Geographically-Enhanced Mathematical Models of HIV Dynamics

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Abstract

Mathematical modeling is a relatively new but fast developing area of HIV studies providing researchers with an additional dynamical dimension in epidemiological work that allows scientists to simulate the consequences of various intervention and prevention scenarios. We illustrate these concepts by presenting a model that describes Injecting Drug Users (IDU) networks, injecting behavior and HIV/HCV spread within the networks. This individual-based (also called agent-based) model is used to investigate the impact of the introduction of Integral-cannula syringes (ICS) instead of commonly used Detachable Needle syringes (DNS). Laboratory experiments have shown that ICS retain approximately 1000 times less residual blood (<.001 ml vs. 1ml) following injection and rinsing than DNS thereby decreasing risk of HIV/NCV transmission by nearly 100 times after 2 rinses. The locations of the respondents and the critical mixing sites are assigned graphic coordinates and visually mapped in order to examine respondents' movements and interactions in space over time. Subjects' confidentiality is assured by choosing the appropriate geographic scale and by masking addresses and personal information. We use a Geographic Information System (GIS) and data collected from our HCV study in conjunction with published HIV risk parameters to develop a geographically-enhanced agent-based mathematical model. AnyLogic software is used to construct the model. Through dynamical simulations we have shown that it is necessary to have approximately 80% of users to switch to the Integral-cannula syringes in order to reverse the spread of HIV and more than 93% of users must switch to these syringes to reverse the spread of HCV. These results are quite robust with respect to the network size and frequency of use. The impact of intervention and prevention policy is modeled through the changes in the risk of behavior. The aggregate behavior is calculated through the averaging of the corresponding individual behaviors.

Such mathematical models can serve as information depositories and allow us to identify critical information needs and data gaps in a complex drug using behavior. In addition, validated models that are based on robust estimates allow for the identification of the most sensitive parameters that influence the course of drug using behaviors, developing optimal and cost-effective prevention and intervention policies and practices.

Key words: HIV, Injecting drug users, Agent-based model, Risk behavior, Geographic Information System

RTI 1

Introduction

- **Most injecting drug users (IDUs) in the United States (U.S.) use 1-milliliter (ml) integral cannula insulin syringes that are designed to minimize dead space (Lurie and Reingold, 1993; Grund et al., 1996).**
- **Some IDUs use 1-ml syringes with detachable needles that are commonly referred to as 'dead space' syringes (Zule et al., 2002).**
- **Researchers studying HIV risk factors among IDUs have rarely reported data on the use of dead space syringes and their possible impact on HIV transmission.**
- **Type of syringe may be associated with higher or lower prevalence of HIV infection (Marmor and Hartsock, 1991, Zule et al., 2002).**

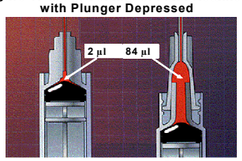
RTI 2

Syringe Description

- **With the plunger depressed, all syringes retain fluid in what has been termed 'dead space.'**
- **Dead space syringes, which usually have detachable needles retain fluid in the syringe cannula, the needle hub, and the needle itself.**
- **Integral cannula or minimal dead space syringes have a needle, which is usually permanently attached, that extends through the cannula to the base of the syringe barrel.**
- **Integral cannula syringes only retain fluid in the needle itself.**
- **The effects of these differences in design on retention of fluid are illustrated in Figure 1.**

RTI 3

Figure 1: Mean Volume of Fluid Retained with Plunger Depressed



RTI 4

Theoretical* and Experimental** Values of Volume of Blood Retained After Rinsing with 0.5 ml Water

Experiment: 0.4 ml saline (drug) solution, 0.1 ml registering with blood injection, 0.1 ml booting with blood 2 x 0.5 ml rinses with saline (water) solution

	1st rinse (theory)	2nd rinse (theory)	2nd rinse (exp.)
Integral cannula	0.008 µl	0.00003 µl	< 0.001 µl
Dead space	12.0 µl	1.7 µl	1.01 µl
Ratio	1,500	54,000	> 1,000

*Zule et al, 2002
**Zule et al, 1997

RTI 5

Blood, Virus, and Probabilities of HIV Infection

The volume of inoculum and quantity of virus in an exposure are important determinants of subsequent HIV infection. In prospective studies:

- **Two of the most important determinants of HIV seroconversion following accidental needle stick were the volume of blood and the quantity of virus in an exposure (CDC, 1995).**
- **HIV viral load in the infected partner was one of the most important determinants of sexual transmission of HIV in discordant couples (Gray et al, 2001).**

RTI 6

Relative Impacts of Syringe Type and Stage of HIV Infection on HIV Epidemics

- **The quantity of virus in an exposure to blood of any given viral load is proportionate to the volume of blood in the exposure.**
- **An exposure involving a dead space syringe would involve 1000 times more virus than an exposure involving an integral cannula syringe.**
- **HIV viral load is 100 times higher during the acute/primary stage than the latent stage.**
- **HIV viral load is 10 times higher during end stage/AIDS than the latent stage (Jacquez et al., 1994).**

Taken together, these postulates suggest that the effect of syringe type on the probability of transmission may be at least 10 times greater than the effect of stage of HIV infection (acute, latent, end stage/AIDS)

RTI 7

Estimated Probabilities of Infection per Exposure

- **Needle stick:**
  - 0.003 to 0.005 [involves transfer of approximately 1 µl of blood] (Gerberding et al., 1997; Hu et al., 1991).
- **Needle Sharing:**
  - between 0.005 and 0.01 (Chin 1992).
  - 0.0067 in New Haven, Connecticut (Kaplan and Heimer, 1992) .
  - 0.0080 among IDUs in Thailand (Hudgens et al., 2001).
- **NOTE:** Needle sharing estimates do not indicate type of syringe involved.
- We use probabilities of infection of .028 and .00008 for exposures involving dead space syringes and integrated cannula syringes respectively because most IDUs outside the U.S. use dead space syringes (Grund et al 1996).
- **Assumptions:**
  - **probability of exposure to approximately 1 µl of infected blood intravenously around .008.**
  - **probability of infection following exposure to less than .001 µl of infected blood at least 100 less than the probability of infection following exposure to 1 µl of infected blood from the same source at the same time.**

RTI 8

Simple Deterministic Model

$I_{n+1}=I_n + I_n*Q*C*(N-I_n)/N - I_n*M$

I_n – number infected at time n

Q – risk factor (Q_1=0.00008, Q_2=0.008)

C – times shared per month (5-40)

M– mortality rate (0.008)

N – network size (10-100)

α- proportion times used safe syringe

$I_{n+1}=I_n + I_n(Q_1 \alpha + Q_2 (1-\alpha))C(N-I_n)/N - I_nM$

Effective Growth Ratio (deterministic) $R_e=I_{n+1}/I_n$;

Effective Growth Ratio (stochastic) R_e=Mean(I_{n+1}/I_n)

R_e= 1+QC-M-I_nQC/N

Fixed points I_n={0, (QC-M)N/ QC }

RTI 9

Geographically-Enhanced Agent-Based Model

- Agents
- Networks
- States
- Rules
- Transitions

RTI 10

Model Details

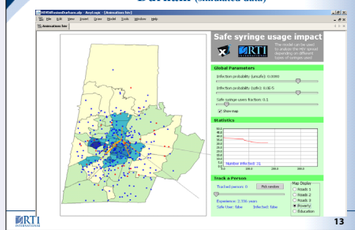
- **Each ID user has network "buddies". Total n=750**
- **Sharing occurs on a daily basis with a fraction (0.2) of users.**
- **Sharing occurs either at the location of the initiator or some other location.**
- **Syringes are used in the order starting from most experienced to least experienced.**
- **Initial infected fraction is 10%**
- **Initial percent of "safer" syringe use is 80%**
- **If a person at the sharing uses "safer" syringe then all of the participants use this type o syringe.**
- **If a syringe passes through an infected person, it becomes infected**
- **The network size is fixed**
- **The ones who die are replaced with the new uninfected**

RTI 11

Dynamics of HIV-Related Behavior in Durham (simulated data)

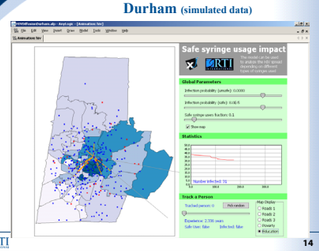
RTI 12

Dynamics of HIV-Related Behavior in Durham (simulated data)



RTI 13

Dynamics of HIV-Related Behavior in Durham (simulated data)



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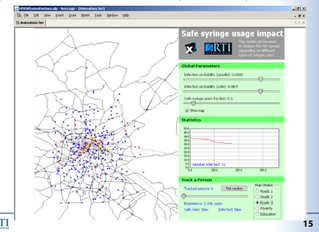
Dynamics of HIV-Related Behavior in Durham (simulated data)



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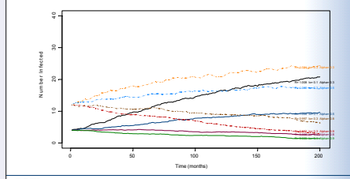
Agent-Based Model for HIV

Q – risk factor (Q1=0.00008, Q2=0.008). Threshold % of safe syringes is 0.86
Averaged over 20 trajectories



RTI 16

Agent-Based Model for HIV

Q – risk factor (Q1=0.00008, Q2=0.008). Threshold % of safe syringes is 0.84
Averaged over 20 trajectories

RTI 17

Results

- **Mathematical models of HIV shows that when high percent (85+%) of IDUs use integral cannula syringes, spread of HIV reverses.**
- **In order to reverse spread of HCV it is necessary that a higher percent (97+%) of IDUs use integral cannula syringes.**
- **Use of the actual geographical maps helps visualize prevalence and dynamics of the disease with respect to risk factors.**

RTI 18

Discussion

- **Results of both stochastic and deterministic models suggest that the course of an injection-related HIV epidemic among IDUs is highly dependent on the proportion of exposures involving dead space syringes.**
- **Dead-space syringes appear to have less impact on HCV epidemics among IDUs probably due to the fact that HCV has higher infectivity rate than HIV**

RTI 19

Discussion (continued)

These findings may have important implications for understanding persistently low levels of HIV among IDUs in some cities despite high levels of injection risk.

Additional research is needed to:

- **Link sharing of dead space syringes to HIV transmission at the individual and network levels**
- **Understand how syringe type affects the relative contributions of injection and sexual transmission among IDUs**
- **Determine why some IDUs use dead space syringes and assess their willingness to switch to integral cannula syringes**
- **How this knowledge could be applicable to other countries such as Russia, where most of HIV transmission is occurring through injecting.**

RTI 20

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