The outcome of infectious disease interventions under age-biased mixing

Joel C. Miller\textsuperscript{1} and Adam Akullian\textsuperscript{2}
\textsuperscript{1}La Trobe University \quad \textsuperscript{2}Institute for Disease Modeling

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Background

- The **prevalence** (proportion infected) of HIV infection is very high in many parts of sub-Saharan Africa.

- The **incidence** (rate of infection per susceptible, often called “force of infection”) is highest in young age groups. [“incidence” is defined in different ways in different subfields of infectious disease epidemiology].

- Mixing is primarily with partners of similar age (though an important proportion of partnerships are young women with older men).

- Two interventions have proven effective to reduce new infections:
  - Voluntary medical male circumcision (primarily prevents acquisition)
  - Anti-retroviral Therapy “treatment as prevention” (prevents transmission)
Shifts in HIV incidence

There is evidence that the age with the highest HIV incidence (infection rate per susceptible person) is shifting older.
Plausible causes

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Plausible causes

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- Changes in partnership patterns
- Interventions preferentially adopted by younger population
- Maybe it’s just a natural consequence of age-biased mixing + effective interventions
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Why do we care?

Policy impacts

- How can we replicate this in other places?
- Where will resources be needed in 10 years?
- How should those resources be distributed?
We know that

- There is age-biased mixing
- Male circumcision and anti-retroviral therapy are effective at reducing transmission.

Is the existence of age-biased mixing + effective transmission reduction enough to plausibly explain the pattern?
Explaining The Proposed Mechanism:

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- Shortly after entering the population, that cohort will begin receiving infections from outside.
- Once established, most transmissions are within the cohort.
- We should see a typical epidemic curve within the cohort.
Single Cohort Perspective

So from the perspective of individuals in the cohort:

▶ We had an epidemic with sporadic introductions from outside.
▶ With intervention, we now have an epidemic with lower transmission rate.
▶ It takes longer for the epidemic to peak in the cohort.

To the outside observer, this looks like a shift in incidence to older groups.
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![Graph of single cohort incidence (over-simplified)](chart.png)
Modeling to test the hypothesis

We build a mathematical model with age-biased mixing. We can write down governing equations from the perspective of a given cohort or a given age. [Lagrangian vs Eulerian].

- SIR model (e.g., accounting for treatment).
- Mixing kernel \( w(\xi) \), assuming that mixing between ages depends only on age gap \( \xi \): \( w(-\xi) = w(\xi) \), \( \int_{-\infty}^{\infty} w(\xi) \, d\xi = 1 \).
Cohort-based Equations

\[
\frac{\partial}{\partial t} S(\alpha, t) = -\beta S(\alpha, t) \int_{-\infty}^{\infty} I(\alpha + \xi, t) w(\xi) \, d\xi
\]

\[
\frac{\partial}{\partial t} I(\alpha, t) = \beta S(\alpha, t) \int_{-\infty}^{\infty} I(\alpha + \xi, t) w(\xi) \, d\xi - \gamma I(\alpha, t)
\]

\[
\frac{\partial}{\partial t} R(\alpha, t) = \gamma I(\alpha, t)
\]

To shift to age-based equations, replace \( \frac{\partial}{\partial t} \) with \( \frac{\partial}{\partial t} + \frac{\partial}{\partial \text{age}} \).
Sample Solutions

As time progresses, the proportion infected as a function of age reaches an equilibrium.

Each curve gives the infected proportion as a function of age at a given time.
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Impact of reduction in $\beta$

Reducing $\beta$ causes the peak incidence to fall and shift right.
Long-term behavior

If we start with infection in one group, it spreads into younger and older cohorts until it reaches one of the boundaries.

It may get pinned to the boundary in the youngest age group. Or…
Disease eradication for $R_0 > 1$

Regardless of $R_0$, we can get elimination if the spread to younger cohorts is slower than the aging of the population.
Infinite ages

- We consider the cohort-focused version on the interval $-\infty < \alpha < \infty$ (so no cutoffs for young/old individuals).
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Equations for the wave front

We look for a traveling wave solution:

\[ I(\alpha + \xi, t) = I(\alpha + \xi - ct). \]
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Then \( \frac{\partial I}{\partial t} = \beta S \int_{-\infty}^{\infty} I(\alpha + \xi - ct)w(\xi)\,d\xi - \gamma I \) becomes

\[-Akce^{k(\alpha-ct)} = A\beta e^{k(\alpha-ct)} \int_{-\infty}^{\infty} e^{-k\xi}w(\xi)\,d\xi - \gamma Ae^{k(\alpha-ct)}\]
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- Divide out the \( Ae^{k(\alpha-ct)} \):

  \[-kc = -\gamma + \beta \int_{-\infty}^{\infty} e^{-k\xi}w(\xi)\,d\xi\]
Rearranging gives

\[
\frac{c}{\gamma} = -\frac{R_0}{k} \mathcal{L}[w(\xi)](k) - \frac{1}{k}
\]

where

- \( \mathcal{L}[w(\xi)](k) = \int_{-\infty}^{\infty} e^{k\xi} w(\xi) d\xi. \)
- \( R_0 = \beta/\gamma. \)

Note the implicit assumption that \( w(\xi) \) decays exponentially fast.
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Recall \( I = Ae^{k(\alpha-ct)} \)

- \( k \) tells us the spatial shape of the leading edge.
- \( c \) tells us the wave speed.
Finding $c$

The equation:

$$\frac{c}{\gamma} = -\frac{R_0}{k} \mathcal{L}[w(\xi)](k) - \frac{1}{k}$$

has multiple solutions pairs $c$ and $k$. Take $c(k)$ as a function of $k$.
Finding $c$

The equation:

$$\frac{c}{\gamma} = -\frac{R_0}{k} L[w(\xi)](k) - \frac{1}{k}$$

has multiple solutions pairs $c$ and $k$. Take $c(k)$ as a function of $k$.

Remarkably, the observed pair is the pair with the **minimal wavespeed** $c$.

$$\frac{dc}{dk} = 0 \Rightarrow \frac{1}{R_0} = kL[\xi w(\xi)](k) - L[w(\xi)](k)$$

So given the mixing kernel $w$, we can find $k$ and then $c$ as a function of $R_0$. 
Discussion

- In some populations the peak risk of infection is shifting to older age groups.
- Our model suggests that this could be a natural consequence of the impact of effective interventions.
- We should anticipate that infection in other places will also shift to “older” age groups.