An Epidemic Model of Nonmedical Opioid Use with Simulated Public Health Interventions

Alexandra Nielsen, Wayne Wakeland and Teresa Schmidt
Systems Science Graduate Program,Portland State University, 10th Avenue, Portland, U.S.A.

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Abstract: We report development of a generalized epidemic model of initiation and nonmedical use of pharmaceutical opioids in the US. The study relies on historical trend data as well as expert panel recommendations that inform model parameters and structure. Derived from current policies, simulated public health interventions are assessed using the model regarding their leverage for reducing initiation and nonmedical use. Preliminary findings indicate that interventions which reduce the perceived attractiveness of opioids for recreational use may significantly reduce initiation and nonmedical use most significantly, while supply restriction effected through drug take back days and prescribing changes may have more modest effects. We argue that system dynamics is an effective approach for evaluating potential interventions to this complex system where the use of pharmaceutical opioids to treat pain is fraught with potentially undesirable distal outcomes in the public sphere.

1 INTRODUCTION

A dramatic rise in the nonmedical use of pharmaceutical opioids in the late 1990's and early 2000's created a substantial public health challenge for the United States (Compton and Volkow, 2006). Despite implementation of public health policies and regulations (Food and Drug Administration, 2013), the high level and increasing prevalence of negative outcomes such as fatal and non-fatal overdoses remains largely unabated (Centers for Disease Control and Prevention, 2012). Resistance to policy interventions likely stems from the complexity of the pharmaceutical opioid system, including multiple interactions between prescribers, pharmacists, persons obtaining opioids for medical or nonmedical use, opioid traffickers, and public health advocates. The resulting chains of cause and effect often result in feedback loops that diminish or even reverse well-intentioned interventions.

This paper presents progress on a system dynamics model of the complex system surrounding the initiation and nonmedical use of pharmaceutical opioids in the United States. In addition to accounting for historical trends in the initiation and escalation of nonmedical use and the acquisition of pharmaceutical opioids via friends and relatives (SAMHSA, 2012), the model may lead to increased understanding of the underlying processes that give rise to this public health problem, and allows for experimentation and direct comparison of a variety of potential policy interventions.

1.1 Background

The number of overdose deaths involving opioids tripled between 1999 and 2006 in the US, rising to 14,800 in 2008 (Warner et al., 2011). As evidenced by the high fraction of opioid overdose decedents without prescriptions (Hall et al., 2008), nonmedical use of pharmaceutical opioids plays a significant role in the prevalence of overdose deaths. Estimates from the National Survey on Drug Use and Health (NSDUH) suggest that the rate of initiation of nonmedical use of pain relievers increased almost three-fold from 1995 to 2003 (SAMHSA, 2006) and has continued at high rates. In 2010, an estimated 2.4 million individuals initiated nonmedical use of pain relievers (SAMHSA, 2012) and 5.1 million individuals used opioids nonmedically within the month prior to the survey (SAMHSA, 2012).

Diversion of opioids from prescription holders is a major source of supply for nonmedical use. Around 70% of respondents to the 2010 NSDUH indicated that they received opioids from friends or relatives. And among those who received the drugs

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for free, 80% identified their source as originally acquiring the drugs from a single doctor. Leftover opioid prescriptions are likely involved in much of this diversion (Compton and Volkow, 2006). A study of post-surgical patients discharged from a urology group practice found that 42% of opioids prescribed were unconsumed, and that 67% of patients had surplus opioids. Further, 91% of patients with leftover medicine kept it in their homes rather than disposing of it (Bates et al., 2011). A recent National Drug Take-Back event in Madison, Wisconsin recovered approximately 100,000 opioid dosage units in one day (Gilson, 2012). These studies suggest that there is a large reservoir of unused opioids stored in homes, and the high fraction of individuals receiving drugs for free from friends and family is likely to be strongly correlated with the size of this reservoir.

2 A SYSTEM DYNAMICS SIMULATION MODEL

The system dynamics modelling approach uses a set of differential equations to simulate system behaviour over time. This approach provides a framework in which to capture the underlying processes involved in a system and the feedback loops that generate its behaviour. When applied to public health problems, system dynamics modelling allows for the simulation of intervention alternatives in order to provide policymakers with a tool to assess interventions for magnitude of impact and potential for unintended consequences–information that is not available from research focused on individual aspects of a system (Sterman, 2006). In the current research, a system dynamics model complements and leverages results from existing research, primarily historical trends available from NSDUH (SAMHSA, 2012), and holds promise for the simulation of intervention alternatives.

Figure 1 provides a high level picture of the current model, which features one of the main pathways by which people may initiate nonmedical use of pharmaceutical opioids and transition from casual usage based on free access to paying for drugs through illicit channels. The ease of obtaining drugs for free depends in the model on the amount of leftover and undisposed pharmaceutical opioids that are stored in homes ("medicine cabinets"). A complete model and exact parameter values are available upon request from the authors.

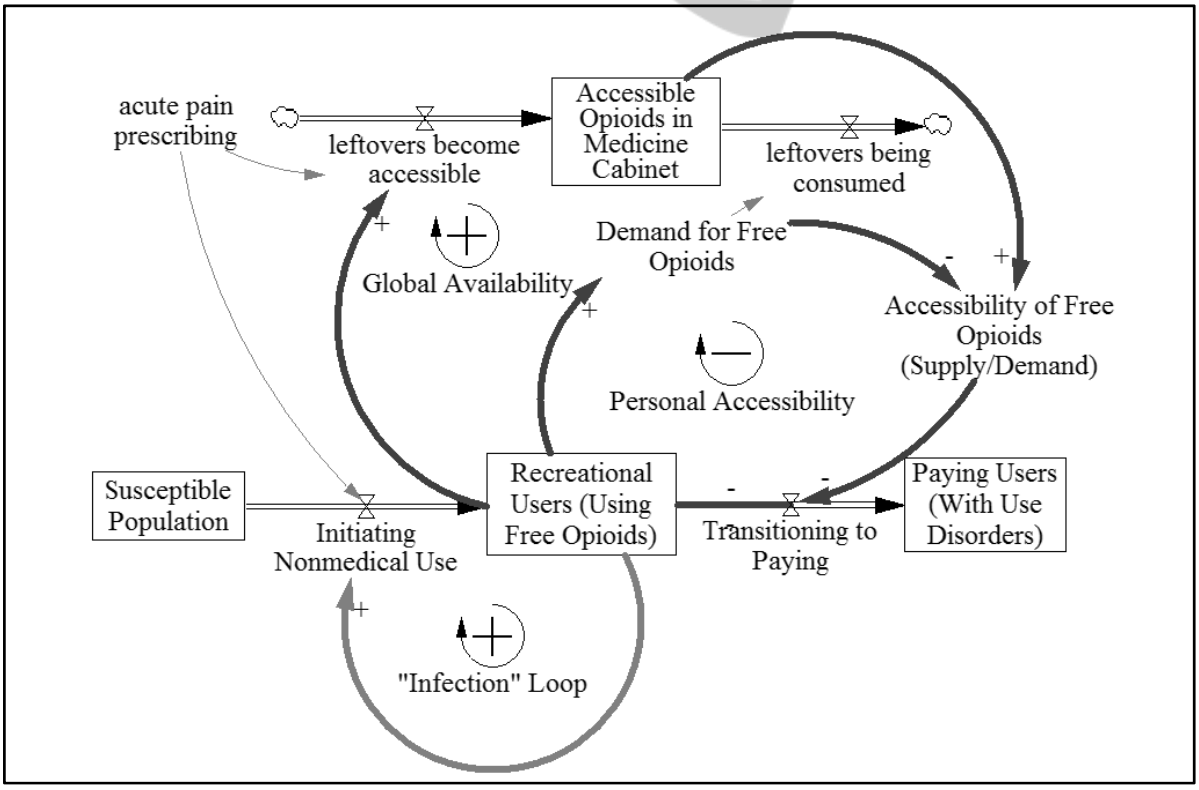

Figure 1: High level diagram of model structure.

2.1 Dynamics of the Opioid Nonmedical Use Initiation System

The rate of prescribed opioids for acute pain treatment is shown in the upper left corner of Figure 1, which serves as a key exogenous input to the model. The model assumes that leftover prescriptions from acute pain conditions are more likely to constitute free sharing than prescriptions for chronic pain diagnoses. The lower part of Figure 1 depicts the progression of people from initiating nonmedical use to paying for drugs, which implies the development of a use disorder (such as opioid abuse or addiction) and other increasingly risky behaviours.

Figure 2 details a recruitment mechanism whereby casual users, who acquire opioids for free from friends or family, influence their peers to initiate nonmedical opioid use. This recruitment is modelled as an infectious disease process using the SIR (susceptible, infected, recovered) epidemic modelling framework.

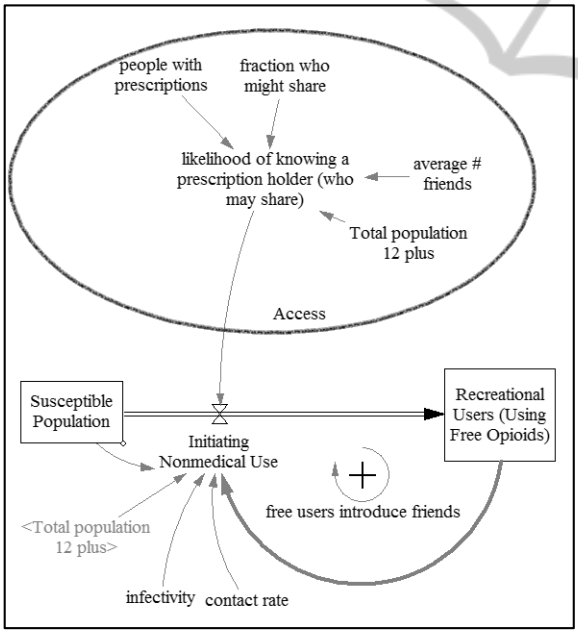

Figure 2: Simple zoomed in view of the infection loop.

In SIR disease models, an infected party will make contact with susceptible individuals based on a contact rate. The infectivity of the disease determines whether contact results in infection of the susceptible. When the number of infected individuals becomes large, a susceptible is likely to have multiple contacts with infected people and infection becomes more likely. Thus the infected population becomes larger causing infection to spread more quickly, resulting in a disease epidemic.

While nonmedical pharmaceutical opioid use is not an infection per se, the SIR epidemic model is a compelling framework to explain initiation. Susceptibles in this case are people who have never used opioids nonmedically, and infected individuals are those who use opioids recreationally. When individuals in these two populations make contact, the idea of using opioids recreationally can spread to the susceptible who then initiates opioid use based on the "infectivity" of the idea. The infection of a susceptible by an infected individual could be active, as when a peer is pressured or persuaded to use drugs by other peers, or passive in which a susceptible observes drug use behaviours in peers, parents, or through the media and copies those behaviours (Dasgupta et al., 2009); (Andrews et al., 1997). When the number of nonmedical users increases, the rate of initiation increases resulting in a positive feedback loop, or vicious spiral.

In order to initiate opioid use, a susceptible must have both the desire to use opioids and access to them. In this model, the initiation rate is mediated by the likelihood that a potential initiator knows *at least one* prescription holder who is willing to share. This likelihood is based on a binomial probability calculation. The probability that at least one of a susceptible's family or friends has an opioid prescription and is willing to share is determined by the number of friends and by what fraction of the total population meet these criteria (see Figure 3).

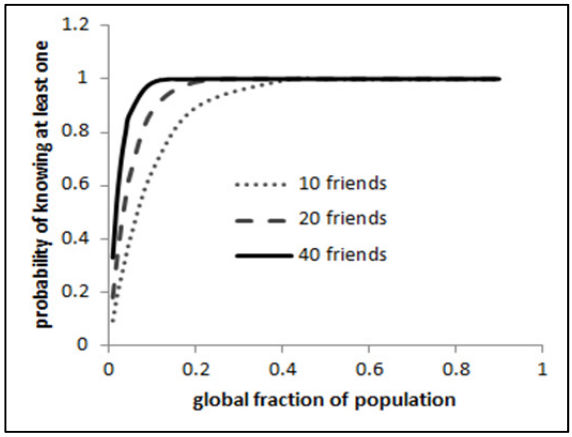

Figure 3: Binomial probability calculation of likelihood parameters with 10, 20 and 40 friends. Initiation depends on the fraction of the total population who are prescription holders willing to share. Opening opioid supply depends on the fraction of the total population who are casual opioid users seeking free supply.

When the number of friends is fairly large, the likelihood that a susceptible knows someone who will share opioids is high even when a relatively small fraction of the total population has prescriptions and will share them, as in the solid plot. However, even when the number of friends is small, the likelihood of knowing at least one person who will share is still greater than this global fraction. The probability curve is always bowed outward. Therefore, it doesn't matter if a susceptible can get opioids from one, five or twenty-five sources; if she knows at least one source, she has access.

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In the classic SIR disease model, people who recover from infection do not spread the disease, nor are they susceptible to reinfection. In this model nonmedical users are organized into three groups, recreational users with and without a use disorder (heretofore shown as the aggregated recreational user group), and people with use disorder who use more than they can obtain for free and have to pay for some of their drugs. Individuals in the third group are assumed not to participate in the recruitment process (Winkler et al. 2004). These users may no longer be peers of susceptibles as they become increasingly socially isolated, and instead of sending positive messages about drug use behaviour that susceptibles want to mimic, they may send negative messages.

Figure 4 describes the relationship between the free supply of opioids in medicine cabinets, and the progression of users from casual (free) use, to development of a use disorder, to paid use. The outermost arrows represent the global dynamics of opioid availability: Much leftover medicine is not accessible because prescription holders may not have any desire to use it nonmedically or know anyone who does. However, as the population of recreational users increases (the circled group in Figure 4), the likelihood that individuals with leftover medications know at least one person who would use them also increases, again based on a binomial probability calculation. A fraction of these

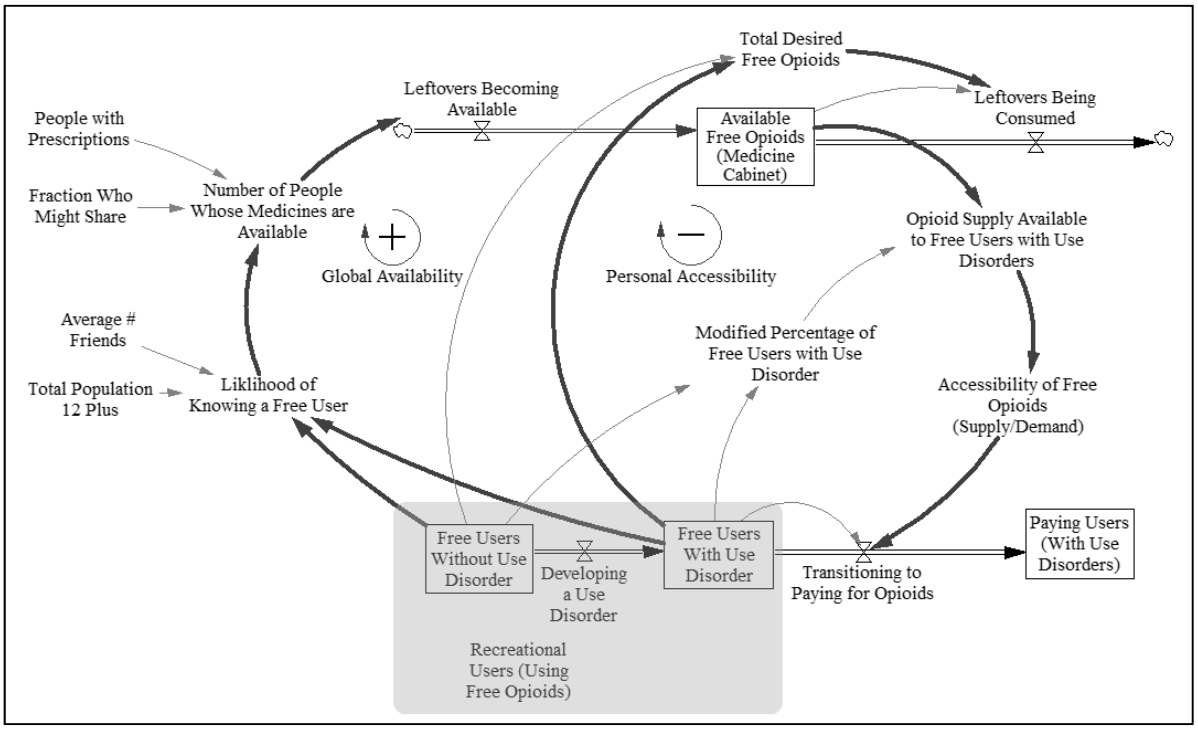


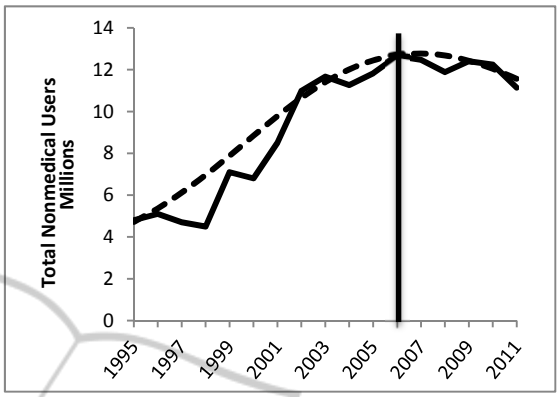
Figure 4: Impact of supply on user progression to paying for drugs.

prescription holders who know a person seeking free opioids for nonmedical use will choose to share them. Their leftover medicine then flows into the available free opioid supply, also called the "medicine cabinet." Thus, increases in initiation lead to *increased* accessibility of leftover prescription opioids, which tends to increase the population of casual users because fewer of them transition to paid use to due loss of access to free opioids, constituting a second positive feedback loop.

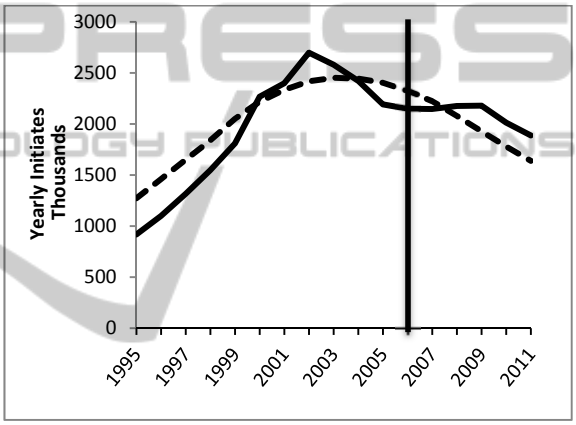
On the other hand, the inner arrows in Figure 4 represent local dynamics of opioid availability, which operate differently than the global dynamics. Repeated use of pharmaceutical opioids can lead to the development of opioid use disorders (Fishbain et al., 2008) and, with them, consumption levels that cannot be sustained by free leftover medicines prescribed to those in one's personal network. When the demand for opioids exceeds what these individuals can access through their personal contacts, they may begin purchasing opioids through the black market. This advancement to paid use is assumed to be associated with the development of an opioid use disorder and with a higher risk of adverse outcomes. Therefore, although an increase in the number of casual users "loosens up" opioid supply by increasing access to leftover prescription holders at the global scale, it also results in the exhaustion of sources of supply at the local scale. Because of these local dynamics, an increase in the population of casual users leads to decreases in accessibility, as represented by a balancing (negative) feedback loop.

3 MODEL TESTING

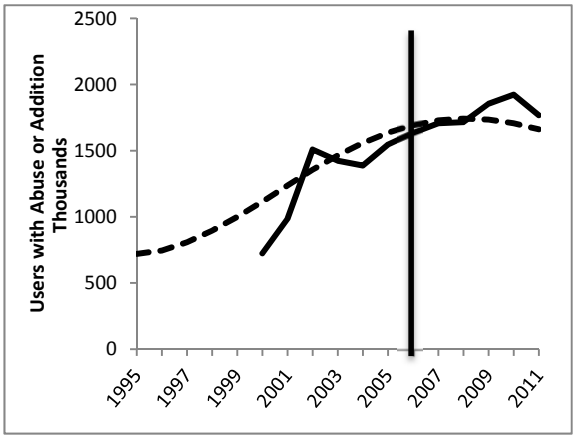
This model is a proof of concept as empirical support is still being sought for many model parameters. Currently, most parameters have been set to plausible values under the guidance of expert panel members and calibrated to fit three time series from the NSDUH for the years 1995-2005: total past year nonmedical opioid users, total past year initiates of opioid use, total past year opioid users who meet the criteria for opioid abuse or addiction. To build confidence in the model concept, model outputs were tested for fit against 2006-2011 data. Results of calibration and tests of fit are shown in Figure 5. Degree of fit to 2006-2011 data was calculated using mean absolute percent error (MAPE), which is reported in figure captions (see Sterman 2000 for a discussion of fitness tests for SD models). Having passed tests of face validity with expert panel members and behaviour reproduction after calibration to reference data, the model was deemed sufficiently plausible for exploratory policy analysis.



a. Total past year nonmedical users. MAPE 3.76%.



b. Total past year initiates of nonmedical use. MAPE 6.14%.



c. Total past year users who meet the criteria for abuse or addiction. Data prior to 2000 could not be obtained. MAPE 3.47%.

Figure 5: Model outputs (dashed) versus data (solid). Data prior to 2006 used for calibration. 2006 onward used for tests of fit and confidence building.

4 PRELIMINARY MODEL RESULTS

The current model increases understanding of the dynamics associated with initiation and nonmedical use of pharmaceutical opioids. Initial testing suggests that the model replicates historical trends of initiation and nonmedical use in the United States, and, following more rigorous testing, the model will be expanded to allow for the evaluation of several specific policy interventions. While more testing of the model is required to establish its credibility and validity, preliminary logic for three initiation reduction scenarios was developed to illustrate the potential for evaluating policy impacting the initiation and nonmedical use of opioids. The baseline run begins in 1995 and runs until 2011, and all scenarios begin arbitrarily in 2005 to demonstrate what their relative impacts on nonmedical opioid use might have been over the six-year period from 2005 to 2011. The scenarios presented here are implemented as simple toggles or switches that affect a single stock or parameter.

4.1 Prescription Drug Take-back Initiative

The first scenario, a prescription drug take-back initiative, simulates an expansion of the DEA's National Prescription Drug Take-Back Day program (Drug Enforcement Administration, 2012) to collect unneeded medications by asking individuals to bring leftover prescriptions to a disposal location. Disposal records from one Take-Back Day in Madison Wisconsin suggest that as many as 100,000 opioid dosage units can be collected in a major city on one day (Gilson, 2012). In the current model, the national take-back program is simulated as a removal of one hundred million dosage units from the "medicine cabinet" supply of available opioids each year, starting in 2005. This amount is largely speculative, but could be possible if all 50 states facilitate Take-Back Days in at least two major cities on 10 days per year, with the degree of success as was witnessed in the recent Madison Take-Back Day.

4.2 Reducing Initiation through Drug-resistance Strategies

The second simulated scenario features a reduction in the "infectivity" of opioids as a desirable substance for nonmedical use. Some interventions, such as "Keepin' it R.E.A.L (Gosin et al., 2003), may deter or delay initiation of nonmedical opioid use, even if opioids are freely available and recommended by peers, through teaching culturally specific drug-resistance strategies. In the current model, infectivity was reduced by 25% in 2005, so that uninitiated individuals were 25% less likely to initiate nonmedical use even if exposed to the idea.

4.3 Reducing Willingness to Share Opioids

The third simulated scenario features a reduction in

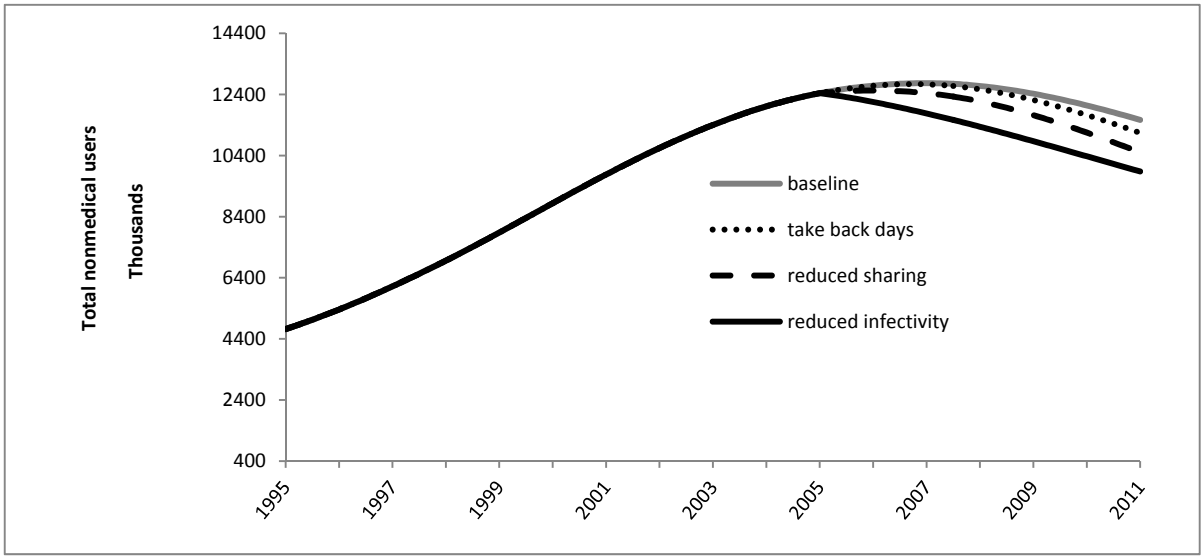


Figure 4: Impact of interventions on number of recent and recreational users.

the fraction of individuals who are willing to share their opioids with others for nonmedical use. Individuals with leftover prescriptions might also be educated about the risks involved in sharing medications, or might be encouraged to adopt safety features, such as locked medicine cabinets. This intervention is currently modelled as a 25% reduction in the number of individuals who are willing to share their leftover opioid prescriptions with others, starting in 2005.

4.4 Preliminary Scenario Comparison

Figure 6 shows a comparison of the three interventions in terms of the impact on total number of nonmedical users over time. These preliminary results suggest that behavioral interventions either on the supply side or the demand side may have a greater impact on the number of users than supply restriction.

Demand reduction achieved through reducing the infectivity of the opioid use idea had the greatest impact on the total number of nonmedical users. This is because a 25% reduction in infectivity results in a 25% reduction in the initiation flow. This reduction is then amplified by positive feedback as a lower initiation rate results in fewer recreational users who subsequently infect fewer susceptibles.

Supply reduction achieved through reducing prescription holders' willingness to share acts on two feedback processes, but has a smaller impact. This is because a 25% reduction in willingness to share does not result in a 25% reduction in opioid access to initiates due to the nonlinear likelihood parameter. A 25% reduction in the global fraction of prescription holders willing to share medicines is a leftward movement down the binomial probability curve shown in Figure 3, and in the reduced sharing scenario, translates to a 7% reduction in initiation due to restricted opioid access to potential initiates. This change is similarly amplified by positive feedback as in the reduced infectivity scenario. Reducing sharing also reduces the flow of medicines into the available free supply, however, the impact on the number of nonmedical users is minimal because supply constriction primarily shifts nonmedical users with use disorder from the free user stock to the paying user stock without changing the total number of users.

The prescription take back scenario has little impact on the total number of nonmedical users for the same reason.

5 DISCUSSION AND FUTURE DIRECTIONS

The model presented in this paper is useful primarily because it extends our understanding of the dynamics of pharmaceutical opioid abuse problem in the United States and comparatively demonstrates policy leverage points for intervention The model proposes that nonmedical opioid use spreads in fashion similar to the spread of a disease. Some communities in the United States are deeply impacted by opioid abuse and others are not (Butler et al., 2007); (Brownstein et al., 2010). Using the disease metaphor we might suggest that in some areas the opioid use *idea* had infected too few people for the idea to spread, while in others the infected population is large so the "disease" of opioid use has become endemic. The disease metaphor can be broadened to encompass possible additional intervention strategies. Reducing infectivity (of the idea of using opioids nonmecially) was shown to be highly impactful. What might an "immunization" intervention strategy look like? How would it impact initiation? Could a policy be formulated that acts like a quarantine? Because the infectious disease metaphor has been formalized into a model and calibrated against historical data, these types of ideas may merit exploration.

The other two hypothetical interventions appeared to be less effective in this model, but further investigation seems warranted regarding ways to reduce the free supply, whether it be drug take back day programs, campaigns to reduce prescription holders' willingness to share, other ideas not yet considered. While the vast majority of nonmedical users use very little and do not develop use disorders, a small fraction do, and smaller fraction still buy opioids to support high levels of use (SAMHSA, 2012). Even though this fraction is small, it is included in this model because the high price of pharmaceutical opioids for those who cannot obtain them for free may be an important factor in the recent rise in heroin use (SAMHSA, 2012). The street price of pharmaceutical opioids is high compared to heroin, and qualitative studies suggest that many opioid users switch to heroin due to its lower cost (Levy, 2007); (Young and Havens, 2012). Modelling a progression of opioid use that includes a transition to paying may provide a jumping off point for an investigation of the recent rise in heroin use.

5.1 Limitations

This manuscript describes a work in progress, and stronger empirical support is being sought for all model parameters. Parameter validity tends to be the primary limitation in this type of study (Wakeland et al., 2010).

The scenarios presented in this preliminary analysis are too simple for a rigorous comparison of effectiveness. These scenarios compare the system level impact of hypothetical interventions with specific and stable proximal effects (such as a 25% reduction in the infectivity of the idea of nonmedical drug use), on the number of people who become nonmedical users and on the number of people who escalate their usage and manifest use disorders. Framing scenarios in terms of their proximal effects leaves several important questions unanswered: How can these reductions be achieved? Are reductions of the desired magnitude achievable, given constraints such as limited budgets? How can we compare interventions if some are easy but low impact, and others are difficult but high impact? In order to compare the effectiveness of interventions themselves, model structures would need to be developed that transform exogenous inputs, such as dollars spent on drug resistance programs, into local outcomes that impact model parameters or structure, such as a two year delay in initiation. A more rigorous treatment of intervention strategies is necessary for this preliminary model to become a useful policy evaluation instrument.

Additionally, the population represented in the current model is derived from the NSDUH, which is known to be limited in its representation of hidden drug using communities such as the incarcerated, members of the armed forces, and the homeless (Crum, 2005). The current model presents only one of several possible routes of initiation and does not include initiation of nonmedical use through medical exposure, or as a substitute for or complement to other illicit drug use. Furthermore, the potential impact of the availability of chronic pain medicine is not considered, and may be an important factor.

5.2 Future Research

Future work will include additional efforts to locate empirical support for model parameters and model structure to develop the model beyond the proof of concept stage. Expansion of the model logic for policy interventions is also planned. A variety of model testing techniques, including sensitivity analysis and more rigorous comparisons to reference behaviour, will help to strengthen the model's validity and credibility. In addition, model development is underway for several other aspects of the pharmaceutical opioid system, including the dynamics of black market opioid purchasing and the negative outcomes associated with nonmedical use, including transition to heroin use and fatal overdoses. Integration of the current model with these other sectors will enable future simulations to yield greater insights regarding the likely magnitude of impact, and rigorous testing will increase confidence in the model's results.

6 CONCLUSIONS

Initiation and nonmedical use of pharmaceutical opioids has seen a dramatic rise from 1995 to 2005, and stabilization at a high level toward the end of the last decade (SAMHSA, 2012). The current model replicates historical trends in initiation and nonmedical use, and in doing so provides increased understanding of underlying processes and feedback loops that may give rise to observed historical trends in the pharmaceutical opioid system. Based on initial simulation runs, the model also demonstrates the potential for the system dynamics approach to be useful in evaluating policy alternatives in terms of their likely impact on negative consequences. While further testing and elaboration of intervention logic are needed, preliminary results suggest that the public health interventions described here could potentially have sufficient leverage to appreciably decrease the number of individuals who use opioids nonmedically.

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