

Scalable Mathematical Models for Substance Use: From Social Networks to the Whole Populations

Georgiy V. Bobashev, PhD^{1*}; William A. Zule, DrPH¹; Elizabeth D. Root, MA¹; Wendee M. Wechsberg, PhD¹; Andrei V. Borshev, PhD²; Alex E. Filippov, MS²

¹RTI International, Research Triangle Park, NC; ²Xjtek, St. Petersburg, Russia

*Presenting author
 RTI · 3040 Cornwallis Road · Research Triangle Park, NC 27709
 Phone 919-541-6167
 Fax 919-541-5966
 Email bobashev@rti.org
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Abstract

Mathematical modeling is a relatively new but fast developing area of substance use field providing researchers with additional dynamical dimension in epidemiological work and allowing scientists to simulate the consequences of various intervention and prevention scenarios. We illustrate these concepts by presenting two models. The first model describes Injecting Drug Users (IDU) networks, injecting behavior and HIV/HCV spread among the networks. The size, structure of the networks as well as frequency of injecting and HIV risks were obtained from published literature on urban IDU networks. This individual-based model was used to investigate the impact of introduction of Integral-cannula syringes (ICS) instead of commonly used Detachable Needle syringes (DNS). Laboratory experiments have shown that ICS retain about 1000 times less residual blood (<.001 ml vs. 1 ml) following injection and rinsing and thus provide about 100 times less risk of HIV/HCV transmission after 2 rinses than the DNS. Through dynamical simulations we have shown that it is necessary to have about 80% of users to switch to the ICS in order to reverse the spread of HIV and it takes more than 93% of users to 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. We show how these simulations could be matched on the actual geographical maps and followed in space over the time. The second individual-based model simulates substance use events among the US population allowing to estimate prevalence and incidence. Initially limited to alcohol, tobacco and marijuana use the model is using published age-specific rates of initiation and quitting for these substances. Such models allow identification of critical data gaps and validated models that are based on robust estimates allow 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.

1. Introduction

Mathematical Modeling in Substance Use Studies

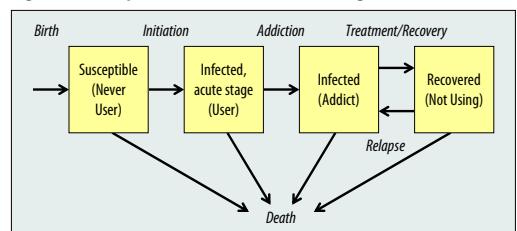
Mathematical modeling is a relatively new but fast developing area of substance use studies providing researchers with additional dynamical dimension in epidemiological work and allowing scientists to simulate the consequences of various intervention and prevention scenarios. Mathematical modeling has been known for decades in economics, ecology, epidemiology of infectious diseases, population biology (Anderson and May, 1992). Application of mathematical modeling to drug use problems is complicated by lack of traceable indicator of use such as antibody for infectious diseases. Nevertheless, drug use studies can dramatically benefit from mathematical models in at least two cases: One is when the main question of the study is "What if..." which is usually asked when planning and/or evaluating intervention. Knowing the major transition parameters and distributions a researcher can simulate various intervention (whether prevention, treatment, or law enforcement) scenarios and evaluate their impact in time. The second case when a mathematical model becomes useful is when geographical component provide insight on local or global dynamics of drug-related behavior in conjunctions with the distribution of risk and protective factors.

Types of Models

Compartmental Deterministic/Stochastic

- Population is divided into compartments and individuals move from one compartment to another according to some rate.
- Deterministic if the rate is considered the same for everyone in the compartment
- Stochastic if the rate is randomly distributed

Figure 1. A Simple Deterministic Model of Drug Use



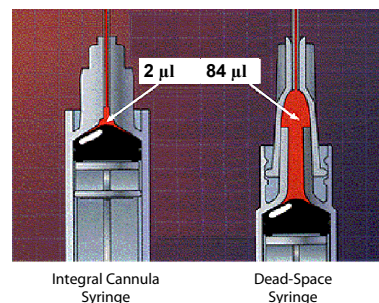
Individual-Based (Agent-Based) Models

- Individuals (Agents)
- States
- Events
- Rules for moving from state to state and for events to occur.

2. Example A: Impact of Type of Syringe on the Risk of HIV Transmission among IDUs

- 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). Use of dead space syringes may be more common in the U.S. than generally thought, and their use may be associated with higher prevalence of HIV infection (Zule et al., 2002).
- With the plunger depressed, "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.

Figure 2. Mean Volume of Fluid Retained with Plunger Depressed



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 .008 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.

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
 $I_{n+1} = I_n + I_n * (Q_1 * \alpha + Q_2 * (1 - \alpha)) * C * (N - I_n) / N - I_n * M$
 Effective Growth Ratio (deterministic) $R_0 = I_{n+1} / I_n$
 Effective Growth Ratio (stochastic) $R_0 = \text{Mean}(I_{n+1} / I_n)$
 $R_0 = 1 + QC - M - I_n * QC / N$
 Fixed points $I_n = 0, (QC - M) / (QC)$

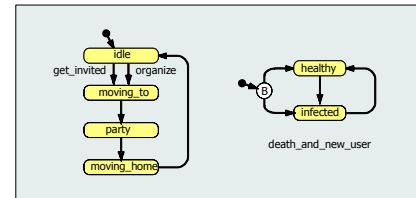
Geographically-Enhanced Agent-Based Model

- 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 of 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

IDUs reside in their neighborhoods and once in a while (according to an empirical distribution law) get together to inject drugs. For that they invite subjects from a number of their acquaintances (buddies) to a particular location for joint injection (party). The matrix of acquaintances is predefined according to published network characteristics, or could be defined as random.

The order of sharing is defined by the number of years of drug use experience. Some IDUs are HIV positive at the beginning. Some of the users insist on using "safer" syringes.

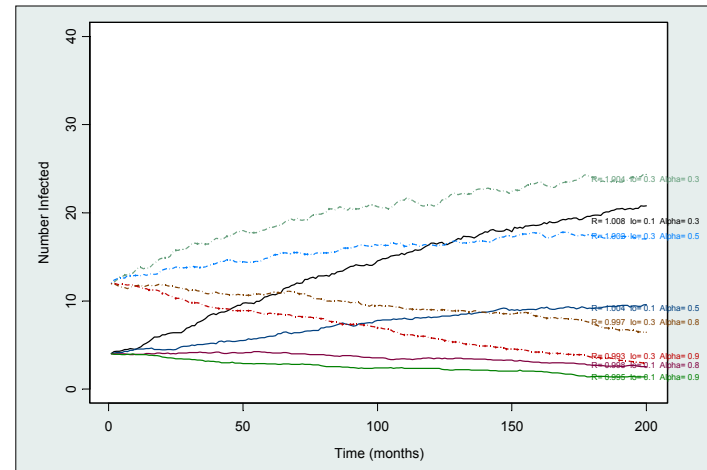
Figure 3. Transition Diagrams for an Individual



Results

Figure 6. Results of the Agent-Based Model Simulation for HIV

Q – risk factor ($Q_1=0.00008, Q_2=0.008$). Threshold % of safe syringes is 0.86 Averaged over 20 trajectories



Conclusions

Results of both the 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. However, dead space syringes appear to have less impact on HCV epidemics among IDUs.

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

Figure 4. Dynamics of HIV-Related Behavior in Durham, NC with Poverty Data Overlay

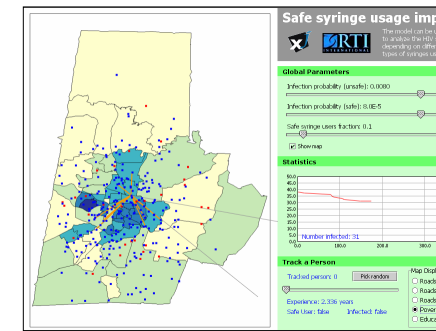
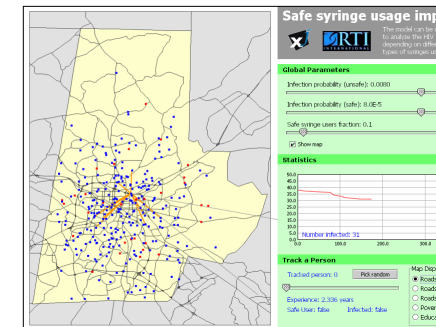


Figure 5. Dynamics of HIV-Related Behavior in Durham, NC with Roads Data Overlay



3. Example B: Impact of Preventive and Cessation Interventions on Dynamics of Drug Use in the U.S.

We consider an age-structured US population where each individual can start using any of the drugs: alcohol, tobacco and marijuana with initiation rates calculated from National Household Survey on Drug Abuse. After using the drug(s) a person can develop drug-related health problems with certain probability which is specific to drug, age and length of the use. An individual can also get recovered and/or quit using the drug. If the person quits there is a chance of relapse. We model impacts of hypothetical interventions that aim to reduce the initiation rate and/or increase quitting rate. We can calculate the effectiveness of such intervention by assigning cost to conducting intervention as well as economical gains due to increase in quality of life.

Figure 7. State Diagram for an Agent-based Model

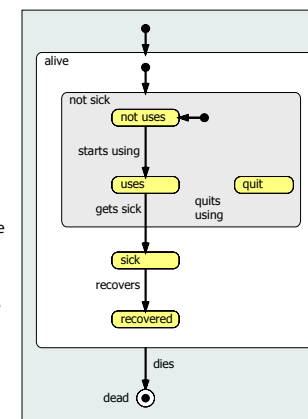


Figure 8. Health Economic Benefit of an Intervention for Total Population

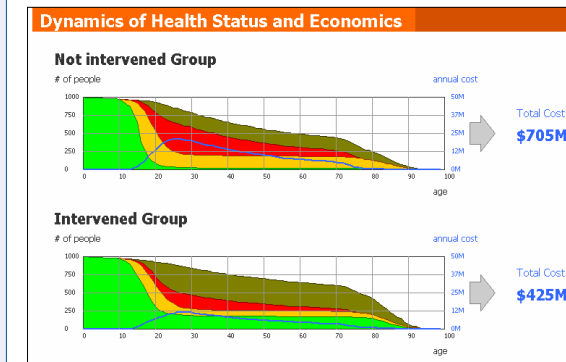


Figure 9. Effects of Intervention on Age Distribution of Health Status

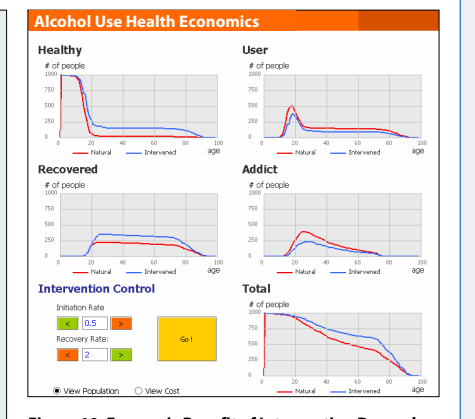
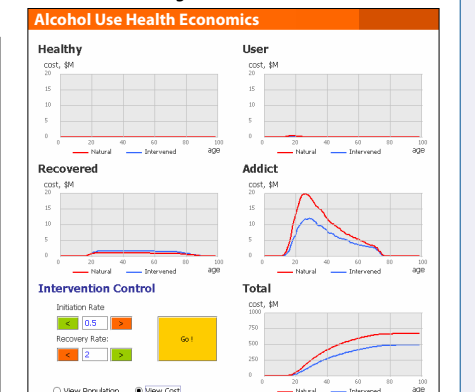


Figure 10. Economic Benefit of Intervention Depends on Health Status and Age



4. Discussion

Mathematical modeling opens new horizons in understanding an interplay of factors at individual, neighborhood, and more global levels. The behavior patterns could be very complex, however the outcome is often binary such as use or not use, disease or no disease. It is virtually impossible to capture all factors and interactions between these factors to explain individual behavior. Statistical modeling does the first step in estimating the major factors and relationships between them and the outcome. Mathematical modeling provides the next step in assembling multiple knowledge pieces into a coherent multi-variable framework. Such frameworks could be then used to illustrate scientific advances, knowledge gaps and provide a hands on tool guiding through numerous mental and practical exercises aimed to predict "What if...". The use of modern theoretical advances, computer power and accumulated data makes mathematical modeling available to a wide range of researchers.

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