Dynamic Simulation of Opioid Misuse Outcomes

Alexandra Nielsen and Wayne Wakeland
Systems Science Graduate Program, Portland State University, 1604 S.W. 10th Av., Portland, OR 97201, U.S.A.

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Abstract: The objective of the study was to develop a system dynamics model of the medical use of pharmaceutical opioids, and the associated diversion and nonmedical use of these drugs. The model was used to test the impact of simulated interventions in this complex system. The study relied on secondary data obtained from the literature and from other public sources for the period 1995 to 2008. In addition, an expert panel provided recommendations regarding model parameters and model structure. The behaviour of the resulting systems-level model compared favourably with reference behaviour data (R^2=.95). After the base model was tested, logic to simulate interventions was added and the impact on overdose deaths was evaluated over a seven-year period, 2008-2015. Principal findings were that the introduction of a tamper resistant formulation unexpectedly increased total overdose deaths. This was due to increased prescribing which counteracted the drop in the death *rate*. We conclude that it is important to choose metrics carefully, and that the system dynamics modelling approach can help to evaluate interventions intended to ameliorate the adverse outcomes in the complex system associated with treating pain via opioids.

1 INTRODUCTION

A dramatic rise in the nonmedical use of pharmaceutical opioid pain medicine has presented the United States with a substantial public health problem (Compton and Volkow, 2006). Despite the increasing prevalence of negative outcomes, such as nonfatal and fatal overdoses, nonmedical use of pharmaceutical opioids remains largely unabated by current policies and regulations (see Fishman et al., 2004). Resistance to policy interventions likely stems from the complexity of medical and nonmedical use of pharmaceutical opioids, as evidenced by the confluence of the many factors that play a role in medical treatment, diversion, and abuse of these products in the United States.

Complex social systems are well known to resist to policy interventions, often resulting in unintended consequences or unanticipated sources of impedance (Sterman, 2000). These undesirable outcomes can result from our inability to simultaneously consider a large number of interconnected variables, feedback mechanisms, and complex chains of causation (Hogarth, 1987). Prescription opioid use, diversion, and nonmedical use constitute a complex system with many interconnected components, including prescribers, pharmacists, persons obtaining opioids from prescribers for medical use, persons obtaining drugs from illicit sources, and people giving away or selling drugs. Interactions among these actors result in chains of causal relationships and feedback loops in the system. For example, prescribing behaviours affect patients' utilization of opioids; adverse consequences of medical and nonmedical use influence physicians' perceptions of the risks associated with prescribing opioids; and physicians' perception of risk affects subsequent prescribing behaviours (Potter et al., 2001); (Joranson et al., 2002).

This paper presents a system dynamics model which simulates the system described above. The model is designed to provide a more complete understanding of how medical use, nonmedical use, and trafficking are interrelated, and to identify points of high leverage for policy interventions to reduce the adverse consequences associated with the epidemic of nonmedical use. An intervention corresponding to the introduction of relatively less-abusable, tamper-resistant formulation is simulated, and possible downstream effects are highlighted.

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2 BACKGROUND

Between 1999 and 2006, the number of U. S. overdose deaths attributed to opioids tripled–increasing more than five-fold among youth aged 15 to 24 (Warner et al., 2009)–signalling the onset of a major public health concern. Overdose deaths involving opioid analgesics have outnumbered cocaine and heroin overdoses since 2001 (CDC, 2010), and estimates from the 2009 National Survey on Drug Use and Health (NSDUH) suggest that 5.3 million individuals (2.1% of the U.S. population aged 12 and older) used opioids for nonmedical purposes within the previous month (SAMHSA, 2010). Earlier data from NSDUH suggest that the rate of initiating nonmedical usage increased drastically from 1994 to 1999 (SAMHSA, 2006), and has continued at high rates, with over 2 million individuals reporting the initiation of nonmedical use of pain relievers in 2009 (SAMHSA, 2010). Recent increases in prescribing opioids stem in part from increases in chronic pain diagnosis and the development of highly effective long-acting pharmaceutical opioid analgesics.

One problem that arose with these new long-acting formulations was the ease with which they could be tampered with to enhance the effects when used non-medically.

Policymakers striving to ameliorate the adverse outcomes associated with opioids could benefit from a systems-level model that reflects the complexity of the system and incorporates the full range of available data. Such a model could be used to study the possible effectiveness of a tamper resistant drug.

3 SYSTEM DYNAMICS SIMULATION MODEL

The current work features a system dynamics simulation model that represents the fundamental dynamics of opioids as they are prescribed, trafficked, used medically and nonmedically, and involved in overdose mortality. The model was developed over a two-year period through collaborative efforts of a modelling team and a panel of pain care and policy experts. The SD modelling approach uses a set of differential equations to simulate system behaviour over time. SD models are well suited to health policy analyses involving complex chains of influence and feedback loops that are beyond the capabilities of statistical models (Sterman, 2006), and have been successfully applied to the evaluation of policy alternatives for a variety of public health problems (Cavana and Tobias, 2008; Homer, 1993; Jones et al., 2006; Milstein, Homer, & Hirsch, 2010). The SD approach can help identify points of high leverage for interventions, as well as possible unanticipated negative consequences of those interventions. This provides policymakers with information that is not available from research focused on individual aspects of a system (Sterman, 2006).

Model development began with a thorough literature review to locate empirical evidence to support key model parameters. Literature sources included a broad spectrum of data sources, survey results, and scholarly articles covering data collect between 1995 and 2009. Multiple data gaps were identified that could not be adequately addressed by existing literature (see Wakeland et al., 2010). Expert panel members provided expert judgment to help fill these data gaps.

The model was developed iteratively, starting with a brainstorming session that included both subject matter experts (SMEs) and computer simulation team members. The system boundary for the initial sketch model describing the various stocks and flows was very broad and included populations of people receiving opioid analgesics to treat pain, people using these prescription drugs nonmedically, people using illicit drugs, plus the overall demand and supply for various drugs. The simulation team then refined the diagram, searched for parameter data, and specified possible equations. Model scope was reduced and the model was simplified due to the lack of data and requisite knowledge. The data and model were reviewed again by the SMEs, and the simulation team further refined the model and sought additional data based on the SME feedback. This process was repeated multiple times.

The model encompasses the dynamics of the medical treatment of pain with opioids, the initiation and prevalence of nonmedical usage; the diversion of pharmaceutical opioids from medical to nonmedical usage; and adverse outcomes such as overdose fatalities. Discussion of each sector includes a description of empirical support, a narrative on model behaviour, and a causal loop diagram showing model structure. Bracketed numbers in the text correspond to specific points in the diagrams. The model contains 40 parameters, 41 auxiliary variables, and 7 state variables, as well as their associated equations and graphical functions.

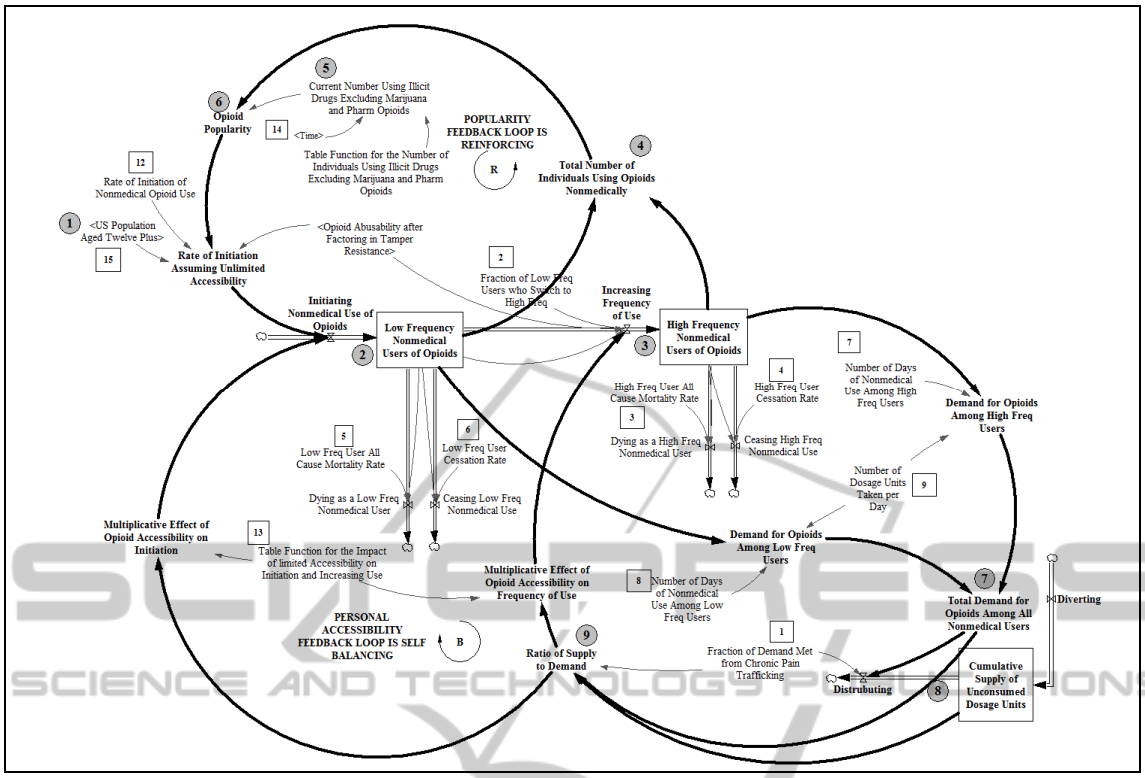


Figure 1: Causal loop diagram of the nonmedical use sector. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to model parameters in the Appendix, Table 1.

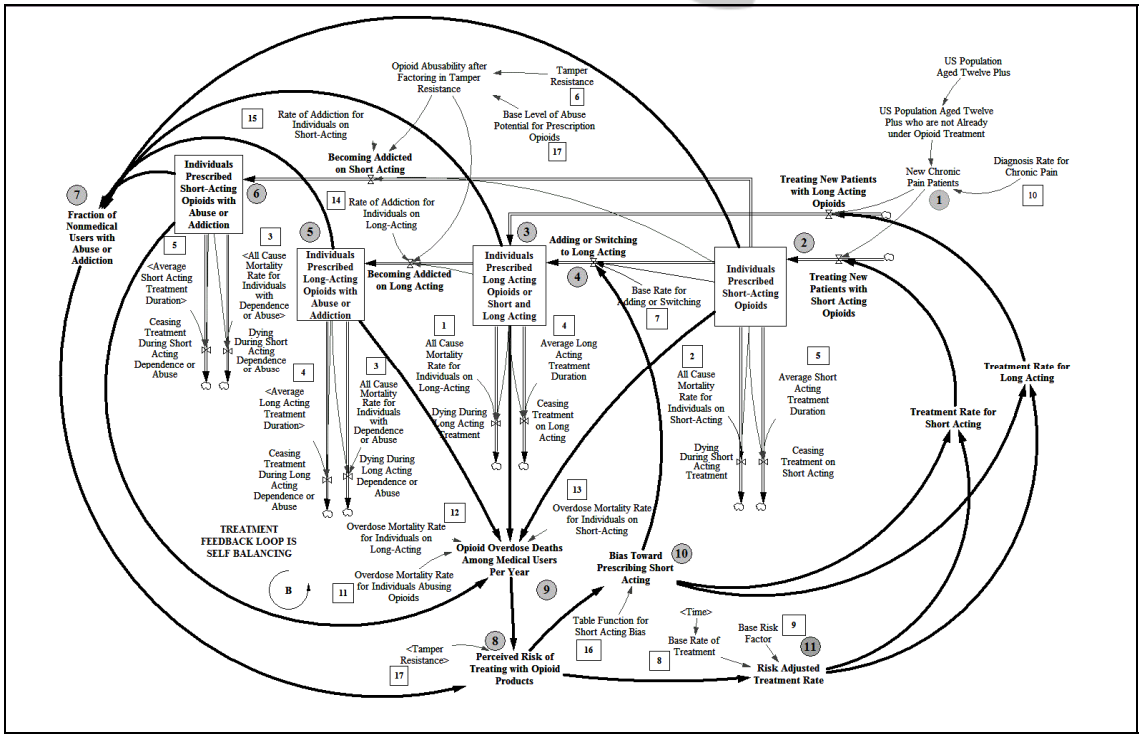


Figure 2: Causal loop diagram of the medical use sector. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to model parameters in the Appendix, table 2.

3.1 Nonmedical Use Sector

12%-14% of individuals who use opioids nonmedically meet the criteria for opioid abuse or dependence (Colliver et al., 2006), either of which is associated with a high frequency of nonmedical use. Extrapolation from heroin findings indicates that higher frequency opioid use is associated with a significantly higher mortality rate (WHO; see Degenhardt et al., 2004); (Hser et al., 2001) and supports a distinction between two subpopulations of nonmedical users (low- and high-frequency) in this model sector.

As illustrated in Figure 1 (with supporting data in the Appendix, Table 1), a percentage of the US population {1} is assumed to initiate nonmedical use each year {2}, all of whom start out in a stock of 'low-frequency nonmedical users,' and a small percentage of whom advance to a stock of 'high-frequency nonmedical users' {3} during each subsequent year. The total number of individuals using opioids nonmedically {4} is divided by the current number of individuals in the US who are using other drugs nonmedically {5} to calculate the relative popularity of opioids for nonmedical use {6}. As the popularity of using opioids nonmedically increases, the rate of initiation increases, creating a positive feedback loop that *ceteris paribus* would result in an exponential increase in the rate of initiation.

Nonmedically used opioids are obtained through many routes, but of key interest for the current research is opioid 'trafficking' (i.e., buying or selling) via persons who are receiving these products ostensibly for treatment. Extrapolation of results from the 2006 NSDUH survey (SAMHSA, 2007) suggests around 25% of the nonmedical demand for opioids is met via trafficking.

In the model, demand for opioids is calculated from the number of individuals in low- and high-frequency populations {7}. As noted above, 25% of demand is assumed to be met by trafficking {8}, with the rest coming from sources not modelled explicitly (mostly interpersonal sharing among friends and relatives, per SAMHSA, 2007). When the trafficking supply is ample relative to demand, the rate of initiation {2} and the rate of advancement from low-frequency to high-frequency use {3} are assumed to be somewhat enhanced. When the trafficking supply is limited, however, rates of initiation and advancement are assumed to decrease dramatically. The ratio of supply to demand {9} indicates the degree to which opioids are accessible for nonmedical use. As the populations of nonmedical users increase beyond what trafficking can support, accessibility becomes limited, decreasing initiation and advancement. This creates a negative feedback loop that eventually equilibrates the otherwise exponential increase in nonmedical use driven by the popularity feedback loop.

3.2 Medical Use Sector

Increases in opioid abuse and addiction have led to regulatory policies which have lead many physicians to avoid prescribing opioids to patients out of fear of overzealous regulatory scrutiny (Joranson et al., 2002). Or, they may decrease the amount of opioids they prescribe, and shift their prescribing towards short-acting opioid products because long-acting opioids have been shown to have a higher rate of abuse than immediate-release opioid analgesics when abuse rates are normalized for the number of individuals exposed (Cicero, Surratt, Inciardi, & Munoz, 2007). Thus, physicians exhibit more caution in prescribing long-acting opioids (Potter et al., 2001).

As illustrated in Figure 2, the system model assumes that a proportion of the US population is diagnosed with a chronic pain condition each year {1}. A fraction of these people are subsequently treated with either short-acting {2} or long-acting {3} opioid formulations, and become members of one of the stocks (populations) of patients under opioid treatment ostensibly for chronic pain. Patients who begin treatment with short-acting formulations may cease treatment if their condition improves, or they may switch to long-acting formulations if their pain conditions appear to worsen {4}.

Each year some individuals move from the stocks of 'individuals receiving opioids' {2-3} to the stocks of 'individuals receiving opioids with abuse or addiction' {5-6}. The fraction of opioid-prescribed individuals with abuse or addiction {7} influences physicians' perception of the risk involved in opioid prescribing {8}, as does the total number of overdose deaths among medical users each year {9}. As physicians perceive higher levels of risk {8} they become increasingly biased toward prescribing short-acting formulations {10}, and their overall rates of opioid prescribing decrease {11}. Because of these balancing feedback loops, the increase in the amount of abuse and addiction {7} is slowed. Physicians' responses to increasing rates of abuse, addiction, and overdose effectively move the model towards a state of dynamic equilibrium.

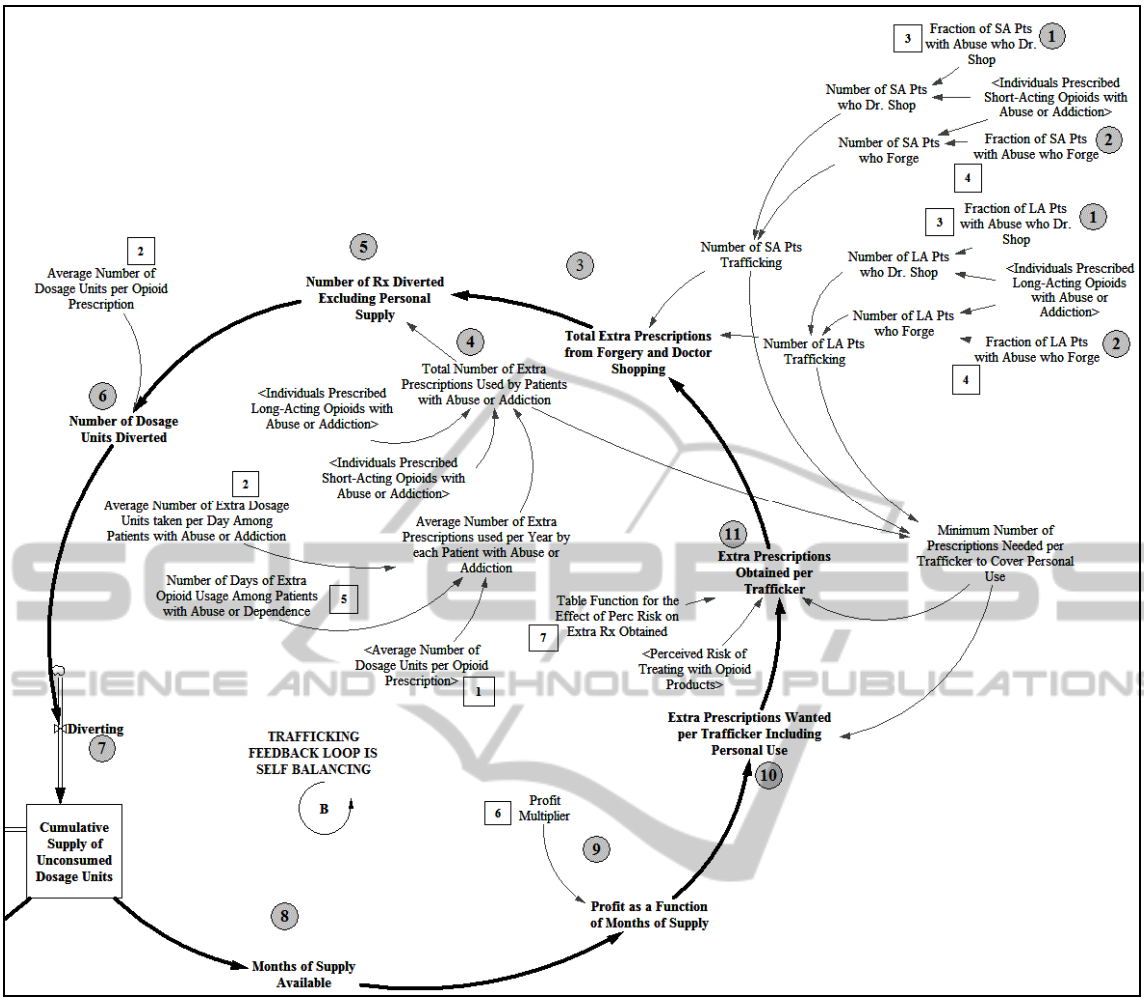


Figure 3: Causal loop diagram of the trafficking sector. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to the model parameters in the Appendix, Table 3.

3.3 Trafficking Sector

Findings from Manchikanti et al. (2006) indicate that 5% of chronic pain patients engage in doctor shopping and around 4% engage in forgery. In the model, forgery and doctor shopping by persons interacting with prescribers are assumed to be exhibited entirely by those with abuse or addiction, which constitute around 7% of individuals receiving opioid prescriptions for chronic pain. This would imply that about 70% of persons with abuse or addiction (5 out of 7) engage in doctor shopping and over half (4 out of 7) engage in forgery. More research is needed to support these parameters and the associated logic.

As shown in Figure 3, a fixed fraction of persons with abuse or addiction are assumed to engage in trafficking each year, including doctor shopping {1} and forgery {2}. The number of extra prescriptions acquired {3} is calculated as a product of (a) the total number of individuals engaging in trafficking and (b) the number of extra prescriptions obtained per trafficker {11}. Some proportion of these excess prescriptions is assumed to be used by the traffickers themselves, rather than diverted to other nonmedical users {4}. This number is calculated as a product of (a) the number of individuals with abuse or addiction and (b) the average number of extra prescriptions used per year by such individuals. The number of prescriptions that are used "in excess" by medical users is subtracted from the number of extra prescriptions acquired. The remainder is converted to dosage units {5} and assumed to be diverted to nonmedical users {6}.

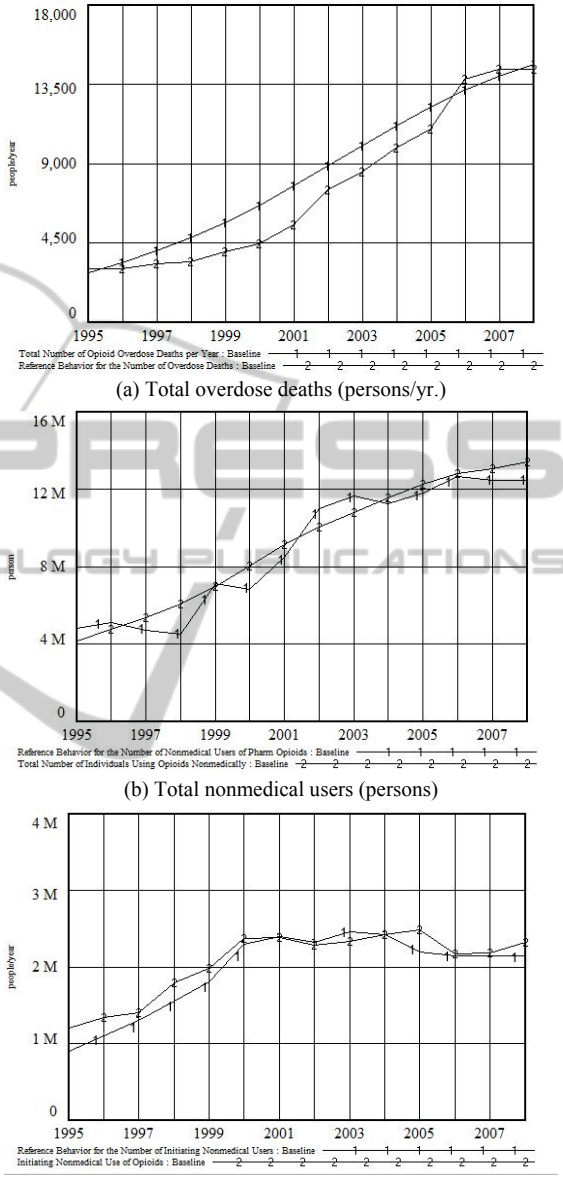
Trafficked opioids accumulate in a stock of dosage units {7} that are consumed according to

demand from the nonmedical use sector. Supply can also be expressed as 'months of supply available' {8}, which indicates the extent to which the trafficked supply is able to meet the demand at any given time. When the supply of opioids becomes limited, a profit motive emerges {9} and motivation to forge and doctor shop increases. When supply is large compared to demand, motivation to commit fraud for the purpose of sale is small. As this motivation fluctuates, the number of extra prescriptions each trafficker would like to obtain {10} also changes. But the number of prescriptions that can be successfully trafficked is attenuated by cautious dispensing when perceived risk is high among physicians and pharmacies {11}, which creates a balancing feedback loop that stabilizes the amount of trafficking.

4 MODEL TESTING

The model was tested in detail to determine its robustness and to gain an overall sense of its validity. As is often the case with system dynamics models, the empirical support for some of the parameters was limited, as indicated in Tables 1-3 in the Appendix. System Dynamics models are generally more credible when their behaviour is not overly sensitive to changes in the parameters that have limited empirical support. Therefore, to determine sensitivity of primary outcomes to changes in parameter values, each parameter in turn was increased by 30% and then decreased by 30%, and the outcome was recorded in terms of cumulative overdose deaths. One parameter with limited empirical support which has a substantial influence on model behaviour is the impact of limited accessibility on the initiation rate. Another parameter, the rate of initiation of nonmedical use, also strongly influenced model behaviour but is less worrisome because it *does* have sufficient empirical support. Because model testing revealed a high degree of sensitivity to certain parameters for which empirical support is limited, study results should be considered exploratory and viewed with caution.

In addition to sensitivity analyses, the model was also carefully checked for dimensional consistency and appropriate integration step-size, subjected to a rigorous model walk through to uncover logical flaws, and subjected to a variety of hypothesis tests. The model walk-through revealed logical flaws that required substantial model revision. Several parameters with a high degree of sensitivity and limited empirical support were replaced, and all tests were re-run. The results of these tests were generally favourable, indicating at least a preliminary degree of model validity.



(a) Total overdose deaths (persons/yr.)

(b) Total nonmedical users (persons)

(c) Total new initiates (persons/yr.)

Figure 4: Model output versus reference behaviour. (a) total prescription opioid overdose deaths per year, (b) total nonmedical users of prescription opioids, (c) total number of individuals initiating nonmedical opioid use per year.

When empirical support was available, model outputs were validated against reference data for the historical period. While this reference period is relatively short, the model does fit the data well, as shown in Figure 4.

Figure 4a shows the number of prescription

opioid overdose deaths from a baseline model run for the historical period overlaid on a plot of the reported number of overdose deaths obtained from the CDC multiple cause of death database.

The total opioid-related deaths resulting from all types of medical and nonmedical use has been reported to be 13,755 in 2006 and approximately 14,000 in 2007. The data suggest that the pattern has been an S-shaped, with modest growth in the late 90s and more rapid growth throughout the early 2000s before levelling off between 2006 and 2007 (Warner, Chen & Makuc, 2009). The baseline model behaviour, also shown in Figure 4a, shows a similar S-shaped growth curve, with the number of opioid overdose deaths calculated to be approximately 13,200 in 2006 and 14,300 in 2007 (R^2 = .90). While additional data are needed to validate these results, the model behaviour does exhibit a preliminary level of credibility for this metric.

Figure 4b shows the total number of individuals using prescription opioids non-medically overlaid on reference data for the historical time period. The graph of historical data is not smooth, but again, the general pattern of growth is S-shaped. The graphical output from a baseline model run is a smooth S-shaped curve that is a good fit for the limited time series data available (R^2 = .95).

Figure 4c gives model output and reference data for the number of individuals initiating nonmedical use of prescription opioids. The reference behaviour pattern here is highly non-linear with the number of initiates more than doubling from 1995 to 2000, then approximately no change between 2000 and 2004, followed by a decrease and levelling from 2004 to 2007. The baseline model run matches the reference behaviour pattern very closely (R^2=.95).

Overall, model results closely track the complex patterns graphs of empirical data despite exhibited. Thus, baseline results were deemed sufficiently plausible to proceed with intervention analysis.

5 RESULTS

To test the intervention, the model time horizon was extended to 2015 and a baseline run was made. The intervention was then formulated and tested.

5.1 Tamper Resistant Formulation

Logic representing the introduction of a tamper resistant drug formulation was added to the model. The model was run over a time period of twenty years, which was divided into an historical period from 1995 to 2008, and an evaluation period from 2008 to 2015. The intervention was represented as simple toggle switch that doubled beneficial parameters and/or halved harmful parameters. The response of the model to this simulated intervention is shown in Figure 5. This intervention of a new drug formulation being introduced in 2008 was implemented as a 50% decrease in: 1) the rate of abuse or addiction among opioid-treated persons, 2) the fraction of low-frequency nonmedical opioid users who become high-frequency users per year, 3) the rate of initiation of nonmedical opioid use, and 4) the perceived risk of opioid abuse amongst prescribers (this increased the prescribing rates for all opioids). Figure 5 shows that this change caused an *increase* in the total number of overdose deaths in the model, due to a sizable increase in deaths among medical users and a small decrease in deaths among nonmedical users. This was not expected. Figure 6 explains why this happened. Subplot (a) shows that the number of individuals receiving treatment increased sharply, and this increase, even when coupled with lower death rates, led to the net increase in the total number of overdose deaths compared to baseline (Figure 5). Figure 6, subplot (b) shows the number of deaths divided by number of individuals receiving opioid treatment (and then divided by 10,000 to yield an indicator in the 0 to 10 range). This indicator, which was beginning to increase as of 2008, declined as a result of the intervention, especially in the nonmedical sector. So, although the fraction of deaths among patients did decrease as anticipated, the rise in patient populations (due to the lower risk perception associated with tamper resistant formulations amongst prescribers) obscured the benefits of the lower death fraction.

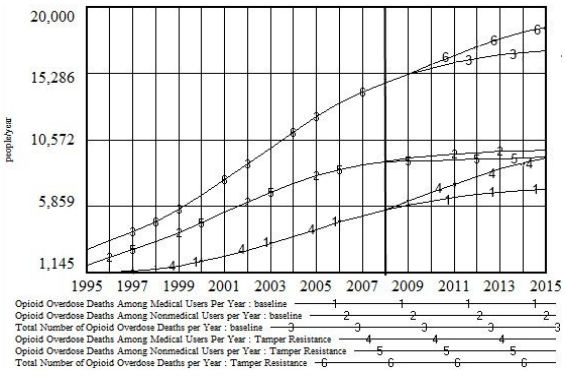
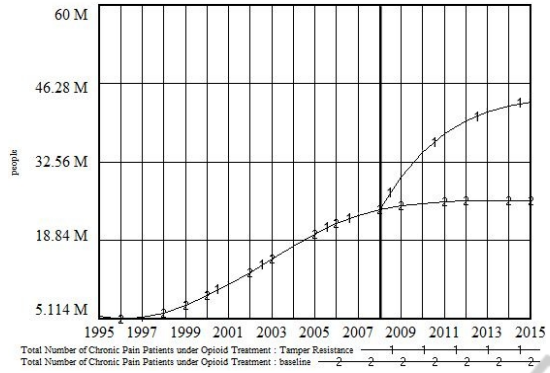
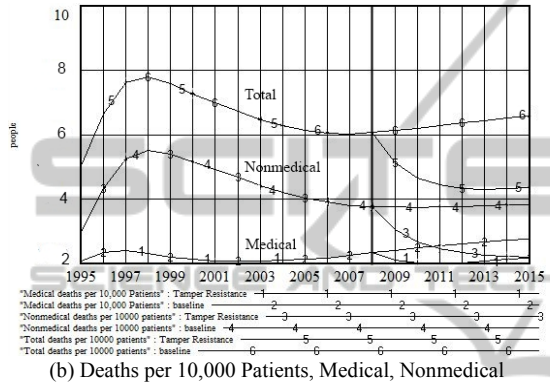


Figure 5: Projected total opioid deaths (top), nonmedical (middle), and medical (bottom). Baseline is shown, plus the impact of a tamper-resistant formulation introduced in 2008.



(a) Total Number of Patients Receiving Opioid Therapy



(b) Deaths per 10,000 Patients, Medical, Nonmedical

Figure 6: A dramatic increase in (a) the number of patients who receive opioids results in a smaller ratio (b) of the overdose deaths divided by the number of patients receiving opioid therapy/10000.

6 DISCUSSION

Results from the model indicate that SD modelling holds promise as a tool for understanding the complex challenges associated with the epidemic of nonmedical use of opioids, and for evaluating the potential impact (on overdose deaths) of interventions to minimize the risks of opioid analgesics. By deliberately exaggerating the direct effects, downstream effects were also accentuated to make as obvious as possible any unintended consequences or counterintuitive results.

Since previous research has indicated that over half of opioid overdose deaths are individuals who have never been prescribed opioids directly (Hall et al., 2008), it is important to consider distal effects of medical sector-related interventions on nonmedical use and overdose deaths. Results of the intervention that simulated the introduction of tamper-resistant formulations also show that it is important to be aware of the metrics used to judge effectiveness. When using the metric deaths per 10,000 treated patients, tamper resistance appears to be effective at reducing the *rate* of overdose deaths as proportion of the medical users.

6.1 Limitations

Tamper resistance is only one possible intervention in the system of opioid misuse. Other interventions not referenced in this article include prescriber and patient education interventions which affect prescribing behavior and the onset of addiction among patients, a prescription monitoring program, which reduces fraud and nonmedical supply, and a popularity intervention which disrupts the vicious cycle of initiation, nonmedical use, and peer pressure that drives up nonmedical use of opioids. Tamper resistance is a pharmaceutical intervention, and as such does not take into account the social forces that influence health behavior or drug use.

Despite great efforts to find empirical support for all model parameters, parameter validity remains a primary limitation in the study (see Wakeland, et al. 2010). Several parameters have weak empirical support, and a number of potentially important factors have been excluded. For example, the model is limited because it focuses on *chronic* pain, and ignores the vastly-larger number of persons who receive opioids to treat acute pain. The prescribing of opioids to treat acute pain accounts for a much larger fraction of the opioids dispensed annually, so it is likely to contribute the supply of opioids for the nonmedical use sector, as well as to physician's perception of risk in the medical use sector.

The model may also be exaggerating the notion of profit as a motive for trafficking. Since the fraction of demand met by interpersonal sharing is large, it may be necessary to model this mechanism in a more detailed fashion.

Additionally, poly-drug use and abuse, opioid treatment programs, alternative treatments, and institutional factors that impact opioid use, such as payer policies and formularies, can all influence rates of medical and nonmedical use of opioids and the outcomes associated with such use. The exclusion of these factors imposes limitations on the model's ability to provide conclusive inferences.

7 CONCLUSIONS

The principal strength of this study is its system-level perspective and deliberate recognition of the complex interconnections and feedback loops associated with the use of opioids to treat pain and

the associated adverse outcomes. From a systems perspective it is clear that interventions focused on prescribing behaviour can have implications beyond the medical aspects of the system, and that a multifaceted approach which also addresses illicit use is warranted. The present study serves well to demonstrate how a systems-level model may help to evaluate the relative potential efficacy of interventions to reduce opioid-related overdose deaths.

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APPENDIX

Table 1: References of support for model parameters in the nonmedical use sector.

	Parameter	Value	Support
1	Base Level of Abuse Potential of Opioids	1.3	Panel Consensus
2	Fraction of Demand Met from Chronic Pain Trafficking	.25	Extrapolation from NSDUH (SAMHSA, 2007)
3	Fraction of Low-Freq Users who switch to High-Freq	0.06	Extrapolated from MTF data (Johnston et al., 2007) and results (Mack et al., 2003)
4	High-Frequency User All-Cause Mortality Rate	0.02	Extrapolated from heroin research findings (WHO; Degenhard et al., 2004; Hser et al., 2001)
5	High-Frequency User Cessation Rate	0.08	Imputation from NSDUH SAMHSA 2009b)
6	Low-Frequency User All-Cause Mortality Rate	0.012	Extrapolated from (Rehm et al., 2005)
7	Low-Frequency User Cessation Rate	0.15	Imputation from NSDUH data (SAMHSA 2009b)
8	Number of Days of Nonmedical Use Among High-Freq Users	220	Extrapolation from NSDUH 2007 results (Lee et al., 2010)
9	Nbr. of Days of Nonmedical Use Among Low-Freq Users	30	Extrapolated from NSDUH 2007 (Lee et al., 2010)
10	Number of Dosage Units Taken per Day	2	Modeling Team Judgment, reviewed by Panel
11	Overdose Mortality Rate for High-Freq Nonmedical Users	0.002	Extrapolated from Fisher et al., 2004; Warner et al., 2009; Warner-Smith et al., 2000
12	Overdose Mortality Rate for Low-Freq Nonmedical Users	0.0002	Extrapolated from Fisher et al., 2004; Warner et al., 2009; Warner-Smith et al., 2000
13	Rate of Initiation of Nonmedical Opioid Use	0.006	Imputed from NDUHS (SAMHSA, 1996)
14	Table Function for the Impact of Limited Accessibility on Initiation and Increasing Use	[(0,0)-(5,2)]	Modeling Team Judgment, reviewed by Panel
15	Table Function for the Number of Individuals Using Illicit Drugs Excluding Marijuana and Opioids	6.7M to 8.6M	Calculated from NSDUH 2006 results (SAMHSA, 2007)
16	US Population Ages 12 and Older	211M to 357M	Imputed from NSDUH (SAMHSA, 1996, 2002)

Table 2: References of support for model parameters in the medical sector.

	Parameter	Value	Support
1	All-Cause Mortality Rate for those receiving Long-acting Opioids	0.012	US Population mortality data, adjusted by panel consensus
2	All-Cause Mortality Rate for those receiving Short-acting Opioids	0.01	US Population mortality data, adjusted by panel consensus
3	All-Cause Mortality Rate for those with Abuse/Addiction	0.015	US Population mortality data, adjusted by panel consensus
4	Average Long-acting Treatment Duration	7 yrs.	Panel Consensus
5	Average Short-acting Treatment Duration	5 yrs.	Panel Consensus
6	Base Level of Abuse Potential for Opioids	1.3	Modeling Team Judgment, reviewed by Panel
7	Base Rate for Adding or Switching (to Long-acting)	0.03	Extrapolation from outcome data: Verispan, LLC, SDI Vector One®: National (Governale, 2008a)
8	Base Rate of Treatment	.05 to .23	Panel Consensus, informed by Potter et al., 2001
9	Base Risk Factor (degree Tx reduced in 1995 due to perceived risk)	1.3	Modeling Team Judgment, reviewed by panel
10	Diagnosis Rate for Chronic Pain	.05 to .15	Panel Consensus & Gureje et al., 2001
11	Overdose Mortality Rate if Abusing Opioids	0.0015	Extrapolation from Heroin data (Sullivan, 2007)
12	Overdose Mortality Rate if on Long-acting	0.0025	CONSORT study (Potter et al., 2001)
13	Overdose Mortality Rate if on Short-acting	0.00005	CONSORT study (Potter et al., 2001)
14	Rate of Addiction for those on Long-acting	0.05	Meta-Analyses (Dunn et al., 2010; Højsted & Sjøgren, 2007)
15	Rate of Addiction for those on Short-acting	0.02	VISN16 data (Fishbain et al., 2008)
16	Table Function[1] for Short-acting Bias (as function of perceived risk)	[(1,0)-(4,1)]	Modeling Team Judgment, reviewed by panel
17	Tamper Resistance (baseline value)	1	Policy variable (1=status quo)

Table 3: References of support for model parameters in the trafficking sector.

	Parameter	Value	Support
1	Avg. Nbr. of Dosage Units Per Opioid Prescription	86	Extrapolation from VONA (Governale, 2008)
2	Avg. Nbr. of Extra Dosage Units taken per Day Among those with Abuse or Addiction	1.5	Panel Consensus
3	Fract. of Abuse/Addicted who Engage in Dr Shopping	.5	Extrapolated from (Manchikanti et al., 2006)
4	Fraction of Abuse/Addiction who Engage in Forgery	.4	Extrapolated from (Manchikanti et al., 2006)
5	Number of Days of Extra Opioid Usage Among those with Abuse/Addiction	50	Generalized from NSDUH 2002, 2003, & 2004 (Table 2.18B in Colliver et al., 2006)
6	Profit Multiplier	15	Modeling team judgment
7	Table Function for the Effect of Rec Risk on Extra Rx Obtained	[(0,0) – (2,1)]	Modeling team judgment