COVERAGE STRATEGIES:
Insights from Population Simulation Models

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COVERAGE AND IMPACT: NON-LINEAR ASSOCIATIONS

- The interplay of prioritization, coverage and impact
  - Earlier ART initiation as an example

- Coverage in the context of combination prevention
  - Multi-dimensional coverage distributions

- Coverage and the sexual network structure
  - Behavioral change as an example
Reducing the period of unsuppressed viral load may reduce HIV incidence

ART initiation immediately after HIV diagnosis appears unfeasible:
- Unfavorable short-term affordability
- Extra coverage and impact
- Fear for poor adherence in asymptomatic patients
- ARV side effects

Could we, should we prioritize earlier ART initiation?
- How much earlier – what shift in CD4 count threshold?
- Which populations could/should be prioritized, and how?
The impact, cost and efficiency of earlier ART initiation: A modeling study

- Deterministic, compartmental model

- Structured by
  - age
  - gender
  - HIV stage (CD4 count and infectiousness)
  - ART status
THE IMPACT, COST AND EFFICIENCY OF EARLIER ART INITIATION: A MODELLING STUDY

- 20-30 year olds most sexually active

<table>
<thead>
<tr>
<th>Average number of partners per year</th>
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</thead>
<tbody>
<tr>
<td>15-20 years old</td>
</tr>
<tr>
<td>20-25 years old</td>
</tr>
<tr>
<td>25-30 years old</td>
</tr>
<tr>
<td>30-35 years old</td>
</tr>
<tr>
<td>35-40 years old</td>
</tr>
<tr>
<td>40-45 years old</td>
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<tr>
<td>45-50 years old</td>
</tr>
</tbody>
</table>

- Relative HIV transmission probability under ART: 0.1

- Average lag time between eligibility and initiation of ART: 1 year

- Average survival after HIV, off ART: 9.5-11.6 years (age dep)

- Average survival after ART initiation: 9.3-20 years (CD4 dep)

- Relative TB Hazard rate under ART: 0.6-0.2 (CD4 dep)
THE IMPACT, COST AND EFFICIENCY OF EARLIER ART INITIATION: A MODELLING STUDY

- Comparison scenarios:
  - Current ART initiation practice (scenario 1)
  - ART eligibility regardless of age and CD4 count (scenario 5)
  - Age-prioritization of ART eligibility from 350 CD4 cells/μL, 500 CD4 cells/μL, or regardless of CD4 count (scenarios 2,3,4)

- Time horizon: 10 years (2011-2021)

- Impact indicators:
  - Averted HIV infections
  - Averted TB cases
  - Averted HIV-related deaths
  - Years of Life Saved

- Cost indicator:
  - Person-years of ART

- Efficiency indicators (Reference = Current ART initiation practice):
  - Incremental person-years of ART per incremental averted HIV infection, averted TB case, averted HIV-related death and year of life saved
THE IMPACT, COST AND EFFICIENCY OF EARLIER ART INITIATION: A MODELLING STUDY

- Impact

<table>
<thead>
<tr>
<th>Scenario</th>
<th>HIV incidence</th>
<th>TB incidence</th>
<th>HIV mortality</th>
<th>Years of Life</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HIV infections averted (millions)</td>
<td>TB cases averted (millions)</td>
<td>HIV-related deaths averted (millions)</td>
<td>Year of Life Saved (millions)</td>
</tr>
<tr>
<td>Scenario 1</td>
<td>6.60 (7.33) *</td>
<td>4.63 (4.75) *</td>
<td>6.04 (6.25) *</td>
<td>NA</td>
</tr>
<tr>
<td>Scenario 2</td>
<td>0.58 (0.57)</td>
<td>0.19 (0.20)</td>
<td>0.28 (0.29)</td>
<td>0.87 (0.90)</td>
</tr>
<tr>
<td>Scenario 3</td>
<td>1.04 (1.00)</td>
<td>0.34 (0.35)</td>
<td>0.44 (0.45)</td>
<td>1.32 (1.37)</td>
</tr>
<tr>
<td>Scenario 4</td>
<td>1.60 (1.38)</td>
<td>0.47 (0.49)</td>
<td>0.51 (0.51)</td>
<td>1.49 (1.52)</td>
</tr>
<tr>
<td>Scenario 5</td>
<td>2.36 (2.06)</td>
<td>0.88 (0.92)</td>
<td>1.05 (1.08)</td>
<td>3.42 (3.51)</td>
</tr>
</tbody>
</table>
Multiple HIV prevention methods have proven to reduce the risk of transmission and/or acquisition of HIV.

<table>
<thead>
<tr>
<th>Prevention method</th>
<th>Direction of protection</th>
<th>Relative risk</th>
<th>Potential users</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condoms</td>
<td>T+A</td>
<td>0.05</td>
<td>M+W</td>
</tr>
<tr>
<td>Medical Male Circumcision</td>
<td>A</td>
<td>0.41</td>
<td>M</td>
</tr>
<tr>
<td>Microbicides</td>
<td>A</td>
<td>0.46</td>
<td>W</td>
</tr>
<tr>
<td>Pre-exposure Prophylaxis</td>
<td>A</td>
<td>0.27</td>
<td>HIV- M+W</td>
</tr>
<tr>
<td>Antiretroviral treatment</td>
<td>T</td>
<td>0.04</td>
<td>HIV+ M+W</td>
</tr>
</tbody>
</table>

Not all methods are applicable to everybody.

Within potential users, coverage is constrained by acceptability, adherence and affordability.
If we cannot protect everybody all the time, what would be the optimal mix of interventions delivered to whom?

- **Q:** Protect more sex acts per person or protect people?
  - **A:** More acts protected: reduce intra-subject heterogeneity in risk of acquisition and transmission

- **Simple example:** Condom distribution

- **Consequences:** Consistency/adherence is more important than the number of users
  - Promote consistent condom use and high levels of adherence to ART (and microbicides/PrEP)
  - Male circumcision has high consistency by design
If we cannot protect everybody all the time, what would be the optimal mix of interventions delivered to whom?

- **Q**: More transmission reduction per sex act or more people with transmission reduction?
- **A**: More people with transmission reduction: reduce inter-subject heterogeneity in risk of acquisition and transmission

- **Simple example**: Distribute PrEP and MC

- **Consequences**: Avoid over- and under-delivery of interventions
  → Allocate interventions according to baseline risk of acquisition and transmission
If we cannot protect everybody all the time, what would be the optimal mix of interventions delivered to whom?

- **Special case**: Split coverage of intervention over M+W or prioritize only M or W?

- **Simple example**: age-prioritization of earlier ART initiation

\[ \sqrt{(C_m RT_m + (1 - C_m))(C_w RT_w + (1 - C_w))} \]

\[ \sqrt{0.52 \times 0.52} = 0.52 \]

\[ \sqrt{0.04 \times 1} = 0.2 \]

- **Consequences**: Impact/Equity trade-off
COVERAGE IN THE CONTEXT OF COMBINATION PREVENTION

- A semi-static impact optimization method
  1. Estimate maximal feasible coverage for each intervention
  2. Define time horizon and outcome or combination of outcomes to be maximized
  3. Estimate cost and impact for range of coverage up to maximal feasible level
  4. Estimate baseline intra- and inter-subject heterogeneity of acquisition and transmission risk
  5. Maximize coverage of most cost-effective intervention first, in a way that minimizes intra- and inter-subject heterogeneity of acquisition and transmission risk
  6. Add interventions until budget cap is reached
  7. Reevaluate algorithm to account for potential changes in cost, risk distribution, feasible coverage, budget and impact estimate
Interventions that effectively discourage the formation of concurrent relationships impact on HIV transmission dynamics through changes in the sexual network structure.

Does the impact depend on the baseline structure of the sexual network?
COVERAGE AND THE SEXUAL NETWORK STRUCTURE

- Interventions that effectively discourage the formation of concurrent relationships impact on HIV transmission dynamics through changes in the sexual network structure.

- Does the impact of concurrency reduction depend on the baseline structure of the sexual network?
  - Individual-based modelling work ongoing using
  - Assortative, dis assortative or random wrt overlapping relationship?
  - Correlate facilitating behaviors? E.g. age-disparity, sex frequency, alcohol use and unprotected sex.
KEY MESSAGES

- Population impact/efficiency trade-off of targeting

- To learn new lessons in optimal coverage distribution we need gradually more complex models, and lots more empirical evidence

- The entire sexual network structure is indeed unknown, but modelling may provide range of plausible impact measures, and can help with post-hoc interpreting observed exposure-behavior-impact associations
THANKS

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