Dynamic Simulation of the Effect of Tamper Resistance on Opioid Misuse Outcomes

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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 the a tamper resistance intervention 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 behavior of the resulting systems-level model compared favorably with reference behavior data. After the base model was tested, logic to simulate the replacement of all opioids with tamper resistant formulations was added and the impact on overdose deaths was evaluated over a seven-year period, 2008-2015. Principal findings were that the introduction of tamper resistant formulations 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 with opioids.

Keywords: Prescription Drug Abuse, System Dynamics Modeling, Opioid Analgesics, Public Health.

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 [6]. 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 [8]. 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 US.

Complex social systems are well known to resist to policy interventions, often resulting in unintended consequences or unanticipated sources of impedance [24]. These undesirable outcomes can result from our inability to simultaneously consider a

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large number of interconnected variables, feedback mechanisms, and complex chains of causation [10]. 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 behaviors 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 behaviors [19,14].

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.

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.

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 [26]–signaling the onset of a major public health concern. Overdose deaths involving opioid analgesics have outnumbered cocaine and heroin overdoses since 2001 [3], 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 [23]. Earlier data from NSDUH suggest that the rate of initiating nonmedical usage increased drastically from 1994 to 1999 [21], and has continued at high rates, with over 2 million individuals reporting the initiation of nonmedical use of pain relievers in 2009 [23]. 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 [15,20,28]. To combat this trend in abuse, many manufacturers are developing or have already developed opioid formulations that use a physical barrier to resist tampering, or a mix of pharmacologically active ingredients that deter abuse [16]. Post-marketing studies have been conducted on tamper resistant opioids currently on the market that imply lower abuse rates (e.g. [1] for OxyContin), but the long term effects of large scale adoption of tamper resistant opioids on the treatment of pain and opioid abuse are still unknown.