TUPE
0244

Projecting Sexual and Injecting Risks into Future HIV Outcomes with Agent-Based Modeling

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1. Abstract

Background: Risky behavior does not always result in HIV acquisition. It is important for prevention research to understand who is at the highest HIV risk in real-world settings. Estimating individual and group chances of HIV infection in the observable future not only requires the knowledge of risky sexual and injecting practices but also information about sexual and injecting networks. Because direct experiments with HIV transmission are not ethical and feasible, modeling can uncover how the combination of social, behavioral, and biological factors can lead to increased HIV risk.

Methods: A total of 881 drug users and men who have sex with men (MSM) were recruited using respondent-driven sampling (RDS) in central North Carolina between 2005 and 2008. An agent-based model (ABM) was developed to represent behavior and sexual/injecting networks of the population at risk. This behavior was projected into the future (1, 3, and 5 years) to estimate the chances of HIV acquisition and relate them to behavioral and network factors.

Results: Data analysis ignoring the dynamic nature of behavior and network structure produced strongly biased results underestimating the role of sexual and injecting risks, use of stimulants, and use of high dead-space syringes in acquiring HIV. Analysis of simulation modeling results that include networks and dynamic behavior produced results comparable with those observed in longitudinal studies.

Conclusions: The ABM approach, accounting for dynamic behavior and social structure from a cross-sectional representative study, allows one to project the behavior into the future so that the risks of acquiring HIV (e.g., survival HIV free) could be studied in a dynamical/temporal sense. ABM allows one to obtain longitudinal-type results from a cross-sectional study for the price of added uncertainty.

Key Words

1. HIV transmission
2. Sexual risk
3. Injecting risk
4. Agent-based model
5. Survival analysis

2. Background

Main Question

- Longitudinal studies are expensive, long, and cumbersome, leading to smaller and less-representative samples.
- Can cheaper, shorter, and larger cross-sectional studies be used instead of longitudinal studies to estimate risks associated with dynamically changing behaviors?

Table 1. Longitudinal vs. Cross-Sectional Studies

	Longitudinal	Cross Sectional
Representative	More difficult	Less difficult
Time frame to collect	Longer	Shorter
Establishing causality	Easier	Difficult or impossible
Temporal bias	Less	More
Parameter estimates	Dynamic (can change in time)	Static
Cost	More	Less

Compromise

Combine the advantages of longitudinal analysis with the "simplicity" of cross-sectional data by using modeling.

- Gains: dynamic parameter estimates, less expensive
- Price: introduction of uncertainty

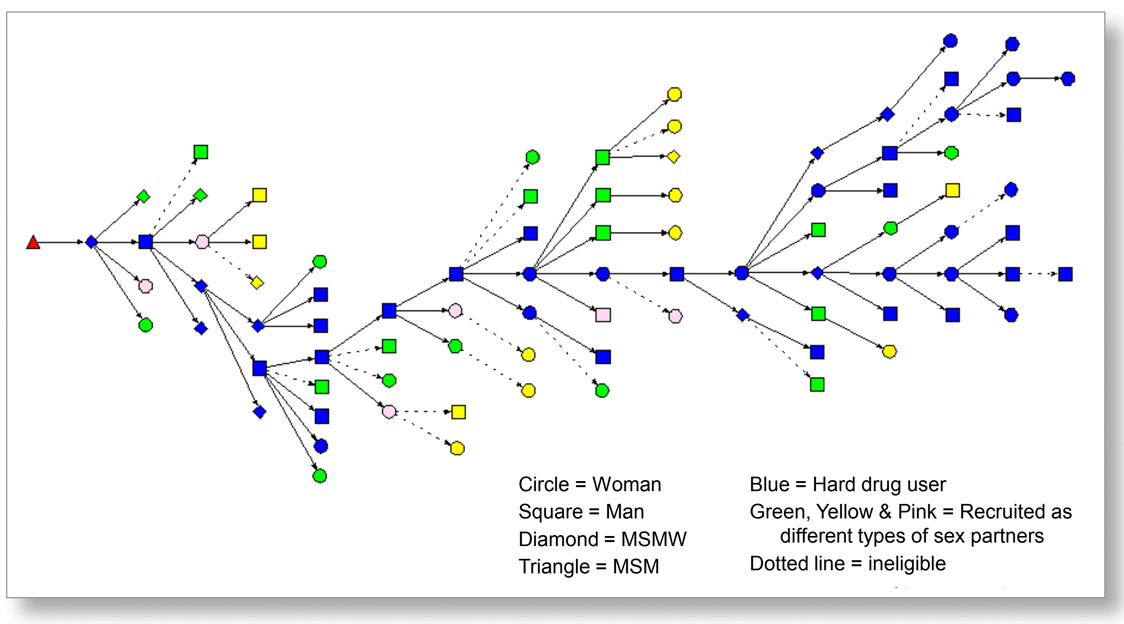
Study of HIV Spread on Sexual and Drug-Using Networks

- Sexual Acquisition and Transmission of HIV Cooperative Agreement Program (SATH-CAP), funded by NIDA, William Zule, PI.
- How does HIV spread within the at-risk population?
- Who are the main spreaders?
- Who are the most likely persons to get HIV?
- How do risk factors, such as the number of sex partners and rate of partner change, affect the chances of contracting HIV in 1, 5, 10 years?

Sample

- About 2,000 members of at-risk group:
  - Men who have sex with men (MSM)
  - Men who have sex with men and women (MSMW)
  - Drug users (DU)
  - Sex partners (SP)
  - Sex partners of sex partners (SPSP)
- Respondent-driven sample (RDS) for data collection

Figure 1. RDS Sample



3. Agent-Based Model of HIV Spread on Sexual and Drug-Using Networks

Components of the Model

- Viral load and HIV progression
- Sexual behavior
- Drug-using behavior
- Structure of sexual and equipment-sharing networks
- Types of syringe used
- Sexual and drug use mixing matrices (who has sex with whom)
- Network turnover

Figure 2. Individual State Diagram

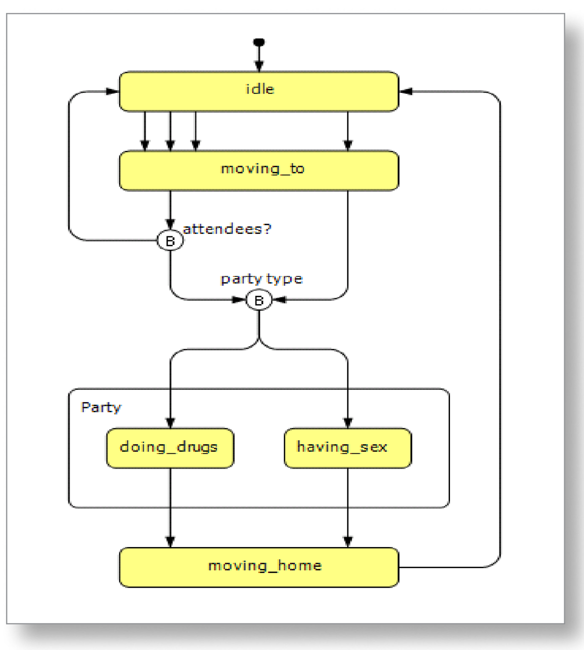
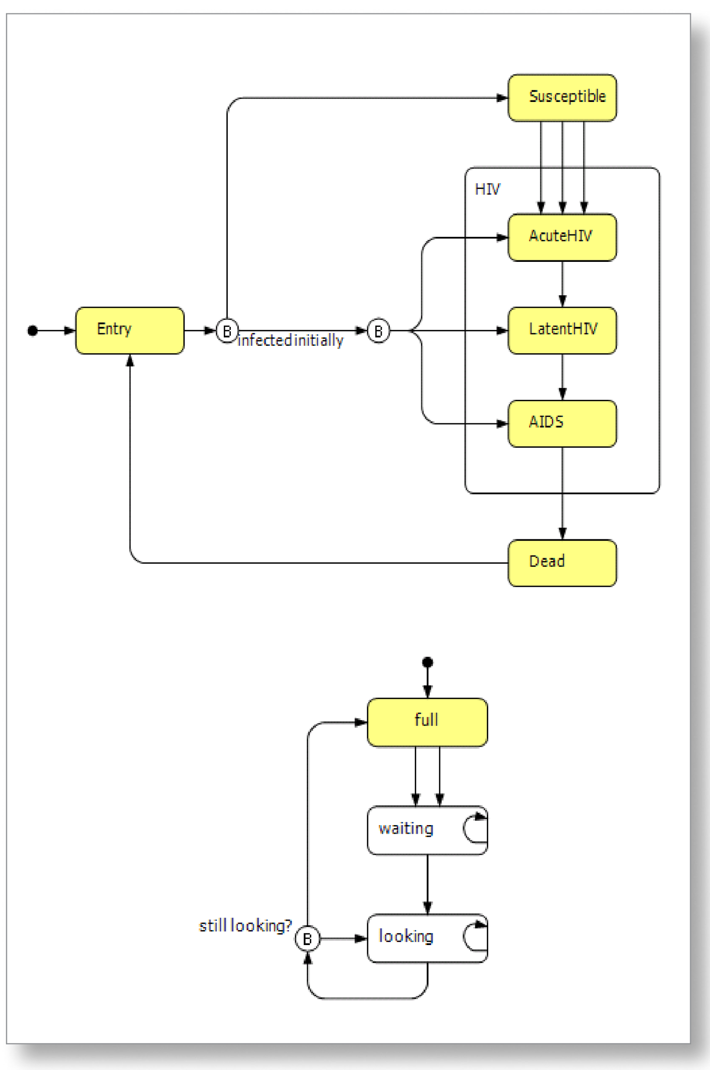


Figure 3. Model of HIV Spread on Sexual and Drug-Using Networks



Populations and Network

- Increase the sampled group by factor of 10 based on independent estimates
- Estimate a mixing matrix (who has sex with whom and who injects with whom)
- Connect agents based on the link's distribution to ensure approximate balance of the egocentric link reports
- Add function and evolution to networks

Figure 4. Sexual and Drug-Using Network

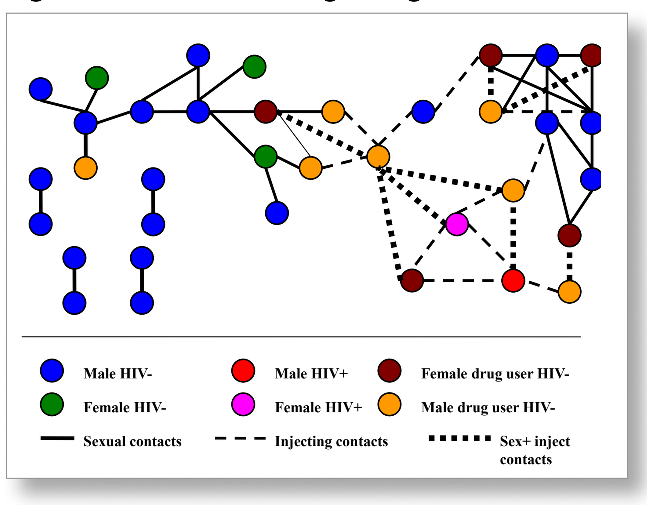


Figure 5. HIV Spread on Networks (1 year later)

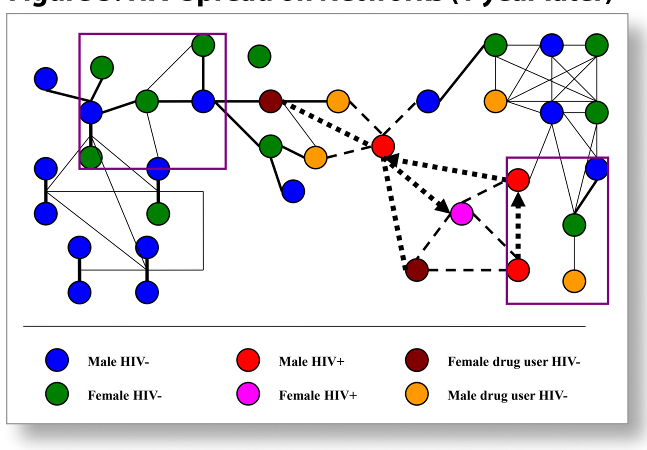
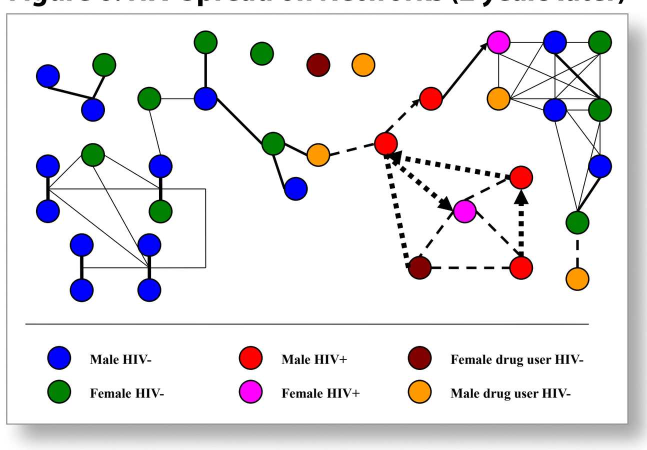


Figure 6. HIV Spread on Networks (2 years later)



3. Agent-Based Model of HIV Spread on Sexual and Drug-Using Networks *(continued)*

Model Parameters Estimated from the Survey Data

- Demographics
- Sexual behaviors
  - Frequency
  - Number of partners
  - Condom use
- Drug-use behaviors
  - Frequency
  - Number of partners
  - Use of dead-space syringes
- Frequency of sharing needles/equipment
- Mixing matrix

Model Parameters Taken from the Literature

- Partner change dynamics
- HIV transmission probabilities
  - Vary by sexual behaviors
    - Sex of partner
    - Type of sex (oral, anal, vaginal)
    - Condom use
  - Vary by drug-use behaviors
    - Using safe syringe
    - Sharing syringes

Parameters Based on Educated Guess

- Network structure and contacts
- Dynamics of links
  - Concurrency
  - Serial monogamy
- Behavior details such as group sex (to be added in future)

4. Results

Figure 7. Probability of Staying HIV Negative is Related to the Number of Sexual and Injecting Partners

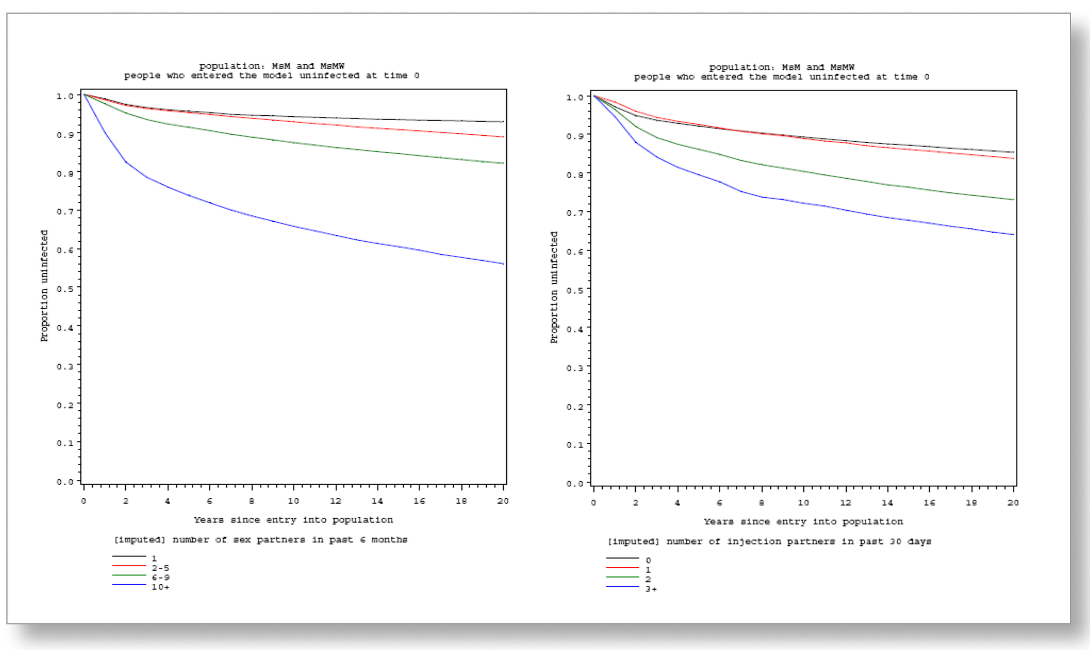
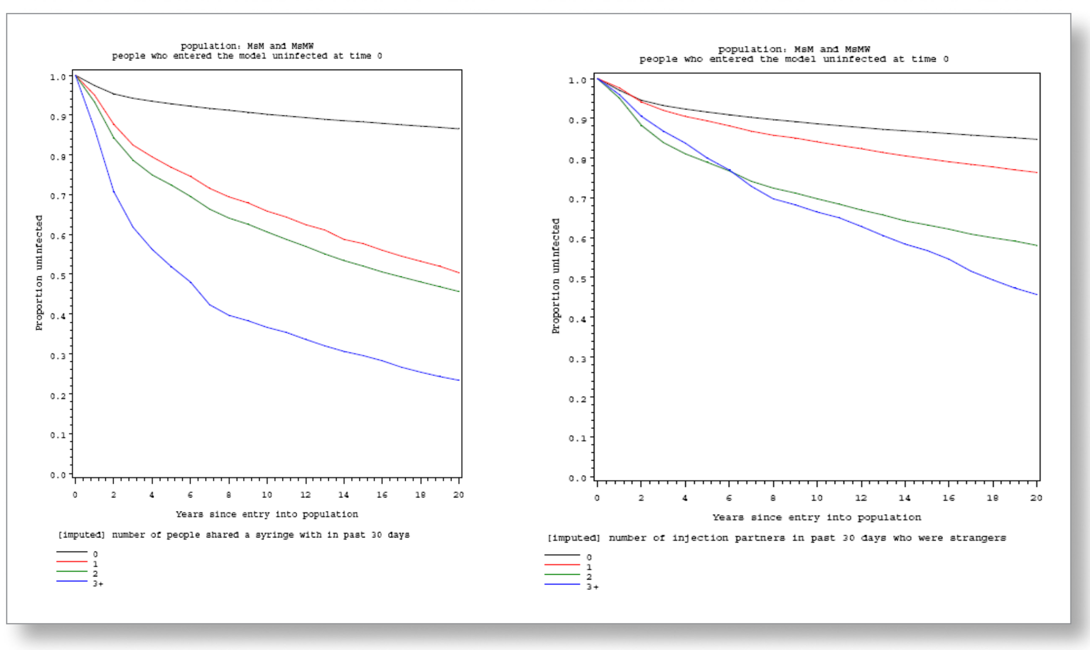


Figure 8. Probability of Staying HIV Negative is Related to the Number of Times Sharing Equipment with Partners and Strangers



Dynamic Risks vs. Static Risks

Table 2. Use of Stimulants in Past 6 Months
MSM and MSMW who entered the model at time 0.
Naïve case-control analysis.

Level	Rel_risk of HIV	Odds	Odds Ratio
No	ref	0.53	ref
Yes	0.41	0.16	**0.31**

Table 3. Use of Stimulants in Past 6 Months
MSM and MSMW who were not infected at the baseline.
Assessed after 5 years. Analysis of projected trajectories.

Level	Rel_risk of HIV	Odds	Odds Ratio
No	ref	0.16	ref
Yes	1.13	0.19	**1.15**

Table 4. Number of Sex Partners in Past 6 Months
MSM and MSMW who entered the model at time 0.
Naïve case-control analysis.

Level	Rel_risk of HIV	Odds	Odds Ratio
1	ref	0.21	ref
2–5	1.65	0.40	1.91
6–9	0.83	0.17	0.81
10+	0.80	0.16	**0.76**

Table 5. Number of Sex Partners in Past 6 Months
MSM and MSMW who were not infected at the baseline.
Assessed after 5 years. Analysis of projected trajectories.

Level	Rel_risk of HIV	Odds	Odds Ratio
1	ref	0.06	ref
2–5	1.02	0.06	1.03
6–9	1.88	0.12	1.98
10+	5.29	0.44	**7.17**

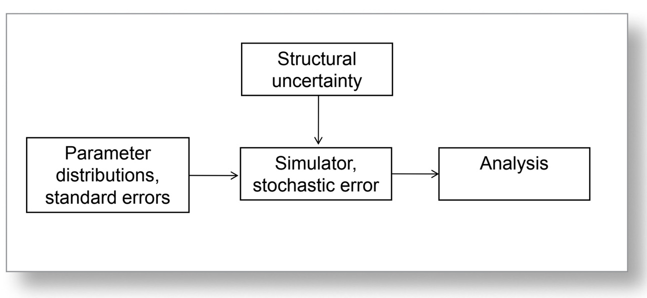
Why Discrepancy?

- Naïve case-control approach is wrong because of the implied causality.
- Many HIV-positive people contracted the disease a while ago when they might have been engaging in risky behavior.
- HIV treatment programs emphasize prevention and reduce risky behavior.
- Projected behavioral trajectories provide more realistic assessment of risks associated with specific behavior.
- In ABM, causality is modeled directly through mechanistic pathways.

Uncertainty

- Additional sources of error:
  - Stochastic assignment
  - Stochastic behavior
  - Uncertainty in parameter values
- Analysis of uncertainty produces 95% bounds for the predictive trajectories; not to be confused with 95% confidence interval.
- Sensitivity analysis of regression models of the outcomes.

Figure 9. Sources of Uncertainty



Components of Variance for Simulation Results

Pseudo-longitudinal study of n subjects. Odds ratio estimate would have the form:

$$\hat{\theta} = E_{\text{over j}}(\hat{\theta}_j \mid Y_{ij}, X_{ij}, U, n)$$

The variance of the estimate

$$Var(\hat{\theta}) = Var_{\text{over } j}(f_j \mid Y_{ij}, X_{ij}, U, n) + E_{\text{over } j}(g_j \mid Y_{ij}, X_{ij}, U, n)$$

The variance could be represented as a sum; each of the components could be estimated separately.

Conclusions

- Advantages of longitudinal analysis conducted on cross-sectional data
- Loss of inference is the price of the advantage
- Statistical challenges to address inferential issues
- Evaluation of specific behavior vs. specific persons/populations
- True validation could be only done by a prospective study

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