

ORIGINAL RESEARCH

OxyContin, prescription opioid abuse and economic medicalization

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Faculty of Business Administration, Simon Fraser University, Vancouver, BC, Canada **Abstract:** This paper examines the relevance of OxyContin diversion and abuse to the economic medicalization of substance abuse and addiction. Given that medicalization is the general social process of nonmedical problems being transformed into medical problems, economic medicalization occurs where the motivation for the transformation is commercial profitability or, in a corporate context, achieving the objective of shareholder wealth maximization. After considering potential conflicts between medical ethics and business ethics, practical aspects of economic medicalization are detailed by considering the methods used to market OxyContin by Purdue Pharma. Illegal practices are identified and contrasted with legal practices that facilitated economic medicalization. Implications of medicalization research for designing public heath solutions to the epidemic of prescription opioid abuse are discussed.

Keywords: medicalization, OxyContin, prescription drug abuse, medical ethics

Introduction

OxyContin is a controlled-released version of the opioid oxycodone, a Schedule II controlled substance under the Controlled Substances Act in the US. Having received FDA approval in 1995 for the management of chronic pain, the aggressive marketing campaign pursued by Purdue Pharma resulted in an increase in sales from \$44 million and 316,000 prescriptions in 1996 to a combined total of nearly \$3 billion and 14 million prescriptions in 2001 and 2002. By 2001, OxyContin had become "... the most prescribed brand-name narcotic medication for treating moderate-to-severe pain." By 2003, the societal implications of OxyContin abuse had become so severe that the US House of Representatives requested the Government Accounting Office (GAO) investigate and prepare a report on OxyContin abuse and diversion.³ While the GAO report did identify the aggressive marketing tactics by Purdue Pharma, the report only went so far as to recommend that the FDA ensure that "... risk management plan guidance encourages pharmaceutical manufacturers that submit new drug applications for these substances to include plans that contain a strategy for monitoring the use of these drugs and identifying potential abuse and diversion problems."2

Despite sidestepping direct Congressional action, the marketing tactics used by Purdue Pharma did not escape the attention of the US Justice Department. "Misrepresenting the risk of addiction proved costly for Purdue. On May 10, 2007, Purdue Frederick and Company Inc, an affiliate of Purdue Pharma, along with 3 company executives, pled guilty to criminal charges of misbranding OxyContin by claiming that it was less addictive and less subject to abuse and diversion then other opiods." The outcome of

Correspondence: Geoffrey Poitras Faculty of Business Administration, Simon Fraser University, 8888 University Drive, Burnaby, BC V5A 1S6, Canada Tel +778 782 4071 Fax +778 782 4920 Email poitras@sfu.ca United States of America vs the Purdue Fredrick Company Inc et al (WD Va, May 10, 2007, Case 1: 07CR00029) was the imposition of a \$634 million penalty. In addition to criminal actions, Purdue was involved in a variety of civil lawsuits claiming aggressive and deceptive marketing tactics used by Purdue contributed to addictions and overdose deaths. On balance, the promotion and marketing of OxyContin by Purdue Pharma has been correctly described as a "commercial triumph" and "public health tragedy." This begs the question: does the marketing of OxyContin by Purdue Pharma represent a compelling illustration of economic medicalization? Further detailed examination is required.

Given that medicalization is the general social process of nonmedical problems being transformed into medical problems, economic medicalization occurs where the motivation for the transformation is commercial profitability or in a corporate context achieving the objective of shareholder wealth maximization (SWM). Recognizing the remarkable technological and economic evolution of the medical profession in the last two decades, various studies find that medicalization is too diverse a concept to be analyzed with a unifying methodology.4-7 As a consequence, it is useful to dichotomize the concept of medicalization into two distinct components: economic medicalization, where the commercial profit motive plays a central role; and social medicalization, where traditional concerns of social control predominate. Poitras^{8,9} and Poitras and Meredith⁴ demonstrate that economic medicalization involves a sharp ethical divergence between the goal of SWM, associated with business ethics, and the norms of science and the scientific method, associated with medical ethics.

The following section details the development of the concept of medicalization, from the early contributions by Szasz and Wootton in the 1950s and continuing up to recent contributions by Conrad⁵ and Moloney et al. ¹⁰ The dichotomization of the medicalization concept into economic medicalization and social medicalization is discussed. The third section of this paper examines general differences between medical ethics, as detailed by the American Medical Association (AMA), and business ethics, as reflected in the objective of corporate SWM.11 The relevance of OxyContin abuse and diversion for the loosely defined subject of bioethics is also considered. The fourth section details the economic medicalization of addiction and substance abuse. Attention focuses on contrasting legal and illegal methods used in the direct-tophysician marketing campaign of Purdue Pharma, including the use of "prescriber profile" databases and a bonus system to encourage sales representatives to target physicians with

high rates of opioid prescription. Detailing illegal elements in the Purdue promotional campaign for OxyContin also reveals legal practices that sustain the economic medicalization process. The fifth section considers whether currently observable trends in medicalization have been adequately addressed in public health plans to tackle the epidemic of prescription opioid abuse in the US.¹² Finally, the sixth section provides some Socratic conclusions.

The concept of medicalization

The modern concept of medicalization emerged during the 1950s, when Thomas Szasz, Barbara Wootton, and others attacked the advance of psychiatry beyond the treatment of well-defined mental disorders into areas of dysfunctional behavior related to crime and delinquency. 13-16 These seminal contributions built on Parsons'17 initial identification of medicine as an institution of social control. Following Szasz and Wootton, "science" was replacing traditional areas of social morality as the means of distinguishing the "undeniably mad" from those "who are simply unable to manage their lives". 18 The distinction between "mentally incompetent" and "sinful" needs to be determined by social values. Allowing "medical science" to encroach on this decision shifts attention to the individual rather than the environment as the source of the problem. As Wootton observes: "Always it is easier to put up a clinic than to pull down a slum."13 While insightful, the early contributions by Szasz and Wootton only examined the narrow confines of psychiatry where the social implications of medicalization were readily discernible. The extension of these initial notions to a wider field of applications was proposed by Freidson and Zola during the 1970s, where the connection between medicalization and social control was more firmly established. 19,20

In traditional sociology, where social control is a central concept, the connection between social control and medicalization is appealing. The observation that medicine had "nudged aside" or "replaced" religion as the dominant moral force in the social control of modern societies was a central theme in medicalization research surveyed in the influential review by Conrad.²¹ However, the lack of cohesion in this research is reflected in the considerable effort Conrad dedicates to the search for a precise definition of "medicalization." Driven by the remarkable evolution of the medical profession in the last two decades, it is becoming gradually apparent that the medicalization concept is too diverse to be analyzed with a unifying methodology.^{4,5,7,22} In particular, considerable insight is gained if medicalization is dichotomized into two categories: social medicalization,

dealing with the type of social control issues that originate with Parsons, Szasz, and Wootton; and economic medicalization, dealing with the markets for medical technology and professional services driven by the corporate profit motive.

Defining medicalization as a process where more and more aspects of everyday life come under medical dominion, influence, and supervision ultimately requires "the turning of non-medical problems into medical ones."22 Medicalization can occur for various reasons. Drawing a distinction between economic and social medicalization focuses attention on the ethical motives of the medical professionals involved in the process. Social medicalization is concerned with encroachment of the medical profession into areas traditionally controlled by other professions, such as the legal profession for deviant behavior, eg, drug abuse, or the ecclesiastic profession for reproductive decisions. This often leads to a sociological examination of issues surrounding the competition of the professions for social control. While the profit motive may play some role, the complexity of issues surrounding the ethics of the marketplace is not a central concern. In contrast, economic medicalization encompasses cases where the profit motive plays a substantive role in the transformation of nonmedical problems into medical ones. In particular, Healy identifies economic medicalization with the "marketing of disease."23

Numerous instances of economic medicalization have been identified. For example, Conrad and Leiter⁷ examine the direct-to-consumer marketing campaigns by pharmaceutical companies and the development of private medical markets. Conrad⁵ finds evidence of economic medicalization in numerous cases, such as male disorders associated with aging, including andropause, baldness, and erectile dysfunction; behavioral disorders such as attention deficit/hyperactivity disorder in adults and hyperactivity in children; and certain applications of biomedical enhancement drugs, such as steroids and human growth hormone. Moloney et al¹⁰ examine the economic medicalization of sleeplessness. Avorn details the deceptions pharmaceutical companies have used to hide the evidence of adverse drug effects.²⁴ Jones and Hagtvedt consider the tragic implications of treatments for malaria.²⁵ In contrast, social medicalization includes studies where the profit motive plays a lesser role, such as studies of the determination of death, spouse battering, or gender deviance. The classification of some areas of medicalization research depends on the methodological approach taken, such as studies of childbirth, long-term disability, infertility, and abortion, where the profit motive may or may not be of central concern. Is the

increasing medicalization of substance abuse and addiction social, economic, or both?

Since the public policy disasters created by drugs such as elixir sulfanilamide in 1937 and thalidomide in the early 1960s, it has been recognized that there is an inherent conflict of interest between private sector firms guided by the profit motive and those of government acting in the "public interest" that needs to be managed through regulatory oversight. The corporate profit motive provides strong incentives: to recoup as efficiently as possible research-and-development expenditures or acquisition costs related to the takeover of other firms that have developed potentially marketable technologies for drugs or devices; to exploit first-mover advantages where the danger of a "race to market" with potentially competing innovative drugs or devices may be apparent; to develop alternative (off-label) applications and delivery mechanisms for existing drugs, eg, the extended-release formulation of oxycodone provided by OxyContin; and to extend drug or device patent protection by reformulations combining these drugs with other existing medications. Faced with a limited time to patent expiration and the long time period required to achieve stage III FDA approval, there is great economic pressure on pharmaceutical companies to move drugs to market as quickly as possible. Commercial rewards are more closely tied to the number of prescriptions written for a drug than to the incremental medical value of the treatment.

The marketing of OxyContin by Purdue Pharma is unlike many other instances of economic medicalization, due to the Schedule II classification of opioid-derived pain treatments and the illegality of some, but not all, Purdue Pharma marketing tactics. Though the marketing plan did ultimately result in widespread diversion for use by those with substanceabuse disorders, it is not possible to fully untangle what portion of the commercial success of OxyContin resulted from illegal claims about the risk of addiction impacting the legitimate prescription activities of primary care physicians. The marketing plan also involved tactics that profited from the increased legal use of prescription opioids by primary care physicians in the management of long-term relief from chronic noncancer-related pain. Diversion of the resulting increased supply of legally obtained prescription opioids has led, de facto, to the medical profession extending control over the nonmedical use of illegal drugs by addicted populations, substituting for the use of heroin, cocaine, and methamphetamines.

The emergence of OxyContin as the drug of choice for substance abusers was a key element in the economic medicalization of opioid addiction and substance abuse that gained momentum during the first decade of the twenty-first century. For example, the Centers for Disease Control and Prevention (CDC) report that the number of unintentional overdose deaths from heroin stayed relatively constant from 1999 to 2007 at around 2000 per year, while the number of deaths from opioid analgesics more than quadrupled from less than 3000 to about 12,000 per year. This increase in deaths is largely due to the decision by the medical profession to expand usage of opioids such as oxycodone and methadone to manage long-term, noncancer-related pain. This change in general pain-management practice has had a substantial and predictable impact on the available supply of prescription opioids available for diversion. For example, the CDC reports: "Drug distribution through the pharmaceutical supply chain was the equivalent of 96 mg of morphine per person in 1997 and approximately 700 mg per person in 2007, an increase of >600%. That 700 mg of morphine per person is enough for everyone in the United States to take a typical 5 mg dose of Vicodin (hydrocodone and acetaminophen) every 4 hours for 3 weeks."26 The CDC also observes: "Persons who abuse opioids have learned to exploit this new practitioner sensitivity to patient pain, and clinicians struggle to treat patients without overprescribing these drugs."26

Medical ethics, business ethics, and bioethics

Practical examples of the medical profession extending authority over matters not directly concerned with the analysis and treatment of biophysical disorders are readily available. Ethical analysis of such developments is complicated, because the "medical profession" includes not only practicing doctors and associations of doctors but also the pharmaceutical and medical device corporations, providing the drugs and other medical technologies that are an essential component of modern medicine; the academic institutions, associations, and journals involved in training doctors and sponsoring essential research activities; the medical insurance corporations that process payments for the bulk of medical services; and the government granting agencies and other sponsors that supply essential funding to the research conducted by the medical profession. Significantly, because the global financial markets are an essential source of capital for the corporations associated with the medical profession, the primary motivation of these important players can differ from those of the other players. The implications of this difference are reflected in the legion of studies on the marketing networks of the pharmaceutical companies and the sophisticated efforts involved in selling products. The differing motivations within the medical profession create a range of potential ethical quandaries that are difficult to resolve.

Due to the diverse and competing ethical norms that impact the medical profession, it is not easy to discern the de facto objectives driving particular actions and outcomes. As Poitras and Meredith observe: "There is an ethical transparency problem."4 The difficulty of discerning the ethical motivations of specific players within the medical profession can even occur for physicians, for whom the ethics of professional fiduciary responsibility would seem to be clear-cut, based on standards of medical ethics stretching back to the oath of Hippocrates, which first appeared around the fifth century BC.²⁷ The oath protects the rights of the patient by appealing to the strong character of the physician; no formal sanctions or penalties are contemplated. The oath was "Christianized" around the eleventh century, and remains an essential component of the ideal ethical conduct of physicians up to the present. The evolution of medical practice gradually surpassed the ethical guidance provided by the oath. Building on contributions from the Scottish physician John Gregory (1724–73), in 1803 the English physician Thomas Percival (1740–1804) published a code of medical ethics to address the need for more detailed ethical guidance. The Percival code was, more or less, adopted by the AMA in 1847.²⁸ From that time, a number of major revisions to the code have been made, with four such revisions during the twentieth century (1903, 1912, 1947, and 1994). In addition to specifying nine principles of medical ethics, the AMA provides detailed opinions on ethical behavior for specific situations of medical practice by physicians.²⁸ Ethical opinions for over 200 situational problems are currently provided. Opinions cover a wide range of subjects, from the controversial to the mundane. In the realm of social policy, controversial issues such as cloning, euthanasia, and gene therapy are examined. More mundane opinions cover interprofessional and hospital relationships and patient confidentiality. Though the present code and related opinions have evolved considerably from the early beginnings of the Hippocratic oath and the Percival code, basic principles for ethical behavior by physicians still remain: physicians should base clinical practice and research on the best science available; individual self-interest is secondary to the well-being of the patient; and medical knowledge is a public trust to be used to the benefit of patients and society. Significantly, "Principles adopted by the American Medical Association are not laws, but standards of conduct which define the essentials of honorable behavior for the physician."28

The long-established field of traditional medical ethics is patient-centered. While the AMA aims to provide guidance to physicians for dealing with the increasingly complex ethical issues raised by the relentless progress of modern biotechnology and pharmacology, the AMA Code of Medical Ethics is not able to provide sufficient guidance to deal with the multitude of interdisciplinary ethical problems raised by research into areas such as cloning, stem cells, genetic modification of foods, euthanasia, DNA data banking, genetic manipulation of human DNA, and testing for genetic markers. The issues involved are so varied and significant that the field of bioethics emerged to address such issues.^{29,30} Biotechnology has also impacted research areas that have long-standing social and religious significance, such as abortion and the determination of death. While medical ethics has considerable interest in such issues, bioethics goes beyond medical ethics to incorporate knowledge from moral philosophy, law, sociology, molecular biology, economics, and other subjects. Central to many issues confronting bioethics is the justification for introducing new technologies. In practice, this ethical problem is confounded by the commercial aspects involved in developing these technologies. The substantial capital investments required for biotechnology and pharmacological advances dictate that bioethics also addresses the implications of corporate decision-making.

Because some of the largest multinational corporations in the world are directly involved in the market for medical products and services, bioethics needs to incorporate elements of business ethics in order to accurately assess a range of important issues. In business ethics, it is necessary to recognize that corporations pursue strategies consistent with SWM. The goal of SWM depends on the future common stock price, and as such does not have ethical transparency.¹¹ Some assumption about the efficiency of the stock market in valuing ethical concerns is required. In this vein, the layers of regulatory oversight aimed to restrict unfettered corporate activity coming into play. Ultimately, it is difficult to expect much more than an "ethical is legal" approach to corporate decisions regarding marketing of medical products if SWM is the goal. In the case of OxyContin, a substantial penalty was imposed for violating the minimum legal standard. In general, significantly higher ethical standards than "ethical is legal" may come at a financial cost that impacts corporate profitability, undermining achievement of SWM.

In setting the legal and regulatory environment for the medical profession, governments are inclined to adhere to utilitarian ethics, where decisions are made on the basis of cost–benefit calculations. The precise method of determining

costs and benefits can depend on a range of political and social factors, not just a "dollar-and-cents" calculation. In contrast to the well-established code of medical ethics, the legal environment is a myriad of legislation and associated regulatory oversight established at different times with potentially competing ethical standards. In turn, relevant legislation will vary from issue to issue. In the area of marketing, distribution, and consumption of Schedule II drugs, regulatory oversight in the US would include the Department of Justice, Drug Enforcement Agency, the Federal Trade Commission, the CDC, the FDA, the Substance Abuse and Mental Health Services Administration (SAMHSA), the Office of National Drug Control Policy, the National Institute on Drug Abuse, the Center for Medicare and Medicaid Services, and Health and Human Services, as well as similar state health agencies and criminal justice branches. If military personnel are explicitly identified, the Veterans Administration and the Department of Defense would also be included.

The history of prescription opioid diversion and abuse provides a helpful illustration of the social consequences of making accurate distinctions between medical ethics, business ethics, and bioethics. This subject is not concerned with traditional bioethical subjects, such as cloning, stem cells, genetic modification of foods, and genetic manipulation of human DNA. Similarly, neither medical ethics, which applies to behavior of physicians, or business ethics, which applies to the behavior of commercial entities, deals directly with implications of marketing addictive substances for commercial profit. It is possible for both physicians and commercial firms to be operating within "ethical" bounds while a public health tragedy emerges as the social outcome. More precisely, it is within the bounds of medical ethics for physicians to prescribe opioids for therapeutic treatment of moderate-to-severe noncancer-related pain and for firms legally supplying opioids to be within the bounds of business ethics in promoting the use of such medical practices but at the same time there is an epidemic of prescription opioid abuse. As such, key ethical issues arising from the current epidemic of prescription opioid diversion and abuse need to be identified before the public health issues involved can be resolved.

Direct-to-physician marketing of OxyContin

The marketing of OxyContin by Purdue Pharma provides considerably more information than typical cases of economic medicalization, due to a number of factors, including the investigation and report by the GAO and related congressional hearings; internal company documents and other items made available during the criminal and civil trials; the length of time that has passed since the most egregious actions, which happened in the period from 1996 to 2003, allowing the preparation of numerous academic studies; and, the Schedule II classification of oxycodone, making for more documentation and attention. As a consequence, there is detailed information on the geography, composition, and previous substance-abuse behavior of users; methods used to purchase and consume the drug; and the legal and illegal marketing methods used by Purdue Pharma that contributed to OxyContin diversion and abuse.

The route to achieving the SWM objective associated with economic medicalization differs depending on the product on offer. In many cases, economic medicalization is associated with the direct-to-consumer television marketing campaigns by the pharmaceutical companies. Such campaigns are designed to put in place a public perception of illness and health consistent with the portfolio of prescription drug products on offer.^{31,32} Where bodies were once understood as normatively healthy and only sometimes ill, effective marketing has individuals seeing their bodies as inherently ill, and only able to be brought towards health with effective patient-driven medical treatment.³³ The history of erectile dysfunction drugs attests to the ability of the direct-to-consumer marketing by pharmaceutical companies to transform a nonmedical problem into a medical one. In contrast, the ability to use direct-to-consumer marketing for Schedule II drugs is severely limited through government legislation and regulation. In such a situation, attention focuses on the use of direct-to-physician marketing tactics. This substantively complicates the economic medicalization process, as physicians generally adhere to principles of medical ethics. The OxyContin case is a particular instance where the regulatory infrastructure for monitoring postapproval marketing is juxtaposed against the corporate requirement of profitability through successful marketing. In a world of declining opportunities for highly profitable "new" patentable drug discoveries, the stage is set for serious ethical conflict to emerge between the players. This conflict is central to analyzing instances of economic medicalization where the ethical norms of "science" are confronted with the ethics of the marketplace. 8,34 In science, accuracy of measurement and validity through replication are fundamental elements. In contrast, the objective of profitability is supported by research, biased or unbiased, that recommends prescription of the treatment on offer. Illegally misrepresenting the risk of addiction, Purdue Pharma directed sales representatives to claim a "less than one percent"³⁵ risk of addiction, citing credible scientific studies by Porter and Jick³⁶ and Perry and Heidrich.³⁷ However, these studies dealt only with the immediate treatment of acute pain, not long-term chronic pain, where many studies highlight a high incidence of prescription drug abuse.¹

Misrepresenting scientific evidence was only one aspect of the marketing campaign used by Purdue Pharma. Given the limited oversight of postapproval marketing and promotion of controlled drugs by the FDA and other regulatory authorities, no single aspect of the Purdue Pharma marketing plan taken in isolation would justify the severe monetary penalty imposed. In addition to having "detail men" make unjustified "scientific" claims about the risk of addiction associated with OxyContin, Purdue Pharma employed "prescriber profiles" to identify physicians with high incidence of writing opioid prescriptions, used a "lucrative" bonus system for sales representative based on their sales, substantially increased the number of sales representatives to extend the marketing campaign to primary care physicians, and introduced a "patient starter" program, providing patients with a free 7- to 30-day supply. These initiatives were supplemented by the usual promotional gimmicks offered by pharmaceutical companies, such as "fishing hats, stuffed plush toys" and "more than 40 national pain-management and speaker-training conferences in Florida, Arizona and California" from 1996-2001.

How does the marketing campaign employed by Purdue Pharma differ from the typical types of marketing methods used by medical companies to influence treatment selection? Following Donohue et al, spending on advertising and promotion to medical professionals and consumers in 2005 was \$4.2 billion for direct-to-consumer advertising, \$18.4 billion for free samples, mostly given to physicians, \$6.8 billion for detailing, and \$429 million for journal advertising.³⁸ This only partially identifies the costs of a marketing strategy that is used for a wide range of products, ie, influencing the opinion leaders. In the case of medical drugs and devices, opinion leaders can be identified with groups such as specialists, research faculty, heavy prescribers in a drug/device category, and product champions. Considerable effort is given to finding opinion leaders willing to speak favorably about a company's product. Marketers try to influence opinion leaders because these groups, in turn, affect the purchasing habits of other buyers who respect the opinion leaders' knowledge base and authority in a particular area. In addition to practices such as using "profiler" databases to

identify heavy prescribers, Purdue Pharma averaged eight OxyContin-related pain-management and speaker-training courses per year from 1996 to 2001.

While the enlistment of opinion leaders plays a fundamental role in corporate marketing strategies, it has traditionally been the prescribing physician that drug companies need to influence the most. Though this approach has changed somewhat with the rise of direct-to-consumer marketing, the bulk of advertising and promotion spending is still targeted directly at physicians. A key element in this strategy is the company sales representative or "detail man." The history of the modern detail man can be traced back to the 1940-60 era, when the prescription drug industry was in a period of enormous expansion.³⁹ To address the dramatic changes in the medical profession brought on by the advent of a host of new and important prescription drugs, detail men during the period were transformed ". . . from specialized salesmen into quasiprofessionals." The pharmaceutical companies recognized the value to drug sales if detail men could be seen as assistants to doctors, conveying useful information about important drug developments rather than being mere salesman for products. Greene argues that this change of image "... required a careful negotiation around doctors' spaces, both figuratively and literally."39

The lack of ethical transparency in the activities of detail men is apparent in the OxyContin case. Though detail men cannot be seen as telling doctors what to prescribe, their role is ultimately to influence prescription behaviors. To do this, detail men want to be seen by physicians as allied professionals, consciously modeled as having the same ethical objectives as doctors. For example, Greene reports that manuals for detail men reproduce parts of the AMA's code of ethics.³⁹ To be effective, detail men need to have the ability to interact with doctors, and require training to develop this ability. Detailing has to at least appear to educate, rather than merely to sell. In this process, a research pipeline of positive results is an invaluable tool. Marketing to doctors often takes the form of getting doctors up to speed on the latest research. The range of techniques that can accomplish this goal includes not only marketing by pharmaceutical representatives but also advertisements in professional journals, funding continuing medical education conferences, and preparing promotional videos; all marketing activities pursued by Purdue Pharma.

The misrepresentation of the addiction risk from OxyContin by Purdue Pharma sales representatives and

in related promotional material was deemed to be illegal. However, absent this misrepresentation, other aspects of the marketing plan were legally acceptable and common practice in pharmaceutical marketing. Consistent with practices used by drug companies for a wide range of drugs, Purdue Pharma used prescriber profiles compiled from large national databases on the prescription patterns of physicians to identify and target physicians that were the highest prescribers of opioids. Similarly, Purdue Pharma employed a bonus system to encourage sales representatives that – combined with the availability of prescriber profiles - resulted in targeting of highest-opioid-prescriber physicians. While there were illegal claims of "less than one percent" addiction rates, it was commonly used legal marketing tactics that ultimately contributed to a dramatically expanded usage of opioid prescriptions by primary care physicians for the treatment of long-term noncancer-related pain. While use of opioids for acute and short-term pain has strong "scientific" support, the overall efficacy in cases of chronic long-term pain is unclear.1

Another application by Purdue Pharma of traditional marketing practices to a Schedule II drug was the use of free samples in the form of vouchers for a limited-time 7- to 30-day free supply (this program was discontinued in 2001). A key element in traditional marketing to primary care physicians is the provision of free samples in order to impact on prescriptions patterns. Chew et al conclude that the availability of drug samples led their primary physician respondents to prescribe drugs different from their preferred choice, especially if it avoided costs to the patient. 40 A national US survey reported that 78% of 1255 physician respondents had received free samples.⁴¹ Pharmaceutical companies undertake that level of free-sample distribution because free samples are one of the strongest cues for successful product trial and adoption. Using such cues, sales representatives aim to interact directly with primary care physicians, instead of, say, working through hospital pharmacologists, who possess far greater knowledge of drug efficacy and safety and are much better equipped to evaluate drug alternatives.

Economic medicalization and prescription opioid abuse

Figures 1 and 2 illustrate the tragic social consequences of drug poisonings, which include overdose deaths from prescription drugs. In 2008, there were 30 states in the US where drug poisoning was the leading cause of injury deaths. While the precise contribution from prescription opioid

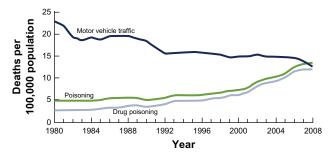


Figure I Motor vehicle traffic, poisoning, and drug poisoning death rates. United States, 1980–2008.

Note: Source – Centers for Disease Control and Prevention National Vital Statistics System.⁴²

abuse cannot be precisely determined, the National Center for Health Statistics is able to determine that:⁴²

Of the 36,500 drug poisoning deaths in 2008, more than 40% (14,800) involved opioid analgesics. For about one-third (12,400) of the drug poisoning deaths, the type of drug(s) involved was specified on the death certificate but it was not an opioid analgesic. The remaining 25% involved drugs, but the type of drugs involved was not specified on the death certificate (for example, "drug overdose" or "multiple drug intoxication" was written on the death certificate).

Recognizing data limitations inherent in death certificates and other sources used to calculate overdose death statistics, it is not possible to determine the fraction of the 14,800-plus opioid analysesic overdose deaths in 2008 directly attributable to OxyContin abuse. However, there are a number of circumstantial factors suggesting that many of these deaths did originate from OxyContin, such as a dramatic increase

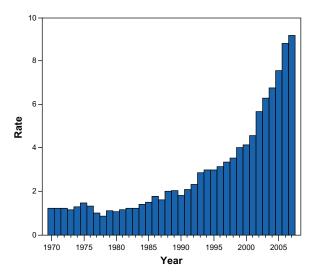


Figure 2 Rate per 100,000 population of unintentional drug overdose deaths in the US, 1970-2008.

 $\textbf{Note:} Source-Centers for \ Disease \ Control \ and \ Prevention \ National \ Vital \ Statistics \ System. \ ^26$

in deaths from the period following FDA approval (see Figure 2), the status of OxyContin as the most prescribed such opioid, and the large number of prescriptions written, as reported by the company. It is significant that despite the sizable number of agencies and government departments responsible for providing data on the prescription drug problem, with few exceptions evidence is only collected by drug category without reference to the companies producing a specific drug formulation.

Fortunately, sufficient time has passed since the introduction of OxyContin that a variety of detailed academic studies have emerged about methods of use, intranasal (IN) vs intravenous intake, 43-45 geographical and demographic distribution of users, 42,46 patterns of diversion and abuse in high-use areas, eg, rural Appalachia^{45,47} and Washington state, 48 and characteristics of abusers. 44,49-52 What has emerged from such studies is a clearer picture of the contribution of OxyContin to the economic medicalization of substance abuse and addiction. In particular, the extended-release formulation of OxyContin may contain "... excipients that may enhance IN drug delivery . . . The direct effects of these excipients on IN oxycodone drug absorption are unknown, but polymer interactions with nasal mucous can enhance mucoadhesion and are used to optimize human IN drug delivery."42 Lofwall et al also find that ". . . crushing and snorting OxyContin tablets is a highly efficient drug delivery method that clearly bypasses the extended-release . . . (Purdue Pharma) drug delivery matrix."43 In effect, when crushed, the formulation of OxyContin was "optimized" to deliver the most potent high for IN opioid drug abusers.

Following Poitras and Meredith, economic medicalization is concerned with the transformation of nonmedical problems into medical problems in order to achieve the goal of SWM.⁴ Given this, accurate analysis of economic medicalization requires the relevant nonmedical and medical problems involved to be defined. Traditional definitions focus on the therapeutic use of prescription drugs. In particular, SAMHSA defines "nonmedical" use as the taking of a prescription drug that "was not prescribed" for that individual or that was taken "only for the experience or feeling it caused."50 This definition includes a range of behaviors, from "non-compliant" use to substance addiction. Using this definition, OxyContin diversion and abuse is a subversive, nonmedical activity. The medical problem is concerned with the legitimate chronic pain for which this opioid is prescribed and the associated increased risk of addiction or overdose death for the individual receiving the prescription. From this mainstream perspective, increased risk of diversion and abuse

is subversive and not a "medical" problem, per se. Only if physicians become ". . . reluctant to prescribe opioid analgesics for fear of causing addiction in their patients" is there a medical problem. ⁵⁰ Hence, there is no basis for claiming (social) medicalization because there is no extension of social control by the medical profession.

In contrast, the case of prescription opioids, in general, and OxyContin, in particular, is concerned with economic medicalization involving medical corporations acting for profit, transforming the nonmedical problem of recreational abuse of illegal drugs into the medical problem of addiction and substance abuse by dramatically increasing the supply of legally issued opioid prescriptions. In the absence of directto-consumer marketing tactics found in previous instances of economic medicalization, the increased supply of prescription opioids available for diversion was generated by marketing tactics aimed at changing the opioid-prescription behavior of primary care physicians, especially those involved in long-term chronic-pain management. Many such physicians have been detailed on the legitimate therapeutic value of prescription opioids. The resulting increased aggregate supply of prescription opioids has created a "medical problem" associated with increased addiction, substance abuse, and overdose deaths in the greater community. In this process, the medical profession has extended control over the total aggregate supply of legal and illegal drugs available for consumption by addicted populations.

The extent and character of this avenue of economic medicalization on the public health tragedy is identified in numerous studies. For example:^{44,53}

It is clear that many of the people who enter treatment programs for OxyContin abuse/dependence are not naive individuals with accidental addiction... The individuals... are, for the most part, individuals with extensive drug use and involvement in the criminal justice system. Their use of OxyContin as their preferred drug is related to the fact that in some parts of the United States there is easy access to OxyContin. Hence OxyContin use among this group simply represents a drug preference based primarily on convenience.

This result is mirrored in various other studies, eg, "... it appears that the majority of OxyContin users... were already involved in the use of drugs and used OxyContin to get high and in ways to maximize its psychogenic effects." On balance, there is little evidence that OxyContin is a "gateway drug" compared to other prescription opioids; ⁵¹ rather, the availability, formulation, and strength of OxyContin

contribute to the preference for this particular drug among those with preexisting substance-abuse disorders. Figure 3 provides evidence on the preponderance of "experienced" substance abusers in prescription drug-overdose deaths.

Results of the 2009 National Survey on Drug Use and Health are applicable to the diversion of legal prescriptions: "... over 70 percent of people who abused prescription pain relievers got them from friends or relatives, while approximately 5 percent got them from a drug dealer or from the Internet."12 While startling, such claims tend to misrepresent the geographic, demographic, and institutional factors driving the diversion of prescription opioids, in general, and OxyContin, in particular. Table 1 and Figure 4 give a brief overview of the populations involved in prescription opioid diversion and abuse activities. In addition to being predominately rural and non-Hispanic Caucasian or Native American, the CDC further indicates: ". . . higher drug overdose rates in lower-income populations."48 Beyond such general conclusions, there is considerable geographical variation in diversion, abuse, and overdose-death populations, if only because there is considerable cross-state variation in monitoring, enforcement, and access to legal prescriptions and illegal alternatives, eg, heroin and cocaine.

In the case of prescription opioid abuse, the "economics" of economic medicalization extend beyond the commercial profitability for companies such as Purdue Pharma. There is also the economics of prescription purchase, diversion, and illegal purchase and consumption. Because opioid prescriptions are relatively expensive, individuals require funds for the initial, legal purchase. The commercial success of OxyContin was driven by targeting chronic noncancer-related pain

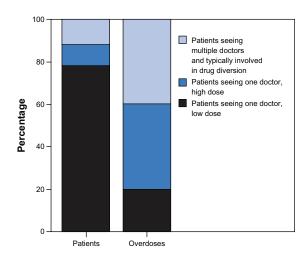


Figure 3 Percentage of patients and prescription drug overdoses, by risk group – United States.

Note: Source – Centers for Disease Control and Prevention National Vital Statistics System.²⁶

Table I Age-adjusted drug-poisoning death rates, by demographic characteristics and intent: United States, 1999–2008⁴²

	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Age-adjusted death rate										
Total	6. l	6.2	6.8	8.1	8.9	9.3	10.0	11.4	11.8	11.9
Sex										
Male	8.2	8.3	9.0	10.5	11.4	11.7	12.7	14.6	14.8	14.8
Female	3.9	4 . I	4.7	5.8	6.4	6.9	7.3	8.2	8.9	9.0
Race and ethnicity										
Hispanic	5.5	4.6	4.4	5.3	5.6	5.2	5.7	6.2	5.9	5.9
Non-Hispanic white	6. l	6.6	7.4	9.2	10.1	10.9	11.7	13.5	14.4	14.7
Non-Hispanic Black	7.5	7.3	7.6	8.2	8.2	3.3	9.4	10.9	9.8	8.5
Non-Hispanic American Indian or Alaska Native	6.0	5.5	6.8	8.4	10.6	12.3	12.9	13.9	13.9	15.6
Non-Hispanic Asian or	1.2	1.0	1.2	1.4	1.4	1.5	1.7	1.9	1.9	1.8
Pacific Islander										
Intent ¹										
Unintentional	4.0	4.2	4.6	5.7	6.3	6.8	7.5	8.8	9.1	9.2
Suicide	1.1	1.2	1.2	1.3	1.3	1.4	1.4	1.5	1.5	1.6
Undetermined	0.9	0.9	1.0	1.1	1.2	1.1	1.0	1.1	1.2	1.1

management by primary care physicians. Low-income, rural populations where heavy manual labor can lead to numerous chronic pain problems are well suited to such a strategy, eg, mining towns of rural Appalachia and logging towns of Maine and Washington state. Low-income populations can often access Medicaid funds to obtain legal prescriptions. For example, based on a Washington state sample, the CDC finds: "45.4% of [prescription opioid overdose] deaths were among persons enrolled in Medicaid. The age-adjusted rate of death was 30.8 per 100,000 in the Medicaid-enrolled population, compared with 4.0 per 100,000 in the non-Medicaid population." Significantly, the bulk of these overdose deaths

were not due to oxycodone but to methadone, which was prescribed primarily for the alleviation of chronic pain, not addiction treatment. The 45- to 54-year age cohort had the largest percentage of deaths.

Even for the portion of the low-income population obtaining OxyContin without medical insurance – from either Medicaid or private plans – the economics of diversion are overwhelming. Though precise data are difficult to obtain, figures from the Office of Alcoholism and Substance Abuse Services indicate a street price of $45\phi-53\phi$ per mg in New York City for a 40 mg tablet of "oxycodone," presumably OxyContin given that 40 mg and 80 mg are the tablet doses.

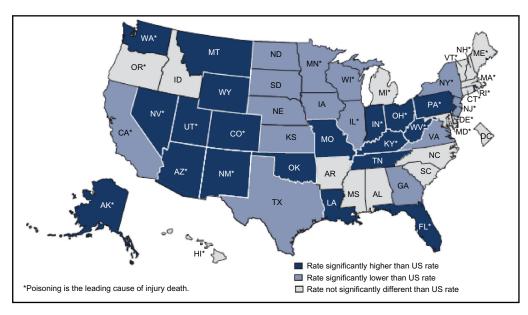


Figure 4 Age-adjusted US poisoning death rates, 2008.

Note: Source – Centers for Disease Control and Prevention National Vital Statistics System. 42

This can be compared to the cost of legally obtained OxyContin of 9¢–13¢ per mg in the same jurisdiction. ⁴⁵ In addition, "Practical issues . . . almost certainly keep the cost of street oxycodone in NYC below the national average." ⁴⁵ Media sources claim street prices up to \$100 per pill (\$2.50 per milligram for 40 mg) in rural areas of Appalachia hardest hit by OxyContin abuse. ⁴⁶ A sample of 503 rural Appalachian drug users indicates that "social capital" benefits result in more diversion for co-use of OxyContin rather than sale for monetary benefits. ⁴⁶

Conclusion

Solutions to the public health tragedy of prescription opioid abuse are elusive. The problem has a history stretching back to 1906, when the Food and Drug Act "mandated that the presence of certain addictive substances be clearly labeled on any products containing these ingredients."54 The White House provides the most recent plan to deal with the tragedy. 12 This plan has four components: education, monitoring, proper disposal, and enforcement. As such, the general components of this plan could apply to a range of toxic products, eg, fluorocarbons. Details of the plan need to be considered. Examining details associated with the education component reveals: "... many people are still not aware that the misuse or abuse of prescription drugs can be as dangerous as the use of illegal drugs, leading to addiction and even death."12 While possibly correct for the general population, this claim is questionable when applied only to the population involved in diversion and abuse of prescription opioids. The target population for the education component is also identified: "Parents and youth in particular need to be better educated about the dangers of the misuse and abuse of prescription drugs" and "Many parents are also not aware that youth are abusing prescription drugs; thus, they frequently leave unused prescription drugs in open medicine cabinets while making sure to lock their liquor cabinets."12 Again, numerous studies reveal that the bulk of the prescription opioid-overdose deaths are not from youth procuring prescription drugs from a parent's medicine cabinet.

At the beginning of medicalization research, Wootton¹³ observed that it is always easier to build a clinic than to tear down a slum. In the present context, this statement can be taken to imply that the problems of prescription opioid abuse are societal, rooted in poverty, social inequality, and marginalization of affected populations. Economic medicalization focuses on the role of medical corporations and other members of the medical profession seeking to profit from such situations. In contrast, the recent White House plan presents

the alternative perspective that focuses on the faults of individuals: ". . . any policy in this area must strike a balance between our desire to minimize abuse of prescription drugs and the need to ensure access for their legitimate use. Further, expanding effective drug abuse treatment is critical to reducing prescription drug abuse, as only a small fraction of drug users are currently undergoing treatment." Key enemies in the battle against prescription opioid abuse are identified as "pill mills" and "doctor shoppers." The addict is at fault for not seeking medical treatment. The doctor shoppers and clinics that "overprescribe" for profit are at fault by making supplies available for nonmedical use.

The economic medicalization of opioid abuse and addiction raises questions about the appropriate definitions to use in analyzing this public health tragedy. What if the "nonmedical" problem is identified with the social problem of "prescription diversion" instead of using the SAMHSA definition associated with individuals taking drugs that were not prescribed? What if the "medical problem" is identified with the social problem of substance abuse, addiction, and overdose deaths instead of increased reluctance of physicians to prescribe opioids for the legitimate treatment of pain? By misleading primary care physicians about the risk of addiction for chronic long-term pain, intentionally or unintentionally, Purdue Pharma targeted populations with a high probability of diversion. Given the Schedule II classification of OxyContin, such diversion activity is different than, say, Parke-Davis promoting the off-label use of gabapentin. This begs the question: how will policies aimed at restricting the supply of prescription opioids solve the social problems that lead to addiction and overdose deaths?

Public health policy surrounding prescription opioid abuse is based on a utopian vision of a world without substance abuse and addiction. The road to achieving this vision depends on tight restriction of illegal drugs and preventing the diversion of legally prescribed opioids. The social consequences of this public health policy vision are reflected in overflowing prisons and increasing marginalization of addicted populations. Is the goal of a "drug-free America" realistic? Can substance abuse and addiction be eradicated by pursuing a policy aimed at supply control? Even if the supply from diversion of legal prescriptions was eliminated, prescription opioid abusers in large urban areas typically have ready access to illegal alternatives such as heroin, cocaine, and methamphetamine (meth), drugs with significant quality fluctuations, and in the case of meth severe health consequences for the addict. Rural Appalachia, a geographical region at the center of OxyContin abuse, is also a region

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with the highest incidence of marijuana cultivation. Meth abuse is already severe in a number of rural Western states, such as Oklahoma. What would be the impact of reducing the supply of prescription opioids on addiction and deaths from illegal alternatives or alcohol?

Waging a war on prescription opioid diversion may have unintended consequences. If use of illegal alternatives increases significantly due to the reduced supply from diversion of prescription opioids, what are the implications for the level of violent criminal activity associated with increased supply and distribution of those illegal drugs? As a response to various legal and regulatory difficulties, in August 2010 the privately held Purdue Pharma corporation reformulated OxyContin claiming the new formulation would deter nonmedical substance-abuse practices. Cicero et al recognize the implications of the change: ". . . an abuse-deterrent formulation successfully reduced abuse of a specific drug but also generated an unanticipated outcome: replacement of the abuse-deterrent formulation with alternative opioid medications and heroin, a drug that may pose a much greater overall risk to public health than OxyContin."55 Despite the reformulation, in 2011 sales of OxyContin were over \$2 billion.

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