How opioids became "safe":
Pharmaceutical splitting and the racial politics of opioid safety

Abstract

This article explores how opioid painkillers, known for over a century to be highly addictive, came to be considered a safe treatment for chronic pain. Based on a critical content analysis of industry-sponsored medical education, biomedical opioid research, and opioid marketing strategy it identifies the unacknowledged racialized category distinctions between 'pain patients' and 'opioid abusers' that have influenced medical opinion on opioid safety since the 1990s. It develops the concept of "pharmaceutical splitting" to understand how distinctions between 'pain patients' and 'opioid abusers' drew on racial and class-based imagery enabling prescribers to reconcile long-standing evidence of opioids' addictive properties with the argument that they were a safe treatment for common chronic pain. Overall, this article contributes to understandings of the cultural and racial politics of pharmaceutical marketing and commercially-sponsored pharmacology.

Keywords: Opioids, Addiction, Pain, Race, Pharmaceutical Splitting, Drug Markets

Introduction

Prior to the 1980s, potent opioid pain relievers were considered to be highly addictive. For this reason, they were primarily prescribed by specialists for cancer, surgery, and end-of life care. In the ensuing decades, many generalist practitioners in the United States came to consider opioids to be a safe treatment for common, chronic pain conditions, and by 2011 opioids were the most widely prescribed class of medications in America (University of Pennsylvania School of Medicine 2011). How did potent opioids known for over a century to be addictive come to be considered safe?

Through a critical content analysis of industry-sponsored medical education, biomedical opioid research, and internal accounts of opioid marketing strategy recently made public through opioid lawsuits, we explore the cultural metaphors and imagery shaping the science and politics of opioid safety in America. We develop the concept of "pharmaceutical splitting" to analyze how category distinctions between types of opioids and types of drug consumers shifted the language and imagery surrounding certain opioids and certain consumers, leading the way for newly patented opioids to be considered safe for use among specified categories of people. By tracing pharmaceutical splitting as it was enacted across marketing materials, consumer and prescriber education, and medical professional consensus statements we highlight how social distinctions that traded on race and class-based images of 'trustworthy patients' versus 'opioid abusers' were crucial to the sea-change in medical opinion on opioid safety that occured in the 1990s.

In psychoanalysis, the term "splitting" references a defense mechanism whereby an individual is unable to reconcile both the positive and negative qualities of self or of others into a cohesive whole, and instead falls into all-or-nothing binary thinking in which the individual projects unidimensional qualities onto others, seeing

some people (or objects) as *all good*, and others as *all bad* (Rubens 1996). Here, we use the term "pharmaceutical splitting" as a metaphor to capture the corporate manipulation and polarization of the imagery attached to certain pharmaceuticals. By our formulation, pharmaceutical splitting refers to an act of category sub-division whereby a drug, its target population, or its associated disorder is split apart in such a manner that some medications, disorders or consumers are depicted as inherently and encompassingly 'good', while other disorders, medications or populations are depicted as inherently and encompassingly 'bad'. Thus, the construct highlights a polarizing all-or-nothing reasoning that is at the heart of clinical and popular understandings of opioid safety.

Our analysis of pharmaceutical splitting reveals that category distinctions between 'good' pain patients and 'bad' opioid abusers traded in racial and class-based imargery to produce a circuitous logic. According to this logic, the implicitly white and middle class 'trustworthy pain patient' to whom opioids were marketed could never, by definition, be addicted. Conversely, the implicitly non-white, poor, 'opioid abuser' who was depicted as 'criminal' and 'prone' to addiction, could not – by definition - consume opioid medications safely. We trace the production of this circouitous logic through an historical chronology of three distinct iterations of pharmaceutical splitting across opioid pain relievers, including: 1) the implicitly white trust-worthy pain patient versus the heroin addict during the early years of opioid prescribing; 2) the implicitly non-white opioid abuser versus the compliant patient on the discovery of opioid mortality from legally produced opioids, 3) the condition of pseudo-addiction versus real addiction in the 2000s following prescribers' doubts as to whether to refill precriptions in the face of clear evidence of opioid misuse, and 4) the patient "susceptable to" addiction versus the patient at "low risk" of addiction, as

elaborated in medical screening tools in the late 2000s. A combination differentiations based on race, class, and criminality have leant structure to each of these distinctions. A deeper understanding of how this process of pharmacetucal splitting works is helpful not only for understanding the sea-changes that have occurred in the prescribing of opioid pain relievers in the United States during the last three decades, but also for understanding the cultural politics of pharmaceutical markets and commercial clinical science more broadly.

Our analysis of pharmaceutical splitting draws on existing work at the nexus of the anthropology of pharmaceuticals, science and technology studies, and critical race theory. We draw on relevant insights from each of these literatures below.

Drug development, marketing, and racialization

Anthropological studies of drug development have often shown that drugs can be designed to have particular identities or personalities. This can occur when pharmaceutical marketers deliberately link drugs with particular attractive images, for example to images of happiness, creativity, balance, or sexual fulfilment (Whyte, Van der Geest, and Hardon 2002; Martin 2006; Jenkins 2010). This can also occur when drugs are discursively associated with or distanced from particular disorders or populations of consumers (Pieters and Snelders 2007; Wentzell 2011; Netherland and Hansen 2016). In her research on Viagra, for example, Emily Wentzell (2011) describes how Pfizer deliberately distanced Viagra from its prior association with gay pleasure. This was achieved through what Wentzell calls "market silencing," whereby marketers avoided discussion of its recreational use within gay communities, enabling Pfizer to target their drug to the larger heterosexual market. "Re-inscription" is another useful construct for understanding how drugs' identities can be altered even

after they have gone to market. Nathan Greenslit (2005) describes how Pfizer re-inscribed a drug that was formerly a depression treatment (fluoxetine) into a treatment for premenstrual disorders through changing its name (from Prozac ® to Sarafem ®) and color (from green and yellow to pink and violet), thus erasing the drug's prior association with depression.

Pharmaceutical splitting is not simply a matter of altering a drug's existing associations. It involves reconciling a drug's positive and negative qualities by splitting its users and their health problems into simplistically opposing 'good' and 'bad' categories. The all-or-nothing reasoning implied by the psychoanalytical concept of splitting is helpful for understanding several important category distinctions that shifted recent understanding of opioid safety. These distinctions include: the pain patient versus heroin addict, the implicitly white trustworthy pain patient conceived as impervious to addiction versus and the implicitly black 'opioid abuser,' conceived as criminal and prone to addiction, and finally 'pseudoaddiction,' conceived as a collection of symptoms that resembles drug addiction but whose etiology 'really' lies in under-treated pain, versus 'true addiction,' conceived as a disorder that -- by definition -- can only emerge by definition among people who 'abuse' opioids, rather than among those who use them 'medically.' As a construct, pharmaceutical splitting draws attention to the flawed logic underlying considerations of opioid safety. It offers a window onto the moralized category distinctions and associated cultural and racial imagery that enabled opioid marketers and prescribers to reconcile longstanding evidence of opioids addictive properties with the idea that opioids are safe for the treatment of common, chronic pain.

Our analysis of pharmaceutical splitting also draws on existing scholarship at the nexus of critical race studies and science and technology studies (Rodríguez-

Muñiz 2016; Benjamin 2016; Hatch 2016). Anthropologists have shown that drug development can be racialized such that medications are designed to have racial identities (Netherland and Hansen 2016; Lee 2005). This racialization is sometimes explicit, as in the case of BiDil, a heart failure drug which in 2005 became the first drug in the US to ever to be approved solely for "self-identifying black patients" (Kahn 2008). More commonly, drugs come to have racial identities through less overt means. These include, for example, the various 'color-blind' laws, regulations, and health insurance markets that lead to racially segregated access to treatment for opioid use disorders (Hansen and Skinner 2012a), or the cultural representations in print and visual media that symbolically associate (accurately or inaccuruately) particular drugs with certain racial or ethnic groups (Anderson, Scott, and Kavanaugh 2015).

A central contention of this article is that unacknowledged racial and class-based imagery has played an important role in shaping medical understanding of opioids safety in the United States. Detecting this cultural imagery is not straightforward, however. As medical historians have long known, cultural imagery and metaphor have a tendency to become invisible in modern medicine because they are so often naturalized through the 'objective' language of epidemiology and clinical practice (Stepan 1986). To uncover this cultural and racial imagery we have therefore had to read dominant narratives against the grain, through a critical analysis of a variety of scientific and advertising materials pertaining to opioids and their safety. Before examining pharmaceutical splitting in more detail, it is necessary to clarify the sources of evidence used in this study. Our selection of sources is informed by recent accounts of opioid marketing as well as by studies of pharmaceutical marketing and its imbrication with science and patient advocacy more broadly, as we explain below.

The blurred interface of pharmaceutical marketing, science, and advocacy

Histories of the US opioid epidemic often begin with OxyContin, a branded name for a pill made of the older drug oxycodone, which was first synthesized in Germany in 1916 and has been available in the United States since 1939. The single feature differentiating OxyContin from oxycodone (making it a new, patentable drug requiring approval from the US Food and Drug Administration) was OxyContin's "controlled release" formulation. Purdue manufacturers embedded oxycodone in a capsule that released only a small amount of opioid at a time and argued that this would lower the risk of addiction. Having changed the delivery device for oxycodone, Purdue obtained approval for OxyContin from the FDA in 1996.

From the early 1990s onwards, Purdue pursued an unprecedented marketing campaign. Rather than focusing directly on consumers, Purdue targeted medical practitioners, professional medical societies, and patient advocacy organizations. Between 1996 and 2001, the company spent half a billion US dollars on pharmaceutical "detailing" – the practice of dispatching sales representatives to visit individual doctors and medical staff in their offices to promote Purdue products (Van Zee 2009). Other manufacturers of similar 'extended release' opioids licensed shortly after OxyContin employed similar strategies, with Janssen, Cephalon, Endo, Actavis (along with Purdue) collectively spend $168 million on detailing branded extended release opioids to doctors in 2014. This figure includes $34 million by Janssen, $13 million by Cephalon, $10 million by Endo, $2 million by Actavis, and $108 million spent by Purdue (Ohio Attorney General's Office 2017).

Opioid manufacturers also made financial contributions to medical education and training programs. Again, Purdue led the way, funding over 2000 pain-related Continuing Medical Education (CME) programs and dozens of national pain management training conferences, often paying for selected physicians to attend these events (Van Zee 2009; Temple 2015; Sherman 2017). Pharmaceutical companies also elected to work with individual academic scientists whose research favored their products. These "thought leaders," as they are sometimes referred to, often received financial support to attend conferences and present their findings across the United States (Lembke 2016; Meier 2003).

In addition to sponsoring medical education, conferences, and individual academic researchers, opioid manufacturers also made financial donations to various professional societies and patient advocacy organizations. The most influential of these were the American Pain Foundation (APF), the American Academy of Pain Medicine (AAPA), the American Pain Society (APA), and the American Osteopathic Association (AOA), all of which led campaigns advocating to increase access to opioid pain relievers. Pharmaceutical executives sometimes assumed leadership roles on the boards and trustees of these organizations, enabling them to steer advocacy efforts in line with the interests of Purdue and other opioid manufacturers (Lembke 2016). According to a report by the US Senate Homeland Security Committee (2018), which investigated the financial connections between opioid manufacturers, advocacy groups, and professional societies operating in the area of opioids policy, Purdue alone spent over $4.15 million between January 2012 and March 2017 on twelve different advocacy and professional organizations.

The extraordinary amount of money spent by manufacturers on promoting branded opioid pain relievers was, without a doubt, unprecedented in pharmaceutical

history. But the significant innovation here was not the budget but the co-option of clinical research and patient advocacy. As several observers have noted, pharmaceutical marketing is no longer a question of advertising: it also involves the sponsorship of science and the dissemination of favorable, sponsored research (Healy 2006, 2003; Healy and Cattell 2003; Healy 2000). Two terms that have recently gained currency in analyses of drug development in the US are illustrative of this trend: "ghost-writing" refers to the enlistment by industry of scientists who have very little to do with the research design, but who lend their names to scientific publications, thereby conferring a veneer of independence onto industry-sponsored research (DeTora et al. 2019). "Ghost-management" refers to the management of clinical trials and scientific publications by the pharmaceutical industry, without that management ever being disclosed in publications (Sismondo 2007). Given the well-documented stream of funding donated to patient advocacy groups by pharmaceutical companies, 'ghost-advocacy' seems an apposite term for describing the co-option and enlistment of patient advocacy into pharmaceutical marketing strategy.

This body of work points clearly to the blurred interface between pharmaceutical marketing, science, and advocacy and highlights the artificiality of distinctions between any 'pure' science of opioids on the one hand and any 'pure' marketing or advocacy efforts on the other. The intersection of these entities - pharmaceutical marketing, science, and advocacy – has methodological implications for both our selection of sources and our analytical approach to them. First, it demands that in addition to overt forms of pharmaceutical advertising we also analyze materials of scientific knowledge and patient advocacy. Second, it requires that we read these materials critically or 'against the grain' so as to uncover the unacknowledged ways in which they may resonate with each other.

Methodologically, this means crossing back and forth across the borders between pharmaceutical adverts, scientific publications, and patient advocacy materials, not so much to show how a particular marketing strategy caused scientific knowledge to change, or to prove how a particular scientific study or advocacy effort caused opioid marketing to develop in a particular way. Instead, we juxtapose what scientists and advocates publish with what opioid marketers say in order to better elucidate how evolving category distinctions in overlapping fields, shaped by explicit and implicit cultural and racial imagery, have helped to radically alter clinical consensus on opioid safety.

The (white) trusthworthy pain patient

Having successfully pivoted from the cancer market to the much larger non-cancer pain market, in the early 1990s opioid marketers set about specifying and targeting a more delineated population of future opioid consumers. When conceiving of their target consumers, the most lucrative avenue for opioid manufacturers was to prioritize those who were insured through private or public health insurance plans with generous prescription benefits. Thus, the opioid public that was constructed in the 1990s mapped onto the clientele base of some of the largest health insurance companies in the US: Medicare (US national insurance for the elderly and disabled), Veterans Insurance, and the Bureau of Workers Compensation (Massachusetts Attorney General's Office 2019). To translate what was primarily a profit-maximizing consideration into a marketing campaign that would be persuasive enough to assuage clinicians' long-held concerns about the dangers of opioids, marketers drew on the long-standing cultural imagery surrounding drug addiction to distinguish between two categories of opioid consumers: the trust-worthy pain patient and the heroin addict.

Before examining how this process splitting worked in more detail, it is helpful to consider two characteristics of the symbolism of narcotics addiction in the US during the previous century: first, its tendency to be racialized and explicitly non-white, and second, the unmarked and assumed whiteness of "Americans" unless otherwise racially specified in media and public policies. A large body of historical and political scholarship on the racial symbolism of US drug policy has documented the systematic coding of narcotics users as racial "others" as a way to build political support for prohibitionist laws. In the early 20th century, for example, images of Chinese opium dens engaging in sex slavery, of so-called Mexican Marijuana madness, and of "Negro cocaine fiends" attacking white employers in the American South stimulated public support for prohibition (Musto 1999, Courtwright, 1982). In the later 20th century, racialized representations of narcotics use assumed new forms: from inner city Black and Latinx heroin "junkies" and "pushers" in the 1960s and 1970s, to Black and Latinx crack cocaine addicted "superpredators" and "crack whores" in the 1980s and 1990s (Peffley, Shields, and Williams 1996; Reinarman and Levine 2004). This association of narcotics with urban Black and Latinx neighborhoods leant political justification to new restrictions on social security and welfare benefit eligibility (Wailoo 2014, Muhammad 2019) and facilitated reductions in public funding for economic development in Black and Latinx US city centers (Kohler-Hausmann 2019, Schneider 2011).

Thus, the racialized coding of narcotics users as non-white has long been intertwined with racially discriminary policies in the United States. In fact, the US "War on Drugs" itself grew out of decades of the Federal Bureau on Narcotics' targeting of communities of color with surveillance and arrests. President Nixon coined the term "War on Drugs" in 1971 as a strategy to suppress Black civil rights

activism and white college student protests (Baum 2016, Provine 2007). In the 1980s, War on Drugs policies assumed more sharply discriminatory forms. In particular, the racialized distinction made by popular media and politicians between crack cocaine as a violence-promoting, neurotoxic Black and Latinx drug, and powder cocaine as a recreational white affluent drug, led to passage of the 1986 Anti-Drug Abuse Act. The act mandated minimum prison sentencing for 1/100th the weight of crack cocaine as opposed to powder cocaine, and fed exponential growth in mass incarceration of Black and Latinx Americans in the two decades that followed (Alexander 2010).

Despite consuming illegal narcotics at similar rates as Black or Latinx Americans, and consuming prescribed narcotics at far higher rates given their disproportionate access to prescribers, white Americans have not been portrayed as susceptible to addiction in popular media and public policy discourse of the last century (Herzberg 2020). This unmarked status of white Americans as "normal," and not addiction-prone, in contrast to drug-seeking racialized "others," is thus a crucial element of the cultural and historical context in which opioid manufacturers sought to market their products.

During the early years of opioid marketing in the 1990s, opioid manufacturers took advantage of these long-standing racialized associations when they constructed the implicitly white 'trust-worthy patient' as the legitimate consumer of opioid pain relievers. In contradistinction to the implicitly black heroin addict, the trust-worthy patient was portreyed as impervious to complications such as opioid addiction or overdose. As evidenced in our analysis of branded adverts, the legitimate consumer of opioids was constructed on the basis of two social figures that hold considerable public trust in America. The first was the American grandparent, an implicitly white social figure culturally considered highly unlikely to abuse drugs and

thus providing a contrasting figure to the heroin addict. The second was the injured Veteran, another implicitly white social figure, able to provide a masculine counterimage to the heroin addict. We review specific marketing materials that drew on images of each of these figures below, beginning with the American grandparent.

Throughout the late 1990s and the early 2000s, Purdue circulated hundreds of thousands of pamphlets to medical prescribers with descriptions and photographs of target patients. One widely circulated pamphlet featured an image of a patient called Pam, who was elderly, white, and suffering from chronic back pain due to osteoarthritis. Non-incidentally, Pam was also insured through Medicare (see Figure 1).

[Insert figure 1]

As evidenced in Figure 1, Pam symbolizes whiteness, family, and innocence, signifiers that crop up repeatedly in Purdue's marketing materials from the mid 1990s onwards. One widely circulated prescriber pamphlet presented a series of "pain vignettes," which were case studies featuring older white patients with pain conditions. One vignette described Paul, a "54-year-old writer with osteoarthritis of the hands" and implied that OxyContin would help the Paul to work more effectively (Ohio Attorney General's Office 2017).

Images of white older patients suffering from pain and osteoarthritis began populating the pages of pain journals, through adverts taken out by opioid manufacturers in journals including the *Journal of Pain*, the *Clinical Journal of Pain*, and also journals with wider audience such as the *Journal of the American Medical Association* (Justia US Law 2015). As shown in Figure 2, an OxyContin®

advertisement featured in JAMA 2002 showed an older white man and a boy fishing with the prominent headline, “There can be life with relief” (JAMA ad 2002).

[Insert figure 2]

In addition to branded adverts, Purdue also trained its salesreps to emphasize the “trustworthiness” of elderly patients in their conversations with clinicians (Ohio 2019). Communicating to prescribers what exactly was meant by ‘trustworthy’ would often involve sharing staged photographs and profiles. Eschewing explicitly racial or class-based descriptors in conversations with clinicians, Purdue trained its sales reps to present clinicians with patient photographs of white elderly patients alongside charts showing Medicare coverage for opioids among the elderly. The targeting of older patients insured through Medicare was referred to in Purdue’s internal documents as its “geriatric strategy” (Massachusetts Attorney General’s Office 2019). Through their interactions with sales reps and through their exposure to branded advertising, prescribers across America gradually learned to identify potential opioid consumers. These ‘trustworthy pain patients were white, older, and middle class.

A second social figure that became a face of the trust-worthy patient was the wounded Veteran, a group to hold considerable public respect in America and whose patriotism made for a strong moral argument for pain relief among men. Non-coincidentally, Veterans also enjoyed subsidized access to opioids through US Veterans insurance plans. Over the course of the 1990s and 2000s, sales reps descended on Veterans’ clinics and hospitals, where they delivered talks to prescribers about Veteran’s injuries, trustworthiness, and insurance coverage. As revealed in lawsuits filed by multiple US states (Ohio Attorney General’s Office

2017; Massachusetts Attorney General's Office 2019; Florida Attorney General's Office 2018), Purdue used patient advocacy groups to target veterans. In 2009, for example, Purdue sponsored a book entitled: "*Exit Wounds: A Survival Guide to Pain Management for Returning Veterans and Their Families."* Though the book was presented as the personal story of a wounded white Veteran (See Figure 3), Derek McGinnis, the author was actually employed by the American Pain Foundation, an organization that received millions of dollars of funding from Purdue (U.S. Senate Homeland Security & Governmental Affairs Committee 2018).

[Insert Figure 3]

In tethering opioid consumption to masculinity, strength, and patriotic service, the wounded white Veteran was designed to overcome gendered ideologies that might deter men from taking pain relievers by providing an explicitly masculine face for legitimate opioid consumption. Thus, through different symbols: frailty, innocence, and family on the one hand, and strength, patriotism and masculinity on the other, both the American grandparent and the wounded Veteran served to communicate whiteness. Each provided a legitimate counterfigure to the 'drug addict' or 'heroin addict.'

Marketing materials did not show visual images of 'drug addicts' or 'heroin addicts.' Nor did they make explicit reference to drug addicts or heroin addicts in their marketing materials. For the first few years of opioid prescribing, the drug addict figured only as a silent referent, a counterfigure that Veterans and Gramdmas were supposed to replace. This changed when evidence of deaths from legal opioids became widely known. Early signs of the emergence of a new social figure can be

seen in the Purdue-sponsored Veterans guide (2009). In this 'self-help' guide for managing injury-related pain, McGinnis tells the story of how opioid pain medications helped to turn his life around, emphasizing the benefits of opioid pain medications throughout:

> The pain-relieving properties of opioids are unsurpassed…Yet, despite their great benefits, opioids are underused. For a number of reasons, healthcare providers may be afraid to prescribe them, and patients may be afraid to take them. At the core of this wariness is the fear of addiction, so I want to tackle this issue head-on… Long experience with opioids *shows that people who are not predisposed to addiction* [authors' emphasis] are unlikely to become addicted to opioid pain medications. (2009:106-107)

Inhering within this white injured Veteran's first-hand assurance that opioids are safe is a second message that became increasingly important in the 2000s. This was the message that opioid pain medications were safe *for some kinds of people*, but not for others. Whereas the previous predominant distinction had been between pain patients and heroin addicts, as mortality data showing a surge in opioid-related deaths became publicly available, articulating a second and illegitimate category of opioid consumers - the "opoid abusers" - became increasingly important. We flesh out the racial coding that constructed the opioid abuser below.

The (non-white) opioid abuser

Five years Purdue launched OxyContin in 1996, Purdue was thrust into public spotlight by media reports linking OxyContin to surging rates of opioid deaths. In emails to company executives, Purdue's founder, Richard Sackler, instructed marketers to pursue a strategy of blame: "We have to hammer on the abusers in every way possible," he wrote in an email in February 2001. "They are the culprits and the problem. They are reckless criminals."

By the mid-2000s, the 'opioid abuser,' defined as risky, criminal, and implicitly nonwhite had become a counterpart (and illegitimate) public for opioid marketers. The opioid abuser represented an almost exact photonegative of the trust-worthy patient. Rather than being elderly, insured, and middle class, the opioid abuser was young, criminal, poor, uninsured, and obtained opioids through illegal rather than legal means. Splitting opioid consumers into these two distinct and opposing categories provided an effective pathway to begin to reconcile the mounting evidence of opioid pain relievers' addictive properties with the notion that they were also a safe treatment for chronic pain. These two figures were increasingly placed side-by-side in opioid marketing materials, where their diametric opposition to each other helped to palliate clinicians concerns about opioids and their risks.

Consider, for example, a 2002 testimony from the American Pain Foundation (APF), an organization that received $1.3M in funding from Purdue between 2006-2016 (Virginia Attorney General's Office 2019). The testimony was written as a guide for patients, and after noting a "false fear" that opioid pain medications "are dangerous or addictive," the APF state: "when taken as prescribed, under the direction of a physician for pain relief, opioids are safe and effective, and only in rare cases lead to addiction" (American Pain Foundation 2002). Where addiction does

occur, APF goes on to state, it does so as a result of the "*illegal* and dangerous use of this medication by drug *abusers*." The binary logic of splitting at play here is clear: opioids are 'safe' when taken 'as prescribed' by trustworthy 'patients', but unsafe when taken 'dangerously' or 'illegally' by 'abusers.' Thus, the splitting of opioid consumers into these two opposing categories was a crucial component in creating the conditions in which it was possible for prescribers and consumers alike to continue to believe opioids were safe.

In constructing opioid abusers through a language of 'criminality' and 'illegality,' opioid marketers engaged in an implicit mode of racial coding. In contrast to the social figure of the trust-worthy patient, who was whitened explicitly through images of white American grandparents and war Veterans, marketing materials did not need to show visual images of 'drug abusers,' nor did they need to use explicitly racial descriptors in their narratives about opioid abusers. Instead, marketers were able to code opioid abusers as non-white implicitly, through their association with pre-existing racialized images of "drug addicts," "criminals" and "illegality" – constructs that have long been coded as non-white in America.

As we described above, the preponderant imagery of "drug addicts" or people with so-called 'predisposition' to drug addiction in American popular culture and media over the preceding century has been non-white. On top of this century-old practice of linking specific drugs with ethnic minorities, Black drug users in particular have long been portrayed in terms of criminality, danger, and illegality. As numerous analyses of films, television, and print media show, Black drug users are routinely portrayed as 'criminal,' 'illegal' and as more dangerous than white drug users, who are more likely to be portrayed as innocent victims of a disease (Peffley et al. 1996;

Reinarman and Levine 2004).

Given the century-old racialized regime of representation surrounding drug addiction in America, opioid marketers' use of the seemingly racially neutral terms ("illegal hands," "illegal use" and "criminals") was more than sufficient to racially code opioid abusers as non-white. In cloaking racial distinctions between groups of opioid consumers in the emotive but non-racial language of abuse, theft, street, illegality, and criminality, Oxycontin's advertisers coded opioid abusers as non-white and pedalled the idea that 'patients' and 'abusers' were fundamentally distinct and non-comparable categories of people. Opioid marketer's manipulation of racialized images of drug addiction was neither explicit nor original; it built on a culturally pervasive regime of racialized representation in America. In what becomes a circular kind of logic, addiction was constructed as the *result* of an underlying and implicitly non-white 'criminality.' Consider one final excerpt that illustrates how opioid abusers were implicitly coded as non-white, taken from patient guide sponsored by Cephalon and Purdue and Teva (2007):

> Opioids get into the hands of *drug dealers* … as a result of pharmacy *theft,* forged prescriptions, Internet sales, and even from other people with pain… Adding to the problem is the increase in *abuse* of prescription drugs in the U.S. Persons with addictive disease … have obtained and *misused* these drugs. Others have taken them *illegally* through pharmacy *thefts* or under *false* pretenses in order to sell them "on the street" for profit [authors' emphasis].

This coded racial imagery was highly effective in conveying a sense of the invulnerability to addiction of the targeted consumer population and, by extension, the safety of opioids. Part of the reason this strategy of splitting was so successful was

that it drew on a century-old system of narcotic segregation in the U.S., in which some drugs became illegal through association with non-white users, and other drugs were legal and deemed "medicines" reserved for white and middle-class consumers. From barbiturate tranquilizers and stimulant diet pills marketed to white women following World War II, to the Librium, Valium, and other sedative benzodiazepines sold as "mother's little helper" in the 1960s, middle class whites have long been protected by an exclusive clinical zone of narcotics use and treatment that provides them permissive law enforcement and medical care (Herzberg 2010).

On the heels of this racially segregationist logic, in the early 2000s a novel category of people emerged in the pharmaceutical advertising materials: "persons with addictive disease."A widely circulated patient guide sponsored by Cephalon and Purdue and Teva entitled: "*Treatment Options: A Guide for People Living with Pain"* (2007), defined the "person with addictive disease" as someone who "may abuse their medications, engaging in unacceptable behaviors like increasing the dose without permission or obtaining the opioid from multiple sources." The 'person with addictive disease' should by now be easily recognizable as another iteration of the same process of pharmaceutical splitting that created the opioid abuser. This time, the differentiation lies not in race but in the seemingly objective language of "misuse" and "predisposition." In the face of evidence of abuse of medical opioids, the "person with addictive disease" provides a morally neutral (not necessarily criminal) figure that can be isolated and separated out from the trust-worthy and legitimate pain patient. Through splitting opioid consumers into simplistically opposing 'good' and 'bad' categories, this time on the basis of ascribed inherent 'predisposition' or 'vulnerability,' it becomes possible to reconcile opioids' positive and negative qualities. In notable departure from the more widely used nomenclature within

clinical medicine of "people with substance use disorders" - terms that foreground *use* of a substance - the category of "person with addictive disease" erases that drug consumption, leaving behind only a diseased person with and individualized in-built disposition and pathology.

The circular logic of vulnerability

This bifurcation of opioid consumers into opposing categories was not confined to industry-sponsored patient and prescriber guides. Similar practices of splitting were also occurring in the scientific literature, although along social axes other than race and criminality. By the early 2000s, scientists' statements about how opioids ought to be prescribed had undergone a shift: they were no longer asking whether opioids were safe in a global sense. Instead, the question now turned to who opioids were safe for. Increasingly, scientists came to use patients' "vulnerability to addiction" and "history of abuse" to explain opioid safety (Savage et al. 2003; Haddox et al. 1997; Chou et al. 2009; Hale et al. 1999). Though presented in the epidemiological language of clinical medicine, rather than in through the emotive and racialized imagery of white American grandparents used in branded advertising, scientists and opioid marketers were making analogous distinctions between legitimate and illegitimate opioid consumers.

Consider, for example, an influential consensus statement published in the prestigious *Journal of Pain* (Chou et al. 2009). The consensus statement, entitled "*Clinical Guidelines for the Use of Chronic Opioid Therapy in Chronic Noncancer Pain,*" was authored by a collective of 21 authors, two of which (Dr. Portenoy and Dr. Fine) are well-known spokespersons for Purdue, though the manuscript reports no

conflict of interest. In the consensus statement, scientists asserted a "legitimate medical need for opioids in *some* [authors' emphasis] patients," with 'legitimate need' illustrated through the example of a patient who was "60 years old, has chronic disabling osteoarthritis pain", and "whose history reveals no … personal or family history of drug abuse or addiction." Scientists then presented a counterexample of a younger patient, who is "30 years old with … recent intravenous drug abuse," for whom opioid pain medication would not be appropriate.

For scientists and opioid marketers alike then, opioid safety was now a question of patient characteristics: "the factor that appears to be most strongly predictive of drug abuse," the scientists note, is "a personal or family history of alcohol or drug abuse." The take-home message here is clear: opioids themselves do not cause addiction; at most, they "increase the risk of such behavior *in those already engaging in them or at high risk to do so"* [authors' emphasis]. Or as stated in another consensus statement[1], this one issued by the American Academy of Pain Medicine in conjunction with the American Pain Society (1997), "the *de novo* [our italics] development of addiction when opioids are used for the relief of pain is low". Similar messages were repeated in various other guidelines (Haddox et al. 1997), including one set published in the *Journal of Pain and Symptom Management*, entitled: "Definitions related to the medical use of opioids: Evolution towards universal agreement" (Savage et al. 2003). In this 'universal agreement' published by six authors (no conflict of interest disclosed), the scientists state: "although some drugs produce pleasurable reward, critical determinants of addiction rest also with the user."

[1] Of this collective of 21 scientists, fourteen are now known to have received financial support from pharmaceutical companies, including six who received financial support specifically from Purdue, and eight who received financial support from other opioid manufacturers (New York Attorney General's Office 2018).

Addiction should not be considered as an effect of opioids, they argued. Rather, it was something that occurs “in vulnerable individuals” (Savage et al. 2003).

By the early 2000s, with growing evidence that the white race and older age of the suburban and rural consumers targeted by opioid marketing did not make them invulnerable to overdose or non-medical opioid use, techniques for maintaining distinctions between trust-worthy patients and opioid abusers underwent an interesting kind of upgrade in the form of new scientific instruments for differentiating among patients. One of these was the ‘opioid risk assessment tool’, an instrument designed to assist prescribers in identifying appropriate opioid patients. Many of these tools were designed by scientists with known financial ties to industry (Lembke 2016). They consisted of a short series of questions concerning patient history, with risk of addiction framed as an issue of patient characteristics, including: criminality, prior illicit drug consumption, and history of mental illness.

One of the most widely promoted instruments was the Opioid Risk Tool (Webster and Webster 2005), developed in 2005 by Dr. Webster, who was a former President of the American Academy of Pain Medicine and also an author of numerous CMEs sponsored by Cephalon, Endo, and Purdue. The Opioid Risk Tool was published in *Pain Medicine,* the same journal that published various supplements funded by Endo that promoted Opana ER. The Opioid Risk Tool was a five question, one-minute self-reported patient questionnaire that purported to predict the risk of opioid dependence. To assess the “abuse liability” of opioids, the instrument questioned patients about their prior drug use and criminality, with specific questions including: 1) How often do you have mood swings?; 2) How often do you smoke a cigarette within an hour after you wake up?; 3) How often have you taken medication other than the way that it was prescribed?; 4) How often have you used illegal drugs

(for example, marijuana, cocaine, etc.) in the past five years?; and 5) How often, in your lifetime, have you had legal problems or been arrested. Other scientists devised similar screening tools, including the Screener and Opioid Assessment for Patients With Pain (SOAPP), the revised SOAPP (SOAPP-R), and the Diagnosis, Intractability, Risk, Efficacy (DIRE) instrument (Inflexxion Inc 2008; Butler et al. 2008; Belgrade, Schamber, and Lindgren 2006).

Thus, both the axes as well as the apparatus for pharmaceutical splitting had evolved over time. Whereas earlier splitting in the 1990s had consisted of opioid marketing materials that relied upon racialized and class-based distinctions between pain patients and drug addicts, by the early 2000s splitting was supported by scientific mechanisms. With the assistance of screening tools, prescribers were now differentiating among patients according to social criteria that included criminal status, mental health, and lifestyle.

By the 2000s, this enduring cultural logic that split narcotics consumers into racialized categories of trustworthy patients and opioid abusers was evident in significant racial inequalities in opioid prescriptions for acute pain. Many US physicians believed that non-white patients were more likely to abuse opioids (Hausmann et al 2013, Shavers 2010); as a result, physicians more frequently prescribed opioid pain relievers to whites than to non-whites (Chen et al 2005, Pletcher 2008, Joynt et al 2013). The public health effects of this racial segregation of narcotics use was soon evident in the mortality rates of white Americans: in the mid-1990s, a time when the life expectancy among nearly all ethnic groups in the US was rising, life expectancy among middle-aged white Americans began to plunge. By 2010, white Americans were dying from opioid-related overdose at over double that of Black Americans (Alexander, Kiang, and Barbieri 2018). Paradoxically then, the

racial privilege that assured whites access to an exclusive clinical zone of narcotics use and medical care was now manifesting through white mortality.

"True addiction" vs. "pseudo-addiction"

If the splitting apart of trustworthy patients and opioid abusers had enabled many prescribers to consider opioids safe for some (white) people, there still remained a problem. By the mid 2000s, prescription opioids were killing 11,500 people each year, a larger death toll at the time than heroin and cocaine combined (Okie 2010). With mounting evidence to suggest that trustworthy white patients were not, in fact, invulnerable to addiction and overdose, an additional and new mode of pharmaceutical splitting was called for. This mode of splitting entailed pulling apart not the consumers, but the disorder of addiction itself, which was subdivided into two: "true addiction" and "pseudo-addiction." The construction of these two opposing disorders would help physicians to reconcile the evidence of opioids addictive properties with the notion they were a safe treatment only by recasting obviously addicted patients as undertreated pain patients. Below, we outline the origin and germination of this idea across academic biomedicine and opioid marketing.

In 1989, David Weissman and David Haddox published an article that would become a critical instrument of opioid marketing, entitled, "Opioid pseudoaddiction—an iatrogenic syndrome." One of the authors, David Haddox, was a past president of the American Academy of Pain Medicine, an organization that received significant financial funding from Purdue. Dr. Haddox also later went on to become a senior medical director for Purdue. In the article, Weissman and Haddox introduced the term "pseudoaddiction" to describe an "iatrogenic syndrome of abnormal behavior" entailing behavioral symptoms that mimic "true opioid psychologic dependence."

Behavioral symptoms such as "overwhelming and compulsive interest in the acquisition and use of opioid analgesics," were argued to be not so much symptoms of addiction, because such symptoms were "caused by the undermedication of pain." In other words, patients who were presenting in clinics with behaviors typically associated with addiction were actually suffering from "pseudoaddiction." According to Weissman and Haddox (1989), the solution to this was to increase the patient's dose of opioid pain medications based on their self-reported level of pain.

The paper, which was published in the prestigious journal *Pain,* leant opioid manufacturers a fortuitous source of scientific authority. Opioid marketers published thousands of copies of educational guides for clinical practitioners and designed dozens of CMEs that taught that pseudoaddiction was real (New York Attorney General's Office 2018; Ohio Attorney General's Office 2017; Florida Attorney General's Office 2018; Virginia Attorney General's Office 2019). For example, a Purdue pamphlet titled *"Providing Relief, Preventing Abuse"* urged doctors to look for pseudoaddiction, which it characterized as "the inaccurate interpretation of [drug-seeking] behaviors in patients who have pain that has not been effectively treated." Similarly, another clinical guide sponsored by Cephalon, Endo, and Purdue titled "*Responsible Opioid Prescribing"* (2007) taught that behaviors such as "requesting drugs by name," "demanding or manipulative behavior," hoarding, and seeing more than one doctor to obtain opioids were all signs of pseudoaddiction rather than true addiction[2].

[2] Though these guidelines are no longer publicly available on the websites of pharmaceutical companies, they can be found in the appendices of numerous court complaints (Ohio Attorney General's Office 2017; Florida Attorney General's Office 2018; Virginia Attorney General's Office 2019; Massachusetts Attorney General's Office 2019).

Purdue also sponsored a CME program entitled *Path of the Patient: Managing Chronic Pain in Younger Adults at Risk for Abuse*. In a specially devised role-play, a chronic pain patient tells his doctor that he is taking twice as many hydrocodone pills as directed. The narrator notes that because of pseudoaddiction, the doctor should not assume the patient is addicted even if he persistently asks for a specific drug, seems desperate, hoards medicine, or "overindulges in unapproved escalating doses." The role-play ends with doctor treating the patient with a high-dose, long- acting opioid (Ohio Attorney General's Office 2017).

Endo took this idea a step further by sponsoring a National Initiative on Pain Control CME program in 2009 (*Chronic Opioid Therapy: Understanding Risk While Maximizing Analgesia*), designed specifically to teach clinicians about pseudoaddiction. To increase opioid prescriptions to patients who were showing signs of drug addiction, Endo even mandated that it would award grants to CME providers *only* if they taught clinicians to differentiate between addiction and pseudoaddiction (Ohio Attorney General's Office 2017). Since Endo was a key funder of the National Initiative on Pain Control - responsible for developing, specifying, and reviewing content - this decision went on to have a profound effect on CME programs.

As clinicians made the rounds of industry-sponsored conferences and educational programs, and as the concept of pseudoaddiction populated pharmaceutical marketing materials, a flawed but circuitous logic took hold. Through splitting apart 'true addiction' and 'pseudo-addiction,' the offending diagnosis (addiction) could be removed from the trust-worthy patient, who could now be recategorized as an under-treated pain patient. Continuing a century-old system of racially segregated narcotic control in the United States, the white pain market to whom OxyContin was targeted was thereby fully insulated from suspicion of

addiction. The overall effect of pharmaceutical splitting, was the production of a circuitous logic in clinical discourse of opioid safety whereby, paradoxically, the (white middle class) chronic pain patients to whom opioids were marketed could never, by definition, be addicted, even if they demonstrated addicted behavior.

Discussion

Eventually, as we now know, the fallacy of splittingand selective invulnerability to addiction surfaced, with public outcries against pharmaceutical companies on the heels of US media coverage of a "New Face of Addiction" (Lee 2013; ABC News 2008). Unlike the earlier imagary of drug use, which for the last century had been Mexican, Chinese, Black and Latinx (Courtwright 2009; Musto 1999; Peffley, Shields, and Williams 1996), the "new face" of addiction was the white suburban housewive (Carroll 2016) and white college athlete (Craig and Leider 2016). These were the trustworthy patients who had initiated pain therapy through prescribed opioids and who had ending up injecting heroin in their bathrooms (Netherland and Hansen 2016).

As images of white mothers, grandparents, professionals and college students who had died from opioid overdose circulated throughout America, white audiences and policy makers sounded surprise and alarm, and the tropes surrounding drug addiction underwent an interesting shift. News coverage of white opioid addiction soon featured humanizing descriptors emphasizing promising backgrounds, civic contribution, and personal struggles. While white race was rarely mentioned explicitily, new items signalled whiteness through photographs and through coded language such as "suburban," or through reference to specific neighborhoods known

to be predominantly white. In contrast, articles from the same time period about Black or Latinx people who were addicted to opioids and heroin almost universally explicitly specified their race. Continuing this practice of coding Black and brown populations as criminal, these stories tended not to tell sympathetic stories of educational achievement but focused instead on crimes committed (Netherland and Hansen 2016).

[Insert figure 4]

As the opioid crisis unfolded and as the face of opioid addiction became white, an additional iteration of pharmaceutical splitting occurred, this time at the level of treatment for opioid use disorder. An old drug, buprenorphine, which had been developed in the 1960s but failed to sell as a "minimally addictive" opioid pain reliever owing to its significant addictive potential (Campbell and Lovell 2012), was re-introduced in the late 1990's as a treatment for opioid use disorder. In the run up to buprenorphine's re-branding as Suboxone®, marketers actively distanced the drug from its pharmacological relative, methadone, a drug that had been around since the 1970's but which was stigmatized and symbolically associated with Black and Latinx populations since its adoption as a "weapon" in President Nixon's War on Drugs in the 1970s (Hansen, Parker, and Netherland 2020). Instead, buprenorphine was marketed as a "smart drug" suitable for the "new face" of addiction, one that was young, suburban or rural, and implicitly, white. It was approved office-based use via private private physicians in 2002 and went on to become the opioid use disorder treatment of choice for white, wealthier patients (Netherland and Hansen 2016).

By the late 2000s, a two-tiered market was in place for the treatment of opioid use disorder (Hansen and Skinner 2012): Black and brown patients continued to be treated in DEA-regulated methadone clinics, where they are required to queue each day for the drug and to consume it under direct supervision. White and wealthier patients, in contrast, were increasingly treated with Suboxone® in private healthcare settings and allowed to take the drug home.

Twenty years later, the effects of this racialized drug development continue to be seen in disparities in access: studies show that buprenorphine continues to be prescribed primarily to white patients (Lagisetty et al 2019), while opioid use continues to be criminalized in low income Black communities (Donnelly et al 2020). One might argue therefore that the pharmaceutical splitting strategies exercised by opioid marketers and scientists continue to endure into the next phase of American drug policy: as opioid-maintenance interventions developed to treat opioid addictions are targeted towards some (white middle class) people, while addiction among Black and Brown opioid users continues to criminalized.

The story of how opioids became “safe” reveals the blurred interface between science with marketing, the cultural and racial metaphors shaping American medicine, and the capitalist impulse to divide consumers by inherent behavioral, biological and racial qualities. Even as new medicines and therapeutics are devised to address the opioid epidemic and other public health emergencies, medical inventions embody social imaginaries of differential potential and deservedness. In the case of opioids, cultural understandings of trust and criminality continue to fuel this racially segregated pharmaceutical consumerism. And it is precisely this continued but unacknowledged salience of race and class in contemporary pharmaceutical markets

that has enabled potent opioid pain relievers, known for over a century to be highly addictive, to come to be considered “safe.”

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