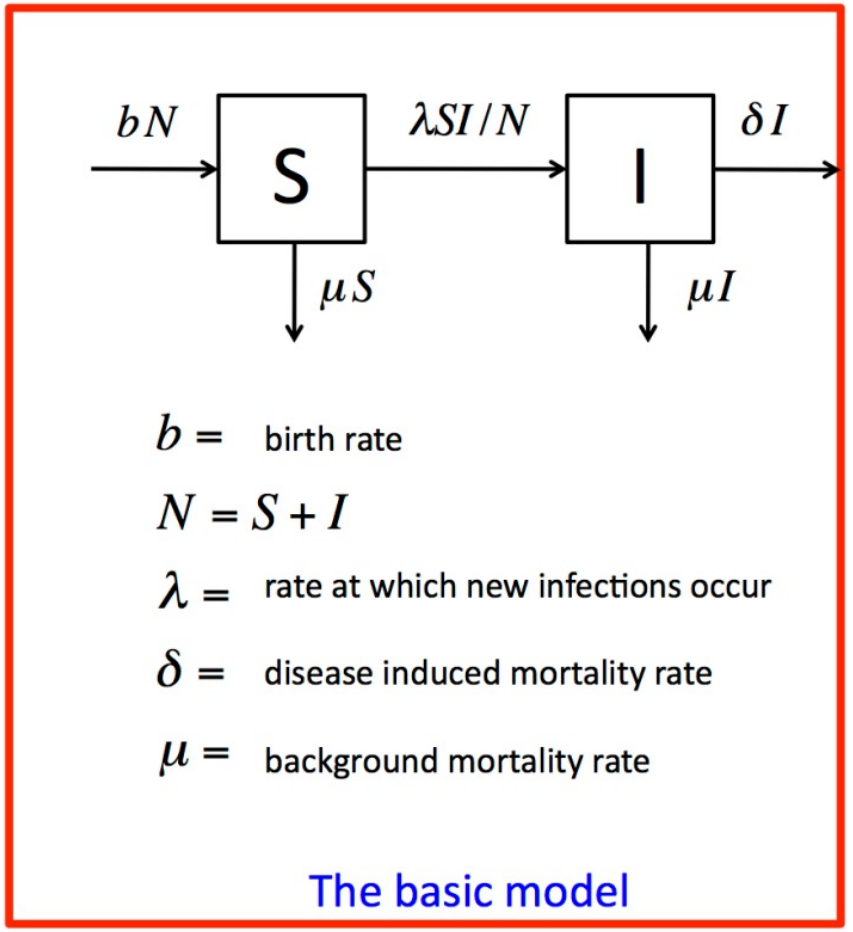



Data from Hargrove et al 2011

# Hargrove et al. 2011 model HIV in Harare, Zimbabwe

- Data from pregnant women being tested in ANC, 1980s-2000
- Model fit to prevalence (proportion infected), incidence (rate of new infections), and mortality data

Model 1



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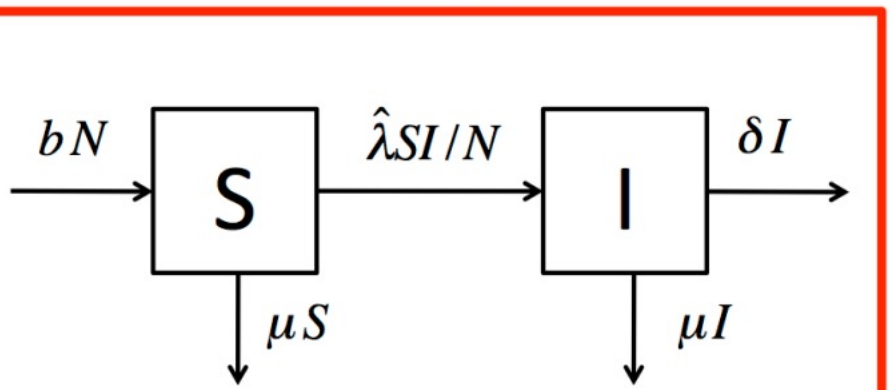
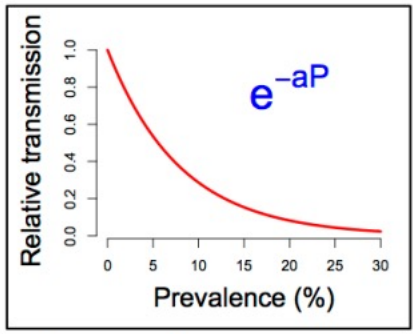
Model 2




$b =$ birth rate

$N = S + I$

$\hat{\lambda} = \lambda e^{-aP}$




$\delta =$ disease induced mortality rate

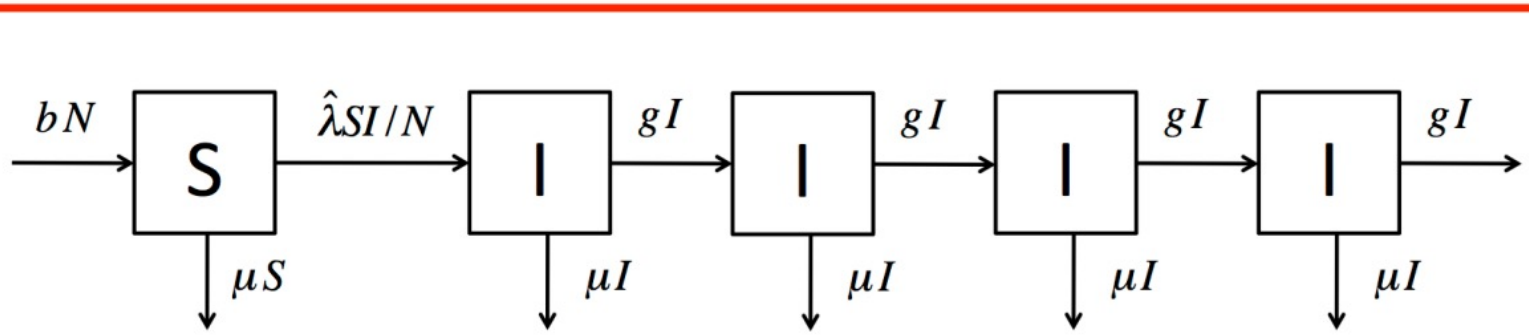
$\mu =$ background mortality rate

Heterogeneity in sexual behaviour

# Hargrove et al. 2011 model HIV in Harare, Zimbabwe

- Data from pregnant women being tested in ANC, 1980s-2000
- Model fit to prevalence (proportion infected), incidence (rate of new infections), and mortality data

Model 3



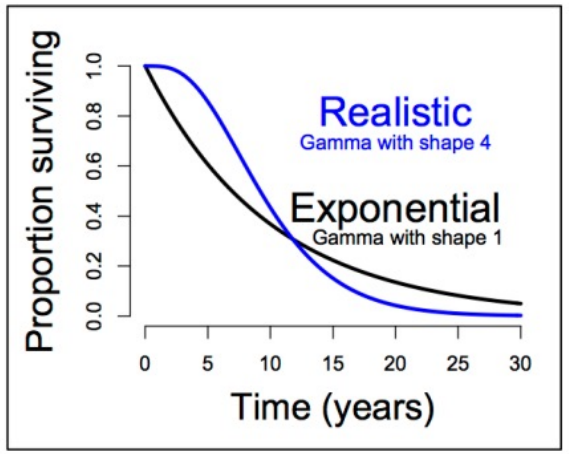

$b =$ birth rate

$N = S + I$

$\hat{\lambda} = \lambda e^{-aP}$

$\delta = g/4$

$\mu =$ background mortality rate




Realistic survival times

# Hargrove et al. 2011 model HIV in Harare, Zimbabwe

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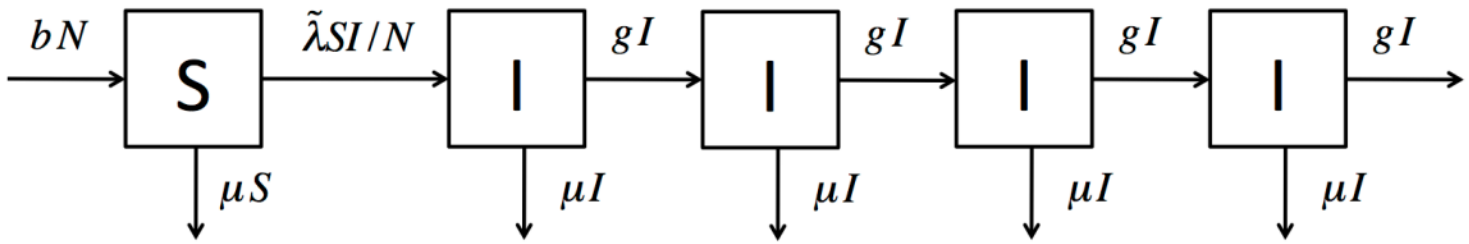
- Model fit to prevalence (proportion infected), incidence (rate of new infections), and mortality data

Model 4




$b =$ birth rate

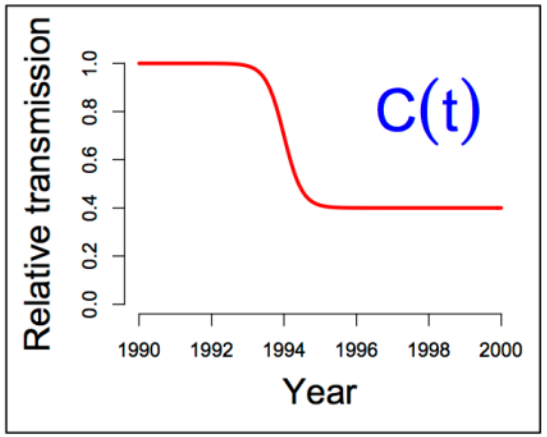
$N = S + I$

$\tilde{\lambda} = \hat{\lambda} C(t)$

$\delta = g/4$

$\mu =$ background mortality rate

Including control



# Hargrove et al. 2011 model HIV in Harare, Zimbabwe

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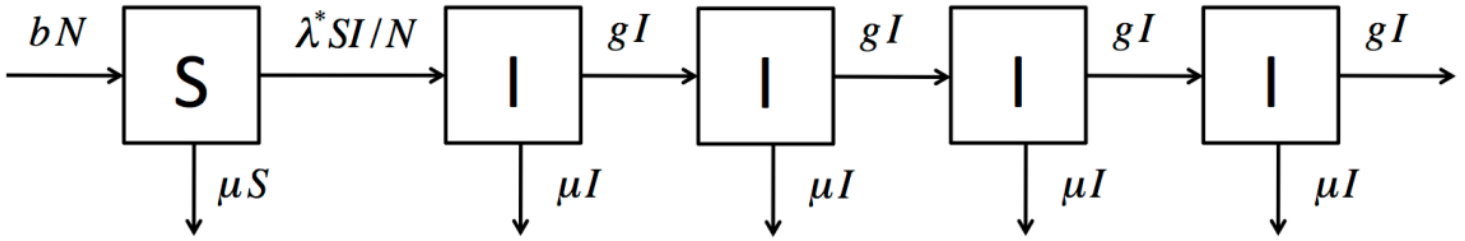
Model 5



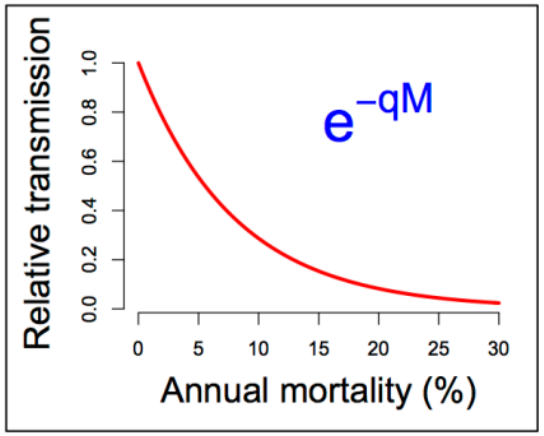

$b =$ birth rate

$N = S + I$

$\lambda^* = \hat{\lambda} e^{-qM}$

$\delta = g/4$

$\mu =$ background mortality rate




Mortality leads to behaviour change