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Modeling opioid addiction treatment policies using system dynamics

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Abstract: Treatment of opioid addiction has historically employed an opioid drug called Methadone that is dispensed in liquid form at treatment facilities. Drawbacks to this treatment include social stigma and relatively high risk due to the pharmacological properties of methadone and also its side effects. A newer therapy uses another opioid drug called Buprenorphine, which is safer and has less social stigma because it can be prescribed and dispensed in tablet form. Policy makers have been cautious, however, and have placed a cap on the number of patients that a physician can treat using Buprenorphine, leading to a concern that even though it is safer, people seeking treatment might not be able to locate a physician and access the treatment because of the cap. An SD model was developed to represent the flows of opioid abusers into and out of treatment with Buprenorphine, as well as the number of physicians certified to treat with Buprenorphine. Treatment is constrained by the cap and also by the amount of budget available for subsidizing treatment. The main finding is the treatment budget is by far the most influential policy variable, and that changing the cap would probably not make much difference.

Introduction

This paper describes policy concerns related to drug abuse and drug treatment. The motivation for the research came from a conversation with an official at the Office of National Drug Control Policy (ONDCP) regarding the treatment of opioid addiction using a drug called Buprenorphine (BUP). Currently, physicians licensed to prescribe and support this treatment who have been treating patients with BUP for at least a year can treat up to a maximum (cap) of 100 patients. The official was concerned that this limit might be adversely impacting the ability of people seeking treatment to find a doctor, and she wondered how difficult it would be to estimate the likely impact of raising this limit. Given the dynamics at play, and based on our research on related aspects of drug diversion and nonmedical use (Nielsen & Wakeland, 2012) we suspected that the system dynamics method might be a good fit for such analysis.

Treating opioid addiction has historically been done in a treatment facility setting using a drug called methadone that is dispensed to patients in liquid form because Methadone can be a tricky due to its pharmacological properties and possible respiratory side effects. BUP is a newer treatment that is considered to be safer than Methadone, and is more desirable because it is prescribed and dispensed in tablet form like most other drug therapies.

To study the possible impact of the cap a model is needed which includes the number of opioid abusers receiving BUP therapy, and those not receiving therapy, the number of treatment physicians, and other relevant factors.

Background material is provided next, followed by a description of the model, a brief section on model testing, a section describing a very preliminary use of the model to study policy alternatives, and discussion.

Background

Opiate addiction, a chronic relapsing condition, is a socially and personally injurious public health problem that affects thousands of Americans each year. The Office of National Drug Control Policy estimates that there were 841,000 chronic users of heroin in 2006, and that the number of chronic users was relatively stable, though declining, since 2000 (ONDCP, 2012). At the same time, prescription pain reliever abuse saw a dramatic rise in the 1990s (SAMHSA, 2006), and has stabilized at high rates in the 2000s (SAMHSA, 2012). The National Survey of Drug Use and Health estimates that in 2011, 4.47 million people used prescription opioid (opium-like) pain killers in the last month and that 1.37 million of these users meet the American Psychological Association diagnostic criteria for opioid dependence (SAMHSA, 2012). Chronic heroin users as a group spent an estimated \$10.6 billion on heroin in 2006 (ONDCP, 2012), and untreated heroin use carries with it an estimated social cost of \$21.9 billion (Mark, Woody, Juday, & Kleber, 2001).

There are many treatment options for opiate addicts including detoxification, residential and outpatient rehabilitation programs, antagonist therapy, and agonist therapy. Antagonist therapy involves the use of an opioid antagonist medication such as naltrexone which blocks the effect of an opiate in the brain. Agonist therapy, sometimes called maintenance therapy, involves the managed and supervised use of a different opioid substance to manage opiate cravings and withdrawal. Agonist therapy has consistently been shown to be more effective than no-medication therapy or placebo in retaining clients in treatment and reducing opiate use (see Amato et al., 2005 for a meta-analysis). Retention in treatment is an important metric because relapse after loss of tolerance due to detoxification results in an increased likelihood of opiate overdose and death (Warner-Smith, Darke, Lynskey, & Hall, 2001). Agonist therapy has also

been shown to reduce mortality, HIV risk behavior, levels of crime, and when considering social cost gives more health gain at less cost than no-medication treatment (Connock et al., 2007) due in part to reduced use of emergency services and hospitalization (Clark, Samnaliev, Baxter, & Leung, 2011). Unfortunately, less than 20% of opioid users receive agonist therapy (Fiellin & O'Connor, 2002), which has led the NIH to view expanding access to agonist therapy as a national public health priority (Barry et al., 2009).

Currently the most widely used agonist therapy in the United States is methadone maintenance therapy (MMT). MMT is highly effective, but is problematic in several respects. While methadone can be prescribed in an office based setting for the treatment of pain, methadone for the treatment of opiate dependence can only be administered through hospitals or federal and state approved opioid replacement substance abuse treatment programs (Arfken, Johanson, Di Menza, & Schuster, 2010). Drug dealers and others engaged in drug are known to target vulnerable people in and around methadone clinics (Hunt, Lipton, Goldsmith, & Strug, 1984; Inciardi, Surratt, Kurtz, & Cicero, 2007; Join Together Staff, 2002). Participation in a methadone program carries a social stigma (Barnett, Rodgers, & Bloch, 2002) as the most problematic clients are the most visible, while compliant successful patients often hide their program participation from family and friends (Stancliff, Elana Myers, Steiner, & Drucker, 2002). Mandatory dosing within a clinic has a high time cost and is seen as inconvenient (Barnett, Rodgers, et al., 2002; Stancliff et al., 2002). Many Medicaid programs don't cover MMT, and in 2001 MMT was prohibited in eight states (Barnett, Zaric, & Brandeau, 2002), and, where it is available, there may not be enough clinic openings to meet demand (Stancliff et al., 2002).

In addition to social barriers associated with MMT, methadone itself may also be problematic in some respects. Methadone is a full opioid agonist, which means it works like other opiates in the brain. Use of full agonists for maintenance has some advantages. Induction onto therapy is relatively simple and can begin even when other opioids are present in one's system (Saxon, 2012). However, full agonists can lead to feelings of euphoria, and while some in drug-assisted therapy feel that they need some euphoric feeling to stay in treatment, others feel that one addiction is simply being substituted for another (McKenzie, Nunn, Zaller, Bazazi, & Rich, 2009). Another problem with MMT is the fact that the respiratory depression effects of methadone use can outlast the pain control or euphoric effects, which can result in overdose when people seek greater euphoria or pain control. Further, tolerance to respiratory depression develops more slowly than tolerance to euphoria or pain control, so the risk of overdose is high (Webster, 2005).

Buprenorphine (BUP) maintenance treatment (BMT) is a newer opioid agonist therapy that does not have the same barriers to treatment as MMT. BUP is a partial opioid agonist with a good safety profile, and lower abuse liability than methadone, meaning that there is less euphoric effect and less chance of physical dependence (Mello & Mendelson, 1985; Walsh & Eissenberg, 2003). Because of how it works in the brain, BUP is unlikely to be used in combination with full agonists like heroin because it can force immediate withdrawal (Auriacombe, Fatséas, Dubernet, Daulouède, & Tignol, 2010), or block the effects of the full agonist (Clark et al., 2011). BUP also has a ceiling effect meaning that once a certain dose is reached there is no increased effect on the body—including respiratory depression—with increased dosage (Barnett, Rodgers, et al., 2002). Like methadone, it only needs to be taken once a day, or even every other day for the management of opioid addiction (Mattick et al., 2003). Many studies compare the

effectiveness of BUP and methadone maintenance therapy, and while retention in treatment tends to be better in MMT, BMT has been found to equal MMT in suppression of heroin use (Connock et al., 2007; Mattick et al., 2003), and has been shown to result in lower mean annual spending per patient than MMT (Barnett, 2009; Clark et al., 2011).

Because of its safety profile and lower abuse liability, BUP is the only drug approved for the treatment of addiction in an office setting. BMT has been shown to be equally effective when administered in a clinic or in a primary care setting (Connock et al., 2007), and BUP can be dispensed once a week or once every three weeks with once weekly counseling with the same retention in treatment and reduction in opiate use (Fiellin et al., 2006). Obtaining treatment from a doctor has several advantages over obtaining treatment at an addiction treatment program including the following: absence of stigma (Brady, Verduin, & Tolliver, 2007; Nunn et al., 2009), concomitant monitoring of chronic health conditions that accompany opioid dependence (Barry et al., 2009), reduced travel costs and increased scheduling flexibility (Clark et al., 2011), and potentially less exposure to drug dealer and diverters at clinic sites. While patients who require greater structure or who desire the subjective effects of methadone can be transitioned onto MMT, this flexibility can be beneficial for some patients (Saxon, 2012).

BUP has a lower abuse liability than methadone, but is still potentially abusable and can be diverted to non-patients. Nonmedical use of BUP in other countries has led to cautious regulatory policy that seeks to limit diversion through supply control, and also to the development of an abuse deterrent formulation of BUP combined with naloxone which inhibits the euphoric effects of opioids in 2002 (Arfken et al., 2010). The US Drug Addiction Treatment Act of 2000 (DATA) allowed BUP (a schedule III drug approved for the treatment of opioid addiction) to be prescribed in office-based settings, but also limited the number of patients that

could be treated by a group practice to 30, and mandated certification with at least 8 hours of training in BUP administration (Arfken et al., 2010). In 2006 the 30 patient limit was per practice was changed to a 30 patient limit per prescriber, and in 2007 the 30 patient limit could be raised to 100 patients after a year (Arfken et al., 2010). Relaxation in regulatory requirements has led to expanded BMT capacity, diversification of specialists offering therapy (Arfken et al., 2010), and an expansion of total treatment capacity—MMT and BMT (Clark et al., 2011).

In addition to the treatment cap, which has been identified by some doctors as a barrier to offering BMT, the following barriers have also been identified: physician or practice concerns—poor fit with current practice, disinterest, low demand, logistic concerns, insufficient institutional or nursing support, lack of experience; patient concerns—difficult patients, psychiatric comorbidities, compliance problems, challenges of induction; payment concerns—lack of insurance coverage, reimbursement concerns, high cost of drugs, and Medicaid restrictions (Barry et al., 2009; Clark et al., 2011; Stanton, McLeod, Luckey, Kissin, & Sonnefeld, 2006; Walley et al., 2008). However, the challenges that have the greatest impact on ability to offer treatment in high demand areas are cost, induction concerns, and treatment caps (Stanton et al., 2006).

A System Dynamics Model

An initial model was created based almost entirely on the comments made by the ONDCP official. The main theme of the model was that treatment was being limited by the cap placed on the number of patients each physician can treat. That model showed interesting results, so the literature was reviewed to find relevant structural information and data. This research revealed major flaws in the initial model, which turned out to be overly complex regarding patient dynamics and unrealistic regarding physician dynamics. Significant revisions

were made. Figure 1 shows the current model, which remains very preliminary and not fully tested.

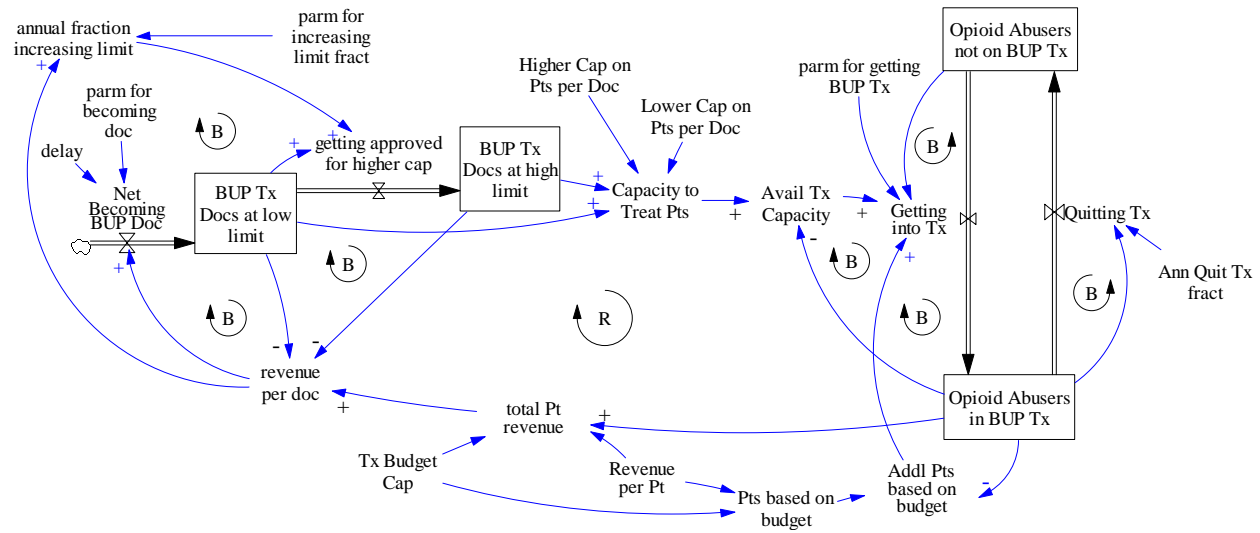


Figure 1. Causal Loop & Flow Diagram

The model assumes a relatively stable population of opioid abusers (pharmaceutical and illicit), which is supported by data from (Substance Abuse and Mental Health Services Administration, 2012) and (Office of National Drug Control Policy, 2012)

All but one of the feedback loops in the model is balancing, and several of the balancing loops are short in length. Although technically there are three balancing loops that involve the variable “revenue per doc” these loops work together essentially as a single loop, such that when “revenue per doc” increases, more physicians choose to become certified to treat with BUP and a larger fraction of those who are limited [initially] to only a small number of patients apply to be certified to treat a larger number of patients. As the number of BUP physicians increases, “revenue per doc” decreases.

The loop in the center of the diagram is reinforcing because as the number of BUP physicians increases and more physicians are certified to treat more patients, the capacity to treat increases, which allows more patients to be treated, which increases revenue and, therefore, “revenue per doc.” Increased “revenue per doc” encourages more physicians to become BUP physicians.

One of the treatment-related balancing loops includes a variable called “available treatment capacity,” which is the “total treatment capacity” minus the current number of people in treatment. If available capacity increases, the rate at which people get into treatment increases. But as more people enter the treatment stock, the available capacity is reduced. The next treatment-related balancing loop involves the variable “Add'l Pts based on budget,” which indicates the degree to which treatment is limited financially. The flow “Getting into Tx” uses the minimum of “Avail Tx Capacity” and “Add'l Pts based on budget” to determine the flow into the treatment stock.

The other two balancing loops reflect the fact that as the two opioid abuser population stocks change, their respective outflows change proportionally.

The model was initialized based on available data for the initial values for the stocks. The number of people in BUP Tx in 2004 is interpolated from (Stanton et al., 2006), and the number of BUP docs in 2004 is inferred from (Arfken et al., 2010). Data for key parameter values were also inferred from the literature, such as the “quitting tx fraction” (Alford et al., 2007)). Three parameters which do not have empirical support (see Table 1) were imputed by adjusting their values so that the model was able to replicate the behavior over time for the

number of people in treatment, and the number of physicians in the two physician stocks. Table 1 shows these equations and the associated parameter values.

Table 1. Key Model Tuning Parameters

Variable	Equation	Parameter	Parameter Value
Getting into Tx	Opioid Abusers not on BUP Tx*MIN(Avail Tx Capacity, Addl Pts based on budget)*parm for getting BUP Tx	parm for getting BUP Tx	6e-7
Net Becoming BUP Doc	DELAY(revenue per doc^2/parm for becoming doc, delay, 3000)	parm for becoming doc	5e5
annual fraction increasing limit	0+STEP(revenue per doc/parm for increasing limit fract,2006)	parm for increasing limit fract	3e5

The equation for Getting into Tx is similar to an epidemic model where the product of two large populations (drug abusers and treatment physicians, in this case) is multiplied by a very small parameter to determine the flow from untreated to treated. The equation for “Net Becoming BUP Doc” is based on the Revenue per doc, which is squared (to reflect a nonlinear relationship) and then divided by a large parameter to normalize the result. The result of this calculation is then delayed (by a year) to allow time for training and to become registered. The equation for “annual fraction increasing limit” starts at 0 at time 2004 because the higher limit was not made legal until 2006 ((Arfken et al., 2010). From 2006 on, the fraction is specified as revenue per doc divided by a large number, yielding a number near 20%.

By using the parameter values shown in Table 1, the model-calculated figures for the number of BUP patients and BUP docs in 2008 were very close to the figures report in (Stanton et al., 2006) and (Arfken et al., 2010).

Model Testing

The model has not yet been thoroughly tested via sensitivity analysis, extreme value testing, hypothesis testing, prediction testing, etc. When the model is deemed ready, the number of BUP docs and patients in 2010, for which we have not yet located the data, will be predicted. We are confident that we will be able to then locate this information and determine if the model's predictions are close to the actual or not. Model testing will be completed well before the conference.

Preliminary Use of the Model to Study Policy Alternatives

Despite the lack of proper testing, in order to determine if the model might be useful as a policy analysis tool, the model was used to estimate future values of the key variables, with surprising results. A key assumption motivating the research was that the current cap of 100 was limiting access and that a policy change might be warranted. The model results were not consistent with this assumption. Instead, the model suggested that physicians would likely continue to become certified to offer BUP treatment, and therefore treatment capacity would continue to increase until a majority of opioid abusers were being treated with BUP. Of course, this is not at all realistic because various other limits would no doubt be reached long before a majority of opioid abusers would be in treatment. For example, the amount of medicine that would be required might not be available, or the number possible physicians might be limited in ways not captured in the model.

In fact, one of the obvious limits to achieving the dramatic levels of treatment shown by the model is the amount of budget (government subsidies, such as Medicaid and the Veteran's Administration) available to help pay for treatment. This idea was already partially embodied in

the model, but some of the necessary logic to fully reflect this limit had not been implemented. Specifically, while the limit in physician treatment capacity was fully reflected, budget to pay for treatment was implicitly assumed to always be available. When the model logic was revised to reflect the plausible effect of budget limitations for treatment, it was clear that treatment budget is likely to be far more important as a policy lever than the cap on the number of patients that each physician can treat.

Experiments with an overall budget cap, the patients per doc cap, and the amount of reimbursement per patient under treatment, both separately and in combination, showed that far and away the most important factor for increasing treatment is the overall budget cap. As currently calibrated, the model suggests that increasing the cap on the number of “patients per doc” would not have a significant effect.

Increasing the reimbursement per patient without increasing the budget would have two disadvantageous outcomes. Immediately, there would be less money for new patients to gain access to treatment and the number people in treatment would begin to decline significantly and the system would find a new and lower steady state. Second, the number of BUP docs increases temporarily, much to their long-term disadvantage. The reason is that prior to this increase, the budget cap had not been reached, so by increasing the revenue per patient, revenue per doc would increase immediately. But this would cause the treatment budget cap to also be reached immediately, which, as mentioned above, would dramatically reduce the inflow of new patients into treatment. Less patients in treatment and more BUP docs would cause the revenue per doc to decline sharply.

Finally, increasing the reimbursement per patient, along with a corresponding increase in the treatment budget cap, did not change the number of patients in treatment, but the number of BUP docs increased, and consequently, the revenue per doc, while significantly larger than the baseline figure, was somewhat less than when only the treatment budget cap was increased.

Discussion

The results appear to be largely consistent with the literature, which indicates that the vast majority of physicians have never had to turn away a potential BUP patient because of the cap, but does note that reimbursement is a barrier to physicians (Arfken et al., 2010). Policy changes that increase the budget for treatment would likely have the most immediate and most direct impact on the number of people being treated. Increasing reimbursement per patient could have an adverse impact unless it is accompanied by a corresponding increase in the overall treatment budget/subsidy. Increasing the cap on the number of patients that can be treated per physician may not have much impact.

The present model has many limitations, not the least of which is the fact that it has not been validated in any way. Many simplifying assumptions were made, including the assumption that once a physician becomes certified to treat with BUP, they remain a BUP physician indefinitely. There is some support for this assumption (Arfken et al., 2010), as long as the time horizon over which the model is run is measured in years and not decades. Many of the factors which might influence a person to seek treatment or not seek treatment are not reflected in the model. The parameter used for ceasing treatment is supported by a citation from the literature (Alford et al., 2007), but the evidence regarding treatment cessation is highly variable, since

people tend to cease treatment after a while and then resume treatment again later. A more definitive analysis of the data is needed.

Next steps include additional model revisions, as needed, including possible changes in scope, locating additional empirical support, and thorough model testing once it is deemed warranted. In particular, a blind prediction test will be performed. If confidence in the model warrants further policy analysis, such analysis will be performed and documented, including potential implementation scenarios.

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