10-2013

Modeling the Impact of Simulated Educational Interventions on the Use and Abuse of Pharmaceutical Opioids in the United States: A Report on Initial Efforts

Wayne Wakeland
Portland State University, wakeland@pdx.edu

Alexandra E. Nielsen
Portland State University, alexan3@pdx.edu

Teresa D. Schmidt
Portland State University

Dennis McCarty
Oregon Health & Science University

Lynn Webster
LifeTree Medical

See next page for additional authors

Citation Details

Wakeland, W., Nielsen, A., Schmidt, T. D., McCarty, D., Webster, L. R., Fitzgerald, J., & Haddox, J. D. (2013). Modeling the impact of simulated educational interventions on the use and abuse of pharmaceutical opioids in the United States: a report on initial efforts. Health Education & Behavior, 40(1_suppl), 74S-86S.

Authors
Wayne Wakeland, Alexandra E. Nielsen, Teresa D. Schmidt, Dennis McCarty, Lynn Webster, John Fitzgerald, and J. David Haddox

Modeling the Impact of Simulated Educational Interventions on the Use and Abuse of Pharmaceutical Opioids in the United States: A Report on Initial Efforts

Wayne Wakeland, PhD[1], **Alexandra Nielsen, BS**[1], **Teresa Schmidt, MA**[1], **Dennis McCarty, PhD**[2], **Lynn Webster, MD**[3], **John Fitzgerald, PhD**[4], and **J. David Haddox, DDS, MD**[4]

[1]Portland State University, Portland, OR, USA

[2]Oregon Health and Sciences University, Portland, OR, USA

[3]LifeSource Foundation, Salt Lake City, UT, USA

[4]Purdue Pharma LP, Stamford, CT, USA

Abstract

Three educational interventions were simulated in a system dynamics model of the medical use, trafficking, and nonmedical use of pharmaceutical opioids. The study relied on secondary data obtained in the literature for the period of 1995 to 2008 as well as expert panel recommendations regarding model parameters and structure. The behavior of the resulting systems-level model was tested for fit against reference behavior data. After the base model was tested, logic to represent three educational interventions was added and the impact of each intervention on simulated overdose deaths was evaluated over a 7-year evaluation period, 2008 to 2015. Principal findings were that a prescriber education intervention not only reduced total overdose deaths in the model but also reduced the total number of persons who receive opioid analgesic therapy, medical user education not only reduced overdose deaths among medical users but also resulted in increased deaths from nonmedical use, and a "popularity" intervention sharply reduced overdose deaths among nonmedical users while having no effect on medical use. System dynamics modeling shows promise for evaluating potential interventions to ameliorate the adverse outcomes associated with the complex system surrounding the use of opioid analgesics to treat pain.

Keywords

alcohol and substance abuse; dynamic modeling; modeling and simulation; nonlinear dynamics; substance use; systems science

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Corresponding Author: Alexandra Nielsen, Portland State University, PO Box 751, Portland, OR 97207-0751, USA. alexan3@pdx.edu.

Declaration of Conflicting Interests
The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: In the 12 months prior to May 1, 2013, Lynn Webster has served either as a consultant, on the advisory board, or has received honoraria from the following organizations: AstraZeneca, Covidien Mallinckrodt, CVS, Jazz Pharmaceuticals, Medtronic, Nektar Therapeutics, Neura Therapeutics, and Theravance. No formal restrictions were placed on research or communication of findings; however, prior to submission for publication, the manuscript was reviewed by a Purdue Pharma L.P. review committee, and minor nonsubstantive changes were made to the manuscript to improve flow and sharpen the vocabulary.

A dramatic rise in the nonmedical use of pharmaceutical opioids has presented the United States with a substantial public health problem (Compton & Volkow, 2006). Despite the increasing prevalence of negative outcomes, such as fatal and nonfatal overdoses, nonmedical use of pharmaceutical opioids remains largely unabated by current policies and regulations (Fishman, Papazian, Gonzalez, Riches, & Gilson, 2004). Resistance to policy interventions likely stems from the complexity of the medical and nonmedical use of pharmaceutical opioids, as interactions among prescribers, pharmacists, persons obtaining opioids for medical or nonmedical use, opioid traffickers, and public health advocates result in chains of causal relationships and instances of information feedback in the system.

This article presents a system dynamics (SD) model of the U.S. opioid-related complex system. This model is designed to foster a more complete understanding of how medical use, trafficking, and nonmedical use are interrelated, and to identify points of high leverage for educational interventions on the epidemic of nonmedical use. Three potential interventions are simulated, relative costs and benefits are estimated, and possible counterintuitive downstream effects are high-lighted. The term *opioids* is used to mean pharmaceutically manufactured opioid (morphine-like) medicines, most of which are indicated for use as analgesics, and does not include heroin or other illicit opioid drug substances.

Background

The number of U.S. unintentional fatal poisonings involving opioid analgesics tripled between 1999 and 2006 (Warner, Chen, Makuc, Anderson, & Miniño, 2011; see Figure 1), increasing more than fivefold among those aged 15 to 24 years (Warner, Chen, & Makuc, 2009). Diversion of opioids is assumed to be a major source of supply for nonmedical use. Among those survey respondents to the 2010-2011 National Surveys of Drug Use and Health (NSDUH) who received opioids for free from friends or relatives, about 82% reported that their source had originally received the drugs from one doctor (Substance Abuse and Mental Health Services Administration [SAMHSA], 2012). Recent increases in opioid prescribing stem in part from increases in the diagnosis and recognition of the need to treat chronic noncancer pain. Data from NHANES (Hardt, Jacobsen, Goldberg, Nickel, & Buchwald, 2008) support an estimate of 29 million Americans aged 20 years or older with chronic pain in the period 1999-2002. Opioid treatment for chronic, noncancer pain is not without controversy (Collett, 2001), but opioids have been found to be more effective at ameliorating pain than alternative medications (see Furlan, Sandoval, Mailis-Gagnon, & Tunks, 2006, for a review), and their prescription and medical use have become increasingly common over the last decade (Governale, 2007, 2008a, 2008b).

In July 2012, the Food and Drug Administration (FDA) approved a shared Risk Evaluation and Mitigation Strategy (REMS) for all Extended-Release and Long-Acting (herein-after “long-acting”) opioid analgesics (FDA, 2012). Unfortunately, nonmedical use of pharmaceutical opioids has tended to resist policy and regulation (Fishman et al., 2004), and the effectiveness of many REMS interventions (e.g., medication guides and prescriber training) remains inconclusive at this time (see Chou, Ballantyne, Fanciullo, Fine, &

Miaskowski, 2009, for a review). Tools are needed to assess intervention alternatives for their capacity to balance the benefits and risks of opioids in the United States. Policy makers, striving to ameliorate the adverse outcomes associated with opioid analgesics, could benefit from a systemslevel model that reflects the complexity of the system and that incorporates the full range of available data.

An SD Simulation Model

The current work features an SD simulation model that represents the fundamental dynamics of opioids as they are prescribed, unlawfully trafficked, used nonmedically, and involved in overdose mortality. SD modeling uses a set of differential equations that are integrated numerically to simulate system behavior over time. This allows researchers to incorporate information on various factors into a single model that represents behaviors at a system level.

SD models have been successfully applied to analysis of a number of public health issues, including tobacco (Cavana & Tobias, 2008), cocaine (Homer, 1993), diabetes treatment (Jones et al., 2006), and health care reform (Milstein, Homer, & Hirsch, 2010). The approach is well-suited to health policy analyses involving complex chains of influence (Sterman, 2006), as these often involve feedback loops and nonlinear relationships that are beyond the capabilities of statistical models. The approach is especially useful for identifying points of leverage for intervention and for indicating potential negative consequences of those interventions (Sterman, 2000). This provides policy makers with information that is not available from research focused on individual aspects of a system (Sterman, 2006).

The current SD model was developed over a 2-year period through collaborative efforts of a modeling team and a panel of experts in policy and the use/abuse of opioid analgesics. This model complements and leverages results from an extensive amount of research on the use and abuse of pharmaceutical opioids in the United States. Much of the current body of knowledge regarding the interrelated public health problems of medical and nonmedical use of opioid analgesics is based on surveys and inferential statistics. Because of limitations of the surveys and differences in their methods, caution is required when defining populations of interest and relationships between variables, especially variables that are similar but not exactly the same across surveys. Guidance was often provided by the expert panel in reconciling apparent differences between sources and making assumptions about how causal relationships would be best represented in the model.

Dynamics of the Opioid System

The system model estimates overdose fatalities in which opioid analgesics were involved based on the dynamics of medical treatment with opioids, initiation and prevalence of nonmedical usage, and drug trafficking supply and demand. Discussion of each sector includes a table of empirical support, a narrative of the model’s behavior, and a diagram depicting model structure. Verbal descriptions contain bracketed numbers that 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.

Medical Use Sector

Diagnostic criteria from *DSM-IV* have been used to differentiate persons who engage in problematic substance use according to whether or not they meet the mutually exclusive specific criteria for either *opioid abuse* or *opioid dependence*—the latter referred to by many as *addiction* (American Psychiatric Association, 1994). Historically, increases in opioid abuse and addiction have led to the implementation of regulatory policies for opioids (FDA, 2008). These have been shown to lead many physicians to avoid prescribing opioids out of fear of overzealous regulatory scrutiny (Joranson, Gilson, Dahl, & Haddox, 2002) and may also lead them to decrease the amount of opioids they prescribe, limit quantities and refills, and shift prescribing to opioid analgesic drug products with a presumably lower risk of abuse, addiction, or overdose (Wolfert, Gilson, Dahl & Cleary, 2010). Specifically, physicians have been found to exhibit more caution in prescribing long-acting opioid analgesics (Potter et al., 2001), due to greater concerns about the development of physical dependence, tolerance, and addiction, and because most of them are classified in the most restrictive schedule defined in the federal Controlled Substances Act. (See Table 1 for additional empirical support for the medical use sector.)

As illustrated in Figure 2, the system model assumes that a proportion of the U.S. 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 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 some 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 individuals with abuse or addiction {7} influences physicians’ perception of the risk involved in opioid prescribing {8}, as does the total number of accidental overdose deaths involving opioid analgesics 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}. This response slows the amount of abuse, addiction, and overdoses {7}, which tends to stabilize the medical use sector of the model.

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. (See Table 2 for additional empirical support.) As shown in Figure 3, a fixed proportion of the persons with abuse or addiction are assumed to engage in trafficking each year, including doctor shopping {1} and forgery {2} of prescriptions for long-acting and/or short-acting medications. The number of extra prescriptions acquired {3} is assumed to be a product of the total number of individuals engaging in trafficking and the number of extra prescriptions obtained per trafficker {11}. Some proportion of these excess prescriptions is assumed to be kept by the traffickers themselves rather than transferred to others {4}. The amount kept for personal use is a product of the number of traffickers with abuse or addiction and the average number of extra prescriptions used per year by them. The number of prescriptions used by the trafficker is then subtracted from the number of extra prescriptions acquired. The remainder is converted to dosage units {5}, representing opioid drug products dispensed from pharmacies from the fraudulently obtained prescriptions, and 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. The “months of supply available” {8} indicates the extent to which the trafficked supply is able to meet the trafficking-oriented demand. When the trafficked supply of opioids becomes limited, an increased profit motive emerges {9} and motivation to forge prescriptions and doctor shop increases. When supply is large compared with demand, the opposite is true. As this motivation fluctuates, the number of extra prescriptions each trafficker would like to obtain {10} also changes. But the number of trafficked prescriptions that can be successfully redeemed for opioid drug products is attenuated by cautious dispensing when perceived risk is high among physicians and pharmacies {11}, which tends to stabilize the amount of trafficking.

Nonmedical Use Sector

Around 12% to 14% of individuals who use opioids nonmedically meet the criteria for abuse or dependence (Colliver, Kroutil Dai, & Gfroerer, 2006), and statistical analysis of the full NSDUH (2009) data set indicated that respondents with abuse or dependence reported a median frequency of opioid usage during the past year 38 times greater than respondents without abuse or dependence. Extrapolation from heroin findings indicates that higher-frequency opioid use is associated with a significantly higher all-cause mortality rate (WHO; see Degenhardt, Hall, Warner-Smith, & Lynskey, 2004; Hser, Hoffman, Grella, & Anglis, 2001) and supports a distinction between two subpopulations of nonmedical users (low and high frequency) in this sector of the model. (See Table 3 for additional empirical support for this sector.)

As illustrated in Figure 4, within the model a percentage of the U.S. population {1} initiates nonmedical use each year {2}, all of whom start out in a stock of “low-frequency nonmedical users,” and a small percentage of whom then 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 United States 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 acting on its own would result in an exponential increase in the rate of initiation.

Nonmedically used opioids are obtained through a variety of routes, but of chief interest for the current research is the prevalence of opioid “trafficking” (i.e., buying or selling) via persons who are receiving these products ostensibly for treatment. Results from the 2006 NSDUH survey (SAMHSA, 2007) indicate that 75% of the nonmedical demand for opioids is met via interpersonal sharing or theft from friends or relatives. The remaining 25% represents the demand met by trafficking {8}. The focus on trafficking in the model reflects the emphasis in the medical sector on prescribing for chronic pain, and the assumption that chronic pain medicines are less likely to be left over or shared.

In the model, demand for opioids (long- and short-acting) is calculated from the number of individuals in low- and high-frequency populations {7}. When the trafficking supply {8} is ample relative to demand, the rate of initiation {2} and the rate of advancement from low-frequency to high-frequency use {3} is somewhat enhanced. However, when the 25% of opioids for nonmedical use supplied by trafficking is limited (or even negative), rates of initiation and advancement decrease appreciably. 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. This decreases initiation and advancement and this balancing loop offsets the exponential increase in nonmedical use driven by the popularity feedback loop.

Model Testing

The model was tested in detail to determine its robustness and ability to endogenously match simulated data against historical data (refer to Sterman, 2000, for a list of standard tests for confidence). Model outputs were compared with reference data for the historical period (1995 to 2008) where these data were available, as shown in Figure 5. Overall, simulated results were consistent with the empirical reference data despite the complex patterns exhibited, and baseline results were considered sufficiently plausible to proceed with exploratory analysis.

Results

To illustrate the potential for evaluating interventions, logic representing three possible interventions was added to the model to calculate their relative potential impacts on the number of opioid overdose deaths in the United States. The model was run over a time period of 20 years, which was divided into a historical period—1995 to 2008—and an evaluation period—2008 to 2015. All interventions were represented as simple toggles, with exaggerated impacts that demonstrate the model's relative response at multiple points of leverage.

Prescriber Intervention

The implementation of a prescriber education program was simulated by doubling prescriber perception of risk and reducing rates of addiction by half. Given a simulated education intervention, prescribers perceived opioid prescribing as twice as risky and were twice as effective in monitoring patients for signs of abuse. The increased risk caused prescribers to treat half as many chronic pain patients with opioids and to be doubly biased toward prescribing short-acting formulations. Their increased effectiveness in monitoring treatment also resulted in a 50% reduction in the number of patients who developed abuse or addiction.

The prescriber intervention simulation caused a marked decrease in the number of overdose deaths among medical users in the model (see Figure 6B), as wary prescribers offered opioid therapy to fewer individuals. Nonmedical overdose deaths also decreased, as there were fewer individuals with abuse or addiction who could engage in trafficking and increased difficulty in obtaining fraudulent prescriptions. Constraining the trafficked supply reduced the number of nonmedical users and nonmedical overdose deaths. However, this intervention also resulted in a denial of therapeutic treatment to individuals with legitimate chronic pain complaints.

Medical User Intervention

This intervention simulated a patient-level education program that halved the rate at which medical users with chronic pain developed abuse or addiction. In contrast to the prescriber intervention, this simulation maintained the baseline level of prescriber risk perception. Not surprisingly, this caused a decrease in the number of medical user deaths (see Figure 6C). However, because the number of deaths among nonmedical users continued to grow, the reduction in deaths among medical users was not enough to prevent an overall increasing trend in overdose deaths in the model.

The increasing trend in the number of nonmedical users stemmed from the vicious cycle of opioid popularity. An immediate cut in the fraction of individuals developing opioid abuse or addiction caused the perception of opioid risk to drop. In a climate of lower risk, prescribers became less cautious and prescriptions were easier to obtain by fraudulent means. This small rise in fraudulent supply available through traffickers permitted a slight increase in the number of nonmedical users. And because of the self-reinforcing nature of the popularity feedback loop, this slight increase led to a noticeable increase in nonmedical use and overdose deaths in the nonmedical sector.

Popularity Intervention

The popularity intervention simulated an education program targeted at nonmedical users that halved the rate of initiation and also the level of perceived popularity of opioids for nonmedical use. Sharply reducing initiation and perceived popularity caused a substantial reduction in the number of overdose deaths in the model (see Figure 6D). Once the user populations declined, the self-reinforcing nature of popularity worked in a *virtuous* cycle of decreased use and decreased popularity. This further reduced rates of nonmedical use and overdose deaths in the nonmedical use sector.

Discussion

Results indicate that SD modeling holds promise as a tool for understanding the phenomena contributing to the nonmedical use of opioids and for evaluating the potential impact of educational interventions on the epidemic of overdose deaths in which pharmaceutical opioids are reported. By deliberately exaggerating the direct effects of three potential options, downstream effects were accentuated to allow for direct comparison of alternatives and to make obvious any possible unintended consequences or counterintuitive results.

Results of the interventions suggest that prescriber-level education initiatives, such as promotion of careful screenings of patients who receive opioid therapy (Fishbain et al., 2008), may be a more effective way to reduce abuse, addiction, and unintentional overdose deaths than patient-level education initiatives. Surprisingly, reducing the rate of abuse or addiction among medical users resulted in *more* overdose deaths, because, in the model, lower rates of abuse and addiction led to lower perception of risk among prescribers, more prescribing, and ultimately more trafficking to nonmedical users.

However, restrictions at the prescriber level suggest that more chronic pain sufferers would also be denied potentially beneficial therapy. By intervening at the level of the medical user, the number of overdose deaths decreased in the medical sector without denying any additional patients treatment. It is possible that a medical user intervention could be amplified with additional efforts to reduce diversion to the nonmedical sector, but among the interventions tested in this study, it appears that patient education interventions may be less effective at reducing overdose deaths in the United States.

The popularity intervention, which directly targeted the nonmedical use sector, was found to be the most powerful point of leverage in reducing deaths among nonmedical users; and research indicates that more than half of opioid overdose deaths are suffered by individuals who have never been prescribed opioids directly (Hall et al., 2008). This intervention would likely have the greatest impact on adolescents and young adults, populations with the greatest rates of nonmedical use (SAMHSA, 2012). However, it is also important to consider the distal impacts of interventions in the medical sector on the nonmedical sector. The prescriber intervention indirectly limited the supply of opioids available for nonmedical use and resulted in the largest reduction in overdose deaths among the three interventions compared.

Limitations

Despite great efforts to find empirical support for all model parameters, parameter validity remains a primary limitation in the study (Wakeland et al., 2010). Several parameters have weak empirical support, and a number of potentially important factors have been excluded, often because evidence to support them remains elusive. For example, the trafficking sector focuses solely on trafficking as a mode of diversion, even though a large fraction of nonmedical use demand is met by interpersonal sharing among friends and relatives. There is very limited empirical evidence on interpersonal sharing, but because of its importance this mechanism would ideally be included in a more detailed fashion. Additional detail on opioid trafficking would also be ideal, as it is currently assumed that only individuals with chronic pain who also abuse or are addicted to opioids engage in trafficking, and that the number of traffickers is stable with changes in supply and demand. There are no reliable data on how many individuals masquerade as pain patients so as to acquire medicine for illicit resale, but anecdotally, some individuals are merely engaged in a criminal enterprise and have no interest in abusing the drugs they buy and sell.

Some additional boundary exclusions include polydrug use and abuse, and the use of substitute substances such as heroin. Without modeling the larger system of nonmedical and illicit use of substances, we are not able to explore the impact of drug switching or polydrug abuse on unintentional overdose deaths in the United States. Opioid treatment programs, alternative treatments, and secular factors—such as payer policies and formularies—are also likely to influence rates of medical and nonmedical use of opioids and the outcomes associated with such use, but were not included in the current model.

Finally, the model focuses exclusively on prescribing and diversion of opioids for the treatment of chronic noncancer pain, without representing the vastly larger number of persons who receive them for acute pain. Chronic pain was of primary interest in the current model because policy interventions that restrict opioid prescribing may have an especially large impact on individuals with long-term pain conditions. However, a larger fraction of the opioids dispensed annually are prescribed to treat acute pain conditions and contribute to the supply of opioids for nonmedical use as well as to physicians' perception of risk in prescribing.

Conclusion

Work is underway to address many of the above limitations, but limitations notwithstanding, the present study serves well to demonstrate how a systems-level model can inform interventions on the nonmedical use of pharmaceutical opioids. It is hoped that the insights achieved by this initial application will demonstrate the value of applying an SD approach to this important public health concern. From a systems perspective, it is clear that interventions focused on prescribing and dispensing behavior can have implications beyond the medical aspects of the system, and it appears likely that a multifaceted approach addressing licit as well as illicit use is warranted.

This initial effort is meant to stimulate the creation of additional models that address the above limitations and that simulate policy interventions more directly tied to those currently under discussion. However, the basic structure of the medical, trafficking, and nonmedical sectors is expected to remain relevant as REMS are implemented and as the policy landscape around this public health area continues to shift. The SD approach allows for analysis of various points of intervention and for evaluation of alternative policies that aim to ameliorate the negative outcomes associated with nonmedical use of pharmaceutical opioids in the United States.

Acknowledgments

The authors appreciate the significant contributions from Jack Homer, PhD, who critiqued the technical aspects of the SD model; Lewis Lee, MS, who developed the primary model logic and located much of the needed data; Louis Macovsky, DVM, who created an initial prototype model and helped locate data sources; and Aaron Gilson, PhD, who provided valuable insight.

Funding

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Wayne Wakeland, Teresa Schmidt, Dennis McCarty, Alexandra Nielsen, and Lynn Webster were compensated through a research grant to Portland State University funded by Purdue Pharma, L.P. J. David Haddox and John Fitzgerald are full-time employees of Purdue Pharma, L.P. Purdue Pharma manufactures opioid products. The manuscript takes as its focus opioid use, diversion, and nonmedical use; however, no mention is made of specific opioid products whether produced by Purdue Pharma or its competitors. Additional support was provided from National Institute on Drug Abuse Grant Number 5R21DA031361-02.

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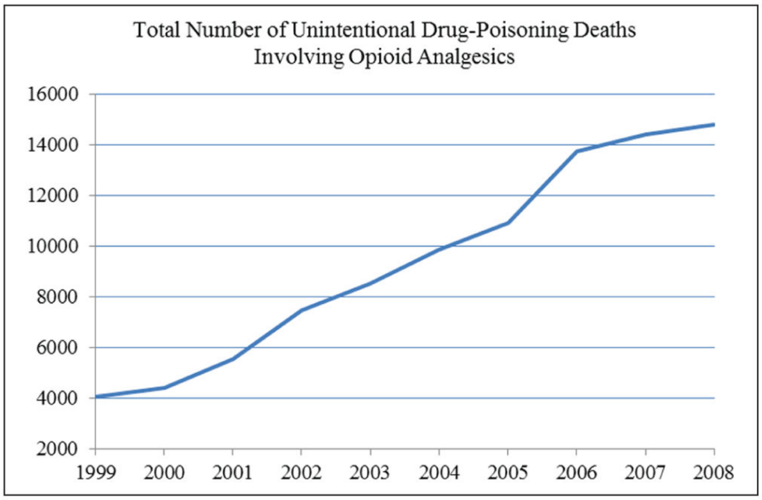

Figure 1.
Escalation of unintentional drug-poisoning deaths in the United States from 1999 to 2008
Source. Warner (2011).

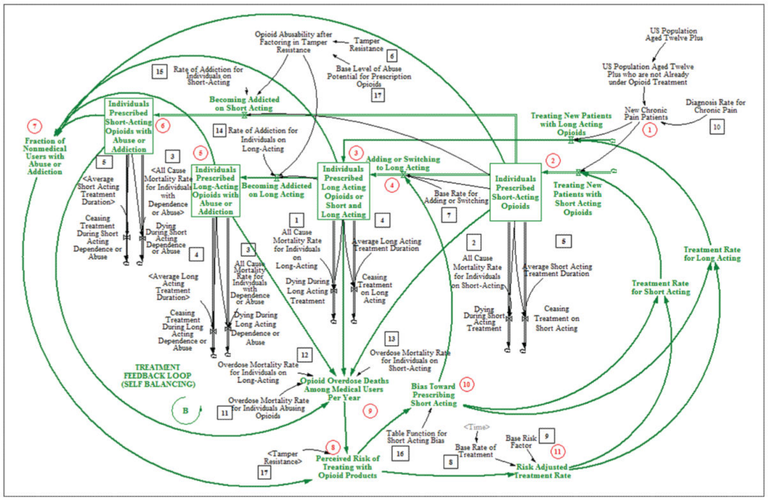

Figure 2.

Stock and flow diagram of the Medical Use Sector.

Note. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to model parameters in Table 1.

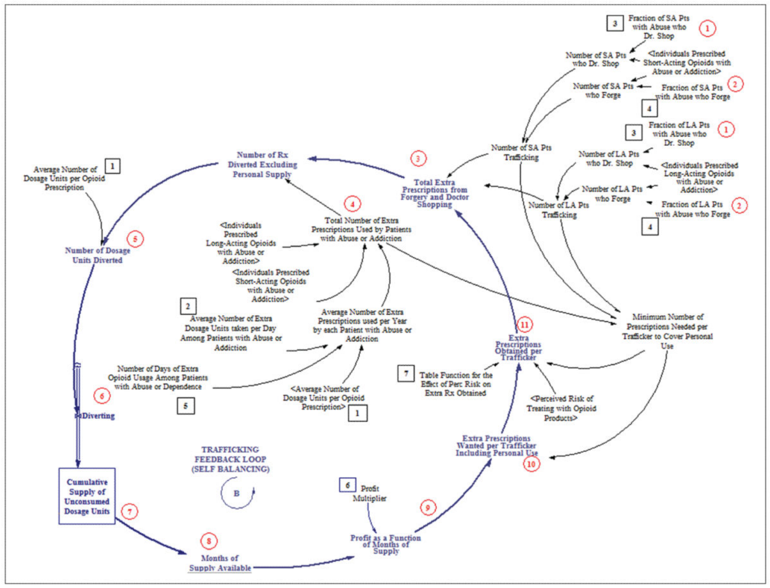

Figure 3.

Stock and flow diagram of the Trafficking Sector.

Note. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to model parameters in Table 2.

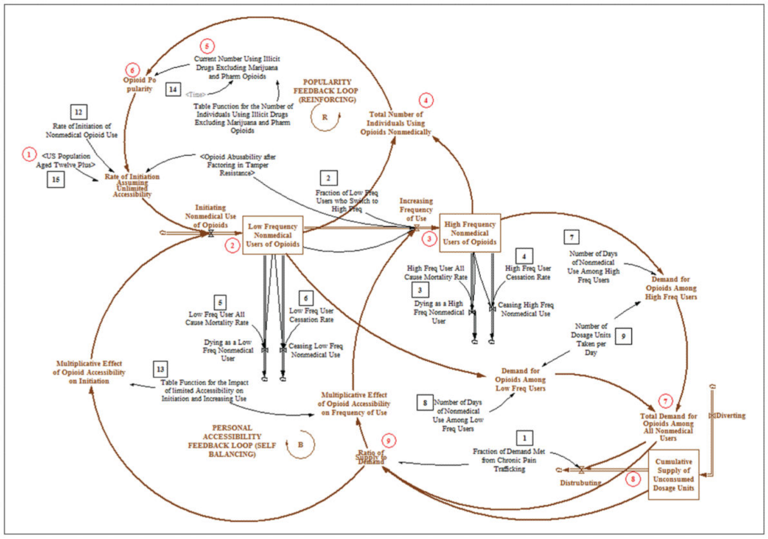

Figure 4.

Stock and flow diagram of the Nonmedical Use Sector.

Note. Circled numbers correspond to bracketed notations in the text. Numbers in boxes correspond to model parameters in Table 3.

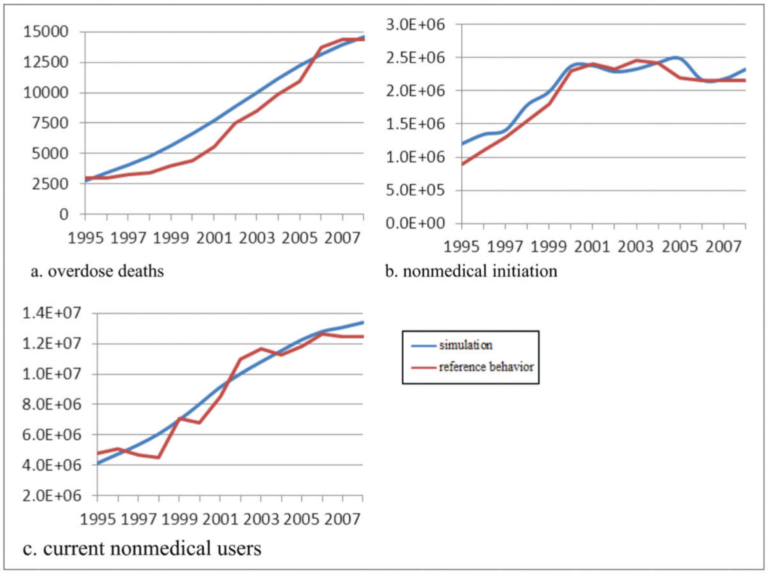

Figure 5.

Model output versus reference behavior.

Note. From top left, clockwise: (a) total prescription opioid overdose deaths per year (Mean Absolute Percentage Error [MAPE] 22%), (b) total nonmedical users of prescription opioids (MAPE 9.1%), (c) total number of individuals initiating nonmedical opioid use per year (MAPE 9.9%). For discussion on MAPE as a metric of model fitness, see Sterman (2000).

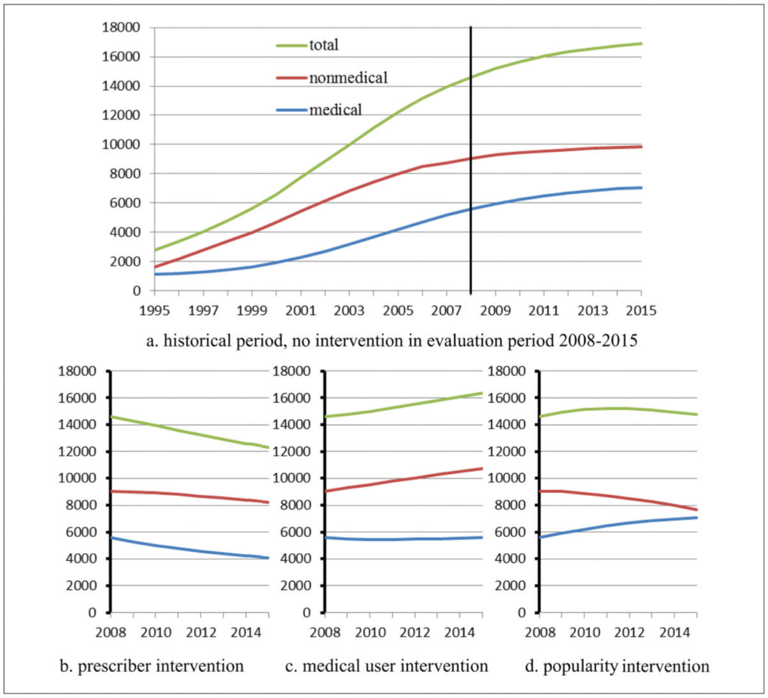

Figure 6.

Effect of simulated interventions on total opioid overdose deaths, overdose deaths among nonmedical users, and medical users.

Note. Baseline results (A) are shown for the historical period and evaluation period. Intervention results (B, C, D) are shown only for the evaluation period.

Table 1

References of Support for Model Parameters in the Medical Use Sector.

	Parameters (Enumerated) and Reference Data	Value	Support
1, 2	All-cause mortality rate for those receiving long-acting and short-acting opioids	0.012; 0.01	U.S. population mortality data, adjusted by panel consensus
3	All-cause mortality rate for those with abuse/addiction	0.015	U.S. population mortality data, adjusted by panel consensus
4, 5	Average long- and short-acting treatment duration (in years)	7; 5	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 (VONA; see Governale, 2008a)
8	Table function[a] for base rate of treatment	From 0.05 in 1995 to 0.23 in 2005	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	Table function[a] for diagnosis rate for chronic pain	From 0.05 in 1995 to 0.15 in 2005	Panel consensus, informed by WHO (World Health Organization; see Gureje, Simon, & Von Korff, 2001)
11	Overdose mortality rate for those abusing opioids	0.0015	Extrapolation from heroin research (see Sullivan, 2007)
12	Overdose mortality rate for those on long- and short-acting	0.0025; 0.00005	CONSORT study (Consortium to Study Opioid Risks and Trends; see Potter et al., 2001)
14	Rate of addiction for those on long- and short-acting	0.05	Meta-analyses (see Dunn et al., 2010; Højsted & Sjøgren, 2007)
15	Rate of addiction for those on short-acting	0.02	VISN16 data (South Central Veterans Affairs Health Care Network; see Fishbain, Cole, Lewis, Rosomoff, & Rosomoff, 2008)
16	Table function[a] for short-acting bias (as function of perceived risk)	From (1,0) to (4,1)	Modeling team judgment, reviewed by panel
17	Tamper Resistance (baseline value)	1	Policy variable (1 = status quo)
	Physicians' fear of overzealous regulatory scrutiny when prescribing opioids		Joranson et al. (2002)
	Physicians' decrease in opioid prescribing after regulation		Wolfert et al. (2010)
	Higher rate of abuse among long-acting than short-acting opioids		Cicero, Suratt, Inciardi, and Munoz (2007)
	Physicians' tendency to exhibit more caution in prescribing long-acting than short-acting opioids		Potter et al. (2001)

[a]A Table Function is a series of *XY* coordinates representing a relationship (usually nonlinear) between two variables; initial and final values given above.

Table 2

References of Support for Model Parameters in the Trafficking Sector.

Parameter	Value	Support
1. Average number of dosage units per opioid prescription	86	Extrapolation from dispensing data: Verispan, LLC, SDI Vector One®: National (VONA; see Governale, 2008a, 2008b)
2. Average number of extra dosage units taken per day among those with abuse or addiction	1.5	Panel consensus
3. Fraction of those with abuse/addict who engage in Dr shopping	0.5	Extrapolation from study results (Manchikanti et al., 2006)
4. Fraction of those with abuse/addict who engage in forgery	0.4	Extrapolation from study results (Manchikanti et al., 2006)
5. Number of days of extra opioid usage among those with abuse/addiction	50	Generalized from NSDUH data (National Survey on Drug Use and Health 2002, 2003, & 2004; see Table 2.18B in Colliver et al., 2006)
6. Profit multiplier	15	Modeling team judgment
7. Table function[a] for the effect of perceived risk on extra Rx obtained	From (0,0) to (2,1)	Modeling team judgment

[a]A Table Function is a series of XY coordinates representing a relationship (usually nonlinear) between two variables; initial and final values given above.

Table 3

References of Support for Model Parameters in the Nonmedical Use Sector.

	Parameters (Enumerated) and Reference Data	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 2006 results (SAMHSA, 2007)
3	Fraction of low- frequency users who switch to high- frequency	0.06	Extrapolation from MTF data (Monitoring the Future; see Johnston, O'Malley, Bachman, & Schulenberg, 2007) and results (Mack & Frances, 2003)
4, 5	Low- and high-frequency user all-cause mortality rate	0.012; 0.02	Extrapolation from heroin research findings (WHO; see Degenhard et al., 2004; Hser et al., 2001; Rehm et al., 2005)
6, 7	Low- and high-frequency user cessation rate	0.15; 0.08	Imputation from NSDUH data (National Survey on Drug Use and Health, 2007; see SAMHSA 2009)
8, 9	Number of days of nonmedical use among low- and high-frequency users	30; 220	Extrapolation from NSDUH 2007 results (Lee et al., 2010)
10	Number of dosage units taken per day of nonmedical use	2	Modeling Team Judgment, reviewed by Panel
11, 12	Overdose mortality rate for low- and high-frequency nonmedical users	0.0002; 0.002	Extrapolation from research findings (Fischer et al., 2004; Warner et al., 2009; Warner-Smith, Lynskey, Darke, & Hall, 2000)
13	Rate of initiation of nonmedical opioid use	0.006	Imputed from National Drug Use and Health Survey Data (NSDUH, 1995; see SAMHSA, 1996)
14	Table function[a] for the impact of limited accessibility on initiation and increasing use	From (0,0) to (5,2)	Modeling Team Judgment, reviewed by Panel
15	Table function[a] for the number of individuals using illicit drugs excluding marijuana and opioids	From 6.7M in 1995 to 8.6M in 2009	Calculated from NSDUH 2006 results, see SAMHSA (2007)
16	Table function[a] for US population ages 12 and older, as a function of time	From 211M in 1995 to 357M in 2007	Imputed from NSDUH data (National Survey on Drug Use and Health 1995, 2002; see SAMHSA, 1996, 2002)
	Proportion of nonmedical users who meet the *DSM-IV* criteria for abuse or dependence	12% to 14%	American Psychiatric Association (1994), Colliver et al. (2006)

[a]A Table Function is a series of XY coordinates representing a relationship (usually nonlinear) between two variables; initial and final values given above.