

University of Chicago Law School

Chicago Unbound

Coase-Sandor Working Paper Series in Law and
Economics

Working Papers

2020

Innovation Institutions and the Opioid Crisis

Daniel J. Hemel

Lisa Larrimore Ouellette

Follow this and additional works at: https://chicagounbound.uchicago.edu/law_and_economics_wp



Part of the [Law Commons](#)

Chicago Unbound includes both works in progress and final versions of articles. Please be aware that a more recent version of this article may be available on Chicago Unbound, SSRN or elsewhere.

**Innovation Institutions
and the Opioid Crisis**

Daniel Jacob Hemel
University of Chicago - Law School

Lisa Larrimore Ouellette
Stanford Law School

John M. Olin Program in Law and Economics
Stanford Law School
Stanford, California 94305

Working Paper Series
Paper No. 547

This paper can be downloaded without charge from the
Social Science Research Network Electronic Paper Collection
<http://ssrn.com/abstract=3534721>

Innovation Institutions and the Opioid Crisis

Daniel J. Hemel¹ & Lisa Larrimore Ouellette²

February 21, 2020

J.L. & BIOSCIENCES (forthcoming 2020)

The United States has recently—and belatedly—come to recognize opioid addiction as a public health crisis. What has gone mostly unrecognized is the degree to which this crisis is intertwined with U.S. intellectual property law and related elements of U.S. innovation policy. Innovation institutions—the legal arrangements that structure incentives for production and allocation of knowledge goods—encouraged the development and commercialization of addictive painkillers, restricted access to opioid antidotes, and (perhaps most importantly) failed to facilitate investments in alternative, non-addictive treatments for chronic pain. Although innovation policy does not bear all the blame for the opioid wave that has washed over communities across the country, innovation institutions are bound up in the ongoing epidemic to a degree that so far has gone underappreciated.

This Article examines the proliferation of opioid use and abuse through the lens of innovation policy, and it envisions ways in which innovation institutions could help to contain the crisis. Along the way, it seeks to derive broader lessons for innovation policy scholarship as well as recommendations for institutional reform. The opioid crisis challenges the conventional understanding of IP law as a tradeoff between allocative efficiency and dynamic efficiency; it highlights the potentially pernicious role of IP protection for addictive and habit-forming products; and it exposes deep flaws in the structure of federal subsidies for and regulation of prescription drugs. It also draws attention to the political and cultural factors that contribute to innovation policy failures. Ultimately, the opioid crisis underscores both the urgency and the limits of institutional change in the innovation policy domain.

¹ Assistant Professor of Law and Ronald H. Coase Research Scholar, University of Chicago Law School; Edwin A. Heafey, Jr. Visiting Professor of Law, Stanford Law School (winter 2020).

² Associate Professor of Law and Justin M. Roach, Jr. Faculty Scholar, Stanford Law School.

For helpful comments, we thank Nora Engstrom, Richard Frank, Keith Humphreys, Mark Lemley, Amy Madl, Doug Melamed, Michelle Mello, Nicholson Price, Rachel Sachs, Heidi Williams, and participants at the Cardozo Intellectual Property Colloquium, PatCon9, the Juniors Scholars in Intellectual Property Workshop, and the University of San Diego Patent Conference.

Table of Contents

Introduction	3
I. The Opioid Epidemic as a Failure of Innovation Institutions	9
A. A Tale of Three Drugs.....	10
1. The \$35 Billion Question: What Explains OxyContin’s Rise?	10
2. Medication Assisted Treatment: Why Is It Harder to Access Addiction Treatments than Addictive Drugs?	12
3. The \$4100 Overdose Treatment: Why Was the Adoption of Opioid Inhibitors So Slow?	15
B. Intellectual Property Law.....	17
1. IP and OxyContin	18
a. Demand Creation.....	19
b. Habit Formation.....	24
2. IP, Suboxone, and Evzio	26
3. Taking Stock	28
C. Regulation and Liability	29
1. Ex Ante Limits: The FDA and DEA.....	29
2. Ex Post Penalties: Tort and Criminal Liability.....	31
D. Demand-Side Subsidies: Medicare and Medicaid.....	33
1. Health Care Coverage and Opioid Use	34
2. The Medicaid Best Price Rule and Private Payers.....	36
E. Where Were the Alternative Pain and Addiction Treatments?.....	40
II. Mixing, Matching, and Layering Innovation Policies to Address the Opioid Crisis	42
A. Incentivizing Pain- and Addiction-Related Innovation.....	43
1. Intellectual Property and Market Incentives	43
2. Ex Ante Government Spending: Grants and Contracts.....	45
3. Ex Post Government Spending: Prizes and Market Subsidies	47
B. Allocating Access to Pain- and Addiction-Related Innovations	51
1. The Case for Open Access	52
2. Carve-Outs, Buy-Outs, and March-Ins.....	53
3. Expanding Coverage and Removing Regulatory Hurdles.....	54
C. Political Economy of Opioid Innovation Institutions	55
III. Beyond Opioids: Avoiding Innovation Institution Failures	57
Conclusion	60

Introduction

Opioid overdoses killed an estimated 46,802 people in the United States in 2018.³ That is a very slight decline from the previous year, but it is still a stunning number. To put that figure in perspective: More Americans now die from opioid overdoses than from motor vehicle accidents,⁴ or from the AIDS epidemic at its peak.⁵ Over one-third of U.S. adults are estimated to have used prescription opioids in 2015, and nearly five percent to have misused them.⁶ The ubiquity of opioids not only put those patients who had prescriptions at risk of addiction but also unleashed a flood of pills that could be used and abused by family members and friends.⁷ Prescription opioids further fed into the spread of other opioids—including heroin, the use of which increased almost five-fold in a decade,⁸ and fentanyl, a synthetic opioid that has seen an even more dramatic and deadly surge.⁹ The economic costs of the epidemic are staggering, likely

³ See Joel Achenbach, *U.S. Life Expectancy Ticks Up as Drug Fatalities and Cancer Deaths Drop*, WASH. POST (Jan. 29, 2020), https://www.washingtonpost.com/health/us-life-expectancy-ticks-up-as-drug-fatalities-and-cancer-deaths-drop/2020/01/29/2f663376-4206-11ea-b5fc-eefa848cde99_story.html. Opioids are drugs that block pain signals by binding to opioid receptors on nerve cells, including opiates derived from the opium poppy plant, such as heroin, morphine, and codeine, as well as synthetic opioids such as oxycodone (OxyContin), hydrocodone (combined with acetaminophen to make Vicodin), and fentanyl. See *Opioids*, NAT'L INST. ON DRUG ABUSE, <https://www.drugabuse.gov/drugs-abuse/opioids> (last visited Feb. 8, 2020).

⁴ See *2017 Fatal Motor Vehicle Crashes: Overview*, NAT'L HIGHWAY TRAFFIC SAFETY ADMIN. (Oct. 2018), <https://crashstats.nhtsa.dot.gov/Api/Public/ViewPublication/812603>.

⁵ See Lenny Bernstein & Christopher Ingraham, *Fueled by Drug Crisis, U.S. Life Expectancy Declines for a Second Straight Year*, WASH. POST (Dec. 21, 2017), <http://wapo.st/2BpGCYg> (citing Stanford University psychiatry and behavioral sciences professor Keith Humphreys); cf. JOSH BLOOM, AM. COUNCIL ON SCI. & HEALTH, *WHATEVER HAPPENED TO AIDS?: HOW THE PHARMACEUTICAL INDUSTRY TAMED HIV* 14 fig.8 (2011) (41,699 deaths from AIDS in peak year of 1995).

⁶ See Beth Han et al., *Prescription Opioid Use, Misuse, and Use Disorders in U.S. Adults: 2015 National Survey on Drug Use and Health*, 167 *ANNALS INTERNAL MED.* 293 (2017).

⁷ Over half of pain relief misusers obtained their drugs from a friend or relative. See *SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., RESULTS FROM THE 2016 NATIONAL SURVEY ON DRUG USE AND HEALTH 170413 tbl.6.53B* (2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

⁸ See Silvia S. Martins, Aaron Sarvet & Julian Santaella-Tenorio, *Changes in US Lifetime Heroin Use and Heroin Use Disorder: Prevalence from 2001-2002 to 2012-2013 National Epidemiological Survey on Alcohol and Related Conditions*, 74 *JAMA PSYCHIATRY* 445 (2017). While the share of the U.S. population that uses heroin remains small (less than two percent of all adults at last count), roughly four in five heroin users began by abusing prescription opioids. See Pradip K. Muhuri, Joseph C. Gfroerer & M. Christine Davies, *Associations of Nonmedical Pain Reliever Use and Initiation of Heroin Use in the United States*, CBHSQ DATA REVIEW, Aug. 2013, <https://www.samhsa.gov/data/sites/default/files/DR006/DR006/nonmedical-pain-reliever-use-2013.htm>.

⁹ See Merianne Rose Spencer et al., *Drug Overdose Deaths Involving Fentanyl, 2011—2016*, 68 *NAT'L VITAL STATS. REPORTS* no. 3, at 1, 9 tbl.1 (2019), https://www.cdc.gov/nchs/data/nvsr/nvsr68/nvsr68_03-508.pdf. In recent years, the synthetic opioid fentanyl has overtaken heroin on the illegal drug market; by 2015, fentanyl and

topping \$500 billion annually.¹⁰ Without a doubt, the opioid crisis is among the primary policy challenges facing the United States today.

Two dominant narratives have emerged in scholarly and popular commentary on the opioid crisis's causes. One narrative casts opioid abuse as a “disease of despair”—a byproduct of poverty and lack of economic opportunity that has hit hardest in deindustrializing regions.¹¹ This account may capture some important social trends, but identifying causal mechanisms behind the growth in opioid overdoses has proven challenging.¹² Econometric evidence suggests that overdoses have more to do with the availability and cost of drugs than with regional economic trends. As one prominent health economist recently wrote, “efforts to improve local economies, while desirable for other reasons, are not likely to yield significant reductions in overdose mortality.”¹³

A second narrative—which we refer to as the “disease of deception” account—emphasizes the role of pharmaceutical companies in hiding addiction risks from the public even as they aggressively marketed opioids for ever-broader uses. The chief antagonists in this narrative are members of the Sackler family that owned and ran Purdue Pharma, the maker of the now-infamous opioid drug OxyContin.¹⁴ The disease-of-deception narrative draws strong support from documents that have surfaced in litigation against Purdue Pharma revealing that company officials knew shortly after OxyContin's introduction in 1996 that the

its analogs were the leading cause of U.S. drug overdose deaths. *Overdose Death Rates*, NAT'L INST. ON DRUG ABUSE, <https://www.drugabuse.gov/related-topics/trends-statistics/overdose-death-rates> (revised Aug. 2018). Fentanyl also has approved medical uses. For a lay overview, see Kathleen Davis, *Everything You Need to Know About Fentanyl*, MED. NEWS TODAY (Oct. 2, 2017), <https://www.medicalnewstoday.com/articles/308156.php>. We are unaware of a study that measures the percentage of fentanyl users who began by abusing prescription opioids.

¹⁰ Opioid-related health care, criminal justice, and lost productivity cost the United States over \$100 billion annually. See CHRIS CHRISTIE ET AL., THE PRESIDENT'S COMMISSION ON COMBATING DRUG ADDICTION AND THE OPIOID CRISIS: FINAL REPORT 31 (2017), https://www.whitehouse.gov/sites/whitehouse.gov/files/images/Final_Report_Draft_11-1-2017.pdf. If one estimates the value of a statistical life at roughly \$10 million, see Cass R. Sunstein, *The Value of a Statistical Life: Some Clarifications and Puzzles*, 4 J. BENEFIT-COST ANALYSIS 237, 240 (2013), the yearly cost in lost lives is over \$400 billion more.

¹¹ See, e.g., Anne Case & Angus Deaton, *Mortality and Morbidity in the 21st Century*, in BROOKINGS PAPERS ON ECONOMIC ACTIVITY 397, 398 (2017) (attributing a rise in deaths from suicide, alcohol, and drug overdoses—which they define as “deaths of despair”—to “a long-standing process of cumulative disadvantage for those with less than a college degree”).

¹² On the exponential growth in drug overdose deaths, largely due to opioids, see Hawre Jalal et al., *Changing Dynamics of the Drug Overdose Epidemic from 1979 Through 2016*, 361 SCIENCE eaau1184 fig.1 (2018).

¹³ Christopher J. Ruhm, *Drivers of the Fatal Drug Epidemic*, 64 J. HEALTH ECON. 25, 25 (2019); see also Case & Deaton, *supra* note 11, at 428 (rejecting economic and income-based accounts for rising “deaths of despair”).

¹⁴ See, e.g., Patrick Radden Keefe, *The Family that Built an Empire of Pain*, NEW YORKER (Oct. 30, 2017), <https://www.newyorker.com/magazine/2017/10/30/the-family-that-built-an-empire-of-pain>; Art Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, 99 AM. J. PUB. HEALTH 221, 221 (2009).

drug was being abused widely—yet concealed that information from the public.¹⁵

Even Purdue Pharma's most withering critics do not allege that the company's cover-up was the sole cause of the opioid crisis, however. Widespread OxyContin abuse was a front page news story as early as 2001, when the opioid epidemic was still in its nascent stage.¹⁶ "[N]o prescription drug in the last 20 years has been so widely abused so soon after its release as OxyContin," the *New York Times* reported in May 2001, citing officials at the federal Drug Enforcement Administration (DEA).¹⁷ Talk radio host Rush Limbaugh drew greater attention to OxyContin in 2003 when he acknowledged on air that he had become addicted to prescription painkillers.¹⁸ And in 2007, a full decade before the annual death toll from opioid abuse reached its peak, Purdue Pharma and three of its executives entered a widely publicized guilty plea to federal criminal charges of misbranding—charges related to the company's concealment of OxyContin's addictive properties.¹⁹ None of this is to suggest that Purdue Pharma and other pharmaceutical companies that marketed prescription opioids are immune from blame for the current crisis. They are not. But deception alone cannot explain how opioids continued to inundate American medicine cabinets long after the addiction risks were widely publicized.

How did opioids overwhelm a nation well aware of their addictive properties, claiming victims across the socioeconomic spectrum? To understand that, one must understand not only how opioid manufacturers aggressively marketed their wares and why physicians profligately prescribed these drugs but also why alternative pain management strategies failed to emerge and why opioid antidotes and abuse treatments were so much slower to spread. Purdue Pharma and "pill mills" play a part in this story,²⁰ but so does Medicaid's "best price" mandate and the National Institutes of Health's allocation of research funding. Comprehending the origins and persistence of the crisis requires a deep

¹⁵ See, e.g., Barry Meier, *Origins of an Epidemic: Purdue Pharma Knew Its Opioids Were Widely Abused*, N.Y. TIMES (May 29, 2018), <https://www.nytimes.com/2018/05/29/health/purdue-opioids-oxycontin.html>.

¹⁶ See Francis X. Clines with Barry Meier, *Cancer Painkillers Pose New Abuse Threat*, N.Y. TIMES, Feb. 9, 2001, at A1, <https://www.nytimes.com/2001/02/09/us/cancer-painkillers-pose-new-abuse-threat.html>.

¹⁷ Barry Meier, *U.S. Asks Painkiller Maker to Help Curb Wide Abuse*, N.Y. TIMES, May 1, 2001, at A16, <https://www.nytimes.com/2001/05/01/us/us-asks-painkiller-maker-to-help-curb-wide-abuse.html>.

¹⁸ See James Barron, *In Show, Limbaugh Tells of a Pill Habit; Plans to Enter Clinic*, N.Y. TIMES, Oct. 11, 2003, at A1, <https://www.nytimes.com/2003/10/11/us/in-show-limbaugh-tells-of-a-pill-habit-plans-to-enter-clinic.html>; Evan Thomas, *"I Am Addicted to Prescription Pain Medicine,"* NEWSWEEK (Oct. 19, 2003), <https://www.newsweek.com/i-am-addicted-prescription-pain-medication-138721>.

¹⁹ See Barry Meier, *In Guilty Plea, OxyContin Maker to Pay \$600 Million*, N.Y. TIMES (May 10, 2007), <https://www.nytimes.com/2007/05/10/business/11drug-web.html>.

²⁰ See Chris McGreal, *Why Were Millions of Opioid Pills Sent to a West Virginia Town of 3,000?*, GUARDIAN (LONDON) (Oct. 2, 2019), <https://www.theguardian.com/us-news/2019/oct/02/opioids-west-virginia-pill-mills-pharmacies>.

dive into the organizations and policies that drove the opioid wave as well as those that failed to produce a robust response.

This Article takes up that task. We suggest that the opioid epidemic is, in important respects, a *disease of design*. By this, we do not mean to suggest that the opioid crisis is the outgrowth of any single person's grand plan. What we mean instead is that the design of *institutions* created conditions that allowed the crisis to arise and proliferate. We focus in particular on the design of innovation institutions—the legal arrangements that structure the production and allocation of knowledge goods.²¹ These include intellectual property law (patents, trade secrets, trademarks, regulatory exclusivity, etc.), but also the regulatory structures of the Food and Drug Administration (FDA) that determine whether knowledge goods can reach the market and the public benefit programs like Medicare and Medicaid that subsidize access to knowledge goods.²²

The design of innovation institutions enabled the opioid epidemic in a number of ways. First, U.S. innovation institutions produced powerful incentives for pharmaceutical firms to develop and commercialize highly addictive prescription pain medicines while imposing weaker constraints on the rollout of new and more addictive products. Second, systems for allocating access to medical technologies promoted use of addictive medicines while creating barriers to access for addiction treatments. Third, innovation institutions allowed—and indeed, encouraged—manufacturers of opioid antidotes to charge sky-high prices for products that, if more widely accessible, likely could have saved the lives of thousands of opioid overdose victims. Fourth, even while encouraging the rapid diffusion of addictive opioids, innovation institutions failed to sufficiently reward firms for formulating, refining, or popularizing alternative treatments for addiction or for the underlying problem of chronic pain. Again, no one sat down and designed the system to work this way. But a series of institutional design choices—some conscious, others unconscious—allowed a perfect storm to coalesce.

Some of these design flaws are relatively familiar. Intellectual property (IP) is an innovation institution that relies on signals of social value generated by market mechanisms, and market-generated signals can yield inefficient allocations of goods in the presence of externalities. Addictive pain-medications generate negative externalities, and overdose and addiction treatments produce positive externalities, so it is perhaps unsurprising that America ended up with too many addictive prescription opioids and too few overdose and addiction treatments. Furthermore, IP distorts investments in research and development

²¹ For an overview of the main innovation institutions, see Daniel J. Hemel & Lisa Larrimore Ouellette, *Innovation Policy Pluralism*, 128 YALE L.J. 544 (2019).

²² The term “knowledge good” refers to “anything that can be digitized.” Daniel J. Hemel & Lisa Larrimore Ouellette, *Knowledge Goods and Nation-States*, 101 MINN. L. REV. 167, 168 & n.1 (2016) (quoting HAL VARIAN, *MARKETS FOR INFORMATION GOODS* 3 (1999)). The knowledge goods we have in mind here are, principally, pharmacological formulas and therapeutic methods for the treatment of addiction and pain. Although pharmaceuticals are physical goods as well as knowledge goods, the primary value lies in the information underlying the product.

toward patentable technologies like pharmaceuticals,²³ so it is no surprise that the patent-centric U.S. innovation institutions resulted in a nation awash in pills but wanting for alternative pain treatments.

In other respects, our examination of the role of innovation institutions in the opioid epidemic challenges traditional understandings of IP in particular and innovation institutions more broadly. The conventional view posits that IP policy's fundamental tradeoff is between innovation and access, or what economists call dynamic efficiency and allocative efficiency.²⁴ IP incentivizes the development and commercialization of new and better products (the dynamic-efficiency benefit), but it also encourages IP holders to raise prices and restrict access (the allocative-inefficiency cost). The opioid epidemic presents a contrasting image of IP's potential consumption-expanding effects. Opioid patents induced investments in efforts to create demand for products that consumers did not previously believe they wanted.²⁵ This demand-creation effect was especially powerful because the patented product was habit-forming—Purdue's lower prices for OxyContin in the short term could thus raise consumption in the long term.²⁶ And this problem was exacerbated by the effective cost often being lowered through prescription drug insurance. Although scholars typically view increased use of patented technologies as a welfare gain, the example of prescription opioids illustrates that patents' consumption-expanding effects can be pernicious.

Ideally, the government would counteract the biases embedded in the patent system through other innovation institutions, including regulations, taxes, and government-directed financial rewards such as grants and prizes. For example, market-based prizes in the form of insurance reimbursement policies appear to be a particularly promising intervention.²⁷ But in the context of pain treatment, the federal government's non-patent interventions exacerbated the skew toward prescription opioids and away from other pain management and mitigation strategies. At the same time, government policies created barriers that limited access to addiction treatments. Additionally, and paradoxically, the federal government's subsidies for opioid antidotes may have *reduced* access to these life-saving products, challenging the view that demand-side subsidies are a solution to the patent system's pitfalls.

²³ See Amy Kapczynski & Talha Syed, *The Continuum of Excludability and the Limits of Patents*, 122 YALE L.J. 1900 (2013).

²⁴ See, e.g., Bhaven Sampat and Heidi L. Williams, *How Do Patents Affect Follow-on Innovation? Evidence from the Human Genome*, 109 AM. ECON. REV. 203, 204 (2019) (“Dating back at least to analyses such as Nordhaus (1969), optimal patent policy design has traditionally been framed as a trade-off between this benefit of providing incentives for the development of new technologies and the cost of deadweight loss from higher prices during the life of the patent.”).

²⁵ The same is true for many non-opioid innovations, of course—which is part of why we think the story of opioid innovations has lessons for innovation policy more broadly.

²⁶ As we will discuss, the economics literature has demonstrated that it is sometimes rational to price addictive products even below marginal cost. See *infra* Section I.B.2.

²⁷ See generally Rachel E. Sachs, *Prizing Insurance: Prescription Drug Insurance as Innovation Incentive*, 30 HARV. J.L. & TECH. 153 (2016) (explaining how manipulation of the market through insurance reimbursement policies feeds back into innovation incentives).

Recognizing the role of America's innovation institutions in the opioid epidemic helps inform the search for paths out of the current crisis, but it is essential to emphasize that no magic-bullet policy will bring the opioid epidemic to an end. The proliferation of prescription opioids was both a function of incentives generated by the current innovation ecosystem and a response—misguided as it may have been—to the very real problem of chronic pain afflicting an estimated one in five U.S. adults.²⁸ Any comprehensive effort to curtail opioid abuse will require interventions aimed at addressing chronic pain in ways that do not put patients at risk of addiction. The solution likely will involve regulated use of opioids by the populations for which they are justified as well as both existing and novel nonaddictive analgesics.²⁹ At the same time, wider access to existing non-pharmacological pain treatments such as acupuncture, physical therapy, exercise, meditation, and cognitive behavioral therapy may do as much to mitigate the overuse of prescription opioids as any pharmacological leap.³⁰ Moreover, any comprehensive national strategy to contain the opioid epidemic also will require interventions aimed at individuals already in the throes of addiction (medically known as “substance use disorder” or “opioid use disorder”).³¹ Initiatives at the federal, state, and local level suggest progress in this regard, though still on a scale far too small relative to the problem that they aim to solve.³²

This Article is an attempt to understand how innovation institutions are bound up in the opioid crisis, how they might help to bring the crisis to an end, and what lessons the opioid crisis offers for innovation policy going forward. Part I investigates the relationship between innovation institutions and the sky-high rates of opioid use, abuse, and overdose. Part II draws on insights from the study of innovation policy and comparative institutional analysis to evaluate the ways in which innovation institutions can respond to the opioid epidemic. For example, distortions caused by patent law might be addressed through interventions in areas such as FDA regulation, tort law, and antitrust. And direct public support can address problems on both the incentive and allocation side of innovation policy. As we discuss, there are significant political hurdles to reform, although it is at least promising that opioid misuse is now being viewed as a

²⁸ See James Dahlhamer et al., *Prevalence of Chronic Pain and High-Impact Chronic Pain Among Adults — United States, 2016*, 67 MORBIDITY & MORTALITY WKLY. REP. 1001 (2018), <https://www.cdc.gov/mmwr/volumes/67/wr/mm6736a2.htm>.

²⁹ See, e.g., *infra* notes 107–109 and accompanying text (describing recent randomized controlled trials suggesting that certain non-opioids are as effective as opioids at treating both acute and chronic pain).

³⁰ See *infra* note 216 and accompanying text (describing a call from the National Academies for more research in these areas).

³¹ See Allison L. Pitt, Keith Humphreys & Margaret L. Brandeau, *Modeling Health Benefits and Harms of Public Policy Responses to the US Opioid Epidemic*, 108 AM. J. PUB. HEALTH 1394 (2018).

³² Cf. Rebecca L. Haffajee & Richard G. Frank, *Making the Opioid Public Health Emergency Effective*, 75 JAMA PSYCHIATRY 767, 767 (2018) (describing four aspects of the opioid crisis that meet the federal definition of a public health emergency and arguing that the epidemic “requires much greater funds, quickly”).

public health problem. Finally, Part III asks what lessons we can learn from the opioid crisis for innovation policy more broadly.

I. The Opioid Epidemic as a Failure of Innovation Institutions

Although a number of social, economic, and political factors have fueled the opioid epidemic, three phenomena in particular have contributed to the epidemic's spread and severity: (1) the proliferation of prescription opioids from the late 1990s onwards, (2) restrictions on access to opioid antidotes and medication-assisted treatment for opioid use disorder, and (3) the limited availability of non-pharmacological treatments or studies on new uses of nonaddictive existing drugs for either chronic pain or addiction. Each of these phenomena involves the production and allocation of knowledge goods. This Part highlights the role of America's innovation institutions in fueling these trends, while also recognizing the complexity of this history and the influence of other actors and structures.

To illustrate how innovation institutions are bound up in the opioid crisis, we begin in Section I.A with the stories of three pharmaceutical knowledge goods that have affected different aspects of the epidemic: (1) OxyContin, a controlled-release form of an opioid called oxycodone, for treatment of chronic pain; (2) Suboxone, a treatment for opioid use disorder; and (3) Evzio, a device for injecting medicine to halt opioid overdoses. Of course, these three drugs capture only part of the story of the American opioid epidemic. For one thing, as we discuss in more detail below, OxyContin is just one of many opioids contributing to the overdose epidemic; Suboxone is just one among several drugs used to treat opioid use disorder; and Evzio is not the only delivery mechanism for overdose treatments. Nonetheless, the histories of OxyContin, Suboxone, and Evzio capture important aspects of the opioid epidemic's emergence and expansion, helping us show how America became awash in prescription opioids and not in the drugs needed to treat addiction and reverse overdoses.

Sections I.B–D then relate these narratives to specific innovation institutions: intellectual property law (including patents, regulatory exclusivity, and their antitrust limits), institutions for ex ante and ex post drug regulation, and public benefit programs that subsidize access to pharmaceuticals and health care. All of these institutions are deeply intertwined with the opioid epidemic, though often in tangled ways.

In Section I.E, we turn to the innovations that existing institutions *failed* to produce for treating both pain and opioid addiction. Opioids are not the only (and often likely not the best) way to treat chronic pain; pharmaceuticals may not be the only effective treatment for addiction;³³ and the Evzio injector is not the only way to halt an opioid overdose. Yet American innovation institutions

³³ Evidence of the efficacy of medication assisted treatment for opioid use disorder is, however, quite robust. For an overview, see Hilary Smith Connery, *Medication-Assisted Treatment of Opioid Use Disorder: Review of the Evidence and Future Directions*, 23 HARV. J. ON PSYCHIATRY 63 (2015).

failed to promote the development and commercialization of alternative treatments involving existing drugs or non-pharmacological interventions. This is—if not quite by conscious design—nonetheless a byproduct of the design of innovation institutions, which promote technologies that are amenable to IP protection but provide insufficient incentives for technologies that are not. And while non-IP policies potentially can offset some of the IP system’s biases, the U.S. federal government’s non-IP interventions have often done the opposite—exacerbating rather than mitigating the failures of patent-centric innovation institutions.

A. A Tale of Three Drugs

1. *The \$35 Billion Question: What Explains OxyContin’s Rise?*

In the early 1990s, MS Contin, a controlled-release form of morphine sulfate, was generating millions of dollars in sales for Purdue Pharma.³⁴ But MS Contin no longer had IP-protected exclusivity,³⁵ and Purdue expected generic competition to eat into its profits.³⁶ The firm pivoted to a new pain-treatment market strategy. In November 1993, the U.S. Patent and Trademark Office (PTO) granted Purdue’s application for Patent No. 5,266,331, which claimed a controlled-release form of the opioid oxycodone.³⁷ Just over two years later, in December 1995, the FDA approved Purdue’s application to market OxyContin for treatment of chronic pain.³⁸ Purdue’s strategy, according to its 1996 budget plan, was “to switch patients who would have been started on MS [Contin] to OxyContin, as quickly as possible.”³⁹

The new drug would prove to be a commercial blockbuster. Purdue Pharma set the price of OxyContin at levels that put it within reach even of patients who lacked prescription drug coverage: \$1.25 per 10-milligram tablet as of 2000.⁴⁰ The number of OxyContin prescriptions dispensed nationwide

³⁴ See *Purdue and the OxyContin Files*, KAISER HEALTH NEWS (June 13, 2018), <https://khn.org/news/purdue-and-the-oxycontin-files> (page 61 of 1996 Budget Plan).

³⁵ Although numerous articles describe Purdue as having a patent on MS Contin that was set to expire around 1995, no such patent is listed in the FDA Orange Book in the 1980s or 1990s; rather, Purdue had regulatory exclusivity that expired in 1990. See FOOD & DRUG ADMIN., APPROVED DRUG PRODUCTS WITH THERAPEUTIC EQUIVALENCE EVALUATIONS AD27 (10th ed. 1990) (listing MS Contin as having new dosage form exclusivity that would expire on May 29, 1990, and no listed patents), http://data.nber.org/fda/orange-book/historical/1986-2016/1_orange_book_PDFs/full_books_1980-2016/1990.pdf.

³⁶ See *Purdue and the OxyContin Files*, *supra* note 34 (page 6 of 1996 Budget Plan).

³⁷ U.S. Patent No. 5,266,331 (filed Nov. 27, 1991; issued Nov. 30, 1993).

³⁸ *Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, U.S. FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm338566.htm> (last updated Nov. 28, 2018).

³⁹ See *Purdue and the OxyContin Files*, *supra* note 34 (page 6 of 1996 Budget Plan).

⁴⁰ See *OxyContin Diversion and Abuse*, NAT’L DRUG INTELLIGENCE CTR. (Jan. 2001), <https://www.justice.gov/archive/ndic/pubs/651/abuse.htm>.

each year reached six million that year, bringing in over \$1 billion in sales.⁴¹ Thanks to its patent rights, Purdue Pharma controlled the entire controlled-release oxycodone market until 2005.⁴² Due to a temporary patent litigation loss, generics briefly captured up to a third of the market in terms of number of prescriptions, but Purdue ultimately prevailed in litigation and forced competitors out of the market by 2010.⁴³ In 2010, Purdue also engaged in “product hopping”⁴⁴ by replacing its original OxyContin formulation with a new “abuse-deterrent” formulation, which is protected until 2030 by later-expiring patents.⁴⁵ (The new crush-resistant formulation seems to have been only moderately effective at deterring abuse.⁴⁶) By 2018, Purdue Pharma’s all-time total OxyContin revenue topped \$35 billion.⁴⁷

To be clear, OxyContin is just one of several prescription opioids that have contributed to America’s overdose epidemic. In a recently released federal database, Purdue ranked fourth among prescription opioid manufacturers from 2006 to 2012, with just over three percent of the market.⁴⁸ This small market share likely understates Purdue’s role in the epidemic, however. OxyContin was

⁴¹ See GARDENIA HARRIS, JOHN Q. HODGES & CAROL A. SNIVELY, OXYCONTIN IN MISSOURI: A POLICY BRIEF EXPLORING PATTERNS OF ABUSE, PREVENTION, TREATMENT AND INTERDICTION STRATEGIES 8 (2002); Van Zee, *supra* note 14, at 221.

⁴² See *Purdue Pharma L.P. v. Endo Pharm. Inc.*, 438 F.3d 1123 (Fed. Cir. 2006) (withdrawing a 2005 opinion that had affirmed a judgment that Purdue’s patents were unenforceable for inequitable conduct—which had allowed generic oxycodone launches—and instead concluding that the generic manufacturer’s product would infringe Purdue’s patents); Catherine S. Hwang, Hsien-Yen Chang & G. Caleb Alexander, *Impact of Abuse-Deterrent OxyContin on Prescription Opioid Utilization*, 24 PHARMACOEPIDEMOLOGY & DRUG SAFETY 197, 198–200 (2015) (describing the history of generic oxycodone launches and then removal from the market due to patent settlements and showing Purdue versus generic sales numbers).

⁴³ See Hwang et al., *supra* note 42, at 199 fig.1.

⁴⁴ See generally Michael A. Carrier & Steve D. Shadowen, *Product Hopping: A New Framework*, 92 NOTRE DAME L. REV. 167 (2016) (describing this practice and providing a framework for antitrust analysis).

⁴⁵ See Hwang et al., *supra* note 42, at 200 tbl.1; *Patent and Exclusivity for N022272*, U.S. FOOD & DRUG ADMIN. ORANGE BOOK, https://www.accessdata.fda.gov/scripts/Cder/ob/patent_info.cfm?Product_No=001&AppL_No=022272&AppL_type=N (last visited July 21, 2019). Some of these patents have been found invalid as obvious. See *Purdue Pharma L.P. v. Epic Pharma, LLC*, 811 F.3d 1345 (Fed. Cir. 2016).

⁴⁶ See Hwang et al., *supra* note 42, at 200–01.

⁴⁷ See Patrick Radden Keefe, *The Family that Build an Empire of Pain*, NEW YORKER (Oct. 30, 2017), <https://www.newyorker.com/magazine/2017/10/30/the-family-that-built-an-empire-of-pain>; *OxyContin Maker Purdue Pharma to Stop Marketing Opioids to Doctors*, MARKETPLACE (Feb. 10, 2018), <https://www.marketplace.org/2018/02/10/health-care/uncertain-hour/oxycontin-maker-purdue-pharma-stop-marketing-opioids-doctors> (citing data from IQVIA).

⁴⁸ See Scott Higham, Sari Horwitz & Steven Rich, *76 Billion Opioid Pills: Newly Released Federal Data Unmasks the Epidemic*, WASH. POST. (July 16, 2019), https://www.washingtonpost.com/investigations/76-billion-opioid-pills-newly-released-federal-data-unmasks-the-epidemic/2019/07/16/5f29fd62-a73e-11e9-86dd-d7f0e60391e9_story.html.

for a time the “drug of choice among abusers,”⁴⁹ and it still appears to be the most abused *single-entity* prescription painkiller.⁵⁰ Approximately 14.1 percent of adults who reported misuse of a prescription pain reliever in 2015 said they misused OxyContin specifically.⁵¹ Moreover, there is some evidence to suggest that oxycodone is more prone to abuse than other common opioids.⁵² A recent empirical study of cross-state variation in OxyContin exposure concluded that “the recent heroin epidemic is largely due to the reformulation of OxyContin.”⁵³ Additionally, some of Purdue’s efforts to promote controlled-release oxycodone may have had spillover effects on other opioid products.⁵⁴

Our focus on OxyContin should not be misinterpreted as a monocausal explanation for what is in fact an epidemic with multiple and converging root causes. Rather, its prominence makes it a useful example for illustrating the relationship between opioids and innovation institutions. But before we turn to this relationship, we introduce two other illustrative drugs—each of which might have done more to contain the epidemic had it been more widely distributed: Suboxone and Evzio.

2. Medication Assisted Treatment: Why Is It Harder to Access Addiction Treatments than Addictive Drugs?

Rising addiction to opioids such as OxyContin has been accompanied by growing business interest in drugs for treating individuals suffering from opioid use disorder, which are commonly described as medication-assisted

⁴⁹ U.S. GENERAL ACCOUNTING OFFICE, PRESCRIPTION DRUGS: OXYCONTIN ABUSE AND DIVERSION AND EFFORTS TO ADDRESS THE PROBLEM 33 (2003).

⁵⁰ See SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., RESULTS FROM THE 2016 NATIONAL SURVEY ON DRUG USE AND HEALTH: DETAILED TABLES 170525 tbl. 1.97A (Sept. 7, 2017), <https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2016/NSDUH-DetTabs-2016.pdf>.

⁵¹ *Id.* That figure dropped to 12.5 percent in 2015. *Id.* Note that this does *not* mean that OxyContin accounted for 14.1 percent of all misused prescription pain relievers, because some OxyContin misusers may have misused other prescription pain relievers as well.

⁵² See Rachel Wightman et al., *Likeability and Abuse Liability of Commonly Prescribed Opioids*, 8 J. MED. TOXICOLOGY 335 (2012) (“Oral oxycodone has a substantially elevated abuse liability profile compared to oral morphine and hydrocodone due to high likability scores and a relative lack of negative subjective effects.”). Cf. SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., *supra* note 50, at 170525 tbl. 1.97A (indicating that OxyContin accounted for 10% of prescription pain reliever use and 12% of abuse in 2016). But see Sharon L. Walsh et al., *The Relative Abuse Liability of Oral Oxycodone, Hydrocodone and Hydromorphone Assessed in Prescription Opioid Abusers*, 98 DRUG & ALCOHOL DEPENDENCE 191, 200 (2008) (“[T]he abuse liability of [oral hydrocodone, oxycodone and hydromorphone] does not differ substantially from one another . . .”).

⁵³ Abby Alpert, David Powell & Rosalie Liccardo Pacula, *Supply-Side Drug Policy in the Presence of Substitutes: Evidence from the Introduction of Abuse-Deterrent Opioids*, AM. ECON. J.: ECON. POL’Y, Nov. 2018, at 1, 1.

⁵⁴ See U.S. SENATE HOMELAND SECURITY & GOVERNMENTAL AFFAIRS COMM., FUELING AN EPIDEMIC: REPORT TWO – EXPOSING THE FINANCIAL TIES BETWEEN OPIOID MANUFACTURERS AND THIRD PARTY ADVOCACY GROUPS (2018) (noting that payments from Purdue account for almost half of the \$9 million in funding to advocacy groups and professional societies working on opioid policy, and concluding that this “opioids-friendly messaging . . . may have played a significant role in creating the necessary conditions for the U.S. opioids epidemic”).

treatments. The FDA has approved three drugs for treating opioid use disorders—buprenorphine, methadone, and naltrexone—which are available in various combinations and formulations.⁵⁵ Buprenorphine is a partial opioid agonist, meaning that it partially binds to opioid receptors to reduce cravings and to reduce the impact of other opioids taken while using the drug.⁵⁶

The buprenorphine market leader is Indivior, whose buprenorphine-naloxone combination drug Suboxone is, according to some studies, a more effective opioid substitution treatment than buprenorphine alone or the more familiar methadone.⁵⁷ Suboxone was introduced in 2002 as a sublingual (under the tongue) tablet subject to a seven-year period of exclusivity under the Orphan Drug Act.⁵⁸ The approaching end of Indivior's exclusivity period brought another example of product hopping.⁵⁹ The company developed and gained FDA approval for a sublingual film version of Suboxone, with patent protection extending until 2030.⁶⁰ As alleged in an antitrust suit brought by thirty-five states, Indivior then engaged in a campaign to shift patients from the tablet version to the film version, thus negating the threat of competition from generic tablets that could go on the market starting in 2009.⁶¹ According to the states' complaint, Indivior's campaign took several forms. The company "aggressively" promoted the superiority of the film version to physicians, pharmacists, and payors.⁶² It priced the film version below the tablet version even though the film version is more expensive to produce.⁶³ And then in 2012, it followed Purdue's lead in protesting the safety of its own soon-to-be-generic product to remove it from the market.⁶⁴ Indivior announced that it would take the tablet form off the

⁵⁵ See *Information About Medication-Assisted Treatment (MAT)*, FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm600092.htm> (last updated Feb. 14, 2019).

⁵⁶ See NAT'L ACADS. OF SCIS., ENG'G, & MED., *MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES* 35–36 (2019).

⁵⁷ See CANADIAN AGENCY FOR DRUGS & TECHNOLOGIES IN HEALTH, *RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL—SUBOXONE VERSUS METHADONE FOR THE TREATMENT OF OPIOID DEPENDENCE: A REVIEW OF THE CLINICAL AND COST-EFFECTIVENESS* (Nov. 14, 2013), <https://www.ncbi.nlm.nih.gov/books/n/rc0495/pdf>.

⁵⁸ See *In re Suboxone (Buprenorphine Hydrochloride & Naloxone) Antitrust Litig.*, No. 13-MD-2445, 2017 WL 3967911, at *2 (E.D. Pa. Sept. 8, 2017).

⁵⁹ See *supra* note 44 and accompanying text.

⁶⁰ See *In re Suboxone*, 2017 WL 3967911, at *3; *Patent and Exclusivity for N022410*, U.S. FOOD & DRUG ADMIN. ORANGE BOOK, https://www.accessdata.fda.gov/Scripts/cder/ob/patent_info.cfm?Product_No=001&AppL_No=022410&AppL_type=N (last visited July 21, 2019).

⁶¹ See *In re Suboxone*, 2017 WL 3967911, at *4. The district court has denied defendants' motion to dismiss, *id.* at *24, and has certified two classes in the litigation, *In re Suboxone (Buprenorphine Hydrochloride & Naloxone) Antitrust Litig.*, No. 13-MD-2445, 2019 WL 4735520 (E.D. Pa. Sept. 27, 2019).

⁶² *Id.*

⁶³ *Id.*

⁶⁴ For a more detailed analysis of how branded firms use citizen petitions to delay generic approval, see Michael A. Carrier & Carl Minniti, *Citizen Petitions: Long, Late-Filed, and At-Last Denied*, 66 AM. U. L. REV. 305 (2016). The FDA has recently announced draft guidance that

market due to a “pediatric exposure safety issue” and petitioned the FDA to deny approval for generic versions of the Suboxone tablet due to purported safety concerns.⁶⁵

Because Indivior believed it would enjoy monopoly power over Suboxone film but would soon face competition from generic tablets,⁶⁶ the company apparently sought to cannibalize the tablet market and induce demand for a new product. Indivior’s efforts to transition patients to the patented film version of Suboxone bore fruit: by 2013, eighty-five percent of prescriptions for Suboxone were written for the film formulation,⁶⁷ and Suboxone has consistently held over fifty percent of the buprenorphine market.⁶⁸ But it did not come cheap—about \$8.56 per dose as of early 2019, or slightly more than \$500 per month for twice-a-day use.⁶⁹ Indivior’s annual revenue from Suboxone topped \$1 billion each year from 2014 to 2018.⁷⁰

While a lucrative business for Indivior, medication-assisted treatment continues to be underused in the United States, reaching—by the National Academies’ estimate—only about twenty percent of patients who are estimated to need it.⁷¹ Moreover, it is far from clear that Suboxone film carried any advantage over Suboxone tablets. The FDA has not found Indivior’s claims regarding the dangers of Suboxone tablets to be supported by evidence,⁷² and in 2019, Indivior was federally indicted for fraudulently marketing Suboxone film as safer than the tablet form.⁷³

would give them greater authority to deny these petitions. Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act; Draft Guidance for Industry; Availability, 83 Fed. Reg. 49,935 (Oct. 3, 2018).

⁶⁵ *In re Suboxone*, 2017 WL 3967911, at *4–5.

⁶⁶ This belief might turn out to be inaccurate. Indivior is now fighting a challenge from rival Dr. Reddy’s to the patents on the film version of Suboxone. See *Indivior Inc. v. Dr. Reddy’s Labs., S.A.*, No. 2018-2167, 2018 WL 6069706 (Fed. Cir. Nov. 20, 2018) (vacating a preliminary injunction against Dr. Reddy’s).

⁶⁷ *In re Suboxone*, 2017 WL 3967911, at *5.

⁶⁸ See *Annual Reports*, INDIVIOR, <http://www.indivior.com/annual-reports> (last visited July 21, 2019).

⁶⁹ See Ari Alstedter, *America’s Best Weapon in the Opioid Epidemic Just Got Cheaper*, BLOOMBERG (Mar. 20, 2019), <https://www.bloomberg.com/news/articles/2019-03-20/america-s-best-weapon-in-the-opioid-epidemic-just-got-cheaper>.

⁷⁰ See *Annual Reports*, *supra* note 68. Indivior started as the buprenorphine division of Reckitt Benckiser in 1994 and was spun off into a separate company in 2014. See *History*, INDIVIOR, <http://www.indivior.com/about/our-history> (last visited July 21, 2019).

⁷¹ See NAT’L ACADS. OF SCIS., ENG’G, & MED., *supra* note 56, at 19.

⁷² *In re Suboxone*, 2017 WL 3967911, at *5.

⁷³ See Press Release, U.S. Dep’t of Justice, *Indivior Inc. Indicted for Fraudulently Marketing Prescription Opioid* (Apr. 9, 2019), <https://www.justice.gov/opa/pr/indivior-inc-indicted-fraudulently-marketing-prescription-opioid>; Indictment, *United States v. Indivior Inc.*, No. 1:19-cr-00016 (W.D. Va. Apr. 9, 2019), <https://www.justice.gov/opa/press-release/file/1153066/download>. The district court denied Indivior’s motion to dismiss. *United States v. Indivior Inc.*, No. 1:19-CR-00016, 2019 WL 6039969 (W.D. Va. Nov. 14, 2019).

3. The \$4100 Overdose Treatment: Why Was the Adoption of Opioid Inhibitors So Slow?

For patients underserved by addiction treatments, medications to halt the effects of an overdose are another evidence-supported intervention to reduce the human costs of the opioid crisis. One such drug is naloxone—the drug combined with buprenorphine in Suboxone—which binds to opioid receptors to block the effects of other opioids. It was first approved by the FDA in 1971 to reverse opioid overdose.⁷⁴ Naloxone is widely used for this purpose by medical professionals, but it has been difficult for lay people to use effectively.⁷⁵

To address this problem, the pharmaceutical company Kaléo developed an naloxone auto-injector, which was approved by the FDA in 2014.⁷⁶ Evzio's delivery mechanism resembles the much more familiar epinephrine auto-injector EpiPen, and the product has been described as “an EpiPen for naloxone.”⁷⁷ A distinguishing feature of Evzio, however, is that each packet comes with an audio recording and visual cues that guide users through the injection process. That—plus the auto-injector format—is reported to give Evzio a significant ease-of-use advantage over other naloxone delivery mechanisms, including the nasal spray branded as Narcan.⁷⁸

Evzio's approval appears to have been based on relatively little R&D compared with most new therapeutics. In general, FDA approval of a new drug requires multiple clinical studies that examine the drug's effectiveness compared with a placebo or a different active drug in a large sample of patients who are observed over many months.⁷⁹ The direct costs of these trials are typically tens or hundreds of millions of dollars.⁸⁰ But given that naloxone had been used successfully since the 1970s and that Evzio's novelty was in the delivery system, the FDA did not require a new clinical efficacy study. Rather, it granted approval based simply on (1) demonstrated bioequivalence to existing naloxone products, (2) prior EpiPen studies showing the safety of auto-injectors, and (3) a human factors validation study showing that 30 out of 40 participants were able to

⁷⁴ See Mark A. Merlin, Navin Ariyaprakai & Faizan H Arshad, *Assessment of the Safety and Ease of Use of the Naloxone Auto-Injector for the Reversal of Opioid Overdose*, 7 OPEN ACCESS EMERGENCY MED. 21, 21 (2015).

⁷⁵ See *id.* at 22.

⁷⁶ See *id.*

⁷⁷ See, e.g., *Episode No. 180: The Ongoing Opiate Crisis*, SMART DRUG SMARTS (May 12, 2017), <https://smartdrugsmarts.com/episodes/episode-180-opiates>. The EpiPen is a fascinating story of innovation institutions in itself. See Michael A. Carrier & Carl J. Minniti III, *The Untold EpiPen Story: How Mylan Hiked Prices by Blocking Rivals*, 102 CORNELL L. REV. ONLINE 53 (2017).

⁷⁸ See, e.g., Merlin et al., *supra* note 74; *infra* note 195 and accompanying text.

⁷⁹ See Thomas J. Moore et al., *Estimated Costs of Pivotal Trials for Novel Therapeutic Agents Approved by the US Food and Drug Administration, 2015–2016*, 178 JAMA INTERNAL MED. 1451, 1454 tbl.2 (2018) (examining the 59 novel drugs approved by the FDA in 2015 and 2016 and reporting that the approvals were based on 138 clinical trials, of which over 80% were placebo-controlled, over 94% involved over 100 patients and over 52% involved over 500 patients, and over 35% had a treatment duration longer than six months).

⁸⁰ See *id.* (finding a median estimated direct cost of \$19 million).

adequately deliver naloxone to a dummy using the auto-injector without training or reading the accompanying package insert.⁸¹ Kaléo claims that it “has invested more than \$100 million in the research, development and commercialization” of Evzio,⁸² although a comparison with the firm’s Securities and Exchange Commission filings suggests that much of this funding was on marketing rather than R&D.⁸³

Yet in spite of—or rather, *because* of—Evzio’s relatively quick path to market, the drug enjoys a lengthy period of patent-protected exclusivity: Kaléo has declared that its product is protected by thirty-one patents, expiring as late as 2035.⁸⁴ (As with OxyContin and Suboxone, this exclusivity period has been extended through product hopping.⁸⁵) We say that this lengthy period of exclusivity is the result of the short R&D process because firms file for patents early in the process of developing a drug, well before the drug is approved by the FDA and available to consumers.⁸⁶ This means that drugs for which the “time to market” is short enjoy longer periods of market exclusivity than drugs for which the time to market is long, since long time-to-market drugs “burn” much of their twenty-year patent life during the R&D phase.⁸⁷ The relationship between time to market and length of exclusivity arguably leads to an upside-down system of incentives, where the financial rewards for easier-to-develop drugs are greater than the rewards for drugs that take years to fine-tune and test.⁸⁸

⁸¹ See Merlin et al., *supra* note 74. For the FDA analysis, see CTR. FOR DRUG EVALUATION & RESEARCH, U.S. FOOD & DRUG ADMIN., APPLICATION NUMBER 205787ORIG1s000 SUMMARY REVIEW 3 (2014), https://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/205787Orig1s000SumR.pdf. A subsequent Kaléo study with 42 participants found greater success administering Evzio than an intranasal delivery system. See Evan T. Edwards, *Comparative Usability Study of a Novel Auto-Injector and an Intranasal System for Naloxone Delivery*, 4 PAIN THERAPY 89 (2015).

⁸² Press Release, Kaléo, Kaléo Announces the Award of Its 100th Patent (Jan. 25, 2016), <https://kaleo.com/press-release/kaleo-announces-the-award-of-its-100th-patent>.

⁸³ See Alex Wang & Aaron S. Kesselheim, *Government Patent Use to Address the Rising Cost of Naloxone: 28 U.S.C. § 1498 and Evzio*, 46 J.L. MED. & ETHICS 472, 476 (2018).

⁸⁴ See *Patent and Exclusivity for N209862*, U.S. FOOD & DRUG ADMIN. ORANGE BOOK, https://www.accessdata.fda.gov/scripts/Cder/ob/patent_info.cfm?Product_No=001&AppL_No=209862&AppL_type=N (last visited July 21, 2019).

⁸⁵ The original 2014 Evzio was discontinued and replaced with a higher strength version in 2016. For the 2014 version, see *Product Details for NDA 205787*, U.S. FOOD & DRUG ADMIN. ORANGE BOOK, https://www.accessdata.fda.gov/scripts/Cder/ob/results_product.cfm?AppL_Type=N&AppL_No=205787 (last visited July 21, 2019).

⁸⁶ See Benjamin N. Roin, *Unpatentable Drugs and the Standards of Patentability*, 87 TEX. L. REV. 503 (2009).

⁸⁷ See Eric Budish, Benjamin N. Roin & Heidi Williams, *Do Firms Underinvest in Long-Term Research? Evidence from Cancer Clinical Trials*, 105 AM. ECON. REV. 2044 (2015) (showing that this effect leads to more R&D for cancer drugs with longer effective patent life).

⁸⁸ On the implications for patent policy of time-to-market differentials, see generally Benjamin N. Roin, *The Case for Tailoring Patent Awards Based on Time-to-Market*, 61 UCLA L. REV. 672 (2014).

Evzio debuted in 2014 at a list price of \$575 for a two-dose prescription.⁸⁹ Kaléo subsequently hiked the price per prescription to \$750 in 2015, \$3750 in 2016, and \$4100 in 2017.⁹⁰ For comparison, the manufacturing cost for an Evzio unit is \$52.⁹¹ Fewer than 70,000 Evzio prescriptions were filled in the twelve months ending in January 2017.⁹² These high prices have generated complaints from a number of potential purchasers, including state and local governments.⁹³

B. Intellectual Property Law

OxyContin, Suboxone, and Evzio are all protected by IP law—and in particular, by lengthy periods of patent exclusivity—so patent law is a logical culprit in the search for the opioid epidemic’s cause. Indeed, Harvard Medical School researchers Ameet Sarpatwari, Michael Sinha, and Aaron Kesselheim have argued that “non-rigorous patenting standards . . . played an important role in launching and prolonging the opioid epidemic.”⁹⁴ They focus specifically on OxyContin and Suboxone, both of which are covered by patents that—they say—should have been rejected by the U.S. Patent and Trademark Office on grounds of obviousness.⁹⁵ Kesselheim, writing separately, has also assigned blame to patent law for limiting access to Evzio and other naloxone delivery devices.⁹⁶

⁸⁹ See STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, COMM. ON HOMELAND SEC. & GOV’T AFFAIRS, 115TH CONG., COMBATING THE OPIOID CRISIS: THE PRICE INCREASE OF AN OPIOID OVERDOSE REVERSAL DRUG AND THE COST TO THE U.S. HEALTH CARE SYSTEM 32–33 (Comm. Print 2018), <https://www.hsgac.senate.gov/imo/media/doc/Naloxone%20Report%20Final%20with%20Annex1.pdf>.

⁹⁰ *Id.* at 46. Some sources indicate that the 2017 price was as much as \$4,500. See Shefali Luthra, *The \$4,500 Injection to Stop Heroin Overdoses*, WASH. POST (Jan. 27, 2017), https://www.washingtonpost.com/business/the-4500-injection-to-stop-heroin-overdoses/2017/01/27/becaaca4-dcf6-11e6-ad42-f3375f271c9c_story.html.

⁹¹ STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 37. The “unit cost” is \$174, including \$29 in overhead and \$93 in “obsolescence.” *Id.*

⁹² *Id.* at 5.

⁹³ See CHRISTIE ET AL., *supra* note 10, at 77 (“[P]rice increases of the various forms of naloxone continue to create affordability issues, preventing state and local governments, as well as community organizations, from stocking naloxone at the levels necessary to rescue more people from overdose.”); David McFadden, *In Opioid Epidemic, Some Cities Strain to Afford OD Antidote*, U.S. NEWS (Apr. 12, 2018), <https://www.usnews.com/news/best-states/maryland/articles/2018-04-12/in-opioid-epidemic-some-cities-strain-to-afford-od-antidote>.

⁹⁴ Ameet Sarpatwari, Michael S. Sinha & Aaron S. Kesselheim, *The Opioid Epidemic: Fixing a Broken Pharmaceutical Market*, 11 HARV. L. & POL’Y REV. 463, 464 (2017).

⁹⁵ See *id.* at 470–71 (OxyContin); *id.* at 473 (Suboxone). See also Rebecca L. Haffajee & Richard G. Frank, *Generic Drug Policy and Suboxone to Treat Opioid Use Disorder*, J.L. MED. & ETHICS (forthcoming), <https://doi.org/10.1177%2F1073110519898042> (arguing that patent abuse and related strategies limited generic entry for Suboxone and helped maintain high prices, which “limited the volume of drugs purchased, particularly through public health insurance and grant programs”).

⁹⁶ See Wang & Kesselheim, *supra* note 83, at 473–77.

Taken together, these claims about OxyContin, Suboxone, and Evzio present a puzzle. Sarpatwari, Sinha, and Kesselheim contend that patent protection led to the proliferation of OxyContin and the undersupply of Suboxone (and, according to Kesselheim, also the undersupply of Evzio). But why would patent protection result in more of the first drug and less of the latter two? The authors never note this tension or seek to resolve it. This Section takes up that task. We first explain why patent protection plausibly contributed to OxyContin's deadly spread. We then explain why patent protection likely led to undersupply of Suboxone and Evzio. Finally, we consider how these cross-cutting claims can be reconciled and what that reconciliation might tell us about IP's role in the opioid crisis.

1. IP and OxyContin

The notion that patent law contributed to the proliferation of OxyContin cuts decidedly against the conventional wisdom about IP. The conventional view of patent law posits that patent monopolies lead to higher prices and lower quantities of patented products.⁹⁷ This is because patentees can maximize profits by pricing their products well above marginal cost (i.e., the cost of producing an additional unit), which means that some consumers who would have purchased the product in a perfectly competitive market choose not to when the price is marked up.⁹⁸ In mine-run cases, this reduction in quantity is considered to be a downside of patent protection,⁹⁹ but when the product in question is a potentially harmful drug, the reduction in quantity can increase social welfare. Christopher Cotropia and James Gibson have called this latter phenomenon “the upside of intellectual property’s downside”¹⁰⁰: the quantity reduction resulting from patent protection is a feature, not a bug, when the relevant product is a detriment to society.

Under this view, patent protection for OxyContin should have led to *lower* quantities of the drug being produced and sold. But the story of OxyContin did not play out as one might have expected: the drug became widely accessible even to consumers of modest means. Why did the trajectory of OxyContin play out so differently than the conventional view of patent law would suggest?

⁹⁷ See Steven Shavell & Tanguy van Ypersele, *Rewards Versus Intellectual Property Rights*, 44 J.L. & ECON. 525, 529 (2001).

⁹⁸ See, e.g., Jen Christensen, *The 5 Most Expensive Drugs in the United States*, CNN (May 11, 2018), <https://www.cnn.com/2018/05/11/health/most-expensive-prescription-drugs/index.html> (reporting price tags exceeding \$40,000 for a one-month supply of some pharmaceuticals); see generally JAY BHATTACHARYA, TIMOTHY HYDE & PETER TU, *HEALTH ECONOMICS* 235 (2013) (“[I]n exchange for [innovation-related] future benefits, costs are imposed on today’s consumers in the form of higher—and for some people, unaffordable—drug prices”).

⁹⁹ See Sampat & Williams, *supra* note 24; Shavell & van Ypersele, *supra* note 97, at 529 (“[T]here is a deadweight loss in social welfare because too little is sold at the monopoly price.”).

¹⁰⁰ Christopher A. Cotropia & James Gibson, *The Upside of Intellectual Property’s Downside*, 57 UCLA L. REV. 921 (2010). For a similar argument in the antitrust context, see Christopher R. Leslie, *Achieving Efficiency Through Collusion: A Market Failure Defense to Horizontal Price-Fixing*, 81 CALIF. L. REV. 243 (1993).

We think at least two factors are likely to have played some role in OxyContin's proliferation: (a) the incentive IP provides to invest in demand creation, and (b) the habit-forming nature of the drug for both prescribing doctors and patients. These effects complicate the conventional understanding of IP law's tradeoffs between dynamic and allocative efficiency. We consider each in turn.

a. Demand Creation

The first mechanism counteracting patents' quantity-limiting effect is that patents generate particularly strong incentives to invest in demand creation. If a firm is one of several purveyors of Honeycrisp apples, then it has a comparatively weak incentive to promote demand for Honeycrisps because the benefits of demand creation will spill over to other Honeycrisp purveyors.¹⁰¹ If a firm is the sole purveyor of a patented product—whether it be a fruit variety¹⁰² or a pharmaceutical—then its demand-creation incentives are much stronger, as it can capture all of the benefits of its promotional efforts. Purdue Pharma invested enormous resources in creating demand for OxyContin, and while some of that investment might have occurred in the absence of patent protection, it is doubtful that the pharmaceutical company's outlays would have been on the same scale but for the additional IP impetus.

OxyContin's selling points were several. First, Purdue sought to tap into the widespread belief that immediate-release oxycodone was an effective analgesic. "The importance of the familiarity of physicians with oxycodone cannot be overstated," Purdue officials wrote in an internal marketing plan.¹⁰³ "This familiarity is a principal factor that should lead to acceptance of OxyContin," the officials added.¹⁰⁴ Purdue officials also emphasized OxyContin's convenience: the controlled-release formulation meant that patients would have to take the drug only once every twelve hours, as opposed to four-times-a-day dosing for the more common immediate-release versions of oxycodone then on the market. "All of our market research indicates that the most important feature of OxyContin beyond oxycodone is the q12h dosing schedule," according to Purdue materials.¹⁰⁵ Finally, Purdue highlighted the low risk of "adverse events" even at high dosage levels.¹⁰⁶

¹⁰¹ Honeycrisp apples, incidentally, were previously patent-protected, but the University of Minnesota's plant patent has since expired. See Dan Olson, *Honeycrisp Apple Losing Its Patent Protection, But Not Its Appeal*, MINN. PUB. RADIO (Oct. 21, 2007), <https://www.mprnews.org/story/2007/10/11/honeycrisp>.

¹⁰² Cf. Dan Charles, *Want to Grow These Apples? You'll Have to Join the Club*, NAT'L PUB. RADIO: MORNING EDITION (Nov. 10, 2014), <https://www.npr.org/sections/thesalt/2014/11/10/358530280/want-to-grow-these-apples-youll-have-to-join-the-club> (discussing the role of patent and trademark law in protecting the rights to the SweeTango apple variety).

¹⁰³ *Purdue and the OxyContin Files*, *supra* note 34 (page 21 of 1996 Budget Plan).

¹⁰⁴ *Id.*

¹⁰⁵ *Id.* (page 22 of 1996 Budget Plan).

¹⁰⁶ *Id.* (page 28 of 1996 Budget Plan).

At least with the benefit of hindsight, all of these claims now appear to be dubious at best. Rigorous evidence for oxycodone's analgesic efficacy is scant. One recent randomized controlled trial involving acute pain patients found no statistically significant difference in pain outcomes between patients who were administered oxycodone with acetaminophen and patients who were administered ibuprofen with acetaminophen.¹⁰⁷ (Acetaminophen is the generic name for Tylenol, and ibuprofen is available under brands such as Motrin or Advil.) Another year-long randomized study of patients with chronic back pain or with hip or knee osteoarthritis found no significant difference in pain-related function between patients receiving high doses of opioids (including oxycodone) and patients receiving non-opioid treatments.¹⁰⁸ Indeed, the non-opioid treatment group fared significantly better on a self-reported pain scale.¹⁰⁹ But of course, Purdue and other opioid manufacturers had little incentive to develop or disclose this kind of negative information about their products.¹¹⁰ Instead,

¹⁰⁷ Andrew K. Chang et al., *Effect of a Single Dose of Oral Opioid and Nonopioid Analgesics on Acute Extremity Pain in the Emergency Department*, 318 JAMA 1661 (2017). While the Chang et al. study did not administer controlled-release oxycodone, Purdue's marketing efforts did not claim that controlled-release oxycodone was more effective than its immediate-release counterpart. Rather, Purdue's claim was that controlled-release oxycodone was more *convenient* than its immediate-release counterpart. See *Purdue and the OxyContin Files*, *supra* note 34 (noting on page 20 of Purdue's 1996 OxyContin budget plan that OxyContin had "[a]ll the analgesic efficacy of immediate-release oxycodone" with "the ease of [twelve-hour] dosing").

It is worth noting that the oxycodone-plus-acetaminophen treatment group in the Chang et al. study received relatively small doses of both drugs (5 milligrams of oxycodone and 325 milligrams of acetaminophen), while the ibuprofen-plus-acetaminophen treatment group received much larger doses (400 milligrams of ibuprofen and 1000 milligrams of acetaminophen). Chang, *supra*; see also Josh Bloom, *Advil Works as Well as Opioids for Acute Pain? Not So Fast*, AM. COUNCIL ON SCI. & HEALTH (Nov. 7, 2017), <https://www.acsh.org/news/2017/11/07/advil-works-well-opioids-acute-pain-not-so-fast-12089> (post on website of industry-funded group noting low oxycodone dosage in the Chang et al. study). Our main point here is not that there is evidence of the absence of oxycodone's efficacy, but that there is an absence of evidence of oxycodone's efficacy.

¹⁰⁸ Erin E. Krebs et al., *Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients with Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial*, 319 JAMA 872 (2018).

¹⁰⁹ *Id.* at 877 tbl.2. Dosages in the Krebs et al. study were significantly higher than in Chang et al., *supra* note 107. The highest dosage of oxycodone was 100 morphine-equivalent milligrams per day, or 67 milligrams of oxycodone. See Krebs et al., *supra* note 108, at 874. Cf. *Calculating Total Daily Dose of Opioids for Safer Use*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf (last visited Mar. 3, 2019) (conversion factor of 1.5 morphine-equivalent milligrams for oxycodone).

¹¹⁰ See generally Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. TECH. L. REV. 345, 347 (2007) ("Pharmaceutical firms sell drugs rather than selling information as such, and they face powerful incentives to cheat in developing and selectively disclosing information about their products in order to improve sales."); Rebecca S. Eisenberg & W. Nicholson Price II, *Promoting Healthcare Innovation on the Demand Side*, 4 J.L. & BIOSCIENCES 3, 18 (2017) (noting drug manufacturers' incentives to not conduct comparative effectiveness research); Kapczynski & Syed, *supra* note 23, at 1923–27 (describing the lack of incentive to produce negative information about pharmaceuticals).

Purdue promoted OxyContin as a way for patients to “gain control of [their] pain” after over-the-counter analgesics had failed.¹¹¹

As for the twelve-hour dosing advantage, this too now appears to have been illusory. A study by researchers at Oklahoma University College of Medicine published in 2002 found that almost nine in ten patients prescribed OxyContin ended up taking the drug more frequently than twice a day. “[N]early every patient in the analysis reported perceived end-of-dose failure of analgesia as the reason for taking the medicine more frequently,” the researchers wrote.¹¹² A *Los Angeles Times* exposé collected stories from physicians and patients across the country attesting to “OxyContin’s 12-hour problem.” When the drug wears off before the twelve-hour mark—as it often does—“patients can experience excruciating symptoms of withdrawal, including an intense craving for the drug,” the *Times* reported.¹¹³ The high highs and low lows associated with twelve-hour dosing “could be ‘the perfect recipe for addiction,’” the *Times* quoted a leading brain researcher as saying.¹¹⁴

All the while, Purdue sought to persuade physicians and patients that addiction concerns were overblown. In that effort, Purdue relied heavily on a one-paragraph letter published in the *New England Journal of Medicine* in 1980—not a peer-reviewed study—which noted that among nearly 12,000 patients who had received at least one narcotic painkiller, “there were only four cases of reasonably well documented addiction in patients who had no history of addiction.”¹¹⁵ This letter was then heavily and uncritically cited as evidence that opioid addiction is rare, with later writers describing it as an “extensive study” or a “landmark report.”¹¹⁶ By 2001, public health advocates were raising concerns about OxyContin’s addiction risk and petitioning the FDA to recall the drug, and in July 2001, the FDA worked with Purdue to add stronger warnings about the potential for abuse to the OxyContin label.¹¹⁷ But even then, Purdue argued that the warning was “more of an exercise in graphic design” and that

¹¹¹ See *Purdue and the OxyContin Files*, *supra* note 34.

¹¹² D. Adams et al., *Retrospective Assessment of Frequency of Dosing of Sustained Release Opiate Preparations in Chronic Pain Patients*, 3 PAIN MED. 185, 185 (2002).

¹¹³ Harriet Ryan, Lisa Girion & Scott Glover, “You Want a Description of Hell?” *OxyContin’s 12-Hour Problem*, L.A. TIMES (May 5, 2016), <https://www.latimes.com/projects/oxycontin-part1>.

¹¹⁴ *Id.* (quoting Theodore J. Cicero, professor of neuropharmacology and neurobiology at the Washington University School of Medicine in St. Louis).

¹¹⁵ Jane Porter & Hershel Jick, Correspondence, *Addiction Rare in Patients Treated with Narcotics*, 302 N. ENG. J. MED. 123 (1980).

¹¹⁶ See Sarah Zhang, *The One-Paragraph Letter from 1980 that Fueled the Opioid Crisis*, ATLANTIC (June 2, 2017), <https://www.theatlantic.com/health/archive/2017/06/nejm-letter-opioids/528840> (citing Pamela T.M. Leung et al., *A 1980 Letter on the Risk of Opioid Addiction*, 376 N. ENG. J. MED. 2194 (2017)); see also Van Zee, *supra* note 14, at 223 (explaining how Purdue misrepresented the risk of addiction for OxyContin).

¹¹⁷ See BETH MACY, DOPESICK 50–51 (2018); *Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, *supra* note 38.

the real victims were “legitimate patients” who would lose access to pain relief if OxyContin were restricted.¹¹⁸ OxyContin sales continued to climb.¹¹⁹

What made Purdue’s demand-creation strategy remarkable—and remarkably successful—was not just the audacity of its claims but the intensity of its efforts. From 1996 to 2001, Purdue held over forty all-expenses-paid conferences in Florida, Arizona, and California for over 5000 physicians, pharmacists, and nurses.¹²⁰ It distributed more than 14,000 videos claiming that less than one percent of patients who took opioids would become addicted (a figure that—while dubious—is also less impressive than it sounds once one considers that one percent of a third of U.S. adults would still add up to nearly a million individuals suffering from substance abuse disorder).¹²¹ In 2001 alone, Purdue’s marketing expenses came to approximately \$200 million, including \$40 million in incentive bonuses for sales representatives.¹²² This kind of direct-to-physician marketing of prescription opioids has been linked to increased prescription rates and opioid-related overdoses.¹²³

In the absence of patent protection, would Purdue Pharma have had as strong an incentive to invest in creating demand for controlled-release oxycodone? Likely not. Purdue knew that if it persuaded physicians to prescribe controlled-release oxycodone to patients, then Purdue would capture the vast majority of resulting revenues. If it were easy for competitors to sell generic versions of OxyContin, however, then Purdue Pharma would have been less likely to invest so heavily in marketing efforts that would have largely benefitted its rivals.

The example of Pfizer’s drug Viagra is illustrative. Advertisements for Viagra, marketed as a treatment for erectile dysfunction, once dominated the airwaves, with celebrities such as former U.S. Senator Bob Dole and Brazilian football legend Pelé among the drug’s promoters.¹²⁴ Once a generic version of

¹¹⁸ MACY, *supra* note 117, at 51 (quoting a Purdue spokesman).

¹¹⁹ See Ryan et al., *supra* note 113 (graphing OxyContin sales from 1996 to 2014). We are unsure why profits declined from 2003 to 2006 before skyrocketing again; perhaps it relates to the FDA warning letter sent to Purdue Pharma in 2003 for misleading advertisements. See *Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, *supra* note 38.

¹²⁰ Van Zee, *supra* note 14, at 221; see also MACY, *supra* note 117, ch. 2 (detailing OxyContin marketing activities).

¹²¹ Fred Schulte, *How America Got Hooked on a Deadly Drug*, NBC NEWS (June 14, 2018), <https://www.nbcnews.com/health/health-news/how-america-got-hooked-deadly-drug-n883361>.

¹²² Van Zee, *supra* note 14, at 221–22.

¹²³ Scott E. Hadland et al., *Association of Pharmaceutical Industry Marketing of Opioid Products to Physicians with Subsequent Opioid Prescribing*, 6 JAMA INTERNAL MED. 861 (2018). Interestingly, advertising also played a role in America’s first opioid epidemic in the late nineteenth century. See Jon Kelvy, *How Advertising Shaped the First Opioid Epidemic*, SMITHSONIAN (Apr. 3, 2018), <https://www.smithsonianmag.com/science-nature/how-advertising-shaped-first-opioid-epidemic-180968444>.

¹²⁴ See Megan Garber, *Jagged Little (Blue) Pill*, ATLANTIC (Mar. 27, 2018), <https://www.theatlantic.com/entertainment/archive/2018/03/20-years-of-viagra/556343>.

the drug became available in 2017, Pfizer's spending on Viagra ads sharply plummeted.¹²⁵ And Viagra is an especially noticeable example of what is a broader trend: IP-protected exclusivity and marketing expenditures are closely tied. Systematic empirical studies of the pharmaceutical market have found that on average, marketing expenditures decline after patent expiration, and that the resulting negative effect on consumption is equal to or even greater than the positive effect from increased competition and decreased price.¹²⁶

The relationship between patent protection and demand creation points to one way in which “the upside of intellectual property’s downside” may not be an upside after all. By that, we mean that patent protection for socially harmful products will not necessarily reduce the quantity consumed. This also means that when the relevant product generates *positive* externalities, the perceived downside of intellectual property in terms of allocative inefficiency may not be as much of a downside as traditional models suggest. That is, patent protection for positive externality-generating goods may encourage greater investment in demand creation—and ultimately, higher consumption—than if the same good had been unpatented. The overall welfare effect of the patent system will thus depend importantly on whether the system successfully distinguishes between—and offers differential rewards to—socially beneficial and socially harmful products.¹²⁷

¹²⁵ See Anthony Crupi, *Deflategate 2.0: Big-Spending Viagra and Cialis Are Pulling out of the NFL*, ADAGE (July 7, 2017), <https://adage.com/article/special-report-tv-upfront/erectile-dysfunction-viagra-cialis-nfl-pullout/309692>.

¹²⁶ See Darius Lakdawalla & Tomas Philipson, *Does Intellectual Property Restrict Output? An Analysis of Pharmaceutical Markets*, 55 J.L. & ECON. 151, 151 (2012) (“[I]n the short run, patent expirations reduce output and consumer welfare by decreasing marketing. In the long run, patent expirations benefit consumers, but by 30 percent less than would be implied by the reduction in price alone.”); Gautier Duflos & Frank R. Lichtenberg, *Does Competition Stimulate Drug Utilization? The Impact of Changes in Market Structure on US Drug Prices, Marketing and Utilization*, 32 INT’L REV. L. & ECON. 95, 95 (2012) (“Price and marketing expenditure both decline by about 50–60% in the years immediately following generic entry, but the number of prescriptions remains essentially constant during those years.”).

Of course, the full story of pharmaceutical marketing cannot be reduced to a simple narrative of high marketing expenditures during the patent term and low marketing expenditures thereafter. Firms often (and sometimes with success) seek to transition consumers to new versions of a drug with longer patent protection through product hopping, as Purdue did with its 2010 reformulation of OxyContin. See *supra* note 45 and accompanying text. They may also launch low-price versions of their products to compete with generics while raising prices on the original drug to retain the most brand-loyal consumers. See Dipak C. Jain & James G. Conley, *Patent Expiry and Pharmaceutical Market Opportunities at the Nexus of Pricing and Innovation Policy*, in INNOVATION AND MARKETING IN THE PHARMACEUTICAL INDUSTRY 255 (Min Ding et al. eds. 2014). The key point is that the incentives patents provide for promotion and marketing can offset their quantity-limiting effect. Simple models based on patent law’s tradeoff between allocative and dynamic efficiency fail to capture this important element of innovation institutions.

¹²⁷ The net effect of patent law’s incentives for demand creation will also inform proposals to enhance this commercialization incentive. See generally Michael Abramowicz, *The Danger of Underdeveloped Patent Prospects*, 92 CORNELL L. REV. 1065 (2007) (proposing patent extension auctions to incentivize commercialization); Ted Sichelman, *Commercializing Patents*, 62 STAN. L. REV. 341 (2010) (discussing the role patents play in commercialization and proposing a new “commercialization” patent to further this goal).

b. Habit Formation

The prospect of market exclusivity interacted with OxyContin's addictive properties to generate especially strong incentives for the dissemination of OxyContin. The risk of addiction may have altered Purdue Pharma's profit-maximization calculus, causing the company to adopt a pricing strategy that initially aimed at encouraging widespread consumption.

If more people consume an addictive good in the present, then future demand for the good will be higher. As economists have recognized, a rational firm with market power may thus choose to lower the present price of its good to increase future demand.¹²⁸ If, for example, a tobacco company controls a significant share of the cigarette market, then the company is likely to profit from an additional smoker. If, by contrast, the company is one among a large number of players in a competitive cigarette market, then the likely benefit to the company of addicting an additional individual is smaller. Just as patent protection encourages firms to invest more heavily in marketing, it also may encourage manufacturers of addictive products to price more aggressively early in the patent term in order to hook new customers.

Importantly, "addiction" in this context refers to any mechanism through which consumption at one time generates demand at a later time. A drug may be addictive in this sense if patients develop a compulsion to continue using it (as in the case of substance use disorder) or if physicians can become habituated into prescribing it.¹²⁹ Studies of physicians' prescription practices show wide variation across doctors in the frequency of opioid prescriptions and the quantity of opioids prescribed—variation that does not appear to be a function of patient characteristics.¹³⁰ As the author of one of these studies hypothesizes, physicians may emulate their mentors' prescription practices to a large extent—in which case one physician's prescription behavior at one time may influence many more physicians' behaviors at later points in time.¹³¹ If

¹²⁸ On the interaction between market power and addiction, see generally Robert Driskill & Stephen McCafferty, *Monopoly and Oligopoly Provision of Addictive Goods*, 42 INT'L ECON. REV. 43 (2001) (modeling "monopoly and oligopoly provision of an addictive good" and finding "a wide variety of possible steady-state outcomes, including ones with output above the efficient level and price below marginal cost"); Timothy J. Richards et al., *Fast Food, Addiction, and Market Power*, 32 J. AGRICULTURAL & RESOURCE ECON. 425 (2007) ("[A] firm with market power will price below marginal cost in a steady-state equilibrium . . ."); and Mark H. Showalter, *Firm Behavior in a Market with Addiction: The Case of Cigarettes*, 18 J. HEALTH ECON. 409 (1999).

¹²⁹ See Sebastian Potthoff et al., *Planning to Be Routine: Habit as a Mediator of the Planning-Behaviour Relationship in Healthcare Professionals*, 12 IMPLEMENTATION SCI. 24 (2017) ("Healthcare professionals often perform the same clinical behaviours repeatedly until they become routine practice, and once a behaviour has become routine, it is increasingly controlled by habit rather than solely by conscious, in the moment decision-making.").

¹³⁰ See Michael L. Barnett, Andrew R. Olenski & Anupam B. Jena, *Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use*, 376 N. ENG. J. MED. 663, 667-71 (2017); Maureen V. Hill, *Wide Variation and Excessive Dosage of Opioid Prescription for Common General Surgical Procedures*, 265 ANNALS OF SURGERY 709 (2017).

¹³¹ See Julia Belluz, *Certain Doctors Are More Likely to Create Opioid Addicts. Understanding Why Is Key to Solving the Crisis*, VOX (Feb. 16, 2017), <https://www.vox.com/science-and->

prescription behavior is propagated in this way, then firms with long-term market power over a drug have an even stronger incentive to boost present-period consumption.

In the case of OxyContin, Purdue's pricing of the drug more or less conformed to what we might expect from a firm with market power over an addictive product. From 2000 to 2015, the (licit) retail price per tablet of 10-miligram strength OxyContin increased by nearly sixty percent after adjusting for inflation, while the inflation-adjusted price of an 80-miligram tablet increased by more than eighty percent.¹³² But for Purdue's bankruptcy filing in 2019 and a tentative settlement with city and state governments,¹³³ we might have expected a continuing pattern of price increases as the firm's patent exclusivity with respect to OxyContin neared its end. (The tentative settlement restricts Purdue's marketing and sale of OxyContin, which may impede further profit maximization efforts—although there is evidence that the Sackler family's international affiliate is using similar tactics to promote OxyContin abroad.¹³⁴)

Purdue's incentive to generate widespread demand for a highly addictive product can help explain why patents may not have had their conventional quantity-limiting effect in the case of OxyContin. We do not mean to suggest, however, that denying IP protection to OxyContin would have prevented the opioid crisis. As noted above, OxyContin constitutes just a small portion of the prescription opioid market. More importantly, it is difficult to know how the market would have evolved in the counterfactual in which Purdue did not have exclusivity with respect to controlled-release oxycodone. Based on the more systematic economic studies discussed above, it seems clear enough that Purdue would have invested far less in pushing the narratives that opioids are safe and effective treatments for chronic pain. But Purdue is not the only opioid producer that has pushed doctors to increase prescription rates in ways that crossed legal and ethical boundaries,¹³⁵ and it is plausible that had controlled-release oxycodone been available generically, even more people would have died.

health/2017/2/16/14622198/doctors-prescribe-opioids-varies-patients-hooked (interviewing Harvard Medical School professor Anupam Jena).

¹³² See *OxyContin Diversion and Abuse*, *supra* note 40; Complaint at 16 ¶ 58, *Commonwealth v. Purdue Pharma L.P.*, No. 1884-cv-01808 (Mass. Super. Ct. June 12, 2018), <https://www.mass.gov/files/documents/2018/06/12/Purdue%20Complaint%20FILED.pdf>; *CPI Inflation Calculator*, BUREAU OF LABOR STATISTICS, <https://data.bls.gov/cgi-bin/cpicalc.pl?cost1=1.00&year1=200012&year2=201512> (last visited Mar. 17, 2019).

¹³³ See Jan Hoffman & Mary Williams Walsh, *Purdue Pharma, Maker of OxyContin, Files for Bankruptcy*, N.Y. TIMES (Sept. 15, 2019), <https://www.nytimes.com/2019/09/15/health/purdue-pharma-bankruptcy-opioids-settlement.html>.

¹³⁴ See Erika Kinetz, *AP Key Findings About Mundipharma's OxyContin Sales in China*, ASSOCIATED PRESS (Nov. 19, 2019), <https://apnews.com/a9b1324e5b7d4679b5a6d465cea2dd2e>.

¹³⁵ See, e.g., Jonathan Saltzman, *Former Drug Exec Pleads Guilty to Pushing Painkiller Prescriptions*, BOSTON GLOBE (Nov. 28, 2018), <https://www.bostonglobe.com/business/2018/11/28/former-drug-exec-pleads-guilty-pushing-painkiller-prescriptions/qjxlwlvfKy3o6sNuVvoHwJ/story.html> (describing incentives doctors received from Insys Therapeutics to prescribe a fentanyl-based painkiller).

To be clear: None of this is to exonerate Purdue for its role in propagating a false narrative around opioids. Nor is it to exonerate IP law for its role in the opioid epidemic. But as we discuss below, IP's contribution to the crisis—while potentially profound—is also nuanced. OxyContin turns out to play a small part in a much more complicated narrative.

2. *IP, Suboxone, and Evzio*

The effect of IP law on the availability of our other two illustrative drugs—Suboxone and Evzio—looks on first glance like the more traditional tale of IP leading to high prices and restricted quantities. But again, first impressions can deceive, and the overall effect of IP on the use of opioid substitutes and antidotes turns out to be less obvious.

Again, the conventional wisdom is that IP law—whatever its dynamic-efficiency effects—leads IP rightsholders to raise prices and thereby reduce quantities of IP-protected products. Consistent with this conventional story, Sarpatwari et al. blame patent law for Suboxone's high price and attribute the underutilization of Suboxone to that patent-induced pricing problem.¹³⁶ And as noted above, Evzio cost \$4100 per two-dose prescription by 2017—nearly eighty times the unit manufacturing cost—leading to similar arguments that patents limited access.¹³⁷

If Suboxone and Evzio had not received lengthy IP protection, it is possible these products would have been developed anyway, and that generic competitors would have entered the markets for buprenorphine-naloxone addiction treatments and for naloxone auto-injector overdose treatments, decreasing prices and increasing the number of patients with access to these products. On this account, Indivior and Kaléo could be portrayed as villains in the opioid story, using unnecessary patents, product hopping, and high prices to deprive patients of access to lifesaving medical treatments. But it is not obvious that long-lasting patent protection can be blamed for limiting access to Suboxone and Evzio. The two factors behind OxyContin's proliferation—IP-driven demand creation and habit formation—are present to at least some degree for Suboxone and Evzio as well. It is possible that without Indivior's and Kaléo's high-powered IP incentives to develop and promote demand for their products—including to encourage early use by consumers who would then be more likely to make repeat purchases—fewer patients would be using these products today.

First, although Indivior and Kaléo did not spend as extravagantly on marketing as Purdue did, their long-lasting IP protection would seem to provide a similar incentive to increase demand for their products. ProPublica reports that Indivior has spent about \$4 million on payments to physicians and lobbying since

¹³⁶ Sarpatwari et al., *supra* note 94, at 475.

¹³⁷ See *supra* notes 89–93 and accompanying text.

2013,¹³⁸ and the company's annual reports describe its efforts to overcome the stigma of medical treatment for addiction.¹³⁹ Meanwhile, Kaléo's financial statements suggest that it was pouring all its revenues and then some into expanding sales,¹⁴⁰ including through nearly \$2.4 million in Evzio-related payments to physicians and lobbying since 2013.¹⁴¹ Although these payments pale next to ProPublica's estimate of almost \$19 million for OxyContin-related payments by Purdue,¹⁴² they signal at least some effort at demand creation.

Second, even if Suboxone and Evzio do not carry the same risk of medical addiction as OxyContin, demand does seem likely to be linked across time such that consumption today increases demand tomorrow. Suboxone is typically used for long-term maintenance therapy for opioid use disorder, with discontinuation linked to high rates of relapse.¹⁴³ Patients who begin Suboxone treatment are thus very likely to become repeat customers, even in the face of future price increases. And while naloxone has no risk of medical addiction, Evzio purchasers—including first responders, drug treatment centers, and businesses in neighborhoods where overdose is common—may become habituated to Evzio's ease of use. Commentators have noted that Kaléo has distributed over 180,000 free devices, apparently with the hope that some of

¹³⁸ See *Dollars for Docs: Suboxone Sublingual Film*, PROPUBLICA, <https://projects.propublica.org/docdollars/products/drug-suboxone-sublingual-film> (last visited July 21, 2019); *Lobbying Arrangements Results for 'Indivior,'* PROPUBLICA, <https://projects.propublica.org/represent/lobbying/search?search=indivior> (last visited July 21, 2019). Indivior was spun off from Reckitt Benckiser in 2014. See *supra* note 70.

¹³⁹ See, e.g., INDIVIOR, ANNUAL REPORT AND FINANCIAL STATEMENTS 2014, at 4 (2014), http://www.indivior.com/wp-content/uploads/2015/04/INDIVIOR_Annual_Report_2014.pdf. Demand-creation efforts focused on addiction treatments are not necessarily beneficial. In December 2019, the FDA criticized the pharmaceutical firm Alkermes for “misbranding” the opioid addiction drug Vivitrol by failing to communicate the overdose risks associated with the drug. See Lev Facher, *FDA Blasts Alkermes for Underselling the Risks of Opioid Addiction Drug Vivitrol*, STAT (Dec. 11, 2019), <https://www.statnews.com/2019/12/11/fda-blasts-alkermes-vivitrol-branding>.

¹⁴⁰ See Kaleo, Inc. and Subsidiary: Consolidated Financial Statements for the Years Ended December 31, 2016, 2015, 2014, at 5, <https://www.sec.gov/Archives/edgar/data/850429/000085042917000018/kaleofinancialstatements.htm>.

¹⁴¹ See *Dollars for Docs: Evzio*, PROPUBLICA, <https://projects.propublica.org/docdollars/products/drug-evzio> (last visited July 21, 2019); *Lobbying Arrangements Results for 'Kaleo,'* PROPUBLICA, <https://projects.propublica.org/represent/lobbying/search?search=kaleo> (last visited July 21, 2019).

¹⁴² See *Dollars for Docs: OxyContin*, PROPUBLICA, <https://projects.propublica.org/docdollars/products/drug-oxycontin> (last visited July 21, 2019); *Lobbying Arrangements Results for 'Purdue,'* PROPUBLICA, <https://projects.propublica.org/represent/lobbying/search?search=purdue+pharma> (last visited July 21, 2019).

¹⁴³ See CANADIAN AGENCY FOR DRUGS & TECHNOLOGIES IN HEALTH, *supra* note 57, at 9; Brandon S. Bentzley et al., *Discontinuation of Buprenorphine Maintenance Therapy: Perspectives and Outcomes*, 52 J. SUBSTANCE ABUSE TREATMENT 48 (2015).

these recipients would later become paying purchasers of the product.¹⁴⁴ And physicians may become routinized into prescribing Evzio as instructed by Kaléo's substantial sales force.

It seems plausible that the markets for both Evzio and Suboxone were expanded by campaigns aimed at familiarizing doctors and patients with these products. The naloxone auto-injector was a novel approach to treating overdoses, so people who could benefit from Evzio—including first responders, people with opioid use disorder, friends and family members of those at risk of overdose, and those stocking first aid kits—did not know this was a product they needed. Suboxone faced a different hurdle. A 2019 National Academies report concludes that stigma toward opioid agonists like buprenorphine is a barrier to effective treatment “grounded in the misperception that these medications are substituting one drug for another,” but that there is some evidence that “as clinicians gain experience treating patients with [opioid use disorder] with buprenorphine, they gain more positive perceptions about the role of medications in effective treatment.”¹⁴⁵ As the sole provider of the leading buprenorphine product, Indivior arguably had stronger incentives to educate clinicians and patients than it would have had in a market with generic competitors who could capture many of the benefits of these promotional efforts.

3. Taking Stock

What, then, can the stories of OxyContin, Suboxone, and Evzio tell us about the role of IP in the opioid crisis? It might seem that the answer is “not much”: IP's effects on quantity are ambiguous, making it difficult to attribute the spread of OxyContin or the scarcity of Suboxone and Evzio to patent protection or any other form of IP exclusivity. On further reflection, a few important lessons emerge.

First, IP relies on markets, and so market failures are likely to result in IP failures too. Perhaps most obviously, OxyContin generates negative externalities (including, among others, the externality to family members and neighbors who are at increased risk of addiction when OxyContin appears in ever more medicine cabinets¹⁴⁶), and Suboxone and Evzio produce positive externalities (including the externality to individuals other than the prescription holder who may nonetheless be saved from overdose by a naloxone injection).¹⁴⁷ Markets tend to spawn socially supraoptimal quantities of products that yield negative

¹⁴⁴ Shefali Luthra, *Getting Patients Hooked on an Opioid Overdose Antidote, Then Raising the Price*, KAISER HEALTH NEWS (Jan. 30, 2017), <https://khn.org/news/getting-patients-hooked-on-an-opioid-overdose-antidote-then-raising-the-price>.

¹⁴⁵ See NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 56, at 112.

¹⁴⁶ Nazleen F. Khan et al., *Association of Opioid Overdose with Opioid Prescriptions to Family Members*, 179 JAMA INTERNAL MED. (forthcoming 2019), <https://doi.org/10.1001/jamainternmed.2019.1064>.

¹⁴⁷ Suboxone (buprenorphine), like OxyContin (oxycodone), can be diverted and abused, but “buprenorphine and buprenorphine/naloxone generally ranked as the least-abused or misused opioid among those studied.” Michael A. Yokell et al., *Buprenorphine and Buprenorphine/Naloxone Diversion, Misuse, and Illicit Use: An International Review*, 2011 CURRENT DRUG ABUSE REV. 28.

externalities and suboptimal quantities of products that create positive externalities. It is in some ways unsurprising that America—reliant as it was on IP, a market institution, to allocate access—ended up with too much OxyContin and not enough Suboxone and Evzio.

Second, and precisely because IP's effects on quantity are ambiguous, IP is too blunt a tool on its own to produce socially optimal quantities of externality-generating goods. Sarpatwari, Sinha, and Kesselheim suggest that without patent protection for OxyContin and Suboxone, we would have ended up with less of the former and more of the latter.¹⁴⁸ But while those counterfactual claims are plausible, it is also plausible that in a world without patent protection for OxyContin and Suboxone, we could have ended up with more of the former (because of lower prices) and less of the latter (because of lower investment in demand creation). Dialing IP protection down or up will have difficult-to-predict effects on welfare.

Finally, and relatedly, reliance on market institutions to allocate access to externality-generating goods will lead to predictable pathologies unless policymakers use other tools—including ex ante regulation, ex post liability, and supply- and demand-side subsidies—to correct for market failures. In the remainder of this Part, we consider how those tools were used and whether they succeeded.

C. Regulation and Liability

Institutions that regulate new knowledge goods—either in controlling whether and how the goods make it to market ex ante or in penalizing firms whose marketed goods turn out to be harmful ex post—play a key role in mediating IP's effect on welfare. Here, we consider some of these institutions and how they interacted with IP throughout the opioid crisis.

1. Ex Ante Limits: The FDA and DEA

The FDA plays an important role in setting the IP incentives discussed in the prior Section because FDA approval is typically accompanied by a period of regulatory exclusivity.¹⁴⁹ But the FDA also plays a direct role in drug regulation by deciding whether and under what conditions a new drug can reach the market. This regulatory power could be used to cause firms to internalize negative externalities of their products. For example, a 2017 National Academies report on pain management argues that the FDA should incorporate public

¹⁴⁸ See Sarpatwari et al., *supra* note 94, at 464, 470–71, 473.

¹⁴⁹ For example, new small-molecule drugs and biologics receive five and twelve years of data exclusivity, respectively, before the FDA will approve a generic version, and orphan drugs receive seven years of market exclusivity. 21 U.S.C. §§ 355(c)(3)(E)(ii), 355(j)(5)(F)(ii), 360cc; 42 U.S.C. § 262(k)(7)(A).

health considerations into regulatory decisions, including drug approval and monitoring.¹⁵⁰

But even if the FDA aggressively took this social-welfare-based approach to drug approvals, it is not obvious that it would have reached a different outcome. The opioid crisis has had tremendous social cost, but so does chronic pain. Equally problematically, while the costs of opioids are now reasonably apparent, it would have been more difficult for the FDA to assess these costs prior to the height of the epidemic. Controlling the drug supply *ex ante* is a blunt policy tool that is difficult to wield.

While the FDA does not currently consider broader public health considerations when deciding whether to approve new drugs, it has used its regulatory authority to address direct safety concerns with opioids. Since 2007, the FDA has had authority to impose a Risk Evaluation and Mitigation Strategy (REMS) requirement on drugs with serious associated risks,¹⁵¹ though systematic studies have been unable to determine whether REMS affect prescribing and dispensing practices.¹⁵² The agency also has encouraged opioid manufacturers to develop “abuse-deterrent” versions of their products, and it has provided an abuse-deterrent designation for numerous brand-name opioids, starting with Purdue’s OxyContin reformulation in 2010.¹⁵³ But this supply-side intervention may have backfired, at least in the short term: a recent economic study of cross-state variation in OxyContin exposure suggests that the reformulation in OxyContin—by cutting access to an easy source of highs—has accelerated the turn toward heroin as an alternative.¹⁵⁴ Of course, had the FDA required a tamper-resistant formulation from the outset, it would have avoided this problem—but that would have required the FDA to foresee OxyContin’s abuse potential.

Finally, we note that the FDA is not the only drug regulator. For example, another federal agency that plays an important role in *ex ante* drug regulation is the Drug Enforcement Administration (DEA) within the Justice Department. Prescribing or dispensing buprenorphine (one of the active ingredients in Suboxone) requires a DEA waiver—a hurdle that is not required to prescribe OxyContin. Although this rule was motivated by a desire to prevent further abuse, it likely had the opposite effect. The 2017 report from the President’s opioid commission recommended that all addiction patients have access to medication-assisted treatment including buprenorphine but noted that forty-seven percent of counties nationwide and seventy-two percent of the most rural counties did not have a physician who had received the required DEA

¹⁵⁰ NAT’L ACADS. OF SCIS., ENG’G, & MED., PAIN MANAGEMENT AND THE OPIOID EPIDEMIC: BALANCING SOCIETAL AND INDIVIDUAL BENEFITS AND RISKS OF PRESCRIPTION OPIOID USE 410–14 (2017); *see also* Patricia J. Zettler, Margaret Foster Riley & Aaron S. Kesselheim, *Implementing a Public Health Perspective in FDA Drug Regulation*, 73 FOOD & DRUG L.J. 221 (2017) (same).

¹⁵¹ 21 U.S.C. § 355-1(a)(1)(E).

¹⁵² *See* NAT’L ACADS. OF SCIS., ENG’G, & MED., *supra* note 150, at 366.

¹⁵³ *See* Alpert et al., *supra* note 53, at 5–6.

¹⁵⁴ *Id.*

waiver to prescribe this drug.¹⁵⁵ In other words, the DEA may have done more to restrict access to drugs that treat addiction than to drugs that cause it.

2. *Ex Post Penalties: Tort and Criminal Liability*

Separate legal institutions for ex post drug regulation are the tort and criminal law system. A sprawling web of complex litigation is currently playing an important role in forcing Purdue and other opioid manufacturers to internalize some of the social costs of their products.¹⁵⁶ Purdue pled guilty to felony misbranding in 2007,¹⁵⁷ and in March 2019 it agreed to pay \$270 million to settle claims brought by the state of Oklahoma.¹⁵⁸ In September 2019, it filed for bankruptcy and agreed to cede all of its assets to a public benefit trust.¹⁵⁹ The bankruptcy case is ongoing as of this writing, but certainly no one would predict that Purdue will emerge from the experience unscathed. The Sackler family that founded and controlled Purdue has pledged to pay \$3 billion from their own fortune as part of a global settlement (though it is not clear whether that aspect of the deal will hold).¹⁶⁰

Why didn't the threat of tort liability deter opioid manufacturers from aggressively hawking their wares? For one thing, we cannot say for sure that the ex ante effect of the threat of ex post liability was null. It may be (though it seems unlikely) that executives of Purdue and other pharmaceutical companies would have been even more unabashed in puffing up their products' virtues and concealing their vices if tort law had been off the table. We can, however, surmise several reasons why the shadow of ex post liability was short.

The first set of reasons is internal to tort law. The framework of negligence liability—centering on the elements of duty, breach, causation, and damages—provides an awkward fit for claims against opioid manufacturers. It

¹⁵⁵ CHRISTIE ET AL., *supra* note 10, at 34, 68.

¹⁵⁶ For a primer, see Abbe R. Gluck, Ashley Hall & Gregory Curfman, *Civil Litigation and the Opioid Epidemic: The Role of Courts in a National Health Crisis*, 46 J.L. MED. & ETHICS 351 (2018). For a more recent update, see Colin Dwyer, *Your Guide to the Massive (and Massively Complex) Opioid Litigation*, NPR (Oct. 15, 2019), <https://www.npr.org/sections/health-shots/2019/10/15/761537367/your-guide-to-the-massive-and-massively-complex-opioid-litigation>.

¹⁵⁷ See Barry Meier, *Origins of an Epidemic: Purdue Pharma Knew Its Opioids Were Widely Abused*, N.Y. TIMES (May 29, 2018), <https://www.nytimes.com/2018/05/29/health/purdue-opioids-oxycotin.html>

¹⁵⁸ See Jef Feeley, *Purdue Pharma Reaches Deal to Settle Oklahoma Opioid Case*, BLOOMBERG (Mar. 25, 2019), <https://www.bloomberg.com/news/articles/2019-03-26/purdue-pharma-said-to-reach-deal-to-settle-oklahoma-opioid-case>.

¹⁵⁹ See Hoffman & Walsh, *supra* note 133.

¹⁶⁰ See Jan Hoffman, *Purdue Pharma Warns That Sackler Family May Walk from Opioid Deal*, N.Y. TIMES (Sept. 19, 2019), <https://www.nytimes.com/2019/09/19/health/purdue-sackler-opioid-settlement.html>. The bankruptcy judge put lawsuits against Purdue and the Sacklers on hold until April 2020 to give the parties more time to reach a settlement. See Tom Hals & Mike Spector, *Where the Purdue Pharma-Sackler Legal Saga Stands*, REUTERS (Jan. 29, 2020), <https://www.reuters.com/article/us-purdue-pharma-bankruptcy-factbox/where-the-purdue-pharma-sackler-legal-saga-stands-idUSKBN1ZS1H3>.

was far from obvious that, for example, Purdue owed any duty to individuals who stole OxyContin from family members' medicine cabinets, crushed tablets to destroy the controlled-release feature, and then snorted or injected oxycodone. The fact that the FDA approved OxyContin and other prescription opioids would have made breach difficult to establish in court, and even if breach were shown, drawing a causal connection between a manufacturer's distribution of opioids and any given individual's overdose would require a fair amount of legal creativity.¹⁶¹ As for damages, apportionment among manufacturers presents a factual and conceptual challenge. As a court in Connecticut said when dismissing a suit by the city of New Haven against Purdue, attempting to assign liability to a particular pharmaceutical company for a share of opioid crisis costs "would inevitably require determining causation by conjecture."¹⁶² It would be, according to the court, "junk justice."¹⁶³

The Connecticut court's claim of "junk justice" is certainly contestable. "Junk justice," one might fairly respond, is a tort system that allows opioid manufacturers to flood the country with addictive pills, conceal their risks, and escape scot-free. But supporters of the effort to hold opioid manufacturers accountable through tort law forthrightly acknowledged that the battle they were fighting was uphill.¹⁶⁴ The apparent settlement of claims against Purdue may be a victory on one front of that fight, but it is not an outcome that was clearly predictable *ex ante*.

A second set of limits on the power of *ex post* tort liability is external to tort law. The limited-liability structure of the corporation shields shareholders from the financial consequences of corporate wrongdoing. The corporation can always declare bankruptcy—an option that, as noted, Purdue has pursued—and it is difficult (though perhaps not impossible) for plaintiffs to claw back from shareholders the dividends that a corporation paid in solvent times. The Sacklers

¹⁶¹ See Mariano-Florentino Cuéllar & Keith Humphreys, *The Political Economy of the Opioid Epidemic*, YALE L. & POL'Y REV. (forthcoming) (noting that unlike cigarettes, which "were never reviewed and sanctioned for sale in advance by the federal government . . . every pharmaceutical opioid on the market was approved by the [FDA]" and "when prescribed judiciously can dramatically relieve human suffering").

¹⁶² *City of New Haven v. Purdue Pharma, L.P.*, 2019 Conn. Super. LEXIS 55, at *5 (Jan. 8, 2019).

¹⁶³ *Id.*

¹⁶⁴ See Richard C. Ausness, *The Role of Litigation in the Fight Against Prescription Drug Abuse*, 116 W. VA. L. REV. 1117, 1165 (2014) (advocating for the pursuit of civil remedies but acknowledging that "the overall effectiveness of civil litigation in this area is highly questionable"); Cuéllar & Humphreys, *supra* note 161 (describing the "host of constraints" facing tort law as a tool for addressing the opioid crisis); Nora Freeman Engstrom & Michelle M. Mello, *Litigation is Critical to Opioid Crisis Response*, DAILY JOURNAL (Mar. 13, 2019), <https://www.dailyjournal.com/articles/351533-litigation-is-critical-to-opioid-crisis-response> (arguing that "litigation is a critically important component of the response to the opioid crisis" but acknowledging that "the plaintiffs' path forward is studded with obstacles"); Amanda Pustilnik, *The Law's Responses to the Opioid Epidemic: Legal Solutions to a Unique Public Health, Criminal Law, and Market-Related Crisis*, in CONFRONTING OUR NATION'S OPIOID CRISIS: A REPORT OF THE ASPEN HEALTH STRATEGY GROUP 93, 110 (Alan R. Weil & Rachel Dolan eds., 2017) (noting that "the litigation approach as currently practiced has limited deterrent value" and arguing that manufacturers must somehow be forced to internalize future harms).

may prove to be the rare case of successful corporate veil-piercing, but they stand out as an anomaly against the background of limited shareholder liability in American law.¹⁶⁵

Criminal law, meanwhile, may have a role to play in policing the most egregious abuses, but it is a small role in the overall scheme of the crisis. Obstacles to the use of serious criminal sanctions may be partly political—indeed, it was an intervention from the Bush administration that spared three Purdue executives from jail time in 2007¹⁶⁶—but they are also legal and practical. Convincing twelve jurors that blame for the opioid crisis lies with individual corporate executives—executives whose companies were distributing drugs that also addressed post-surgical pain and other very real medical conditions—is not an easy task in any courtroom. Of course, our criminal justice system visits harsh consequences on street-level dealers of chemically similar substances on a daily basis, and the disparities in how we treat street-level drug dealers and high-ranking pharmaceutical executives are stark. But it is far from clear that treating the executive like the street-level drug dealer is the solution. And in any event, the task of criminal justice reform is one of the few that is even more daunting than the opioid epidemic. A broken criminal-justice system is almost certainly not the opioid epidemic's fix.

D. Demand-Side Subsidies: Medicare and Medicaid

Demand-side subsidies are another set of institutions that perhaps could have but did not correct IP's flaws as the opioid crisis sprung up and spread. The largest government programs providing subsidies for prescription drugs are Medicare Part D and Medicaid, which are administered at the federal level by the Centers for Medicare & Medicaid Services (CMS). Medicare Part D is an opt-in federal benefit for people over 65 or with certain disabilities.¹⁶⁷ The formula for benefits is complex, but in 2019, Medicare Part D covers seventy-five percent of brand-name costs up to an initial coverage limit of \$3,820, after a \$415 deductible.¹⁶⁸ Medicaid is a joint federal-state program that provides

¹⁶⁵ See Henry Hansmann & Reiner Kraakman, *Toward Unlimited Shareholder Liability for Torts*, 100 YALE L.J. 1879, 1879 (1991) (noting that “[l]imited liability in tort has been the prevailing rule for corporations in the United States, as elsewhere, for more than a century,” though arguing for a change to this rule).

¹⁶⁶ See Barry Meier, *Why Drug Company Executives Haven't Really Seen Justice for Their Role in the Opioid Crisis*, TIME (June 15, 2018), <https://time.com/5311359/purdue-pharma-oxycontin-lawsuit-opioid-crisis>.

¹⁶⁷ See STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 27–28. Medicare also provides limited coverage under Part B for some physician-administered drugs, which does not include opioids but does include some addiction treatments. See Brett P. Giroir & Kimberly Brandt, *Testimony on Tracking Opioid and Substance Use Disorders in Medicare Medicaid, and Human Services Programs before Committee on Finance*, HEALTH & HUMAN SERVS. (Apr. 19, 2018), <https://www.hhs.gov/about/agencies/asl/testimony/2018-04/tracking-opioid-and-substance-use-disorders-medicare-medicaid-hhs-programs.html>.

¹⁶⁸ *An Overview of the Medicare Part D Prescription Drug Benefit*, HENRY J. KAISER FAMILY FOUND. (Oct. 12, 2018), <https://www.kff.org/medicare/fact-sheet/an-overview-of-the-medicare-part-d-prescription-drug-benefit>. About 13 million out of 44 million Part D beneficiaries receive low-

health care coverage for low-income individuals. Medicaid beneficiaries receive full coverage for prescription drugs, with some states requiring a small co-pay.¹⁶⁹

Within these limits, Medicare and Medicaid have generally reimbursed the costs of prescription opioids such as OxyContin. Indeed, in 2016, opioids were provided to one-third of Medicare Part D beneficiaries (14.4 million individuals).¹⁷⁰ The nearly 80 million opioid prescriptions cost taxpayers \$4.1 billion.¹⁷¹ From 2011 to 2016, Medicaid reimbursed an average of 30 million opioid prescriptions per year.¹⁷² In contrast, even though almost half of nonelderly adults with opioid use disorder are Medicaid beneficiaries, many states deny or limit coverage for medication-assisted treatments such as Suboxone, including by imposing barriers such as prior authorization requirements.¹⁷³ Part of the blame for the proliferation of opioids and the more limited spread of opioid-addiction treatments may thus lie with the institutional design choices that led to subsidies for opioids and not for addiction treatments.

This Section provides an in-depth look at the role of Medicare and Medicaid in the opioid epidemic. First, we consider whether expanding access to health care contributed to the crisis. Next, we examine whether a particular aspect of Medicaid's approach to pharmaceutical pricing had the unintended consequence of limiting access to opioid antidotes. The claim that expanding access to health care made the crisis worse turns out to be tenuous at best. But as we seek to show in Section I.D.2, programmatic features of Medicaid may indeed have had pernicious effects for patients.

1. Health Care Coverage and Opioid Use

Generally, demand-side subsidies for a product should result in lower out-of-pocket per-unit costs for subsidy recipients and higher consumption overall. That appears to be what happened with Medicare Part D. Economists Mark Duggan and Fiona Scott Morton have shown that for drugs with competitors in the same therapeutic class, the introduction of Medicare Part D led to substantial price declines and increases in utilization.¹⁷⁴ Subsequent

income subsidies reducing their out-of-pocket spending. See SUZANNE M. KIRCHHOFF, *MEDICARE PART D PRESCRIPTION DRUG BENEFIT*, CONGRESSIONAL RESEARCH SERVICE 1 (2018), <https://fas.org/sgp/crs/misc/R40611.pdf>.

¹⁶⁹ See *Medicaid Benefits: Prescription Drugs*, HENRY J. KAISER FAMILY FOUND., <https://www.kff.org/medicaid/state-indicator/prescription-drugs> (last visited Feb. 15, 2019).

¹⁷⁰ U.S. DEP'T OF HEALTH & HUMAN SERVS. OFFICE OF INSPECTOR GEN., *OPIOIDS IN MEDICARE PART D; CONCERNS ABOUT EXTREME USE AND QUESTIONABLE PRESCRIBING* 2 (2017), <https://oig.hhs.gov/oei/reports/oei-02-17-00250.pdf>.

¹⁷¹ *Id.*

¹⁷² See Alana Sharp et al., *Impact of Medicaid Expansion on Access to Opioid Analgesic Medications and Medication-Assisted Treatment*, 108 AM. J. PUB. HEALTH 642, 643 (2018).

¹⁷³ See CHRISTIE ET AL., *supra* note 10, at 70; NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 56, at 12–13, 123–26.

¹⁷⁴ Mark Duggan & Fiona Scott Morton, *The Effect of Medicare Part D on Pharmaceutical Prices and Utilization*, 100 AM. ECON. REV. 590 (2010); see also Mark A. Lemley, Lisa Larrimore

studies have confirmed these findings in the opioid context: Part D coverage reduced the out-of-pocket cost of prescription opioids for newly insured seniors by roughly forty to fifty percent, and prescription opioid utilization among the covered population increased more or less commensurately.¹⁷⁵

While Medicare Part D appears to have contributed to the proliferation of prescription opioids, the same does not appear to have been the case for Medicaid. Rather, Medicaid-focused studies have found no statistically significant relationship between Medicaid expansion and opioid use.¹⁷⁶ The contrast between Medicare Part D and Medicaid presents a puzzle with at least two potential answers.¹⁷⁷

First, Medicaid establishes limits on reimbursements to pharmaceutical manufacturers that are based on prices paid by non-Medicaid consumers such that Medicaid receives the “best price” among purchasers.¹⁷⁸ This arrangement gives manufacturers an incentive to raise the prices that they charge to non-Medicaid consumers and thereby extract more revenue from the Medicaid program, and Duggan and Scott Morton have shown that an increase in the Medicaid market share is indeed associated with an increase in the average price of a prescription.¹⁷⁹ The result is that Medicaid coverage likely increases access among Medicaid beneficiaries but has the opposite effect on non-beneficiaries. Since Medicare Part D prices are not explicitly tied to rates in the rest of the market, Medicare Part D does not create the same incentive for manufacturers to hike prices. But this is at most a partial explanation: Medicaid expansion failed

Ouellette & Rachel E. Sachs, *The Medicare Innovation Subsidy*, 95 N.Y.U. L. REV. (forthcoming May 2020), <https://ssrn.com/abstract=3441247> (arguing that access-focused proposals such as “Medicare for All” should recognize how demand-side subsidies are connected to innovation incentives).

¹⁷⁵ See Aparna Soni, *Health Insurance, Price Changes, and the Demand for Pain Relief Drugs: Evidence from Medicare Part D* 16–17 (Kelley Sch. Bus. Research Paper No. 19-4, 2018), <https://ssrn.com/abstract=3268968> (finding 38% reduction in out-of-pocket costs and 74% increase in morphine-milligram-equivalent consumption); David Powell, Rosalie Liccardo Pacula & Erin Taylor, *How Increasing Medical Access to Opioids Contributes to the Opioid Epidemic: Evidence from Medicare Part D* 15 (Nat’l Bureau of Econ. Research, Working Paper No. 21072, 2016), <https://www.nber.org/papers/w21072> (finding 48% reduction in out-of-pocket costs and 28% increase in number of prescriptions).

¹⁷⁶ See Katherine Baicker et al., *The Effect of Medicaid on Medication Use Among Poor Adults: Evidence from Oregon*, 36 HEALTH AFFAIRS 2110 (2017) (finding that Oregon residents who were randomized into a Medicaid expansion program were not more likely to use opioids); Alana Sharp et al., *Impact of Medicaid Expansion on Access to Opioid Analgesic Medications and Medication-Assisted Treatment*, 108 AM. J. PUB. HEALTH 642 (2018) (finding that state populations covered by Medicaid expansions were not more likely to use opioids but were more likely to use medication-assisted treatment (buprenorphine and naltrexone) for opioid use disorders).

¹⁷⁷ These answers are certainly not exhaustive. The different populations treated by Medicare and Medicaid may also play some role; for example, there may be greater unmet demand for pain treatment among the more elderly Medicare beneficiaries.

¹⁷⁸ See Ramsey Baghdadi, *Medicaid Best Price*, HEALTH AFFAIRS (Aug. 10, 2017), <https://www.healthaffairs.org/doi/10.1377/hpb20171008.000173/full>. For an overview of Medicaid pricing, see Sachs, *supra* note 27, at 182, 196.

¹⁷⁹ Mark Duggan & Fiona M. Scott Morton, *The Distortionary Effects of Government Procurement: Evidence from Medicaid Prescription Drug Purchasing*, 121 Q.J. ECON. 1 (2006).

to raise prescription opioid use in a statistically significant way not only at the state level, but also at the individual level among newly covered Medicaid beneficiaries.¹⁸⁰ The null result of Medicaid coverage on prescription opioid use is thus not simply a case of a positive effect on use among Medicaid beneficiaries being offset by a negative effective on use among others.

A second plausible explanation for the Medicare/Medicaid contrast is that while Medicare Part D expanded prescription drug coverage among seniors who already had access to non-pharmaceutical care, Medicaid increased access to both pharmaceuticals and other forms of healthcare. In the pain relief context, healthcare and prescription painkillers may be substitutes, dampening the impact of increased opioid access. Thus, even while Medicaid provides a demand-side subsidy for prescription opioids, it also subsidizes certain forms of non-pharmaceutical care that serve to reduce demand for prescription opioids.

In sum, demand-side subsidies do appear to have played a role in the proliferation of prescription opioids, but the story is not a straightforward one.¹⁸¹ In particular, the contrast between Medicare Part D and Medicaid suggests that subsidies for prescription drugs and broader health care subsidies may have differential effects on opioid use. We return to this subject in Section II.B when we consider the implications of our analysis for potential health care access reforms.

2. The Medicaid Best Price Rule and Private Payers

Like OxyContin, Evzio has been the beneficiary of demand-side subsidies. The federal government spent over \$142 million on Evzio from its 2014 launch through August 2018, primarily through Medicare Part D and Medicaid.¹⁸² Most of these expenditures occurred after Kaléo's sales force began urging prescribing doctors in 2016 to complete paperwork indicating that Evzio was "medically necessary," triggering coverage by both commercial and government plans.¹⁸³ In the first quarter of 2017, Medicare and Medicaid were responsible for 24% of the 2522 units sold but 75% of the \$7.94 million in net sales.¹⁸⁴

When setting the price of Evzio, Kaléo sought advice from a number of industry consultants who offered widely varying recommendations. One consultancy suggested a price of \$125 per device, or \$250 for a double-dose

¹⁸⁰ See Baicker et al., *supra* note 176.

¹⁸¹ The Council of Economic Advisers, in its February 2020 *Economic Report of the President*, argues that the decline in out-of-pocket opioid prices (driven largely by government subsidies) accounts for a significant share of the rise in opioid deaths in recent years. See ECONOMIC REPORT OF THE PRESIDENT 228 (Feb. 2020) ("We estimate that the decline in observed out-of-pocket prices is capable of explaining between 31 and 83 percent of the growth in the death rate involving prescription opioids from 2001 to 2010.").

¹⁸² STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 74–84.

¹⁸³ *Id.* at 4.

¹⁸⁴ *Id.* at 5.

packet.¹⁸⁵ Another firm advised Kaléo to price its packets in the \$300 to \$350 range.¹⁸⁶ A third recommended a target price per packet of \$575, which is where Evzio started out in 2014.¹⁸⁷

Two Chicago-based consultants, Todd Smith and Benjamin Bove, were hired in 2015 and offered up a very different strategy, which Kaléo ultimately adopted.¹⁸⁸ Under the distribution model urged by Smith and Bove, Kaléo promised to cover the copays of patients who received Evzio.¹⁸⁹ These patients would receive Evzio in the mail, bypassing the traditional pharmacy channel.¹⁹⁰ Kaléo would charge sky-high prices (in the several thousands of dollars) to commercial insurers, apparently with the expectation that some would not pay but others would.¹⁹¹ The strategy was described to *60 Minutes* journalists by former Kaléo employees as “a legal shell game to bilk insurance companies.”¹⁹²

Kaléo’s shell game hit a number of roadblocks. Two of the three major U.S. pharmacy benefit managers (PBMs),¹⁹³ Express Scripts and CVS, removed Evzio from their drug menus in 2016 and replaced it with the naloxone nasal spray Narcan,¹⁹⁴ which is generally considered to be less user-friendly than Evzio.¹⁹⁵ Kaléo responded by terminating rebate agreements with the PBMs and with CMS, allowing it to earn a higher profit per device.¹⁹⁶ Kaléo received more than \$140 million in payments from Medicare Part D and Medicaid, but even so, according to a Senate subcommittee report, Kaléo had not turned a profit on Evzio as of 2018.¹⁹⁷ Meanwhile, state and local governments—which were not the beneficiaries of Kaléo’s zero-copay pledge—struggled to afford the \$4100 drug.¹⁹⁸ Ultimately—though only after significant pressure from a Senate

¹⁸⁵ *Id.* at 38.

¹⁸⁶ *Id.*

¹⁸⁷ *Id.* at 39–41.

¹⁸⁸ *Id.* at 47.

¹⁸⁹ *Id.* at 54–55.

¹⁹⁰ *Id.* at 55.

¹⁹¹ *Id.* at 54–55.

¹⁹² *60 Minutes: Evzio: The Overdose-Reversal Drug with a \$4000+ Price Tag* (CBS television broadcast Nov. 18, 2018), <https://www.cbsnews.com/news/evzio-the-opioid-overdose-reversal-drug-naloxone-with-a-4000-price-tag-60-minutes>.

¹⁹³ PBMs are the middlemen between drug manufacturers and healthcare payers (including commercial insurers, Medicare, and Medicaid), and three PBMs—CVS, Express Scripts, and UnitedHealth’s Optum—account for over seventy percent of claims. See John Arnold, *Are Pharmacy Benefit Managers the Good Guys or the Bad Guys of Drug Pricing?*, STAT (Aug. 27, 2018), <https://www.statnews.com/2018/08/27/pharmacy-benefit-managers-good-or-bad>.

¹⁹⁴ STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 66–70.

¹⁹⁵ See *60 Minutes: Evzio: The Overdose-Reversal Drug with a \$4000+ Price Tag*, *supra* note 192 (showing reporter Lesley Stahl struggling to administer Narcan but exclaiming that Evzio is “[r]eally easy”).

¹⁹⁶ STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 67, 79.

¹⁹⁷ *Id.* at 74.

¹⁹⁸ See *supra* note 93 and accompanying text.

investigation and critical news articles¹⁹⁹—Kaléo began offering Evzio to first responders for \$180 in April 2018,²⁰⁰ and in December 2018, Kaléo announced that a subsidiary will sell an authorized generic version for \$178.²⁰¹

One way to describe Kaléo’s strategy is as a failed effort at price discrimination. If successful, price discrimination—charging different prices to different consumers—could alleviate the allocative inefficiencies of patent protection. As long as a firm can charge each consumer less than her willingness to pay, then no one’s access will be limited, even if prices are well above marginal cost for consumers whose willingness to pay is high.²⁰² But a number of factors stood in the way of Kaléo’s price discrimination gambit. For one, drug manufacturers do not typically interact directly with consumers—hence Kaléo’s effort to establish independent relationships through specialty pharmacies and bypass traditional distribution channels. For another, federal law places some limits on price discrimination. Drug manufacturers seeking Medicaid coverage typically enter rebate agreements with CMS, with the rebate size guaranteeing Medicaid the “best price” among purchasers.²⁰³ Specifically, Medicaid receives a minimum rebate of 23.1 percent off the Average Manufacturer Price (AMP), and if any private purchaser (or some public purchasers, including local governments) receives more than this discount, Medicaid receives that “best price.”²⁰⁴ This mandate made it unattractive for Kaléo to negotiate discounts with individual PBMs.²⁰⁵ And even after Kaléo ended its rebate agreements, it could (and did) receive Medicaid and Medicare Part D payments when doctors

¹⁹⁹ See STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89; *see, e.g., 60 Minutes: Evzio: The Overdose-Reversal Drug with a \$4000+ Price Tag*, *supra* note 192; Luthra, *supra* note 90; Dylan Scott, *This Drug Saves Americans from Opioid Overdoses. Its Price Has Been Hiked 600 Percent*, VOX (Nov. 19, 2018), <https://www.vox.com/policy-and-politics/2018/11/19/18103361/opioid-overdose-naloxone-evzio-drug-prices>.

²⁰⁰ See Press Release, Kaléo, EVZIO® (naloxone HCl injection, USP) Auto-Injector Now Available to Patients in Select States Without a Prescription Through Kaléo’s New Virtual Standing Order Pilot Program and to Government Agencies at a Direct Purchase Price (Apr. 5, 2018), <https://kaleo.com/press-release/evzio-naloxone-hcl-injection-usp-auto-injector-now-available-to-patients-in-select-states-without-a-prescription-through-kaleos-new-virtual-standing-order-pilot-program-and-to-govern>.

²⁰¹ See Lev Facher, *Kaleo, Maker of \$4,100 Overdose Antidote, Authorizes a Generic Version for Just \$178*, STAT (Dec. 12, 2018), <https://www.statnews.com/2018/12/12/kaleo-evzio-overdose-antidote-generic>.

²⁰² See generally SUZANNE SCOTCHMER, INNOVATION AND INCENTIVES 37 (2004) (“The deadweight loss imposed by a monopolist can be mitigated, and possibly eliminated, if the monopolist can discriminate on price”).

²⁰³ See Baghdadi, *supra* note 178.

²⁰⁴ *Id.*

²⁰⁵ See *id.* (“One ripple effect of guaranteeing the best price for Medicaid is that it weakens the leverage of private commercial payers and pharmacy benefit managers (PBMs) in negotiations with manufacturers, in effect setting a floor under prices. Private payers argue that they would be able to negotiate even lower prices for patients if manufacturers were not obliged to offer the same price to all fifty state Medicaid programs.”).

certified Evzio as “medically necessary,”²⁰⁶ but these payments could not be higher than “usual and customary charges to the general public,”²⁰⁷ again limiting incentives to negotiate individual discounts.²⁰⁸

Under typical accounts of the patent system—including our own previous work²⁰⁹—demand-side subsidies like Medicaid are viewed as a *solution* to allocative inefficiencies. And there are indeed substantial demand-side subsidies for Evzio through Medicaid and Medicare Part D. But they are not playing the role they play in the classic story; instead, they appear to be exacerbating the allocative problem. If the limits on charging CMS more than the “best price” or the “usual and customary charges” did not exist, Kaléo might well have reached agreements with individual purchasers such as cash-strapped local governments or patients without insurance that preserved patient access to Evzio (thereby lowering deadweight loss). But with these limits in the background, Kaléo had less incentive to strike deals with private purchasers that would have reduced what it could charge the federal government.²¹⁰

The Kaléo story thus confirms and challenges our view of patent law. It confirms the view that monopoly power can, under certain conditions, lead to supracompetitive prices and suboptimal output. It challenges the view of demand-side subsidies as an easy solution to the problem. This is not to say that demand-side subsidies *could not* address the allocative problem here. It is, instead, to illustrate that the design details of those subsidies are critically important, and that non-patent policies can magnify as well as mitigate the patent system’s pathologies.

²⁰⁶ See STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 89, at 74, 80 (reporting that from January to August 2018, Medicare Part D paid over \$45 million and Medicaid paid over \$5 million for Evzio); see *id.* at 1 (describing sales efforts focused on getting doctors to sign “paperwork indicating that EVZIO was medically necessary, which ensured the drug would be covered by government programs like Medicare and Medicaid”).

²⁰⁷ 42 CFR § 447.512(b)(2). This regulation was renumbered from § 447.331 in 2007. See 72 Fed. Reg. 39,142, 39,154 (July 17, 2007).

²⁰⁸ There is relatively little discussion in case law or legal commentary about the effect of this “usual and customary” limit on pharmaceutical prices because most firms voluntarily enter rebate agreements with CMS, but the inability to charge CMS more than the “usual and customary charges to the general public” has limited price discrimination in other pharmaceutical contexts. See *United States ex rel. Garbe v. Kmart Corp.*, 824 F.3d 632, 644 (7th Cir. 2016) (“Regulations related to ‘usual and customary’ price should be read to ensure that where the pharmacy regularly offers a price to its cash purchasers of a particular drug, Medicare Part D receives the benefit of that deal.”).

²⁰⁹ See Hemel & Ouellette, *supra* note 21, at 563, 594–95 (describing Medicaid as the closest example in the United States to “matching” of an IP innovation incentive with a non-IP allocation mechanism to reduce allocative inefficiencies).

²¹⁰ To be clear, the “best price” mandate does permit a variety of novel pricing arrangements, including pay-for-value models, as explained by Rachel Sachs, Nicholas Bagley & Darius N. Lakdawalla, *Innovative Contracting for Pharmaceuticals and Medicaid’s Best-Price Rule*, 43 J. HEALTH POL. POL’Y & L. 5 (2018). But Kaléo could not, for example, charge \$200 to poorer purchasers while charging \$4000 to Medicaid.

E. Where Were the Alternative Pain and Addiction Treatments?

Thus far, this Part has illustrated the history of the opioid crisis through a tale of three drugs. But why is it a tale of three *drugs*? Here, we explain how the U.S. patent system helped lead to the current opioid epidemic not only through its incentives to commercialize prescription pain treatments, but also through its *failure* to provide incentives for alternative non-pharmacological pain and addiction treatments. There are, of course, important differences between the problem of treating chronic pain and the problem of treating those addicted to opioids, including the differential role of politics, which we turn to in Section II.C. We think it is worth emphasizing, however, the common institutional distortions that affected the market for innovations in both contexts.

The patent system is designed to mitigate the problem of underinvestment in innovation. Knowledge goods present a classic public goods problem: producers underinvest because knowledge goods often benefit persons other than the producer (nonrivalry) who are hard to exclude from their benefits (nonexcludability), and rational firms do not account for these benefits in their investment decisions.²¹¹ Patent law addresses this problem by making many knowledge goods more excludable. But as Amy Kapczynski and Talha Syed have explained, this system creates a skew in research toward innovations that can be excluded through patents, such as pharmaceuticals.²¹²

Many solutions to chronic pain are not easily patentable. Even within the pharmaceutical space, it is difficult to patent (or to enforce patents on) new uses of existing drugs.²¹³ Information that corrects misinformation about existing drugs is also difficult to patent or commodify.²¹⁴ Recent randomized controlled trials have suggested that opioids may be no more effective than certain non-opioids at treating both acute and chronic pain.²¹⁵ Why weren't these studies conducted before opioid misuse became a national crisis? Why aren't these non-opioid treatment strategies being aggressively promoted even now? A substantial part of the answer is likely the inability to patent or commodify these findings: no one firm can capture the significant public benefit of correcting misinformation about opioid efficacy.

Patents are even less effective at incentivizing pain-treatment research that is not related to a commodifiable pill. The 2017 National Academies report on pain management stressed the importance of additional research on non-pharmacologic interventions that may be more effective than medications, including acupuncture, physical therapy and exercise, cognitive behavioral

²¹¹ See Daniel J. Hemel & Lisa Larrimore Ouellette, *Knowledge Goods and Nation-States*, 101 MINN. L. REV. 167, 170 (2016) (explaining this theory and numerous caveats).

²¹² Kapczynski & Syed, *supra* note 23.

²¹³ See Benjamin N. Roin, Solving the Problem of New Uses (Oct. 1, 2013) (unpublished manuscript), <https://ssrn.com/abstract=2337821>.

²¹⁴ See Sean B. Seymore, *The Null Patent*, 53 WM. & MARY L. REV. 2041 (2012); *supra* note 110 and accompanying text.

²¹⁵ See *supra* notes 107–109 and accompanying text.

therapy, and mindfulness meditation.²¹⁶ But even if firms could overcome the legal hurdles to patenting improvements to these methods of pain management,²¹⁷ it would be difficult to monitor the dispersed use of these knowledge goods and to enforce these legal rights.²¹⁸

Ideally, these patent law failures could be corrected by government-set incentives such as increased grant spending on alternative pain treatments and increased subsidies to expand the market for resulting interventions. But while CMS generally reimbursed the costs of prescription opioids, it did not reimburse the costs of many non-opioid pain treatments such as acupuncture or behavioral programs.²¹⁹ This coverage choice makes non-pharmacological treatments more expensive to patients, even if they are more cost-effective overall.

Worse yet, CMS may have inadvertently pushed physicians to rely more heavily on prescription opioids through its use of pain management questions on patient satisfaction surveys.²²⁰ Specifically, the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey—introduced by CMS in 2006 and administered to patients after discharge²²¹—asked in its now-controversial Question 14: “How often did the hospital or provider do everything in their power to control your pain?”²²² Providers anecdotally observed that patients who received opioid prescriptions were more likely to provide favorable survey responses.²²³ The stakes for hospitals were reputational as well as financial. Starting in 2007, hospitals receiving payments from Medicare for inpatient stays were required to collect and submit HCAHPS data, which was then made publicly available.²²⁴ The rewards for high HCAHPS scores increased after the Affordable Care Act explicitly tied hospital

²¹⁶ NAT’L ACADS. OF SCIS., ENG’G, & MED., *supra* note 150, at 84–91.

²¹⁷ New knowledge about the relative efficacy of existing treatment methods would fail the novelty and nonobviousness requirements of 35 U.S.C. §§ 102–103, and patents on novel methods would likely be challenged as patent-ineligible abstract ideas or laws of nature, *see* *Alice Corp. v. CLS Bank Int’l*, 573 U.S. 208 (2014).

²¹⁸ Many activities by medical professionals are exempt from liability under 35 U.S.C. § 287(c), and activities that can be performed by patients at home—such as exercise and other healthy lifestyle changes—would be very difficult to monitor.

²¹⁹ *See* CHRISTIE ET AL., *supra* note 10, at 56–57.

²²⁰ *See* Jerome Adams, Gregory H. Bledsoe & John H. Armstrong, *Are Pain Management Questions in Patient Satisfaction Surveys Driving the Opioid Epidemic*, 106 AM. J. PUB. HEALTH 985 (2016); Teresa A. Rummans, Caroline Burton & Nancy L. Dawson, *How Good Intentions Contributed to Bad Outcomes: The Opioid Crisis*, 93 MAYO CLINIC PROC. 344 (2018).

²²¹ *HCAHPS Fact Sheet*, CTRS. FOR MEDICARE & MEDICAID SERVS. (Nov. 2, 2017), https://www.hcahpsonline.org/globalassets/hcahps/facts/hcahps_fact_sheet_november_2017.pdf.

²²² Adams et al., *supra* note 220, at 985.

²²³ *See* Anna Lembke, *The Opioid Epidemic Is a Symptom of Our Faltering Healthcare System*, BMJ OPINION (Oct. 31, 2017), <https://blogs.bmj.com/bmj/2017/10/31/anna-lembke-the-opioid-epidemic-is-a-symptom-of-our-faltering-healthcare-system> (“Doctors’ salary and professional advancement are tied to how well patients rate them on ‘patient satisfaction surveys.’ Doctors are desperate to avoid bad ratings, and will write a prescription for an opioid, even when it’s not indicated, to avoid a dissatisfied customer.”).

²²⁴ *HCAHPS Fact Sheet*, *supra* note 221, at 2.

reimbursements in part to a hospital's HCAHPS performance.²²⁵ Hospitals were effectively rewarded (or, at least, believed they were being rewarded²²⁶) for alleviating short-term pain with opioids and were not subsequently punished when their patients or their patients' relatives started abusing the drugs.

In short, instead of offsetting the patent system's skew toward addictive pharmacological pain treatments, other federal policies amplified patent law's flaws. The patent system is only one among a complex of innovation institutions that can balance each other's biases, but here, non-patent innovation institutions did more to exacerbate than to equilibrate the tilt toward prescription opioids. As we discuss in the Parts that follow, the failures of non-patent innovation institutions in the opioid crisis inform potential near-term policy responses to the ongoing epidemic as well as long-term efforts at innovation policy reform.

II. Mixing, Matching, and Layering Innovation Policies to Address the Opioid Crisis

While the design of U.S. innovation institutions created conditions that allowed the opioid crisis to develop, these institutions also can play an important role in helping resolve (or at least contain) the epidemic. The causes of opioid addiction and overdose are manifold, but knowledge goods (or the lack thereof) play a critical role at each step along the way. Greater access to affordable nonaddictive pain treatment alternatives would stem the spread of prescription opioids in the first place. Technologically assisted early interventions can halt transitions from opioid use to opioid abuse. Medication-assisted treatments can put patients with opioid abuse disorders on the path to recovery. And widespread availability of opioid antidotes such as naloxone can avert catastrophic outcomes when earlier efforts fail.

In prior work, we have drawn a distinction between the *incentives* that innovation institutions provide to producers of knowledge goods and the *allocation mechanisms* that innovation institutions establish to govern access to knowledge goods.²²⁷ Here, we apply this framework to the challenges presented by the opioid epidemic. Section II.A considers ways in which innovation institutions can spur the development of technologies that reduce addiction and overdose risks. Section II.B examines policies that can ensure broader access to knowledge goods that fight the opioid epidemic. Finally, Section II.C places these potential policy responses within a broader political and social context. To some degree, the failures of innovation institutions during the opioid crisis reflect underlying inequalities and political pathologies that innovation policy reform is unlikely to solve. In still other respects, however, the crisis was precipitated and

²²⁵ *Id.*

²²⁶ Whether high rates of opioid prescription actually boosted HCAHPS scores is a subject of some ambiguity. See Jay S. Lee, Hsou M. Hu & Chad M. Brummet, *Postoperative Opioid Prescribing and the Pain Scores on Hospital Consumer Assessment of Healthcare Providers and Systems Survey*, 317 JAMA 2013 (2017) (finding no correlation between postoperative opioid prescribing and HCAHPS scores).

²²⁷ See Hemel & Ouellette, *supra* note 21.

perpetuated by policy mistakes that can be corrected, even though the human and economic costs of past mistakes cannot be erased.

A. Incentivizing Pain- and Addiction-Related Innovation

1. Intellectual Property and Market Incentives

Conventionally, innovation scholars have focused on patent law as the main policy tool to increase production of new knowledge goods.²²⁸ Patents, at least in theory, leverage private information from market actors about the value and viability of potential projects and provide strong incentives for investments in promising ideas.²²⁹ But as emphasized in Section I.B, these same features of the patent system encouraged the development and commercialization of prescription opioids. Given the patent system's pro-pharmaceutical skew—and, in particular, its bias toward addictive goods—one natural response might be to write off patents as a potential solution to a problem that, in many respects, is a product of too many pills.

We think that would be a mistake. As awareness grows among physicians and patients about the addiction risk associated with prescription opioids, demand for nonaddictive pain treatments will increase too. The patent system will generate strong financial incentives for pharmaceutical and biotech firms to invest in the development of non-opioid painkillers,²³⁰ abuse-resistant opioids,²³¹ drugs that can be used to treat addiction,²³² and easier delivery methods for the overdose antidote naloxone.²³³ (Indeed, many firms already have.²³⁴) There is, to be sure, something unseemly about the very firms that

²²⁸ See Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1576 (2003) (“Patent law is our primary policy tool to promote innovation.”).

²²⁹ See Hemel & Ouellette, *supra* note 21, at 554–57.

²³⁰ See Tamara Mathias, *U.S. Regulators Snip Red Tape for Medical Devices to Curb Opioid Crisis*, REUTERS (Nov. 8, 2018), <https://www.reuters.com/article/us-usa-opioids-focus/u-s-regulators-snip-red-tape-for-medical-devices-to-curb-opioid-crisis-idUSKCN1NE0GQ> (“Drugmakers including Pfizer Inc, Eli Lilly and Co, Regeneron Pharmaceuticals Inc and Teva Pharmaceutical Industries Inc have been packing their pipelines with potential solutions to the crisis and there are 120 non-opioid drugs under FDA review this year, up some 650 percent since 2013 . . .”).

²³¹ FDA-approved abuse-deterrent opioids, none of which have generic alternatives, are listed at *Abuse-Deterrent Opioid Analgesics*, FOOD & DRUG ADMIN., <https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm600788.htm> (last updated Apr. 23, 2018).

²³² See *Information About Medication-Assisted Treatment (MAT)*, *supra* note 55 (listing approved products). Most of these products are heavily patented. See *Orange Book*, FOOD & DRUG ADMIN., <https://www.accessdata.fda.gov/scripts/cder/ob> (last visited Nov. 28, 2018) (search for the product name and then click on the “Appl No” and “Patent and Exclusivity Information”); see also *Orexo AB v. Actavis Elizabeth LLC*, 903 F.3d 1265 (Fed. Cir. 2018) (reversing a judgment of invalidity for a buprenorphine patent).

²³³ See *supra* note 84 and accompanying text.

²³⁴ See CHRISTIE ET AL., *supra* note 10, at 88; Nic Fleming, *The Search for the Perfect Painkiller*, GUARDIAN (Jan. 28, 2018), <https://www.theguardian.com/us-news/2018/jan/28/opioids-the>

fueled the spread of prescription opioids also profiting from the problem they helped create. Many Americans were thus understandably outraged to learn that Purdue Pharma has filed for a patent on a drug that could “help wean addicts from opioids,” given that Purdue had helped to hook some of those same people on opioids in the first place.²³⁵ It would be an even crueler irony, though, if the patent system failed to reward investments in innovations that could bring the opioid epidemic under control, and thereby encouraged the proliferation of prescription opioids but not the development of solutions to addiction.

Of course, these powerful patent incentives still may be subject to the same distortions described in Part I. Patents also skew research toward treatments that require repeated use—and thus generate steady streams of revenue—rather than preventatives which are effective after a single administration.²³⁶ Patent law may therefore be more helpful, for example, in encouraging the development of nonaddictive painkillers than in the development of anti-addiction vaccines.²³⁷ Patent law likewise will do little to facilitate research and development directed at ideas that are difficult for a single firm to commodify—for example, reducing the default number of pills per prescription,²³⁸ informing doctors when their patients overdose,²³⁹ or encouraging the use of alternative pain treatments such as physical or behavioral therapy.²⁴⁰ Patents are also ineffective incentives for non-pharmaceutical addiction recovery tools such as mobile-phone reminders that track the number

search-for-the-perfect-painkiller-tens-of-thousands-us-deaths-g-protein-coupled-receptor; Mathias, *supra* note 230. For examples of recent patents on devices for treating pain through neural stimulation, see U.S. Patent No. 9,925,384 (filed Sept. 1, 2016), and U.S. Patent No. 9,855,427 (filed Mar. 9, 2017).

²³⁵ Lindsey Bever, *The Man Who Made Billions of Dollars from OxyContin is Pushing a Drug to Wean Addicts off Opioids*, WASH. POST. (Sept. 8, 2018), <https://www.washingtonpost.com/news/business/wp/2018/09/08/the-man-who-made-billions-of-dollars-from-oxycotin-is-pushing-a-drug-to-wean-addicts-off-opioids/>; see also Lily Dancyger, *OxyContin Maker Granted Patent for Opioid Addiction Treatment*, ROLLING STONE (Sept. 11, 2018), <https://www.rollingstone.com/culture-news/oxycotin-purdue-pharma-patent-opioid-addiction-treatment-722646> (“The idea of Purdue and the Sacklers swooping in with the cure for an epidemic they have profited from, with a new product that will make them even richer, however, feels like the darkest form of capitalist absurdity—and like maybe it’s time to make a corporate version of the Son of Sam laws, which prohibit murderers from profiting from their crimes.”).

²³⁶ See Lisa Larrimore Ouellette & Q. Claire Xue, *Intellectual Property and the Market for Vaccines* (Feb. 5, 2020) (unpublished manuscript); see also Michael Kremer & Christopher M. Snyder, *Preventatives Versus Treatments*, 130 Q.J. ECON. 1167 (2015) (providing an economic analysis of other biases that distort R&D toward treatments rather than preventatives).

²³⁷ On not-yet-successful efforts to create a vaccine against addictive drugs, see Michael Torrice, *Vaccines Against Addictive Drugs Push Forward Despite Past Failures*, CHEM. & ENG’G NEWS (Feb. 19, 2018), <https://cen.acs.org/articles/96/i8/Vaccines-against-addictive-drugs-push.html>.

²³⁸ See Alexander S. Chiu et al., *Association of Lowering Default Pill Counts in Electronic Medical Record Systems with Postoperative Opioid Prescribing*, 153 JAMA SURGERY 1012 (2018).

²³⁹ See Jason N. Doctor et al., *Opioid Prescribing Decreases After Learning of a Patient’s Fatal Overdose*, 361 SCIENCE 588 (2018).

²⁴⁰ See *supra* notes 216–219 and accompanying text.

of days that a patient has remained substance-free,²⁴¹ for creative ideas like using reverse-motion detectors in clinic bathrooms (i.e., devices that detect *lack* of motion) to prevent fatal overdoses,²⁴² and for research on the comparative value of supervised drug use clinics²⁴³ or different drug court protocols or streamlined ER-to-outpatient transfers for preventing relapse.²⁴⁴

Episodes such as Indivior's effort to undermine the tablet form of Suboxone²⁴⁵ highlight the need to consider broad changes to patent law and its interactions with FDA regulatory law, antitrust law, tort law, and other institutions that might cabin its pathologies.²⁴⁶ These changes, however, may take years to formulate and implement. In the meantime, the opioid epidemic's daily death toll reminds us of "the fierce urgency of now."²⁴⁷ While patents may play a role in promoting the development and commercialization of opioid alternatives, antidotes, and addiction treatments, we think it is clear enough that America will not patent its way out of the opioid crisis. Policymakers will need to look elsewhere for solutions.

2. *Ex Ante Government Spending: Grants and Contracts*

Patents, fortunately, are not the only choice in the innovation policy toolkit. Another major innovation lever is direct government R&D spending through grants, contracts, and national laboratories, which collectively account for about one-quarter of the \$500 billion spent on U.S. R&D each year.²⁴⁸ Government-set rewards can encourage innovation in areas where patent law fails (e.g., where welfare-enhancing ideas are difficult to commodify).²⁴⁹ But

²⁴¹ See Orly Nadell Farber, *Can a Phone App's Warnings to Avoid Risky Friends and Places Prevent Opioid Addiction Relapses?*, STAT (Aug. 7, 2018), <https://www.statnews.com/2018/08/07/can-phone-app-prevent-opioid-addiction-relapses>.

²⁴² See MACY, *supra* note 120, at 288.

²⁴³ See Bob Oakes & Martha Bebinger, *Somerville Mayor Plans to Open a Supervised Consumption Site*, *Next Year*, WBUR (Aug. 14, 2019), <https://amp.wbur.org/commonhealth/2019/08/14/curtatone-supervised-illegal-drug-use>.

²⁴⁴ See MACY, *supra* note 120, at 220, 301.

²⁴⁵ See Section I.A.2.

²⁴⁶ See, e.g., NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 150, at 410–14 (arguing that the FDA should incorporate public health considerations into regulatory decisions, which could be used to block products for which the negative externalities swamp the social benefits); Engstrom & Mello, *supra* note 164 (discussing the importance of tort litigation in responding to the crisis); Robin Feldman, *May Your Drug Price Be Evergreen*, 5 J.L. & BIOSCIENCES 590 (2018) (suggesting legal changes to cabin extensions of exclusivity with limited public health benefits); *infra* notes 324–326 (discussing potential doctrinal changes to patent law's utility requirement and remedies rules to incorporate broader social welfare concerns).

²⁴⁷ Martin Luther King, Jr., *I Have a Dream*, Speech Delivered at the Lincoln Memorial (Aug. 28, 1963), *reprinted in* A TESTAMENT OF HOPE 218 (James Melvin Washington ed., 1986).

²⁴⁸ See NAT'L SCI. BD., SCIENCE & ENGINEERING INDICATORS 2018, at 4-20 tbl.4-3 (2018), <https://www.nsf.gov/statistics/2018/nsb20181/assets/nsb20181.pdf>.

²⁴⁹ See Hemel & Ouellette, *supra* note 21, at 555; W. Nicholson Price II, *Grants*, 34 BERKELEY TECH. L.J. 1 (2019).

government-set rewards are, as we discuss below, vulnerable to pathologies of their own.

The United States already does provide direct funding for research related to opioids and alternatives, mostly at federal level through the National Institutes of Health (NIH). In 2017, the NIH spent \$516 million on pain-related research and \$1.6 billion on all forms of substance abuse (of which opioids are only one fraction).²⁵⁰ In fiscal year 2018, Congress nearly doubled NIH funding for research on opioid addiction with an additional \$500 million.²⁵¹ Yet these investments, while nontrivial, are on a scale too small for a problem whose economic costs likely top \$500 billion annually.²⁵² For example, opioid-related research funding is less than the \$3 billion the NIH provides each year for HIV/AIDS research,²⁵³ even though in 2016, there were over ten times more Americans abusing prescription pain relievers than living with HIV,²⁵⁴ and more Americans now die from opioid overdoses than died from the AIDS epidemic at its peak.²⁵⁵

The 2017 National Academies report recommended that the United States invest more heavily in research on pain and on opioid use disorder.²⁵⁶ We agree, and we think understanding the failures of innovation institutions that contributed to the present crisis can help policymakers direct this funding to where it is most needed. For example, although patent law is likely to incentivize investment in new non-addictive pharmaceutical pain treatments, it is less likely to encourage research on non-pharmaceutical (and in most cases unpatentable) pain treatments such as acupuncture, physical therapy and exercise, cognitive behavioral therapy, and mindfulness meditation.²⁵⁷ And while patent law potentially rewards firms for developing opioid antidotes such as Evzio and pharmacological addiction treatments such as Suboxone, it does much less to encourage research into other addiction management mechanisms (e.g., counseling as a complement to medication-assisted treatment²⁵⁸). Grantmaking

²⁵⁰ *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, NAT'L INSTS. OF HEALTH (May 18, 2018), https://report.nih.gov/categorical_spending.aspx.

²⁵¹ Francis S. Collins, Walter J. Koroshetz & Nora D. Volkow, *Helping to End Addiction Over the Long-Term: The Research Plan for the NIH HEAL Initiative*, 320 JAMA 129 (2018).

²⁵² See *supra* note 10 and accompanying text.

²⁵³ See *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, *supra* note 250.

²⁵⁴ Compare SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., *supra* note 50, at 170525 tbl. 1.97A (eleven million), with HIV in the United States and Dependent Areas, CTNS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/hiv/statistics/overview/ataglance.html> (last updated Jan. 29, 2019) (one million).

²⁵⁵ See *supra* note 5 and accompanying text.

²⁵⁶ NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 150, at 162–63.

²⁵⁷ See *supra* note 216 and accompanying text.

²⁵⁸ Findings on the effectiveness of cognitive behavioral therapy for patients simultaneously receiving medication-assisted treatment for opioid abuse are decidedly mixed. Compare David A. Fiellin et al., *A Randomized Trial of Cognitive Behavioral Therapy in Primary Care-based Buprenorphine*, 126 AM. J. MED. 74.e11 (2013) (finding no statistically significant difference on effectiveness measures

agencies should consider the patent system's skews when allocating funds so that their dollars can do the most good—which likely means that resources should be directed at precisely the areas that the patent system leaves untouched.

In making these recommendations, we are cognizant that in the real-world of federal grants and contracts, politics as well as policy considerations shape outcomes. For example, one study finds that each additional member on the House subcommittee that oversees the NIH's budget is associated with a roughly nine percent increase in NIH grants to public universities in that member's state²⁵⁹—suggesting that grant allocations may not be based purely on the merits of potential projects. Universities spend many millions of dollars each year lobbying Congress and federal agencies for more grant money,²⁶⁰ and certainly some of this spending can be fairly characterized as rent-seeking. Increasing the amount of federal spending on opioid-related research will likely increase the social cost of competition among politicians and potential grantees for funds. Yet these rent-seeking costs pale in comparison to the costs of patent litigation²⁶¹ and seem rather trivial when compared with the magnitude of the crisis that opioid-related R&D addresses. That the federal R&D grant process remains far from perfect is, we think, both undeniably true and also not a compelling argument against dramatic increases in opioid-related grantmaking.

3. Ex Post Government Spending: Prizes and Market Subsidies

Government grants—i.e., direct, ex ante public funding for research and development—are both familiar and popular, with polling suggesting that eight in ten U.S. adults think government investments in medical research “usually pay off in the long run.”²⁶² Less well recognized—at least outside the innovation

between patients receiving Suboxone and patients receiving Suboxone plus cognitive behavioral therapy), with Brent A. Moore, *Cognitive Behavioral Therapy Improves Treatment Outcomes for Prescription Opioid Users in Primary Care Buprenorphine Treatment*, 71 J. SUBSTANCE ABUSE TREATMENT 54 (2017) (finding that cognitive behavioral therapy increases probability of abstinence among prescription opioid abusers but not heroin abusers).

²⁵⁹ Deepak Hegde & David C. Mowery, *Politics and Funding in the U.S. Public Biomedical R&D System*, 322 SCIENCE 1797, 1798 (2008).

²⁶⁰ See Rick Cohen, *Universities Pay Plenty for Influence and Access Through Lobbying*, NONPROFIT Q. (July 16, 2014), <https://nonprofitquarterly.org/2014/07/16/universities-pay-plenty-for-influence-and-access-through-lobbying>; Monica Vendituoli, *Top Schools for Federal R&D Grants Are Big Spenders on Lobbying, Campaign Contributions*, OPEN SECRETS (June 5, 2013), <https://www.opensecrets.org/news/2013/06/federal-research-and-development-fu>.

²⁶¹ See Malathi Nayak, *Cost of Patent Infringement Litigation Falling Sharply*, BLOOMBERG NEWS (Aug. 10, 2017), <https://www.bna.com/cost-patent-infringement-n73014463011> (reporting that even with new lower-cost procedures for challenging patents, the median cost for a patent infringement case with \$1 million to \$10 million at stake was still \$1.7 million in 2017); see also Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303, 365 (2013) (estimating the total annual cost of patent litigation to be around \$2.5 billion).

²⁶² See Brian Kennedy, *Americans Broadly Favor Government Funding for Medical and Science Research*, PEW RES. CTR. FACT TANK (July 3, 2018), <http://www.pewresearch.org/fact-tank/2018/07/03/americans-broadly-favor-government-funding-for-medical-and-science-research>.

policy literature²⁶³—is that the government can also choose to reward specific technologies *ex post* through prize systems. Because *ex post* rewards are only given to successful researchers, they can provide stronger incentives for ingenuity and effort, at least as long as researchers can acquire necessary bridge financing until their ideas reach fruition.²⁶⁴

Innovation inducement prizes are a small but growing portion of U.S. innovation institutions,²⁶⁵ including in the opioid context. The NIH is offering \$2.5 million for five challenges related to developing open-source databases, algorithms, and biological assays to streamline development of treatments for pain, opioid use disorder, and opioid overdose.²⁶⁶ Other prize competitions offer financial awards for developing the most promising solutions for tackling a broad portion of the opioid problem, without specifying a particular technological goal.²⁶⁷ For example, the federal Health Resources and Services Administration, an agency within the U.S. Department of Health and Human Services (HHS), is offering up to \$375,000 for innovations that address any “barriers that limit access to quality treatment . . . for those with Opioid Use Disorder (OUD), including pregnant women and new moms.”²⁶⁸ And the HHS two-day Opioid Code-a-Thon distributed three \$10,000 prizes for “data-driven solutions to combat the opioid epidemic.”²⁶⁹ Several states have launched prize competitions of their own. For example, an Ohio prize competition awarded \$200,000 in 2018 to each of twelve winners working on technologies to address drug abuse and addiction.²⁷⁰ And most recently, a New York state prize competition focused on novel solutions to the opioid epidemic awarded a grand prize of \$10,000 to a team developing a new intranasal naloxone patch in January 2019.²⁷¹

²⁶³ Among innovation scholars, debates on the value of prizes as an innovation policy have been ongoing since at least the nineteenth century. See Fritz Machlup & Edith Penrose, *The Patent Controversy in the Nineteenth Century*, 10 J. ECON. HIST. 1, 19 (1950). For a more recent discussion of innovation prizes, see Michael J. Burstein & Fiona E. Murray, *Innovation Prizes in Practice and Theory*, 29 HARV. J.L. & TECH. 401 (2016).

²⁶⁴ See Hemel & Ouellette, *supra* note 21, at 556–57.

²⁶⁵ See Hemel & Ouellette, *supra* note 261, at 317–18.

²⁶⁶ 2018 NCATS ASPIRE Design Challenges, NAT’L INSTS. HEALTH, <https://ncats.nih.gov/aspire/challenges> (last visited Feb. 8, 2018). We have argued that prize competitions may be particularly effective for this kind of computational challenge, where capital constraints typically are not binding. See Hemel & Ouellette, *supra* note 261, at 317–376.

²⁶⁷ See generally Jason Reinecke, *General Innovation Competitions*, 21 STAN. TECH. L. REV. 128 (2018) (describing this kind of competition).

²⁶⁸ *Addressing Opioid Use Disorder in Pregnant Women and New Moms: Timeline*, HEALTH RESOURCES & SERVS. ADMIN., <https://mchbgrandchallenges.hrsa.gov/challenges/addressing-opioid-use-disorder-pregnant-women-and-new-moms/timeline> (last visited Feb. 7, 2019).

²⁶⁹ *HHS Opioid Code-a-Thon*, U.S. DEP’T OF HEALTH & HUMAN SERVS., <https://www.hhs.gov/challenges/code-a-thon/index.html> (last updated Jan. 3, 2018).

²⁷⁰ See *Ohio Opioid Technology Challenge*, OHIO DEV. SERVS. AGENCY (last updated Sept. 2018), https://development.ohio.gov/bs_thirdfrontier/ooc.htm.

²⁷¹ See *Empire State Opioid Epidemic Innovation Challenge*, CAMTECH (Jan. 2019), <http://www.globalhealthmgh.org/camtech/new-york-city-opioid-epidemic-challenge-summit-solutions-sprint>.

Many opioid-related prize competitions offer funding at such a small scale that they seem unlikely to overcome financial barriers to addressing the epidemic—although prizes can have effects beyond direct monetary rewards. Economists Petra Moser and Tom Nicholas have demonstrated that prizes also encourage innovation through publicity, independent from the inducement effect of financial incentives.²⁷² As a possible illustration of this effect, the FDA ran a prize competition for opioid-related medical devices that came with no cash prize—winners received only “enhanced interactions with FDA review divisions” and “Breakthrough Device designation.”²⁷³ Despite the lack of direct financial reward, the competition generated significant interest, with 250 applications, from which eight winners were selected.²⁷⁴

Where innovation inducement prizes are explicitly financial, moreover, they need not be structured as offering a fixed amount of money for a particular technological development. The prize can also be tied to some market outcome, with larger prizes corresponding to greater use of the resulting technology by consumers. For example, rather than offering \$100 million for creation of a new vaccine, a prize sponsor could offer \$50 per person actually inoculated—an intermediate solution between government-set fixed prizes and market-set patent rewards.²⁷⁵ This kind of market-based prize has been used to incentivize distribution of pneumococcal vaccines.²⁷⁶ But such a structure is not limited to small demonstration projects: demand-side government subsidies for certain technologies, such as through insurance programs like Medicare and Medicaid,

²⁷² Petra Moser & Tom Nicholas, *Prizes, Publicity and Patents: Non-Monetary Awards as a Mechanism to Encourage Innovation*, 61 J. INDUS. ECON. 763 (2013).

²⁷³ Press Release, Food & Drug Admin. (May 30, 2018), <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm609188.htm>. The competition was broadly open to any opioid-related devices, including devices related to “diagnostics to identify patients at increased risk for addiction, treatments for pain that eliminate the need for opioid analgesics (such as opioid-sparing or replacement therapies for acute or chronic pain), treatments for opioid use disorder or symptoms of opioid withdrawal, as well as devices or technologies that can prevent diversion of prescription opioids.” *Id.*

²⁷⁴ *FDA Innovation Challenge: Devices to Prevent and Treat Opioid Use Disorder*, FOOD & DRUG ADMIN., <https://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHInnovation/ucm609082.htm> (last updated Nov. 30, 2018). To be sure, the absence of a clear counterfactual makes it difficult to draw any strong conclusions about the causal effect of these programs. *See generally* Heidi Williams, *Innovation Inducement Prizes: Connecting Research to Policy*, 31 J. POL’Y ANALYSIS 752, 768 (2012) (describing this evaluation problem). And while rewards are not directly financial, they may be indirectly so. For example, Breakthrough Device designation may help manufacturers obtain FDA approval at a quicker clip—thus bringing the product to market sooner and increasing total profits over the device’s life. *See Breakthrough Devices Program*, FOOD & DRUG ADMIN., <https://www.fda.gov/medical-devices/how-study-and-market-your-device/breakthrough-devices-program> (last updated May 16, 2019).

²⁷⁵ *See* Hemel & Ouellette, *supra* note 21, at 554.

²⁷⁶ *See generally* Williams, *supra* note 274, at 752, 758–59, 769–70 (describing this pneumococcal prize and the challenges in measuring its effectiveness).

bear some similarities to market-based prizes²⁷⁷ (though they may also introduce new distortions, as discussed above²⁷⁸).

The federal government has offered some targeted subsidies focused on relieving the opioid crisis. Most notably, the U.S. Substance Abuse and Mental Health Services Administration (SAMHSA) distributed over \$1 billion in State Opioid Response Grants, focused on “increasing access to medication-assisted treatment using the three [FDA] approved medications for the treatment of opioid use disorder, reducing unmet treatment need, and reducing opioid overdose related deaths through the provision of prevention, treatment and recovery activities for opioid use disorder.”²⁷⁹ If firms expect this kind of demand-side subsidy to expand the market for a particular medical intervention, the subsidy can enhance incentives to develop technologies in that area in the first place.

Grants administered at the state level also provide some opportunity to learn from state experimentation with opioid abuse treatment models—policy variation is important in the face of uncertainty about which policies are most effective.²⁸⁰ Indeed, SAMHSA grants explicitly include funding for “identify[ing] which system design models will most rapidly and adequately address the gaps in their systems of care.”²⁸¹ Some learning has already occurred from state-level responses: for example, Virginia’s 2017 increase in Medicaid reimbursement rates to addiction treatment providers seems to have reduced opioid-related emergency department visits by expanding the supply of (and thus access to) addiction treatment services.²⁸² To encourage policy experimentation, federal policymakers should consider ways to reward states that use SAMHSA grants or other funding sources to develop innovative approaches that are adopted by other states. To the extent the results of state-level innovation are patentable, states could internalize some out-of-state benefits from their innovation.²⁸³ But while this benefit-internalization approach might work for

²⁷⁷ See Lemley et al., *supra* note 174; Benjamin N. Roin, *Intellectual Property Versus Prizes: Reframing the Debate*, 81 U. CHI. L. REV. 999, 1011–14 (2014); Sachs, *supra* note 27.

²⁷⁸ See *supra* Section I.D.

²⁷⁹ Press Release, U.S. Dep’t of Health & Human Servs., HHS Awards Over \$1 Billion to Combat the Opioid Crisis (Sept. 19, 2018), <https://www.hhs.gov/about/news/2018/09/19/hhs-awards-over-1-billion-combat-opioid-crisis.html>.

²⁸⁰ See Lisa Larrimore Ouellette, *Patent Experimentalism*, 101 VA. L. REV. 65 (2015).

²⁸¹ *State Opioid Response Grants*, SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., <https://www.samhsa.gov/grants/grant-announcements/ti-18-015> (last updated Aug. 3, 2018).

²⁸² See German Lopez, *We Really Do Have a Solution to the Opioid Epidemic—and One State Is Showing It Works*, VOX (May 10, 2018), <https://www.vox.com/policy-and-politics/2018/5/10/17256572/opioid-epidemic-virginia-medicaid-expansion-arts>. For a description of another innovative state program, see German Lopez, *I Looked for a State That’s Taken the Opioid Epidemic Seriously. I Found Vermont.*, VOX (Oct. 31, 2017), <https://www.vox.com/policy-and-politics/2017/10/30/16339672/opioid-epidemic-vermont-hub-spoke>.

²⁸³ See Hemel & Ouellette, *supra* note 21, at 550 (referring to this combination of innovation policies as “layering,” or “the use of different policies at different jurisdictional levels, such as

some technologies such as medical devices, most state-level opioid-related innovations are less likely to generate financial rewards commensurate with their social value, making the need for federal innovation incentives all the more acute.²⁸⁴

The overall efficacy of the SAMHSA grant program is yet to be seen, but a recent investigative report into the District of Columbia's execution of its grants raises an important cautionary note.²⁸⁵ The District won \$4 million through the grant program, but "many programs the city said it would launch never materialized," and "[o]fficials at the clinic contracted by the District with most of its federal funds said not a single patient has been referred to them for addiction treatment."²⁸⁶ This story serves as another reminder that non-market solutions are not a panacea: failures of the political market can be just as devastating, and comparisons of innovation institutions must consider the imperfections of each policy choice. We return to these political concerns in Section II.C.

B. Allocating Access to Pain- and Addiction-Related Innovations

The opioid epidemic stems in part from our failure to develop and refine non-addictive pain treatments, addiction prevention technologies, and successful therapies for substance abuse. But the opioid crisis is not only a crisis of innovation; it is also a crisis of access. In some cases, expensive but effective patent-protected technologies remain out of patients' reach. In other instances, non-patent-protected treatments are available at reasonable cost, but public and private sector health insurance plans fail to cover them or regulatory barriers limit patient access. In this Section, we consider a combination of interventions that would expand access to technologies that can avert, treat, and contain the consequences of opioid addiction.

Importantly, as we have explained, these allocation choices can be largely separated from the choice of innovation incentive, and increasing access does not necessarily imply a decreased reward for the innovator.²⁸⁷ But questions of incentives and allocation are not hermetically sealed off from one another. In some cases, access-related policy levers *should* be used to decrease the reward to the innovator, such as when a product that generates negative externalities is subjected to a Pigouvian tax. In other cases, access-related policies can be used to *increase* rewards to innovation, as when firms expect demand-side subsidies to

using non-IP innovation incentives and allocation mechanisms at the domestic level within an international legal system oriented around IP").

²⁸⁴ See generally Yair Listokin, *Learning Through Policy Variation*, 118 YALE L.J. 480, 546 (2008) ("[F]ree-rider problems, failure to internalize benefits to other jurisdictions from innovation, network externalities, and spillovers may reduce policy variation in multi-jurisdictional systems to a level far below optimality.").

²⁸⁵ Peter Jamison, *'Pure Incompetence,'* WASH. POST (Dec. 19, 2018), <https://www.washingtonpost.com/graphics/2018/local/dc-opioid-epidemic-response-african-americans>.

²⁸⁶ *Id.*

²⁸⁷ See Hemel & Ouellette, *supra* note 21.

boost their profits from new products. Policymakers should remain attentive to the incentive effects of their real-world allocational choices while also understanding the possibility of disaggregating rewards and access.

1. The Case for Open Access

The benefit of expanding access to innovations that will address the opioid crisis should be obvious: stemming the enormous human cost of chronic pain and addiction. But should policymakers be concerned about losing some of the informational value of proprietary pricing? As Glen Weyl and Jean Tirole have explained, market prices often serve a useful screening function: when consumers are willing to pay higher prices for a new product, it signals that they assign a high value to that product relative to any substitutes.²⁸⁸ But there are a host of reasons that the screening function of proprietary pricing fails in the context of pain- and addiction-related innovations.

These problems largely mirror the shortcomings of patent incentives in these contexts. As noted above, market value does not reflect social value in the presence of the externalities and internalities that beset markets for addictive products. These markets have also been plagued with misinformation that further misaligns economic rewards and social value.²⁸⁹ Additionally, even if detailed information about relative clinical efficacy were available, those suffering from opioid use disorder and perhaps some pain patients probably are not operating at full rationality.²⁹⁰ It is hard for lay people and even doctors²⁹¹ to understand the complex statistical evidence needed to evaluate medical information, and it seems implausible that the choice between two treatment options for addiction will typically be grounded in a full understanding of their comparative value.

Just as market prices can fail to accurately signal social value when consumers lack relevant information, they also can fail when consumers are not the ones paying the patent owner's price, such that consumption signals little about the relative value of innovations. Allocation of medical technologies in the United States—and most other countries—is far from a pure user-pays system. As previously discussed, the federal government subsidizes access to new medical technologies through programs like Medicare and Medicaid, which have generally covered prescription opioids.²⁹² All of these factors suggest that the value of proprietary pricing is more attenuated in markets for pain and addiction

²⁸⁸ E. Glen Weyl & Jean Tirole, *Market Power Screens Willingness-to-Pay*, 127 Q.J. ECON. 1971, 1972-75 (2012).

²⁸⁹ See, e.g., *supra* notes 111–118 and accompanying text.

²⁹⁰ See generally CHOICE, BEHAVIOURAL ECONOMICS AND ADDICTION (Rudy E. Vuchinich & Nick Heather eds., 2003).

²⁹¹ See Donna M. Windish et al., *Medicine Residents' Understanding of the Biostatistics and Results in the Medical Literature*, 298 JAMA 1010 (2007) (finding that on average, medicine residents answered only 8 of 20 questions correctly on a multiple-choice test about statistical methods and interpretation of research outcomes).

²⁹² See *supra* notes 170–172 and accompanying text.

treatments than in many other contexts, lessening concerns about some of the policy options discussed below.

2. *Carve-Outs, Buy-Outs, and March-Ins*

Sky-high sticker prices for pharmaceutical products such as Evzio are, we have argued, in part a product of unintended consequences of federal reimbursement policies—and in particular, the limits on charging CMS more than the “best price” or the “usual and customary charges” for other payers.²⁹³ These rules discourage pharmaceutical companies from offering discounts to private health insurance plans and pharmacy benefit managers because those discounts will reduce the amount that the companies can charge the government. Limits on CMS payments aspire to serve the noble purpose of protecting the federal fisc from predatory pharmaceutical pricing. In the case of Evzio, however, these laws appear to have had the unintended consequence of keeping the drug out of many private health plans and pharmacy benefit manager formularies while still leaving the government with an enormous bill.

Fortunately, policymakers are not without tools to address the problem. Specifically, the Affordable Care Act authorizes the Secretary of Health and Human Services to waive the Medicaid best-price mandate, among other restrictions, when testing “payment and service delivery models” that “address[] a defined population for which there are deficits in care leading to poor clinical outcomes.”²⁹⁴ This authority at least arguably allows the Secretary to create a carve-out from the best-price mandate for sales of naloxone products to health plans in the areas hit hardest by the opioid epidemic.²⁹⁵ Exercise of that waiver authority would encourage Kaléo and its leading competitor, Adapt Pharma’s naloxone nasal spray Narcan, to strike deals with private health plans that are currently unwilling to cover the drugs at their list prices.

A bolder approach than a Medicaid best-price carve-out would be for the federal government to offer to buy the family of Evzio-related patents from Kaléo and then to place those patents in the public domain.²⁹⁶ One potential concern with buyouts is that they remove the patent holder’s incentive to invest in commercialization—though by this point, the publicity surrounding the naloxone auto-injector may already have accomplished much of what marketing efforts can achieve. Another, more daunting challenge is how to set the price for such a buyout. Academics have proposed auction systems to place some market bound on patent buyout prices, but perhaps the most straightforward approach for a one-time buyout is for Congress to appropriate a specific amount, in effect making a take-it-or-leave-it offer to the manufacturer. Given that Kaléo does not

²⁹³ See *supra* notes 203–208 and accompanying text.

²⁹⁴ 42 U.S.C. § 1315a(b), (d)(1).

²⁹⁵ On the scope and limit of the Secretary’s authority to waive the best-price mandate, see generally Sachs et al., *supra* note 210, at 14–16.

²⁹⁶ See Hemel & Ouellette, *supra* note 21, at 563–66, 587 (discussing academic buyout proposals including Michael Kremer, *Patent Buyouts: A Mechanism for Encouraging Innovation*, 113 Q. J. ECON. 1137 (1998), as well as how the UK has effectively put these ideas into practice through its system for purchasing and distributing pharmaceuticals).

appear to be turning a profit from Evzio yet,²⁹⁷ it's not crazy to think that the firm would say yes.

Optional patent buyouts are attractive if the optimal buyout price is higher than the patentee's expected market return, which may be the case in the Evzio context given both the product's positive externalities and Kaléo's apparent financial struggles. For unwilling sellers, the government has legal options to effectively force patent buyouts. If all the relevant patents were created under federal grants, the government has a license to practice the invention and can also exercise "march-in" rights to grant additional licenses if "action is necessary to alleviate health or safety needs which are not reasonably satisfied" by the patentee.²⁹⁸ And for any patent, 28 U.S.C. § 1498 allows the government and its contractors to manufacture and use the invention "by or for the United States" in exchange for monetary damages based primarily on the patentee's risk-adjusted research and development costs.²⁹⁹ These statutory mechanisms potentially allow the government to address the problem of "over-reward," although the government has shown reluctance to embrace this authority in other contexts.³⁰⁰

3. Expanding Coverage and Removing Regulatory Hurdles

As discussed in Part I, Medicare and Medicaid generally provided reimbursements for prescription opioids but not for non-opioid pain treatments such as acupuncture or behavioral programs, exacerbating the patent-related distortion toward drugs as opposed to less excludable interventions. Coverage of non-pharmacological treatments through private insurers has been similarly limited.³⁰¹ In addition to incentivizing additional research into these alternative pain treatments, the government should address this bias by requiring or subsidizing coverage for these interventions. Moreover, Part I explained how insufficient insurance coverage has presented a barrier to access not only for non-

²⁹⁷ See *supra* note 197 and accompanying text.

²⁹⁸ 35 U.S.C. §§ 202(c)(4), 203(a)(2). To be sure, march-in rights alone will be of little use when a product is also covered by private-sector patents. See Rachel Sachs, *March-In Rights Alone Won't Solve Our Drug Pricing Problems*, BILL OF HEALTH (Jan. 12, 2016), <http://blog.petrieflom.law.harvard.edu/2016/01/12/march-in-rights-alone-wont-solve-our-drug-pricing-problems>.

²⁹⁹ See Wang & Kesselheim, *supra* note 83 (applying to the Evzio context the argument of Hannah Brennan, Amy Kapczynski, Christine H. Monahan & Zain Rizvi, *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, 18 YALE J.L. & TECH. 275 (2016)); see also Letter from Kim Treanor, Knowledge Ecology Int'l, to Kellyanne Conway, Counselor to the President, and James Carroll, Acting Director, Office of Nat'l Drug Control Pol'y (Mar. 29, 2018), <https://www.keionline.org/wp-content/uploads/2018/03/Conway-Carroll-KEI-1498-Evzio-29mar2018.pdf> (same).

³⁰⁰ See Ryan Whalen, *The Bayh-Dole Act and Public Rights in Federally Funded Inventions: Will the Agencies Ever Go Marching in?*, 109 NW. U. L. REV. 1083 (2015).

³⁰¹ See James Heyward et al., *Coverage of Nonpharmacologic Treatments for Low Back Pain Among US Public and Private Insurers*, 1 JAMA NETWORK OPEN e183044 (2018).

opioid pain treatments, but also for pharmaceutical addiction treatments such as Suboxone.³⁰²

Of course, as with government-set innovation incentives, government interventions on the allocation side raise the risk of political failures, including rent-seeking and mismanagement.³⁰³ Ideally, government interventions in the innovation ecosystem should counteract the patent system's biases. But as illustrated throughout this Article, the federal government's actual interventions in the allocation system for pain treatment likely compounded the problems that facilitated the current crisis.

C. Political Economy of Opioid Innovation Institutions

The opioid crisis dramatically illustrates deep flaws with linking biomedical innovation incentives to patent-based rewards, but it exposes inadequacies of non-patent innovation institutions as well. So far, this Article has illustrated how much purchase we can get on these problems through a law-and-economics analysis, but we are cognizant that the study of innovation institutions is about more than financial incentives. The failure of America's innovation institutions to encourage the development and dissemination of nonaddictive pain treatments arose not only from errors of institutional design but also from deficiencies of political will—deficiencies that non-patent institutions came to reflect.

To put the point in public choice terms, the diffuse individuals who bear the costs of underinvestment in nonaddictive pain management—including chronic pain patients and members of communities ravaged by opioid abuse—lacked the social and political capital to influence resource allocation that other, better organized interest groups enjoy. The opioid epidemic has had the most devastating impact in rural, poor communities with high unemployment³⁰⁴ (although, as noted, the causal connection between higher unemployment and higher rates of opioid abuse is difficult to substantiate empirically³⁰⁵). And the stigma of addiction further limited the political capital of those hardest hit.³⁰⁶ If addiction had not been a taboo subject and if the first people hit were children of congressmen rather than politically marginalized groups, there likely would have been far more political traction to address these problems early on.

³⁰² In addition to gaps in government insurance, private insurance markets have long failed to cover addiction treatments, which was the motivation for the Mental Health Parity and Addiction Equity Act of 2008, 42 U.S.C. § 300gg–26, and its extension through the Affordable Care Act, 42 U.S.C. § 18031(j).

³⁰³ See, e.g., Lev Facher, *Trump Opioid Plan Writes in Favoritism to Single Company's Addiction Medication*, STAT (Mar. 26, 2018), <https://www.statnews.com/2018/03/26/trump-opioid-plan-alkermes-vivitrol>.

³⁰⁴ See Katherine M. Keyes et al., *Understanding the Rural–Urban Differences in Nonmedical Prescription Opioid Use and Abuse in the United States*, 104 AM. J. PUB. HEALTH e52 (2014).

³⁰⁵ See *supra* note 13 and accompanying text.

³⁰⁶ See generally MACY, *supra* note 117, at 8 (explaining how retracing the epidemic across the Appalachians allowed her to “understand how prescription pill and heroin abuse was allowed to fester, moving quietly and stealthily across this country, cloaked in stigma and shame”).

Although political institutions could have done far more to forestall the present crisis, it is at least promising that drug misuse is now being viewed as a public health problem, at least in the opioid context. In October 2017, President Trump declared the opioid crisis to be a national public health emergency,³⁰⁷ and the ensuing President's Commission on Combatting Drug Addiction and the Opioid Crisis issued a comprehensive report on addiction prevention and treatment.³⁰⁸ In contrast, the rise of heroin addiction in the 1970s and crack cocaine addiction in the 1980s and 1990s were largely viewed as criminal justice problems rather than public health problems, leading to mass incarceration rather than mass medical care.³⁰⁹ The difference may reflect racial and class politics; the press has typically portrayed opioid users as sympathetic white suburbanites, compared with urban black and Latino heroin users.³¹⁰ But perhaps greater empathy for those fighting opioid addiction will help the public and policymakers view those suffering from other forms of addiction through a public health lens.³¹¹

Of course, even when opioids began to gain policymakers' attention, government interventions were often too small or were misdirected, as illustrated in Part I. Many of the most significant hurdles to effective policymaking continue to be political and cultural, such as concerns that many addicts are to blame for their own plight and thus less worthy of publicly funded assistance, that scientifically supported medication-assisted treatment is inferior to abstinence-based programs, and that treatment clinics will simply attract more heroin users

³⁰⁷ See *The Opioid Crisis*, WHITE HOUSE (last visited Mar. 14, 2019), <https://www.whitehouse.gov/opioids>.

³⁰⁸ CHRISTIE ET AL., *supra* note 10

³⁰⁹ See generally JAMES FORMAN JR., LOCKING UP OUR OWN: CRIME AND PUNISHMENT IN BLACK AMERICA 147 (2017) (arguing that crack cocaine addiction should have been labeled "a public health disaster" rather than "a criminal justice issue").

³¹⁰ See Julie Netherland & Helena B. Hansen, *The War on Drugs That Wasn't: Wasted Whiteness, "Dirty Doctors," and Race in Media Coverage of Prescription Opioid Misuse*, 40 CULTURE MED. & PSYCHIATRY 664 (2016); see also Cuéllar & Humphreys, *supra* note 161 ("Another proffered explanation is the demographics of prescription drug users: the epidemics of the 1980s and 1990s affected mainly low-income, African Americans (crack cocaine) and low-income, rural whites (methamphetamine), whereas the opioid epidemic includes a large representation of middle-class, white individuals with more political and social capital."). Racial biases may also have been responsible for shielding nonwhite communities from the brunt of the opioid crisis: nonwhite patients are less likely to be prescribed opioids for comparable reported pain, See Diana Jill Burgess et al., *Patient Race and Physicians' Decisions to Prescribe Opioids for Chronic Low Back Pain*, 67 SOC. SCI. & MED. 1852 (2008); Mark J. Pletcher et al., *Trends in Opioid Prescribing by Race/Ethnicity for Patients Seeking Care in US Emergency Departments*, 299 JAMA 70 (2008). Controlling for income level, areas with higher proportions of white residents have higher rates of opioid prescriptions and overdose deaths. See Joseph Friedman et al., *Assessment of Racial/Ethnic and Income Disparities in the Prescription of Opioids and Other Controlled Medications in California*, 179 JAMA INTERNAL MED. 469 (2019). But this is just a silver lining to broader problem of racial and ethnic disparities in health care—including, in this case, the undertreatment of pain. See generally INST. OF MED. OF THE NAT'L ACADS., UNEQUAL TREATMENT: CONFRONTING RACIAL AND ETHNIC DISPARITIES IN HEALTH CARE (2002).

³¹¹ Cf. Leigh Ann Caldwell, *How Trump Unexpectedly Garnered Bipartisan Support for Criminal Justice Reform*, NBC NEWS (Dec. 20, 2018), <https://www.nbcnews.com/politics/congress/how-trump-unexpectedly-garnered-bipartisan-support-criminal-justice-reform-n949706>.

and crime.³¹² It is not enough to recommend that policymakers fix innovation institution failures. Innovation institutions are themselves politically produced, and one reason they failed was because politicians didn't have sufficient incentives to design them otherwise.

These problems illustrate the need for research not just on the science of treating pain and addiction, but also on the science of communicating this knowledge in ways that overcome existing cultural hurdles.³¹³ Analogies to other health policy movements may prove instructive. For example, the AIDS movement is partly a story about patent law incentivizing innovations like novel antiretroviral medications, but it is also a story about changing norms and political power.³¹⁴ Innovations in cancer therapy require not just scientific advances but also the political support to fund those research efforts—compare the amazing success of the pink ribbon movement for breast cancer research³¹⁵ with the low funding rates for stigmatized lung cancer,³¹⁶ even though lung cancer is the deadliest cancer, killing more Americans than breast cancer, prostate cancer, and colon cancer combined.³¹⁷ As opioid deaths have become higher profile and overdose victims acquire the faces of friends and family members rather than statistics, there has already been progress.

In the end, the story of the opioid crisis is to a significant extent an account of failures of institutional design, but it is also a narrative in which the pathological politics of pain and addiction prevented design changes that could have helped address the problem. This may be a dispiriting diagnosis: problems of institutional design are ones that legal scholars can solve, and our analysis suggests that the roots of the opioid crisis are not so easy to snip. More optimistically, recognizing the political and cultural determinants of innovation policy failures will move us incrementally further toward ensuring that those failures are not relived. But it will no doubt be a long and hard journey.

III. Beyond Opioids: Avoiding Innovation Institution Failures

While our primary focus in this Article is on the ways in which America's innovation institutions have contributed to the opioid crisis and can hasten its

³¹² See MACY, *supra* note 120, at 216, 281, 288; NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 56, at S-8; German Lopez, *Needle Exchanges Help Combat the Opioid Crisis. So Why Was the One in Orange County Shut Down?*, VOX (May 29, 2018), <https://www.vox.com/science-and-health/2018/5/29/17389048/needle-exchange-opioid-epidemic-orange-county>.

³¹³ See generally THE OXFORD HANDBOOK OF THE SCIENCE OF SCIENCE COMMUNICATION (Kathleen Hall Jamieson, Dan Kahan & Dietram A. Scheufele eds., 2017).

³¹⁴ See generally Julia H. Smith & Alan Whiteside, *The History of AIDS Exceptionalism*, 13 J. INT'L AIDS SOC'Y 47 (2010).

³¹⁵ See Brian Alexander, *The Politics Behind the Pink Ribbon*, NBC NEWS (Oct. 22, 2008), <http://www.nbcnews.com/id/27283197/ns/health-cancer/t/politics-behind-pink-ribbon>.

³¹⁶ See Lecia V. Sequist, *Stigma Lingers for Deadliest Cancer*, CNN (Oct. 30, 2013), <https://www.cnn.com/2013/10/30/health/sequist-lung-cancer-stigma/index.html>.

³¹⁷ Rebecca L. Siegel et al., *Cancer Statistics, 2018*, 68 CA: CANCER J. CLINICIANS 7 (2018).

end, the opioid epidemic also yields lessons for innovation scholars that apply to other areas of public health and scientific knowledge.

The stories of OxyContin, Suboxone, and Evzio confirm some truths that we have long known about the IP system. IP is an effective innovation incentive for aggregating dispersed information about consumers' willingness to pay for new knowledge goods—but when markets fail, so too will IP.³¹⁸ Two familiar reasons why markets fail to produce socially optimal outcomes are (1) the externalization of harms and (2) the externalization of benefits. OxyContin is an example of a product that generates negative externalities and—unsurprisingly—we ended up with too much OxyContin. Suboxone and Evzio are examples of products that generate positive externalities, and—unsurprisingly—we have ended up with too little of these drugs.

America's apparent underinvestment in non-pharmacological pain treatments likewise fits into our existing mental models. Non-pharmacological pain treatments such as yoga and acupuncture are almost inevitably nonexcludable and ineligible for patent protection. Our innovation ecosystem is well designed to reward patentable technologies, such as pharmaceuticals, and poorly structured to support the development of processes and practices such as checklists, cognitive behavioral therapy, and alternative medicine.³¹⁹

Yet in other ways, our study of the opioid crisis has challenged our beliefs about innovation policy and led us toward new insights. In this final Part, we highlight five lessons from the opioid context for innovation policy more broadly:

First, we think that the traditional view of IP as a tradeoff between dynamic efficiency and allocative efficiency is less accurate than we once believed.³²⁰ In the case of OxyContin, patent protection appears to have encouraged Purdue Pharma's extraordinary investment in demand creation. Aggregate data on the consumption of patented and post-patent pharmaceuticals suggests that the OxyContin story is not an outlier in this regard.³²¹ Especially when a pharmaceutical manufacturer follows a relatively standard pricing strategy (such that the product is available to Medicaid and Medicare beneficiaries and is included in most private health plan formularies), above-marginal-cost pricing seems less likely to prevent the vast majority of U.S. patients from gaining access than conventional IP models suggest.

Second, and relatedly, the fact that IP encourages demand creation should affect our view of IP's overall welfare effects. Do we want to encourage patentees to create demand for products for which demand does not currently exist? There are, perhaps, cases in which the answer is yes—for example, Eli Lilly's promotion of Prozac arguably generated greater attention toward

³¹⁸ See generally Hemel & Ouellette, *supra* note 21, at 555–56.

³¹⁹ See generally Kapczynski & Syed, *supra* note 23.

³²⁰ See *supra* notes 24, 97–100 and accompanying text.

³²¹ See *supra* note 126 and accompanying text.

untreated depression.³²² But we should be aware that the patent system creates incentives for firms to promote products that consumers did not know they wanted (and indeed might not have needed).³²³

Third, the interaction between IP and addiction can be particularly pernicious. As we sought to illustrate in Section I.B.1, firms have an especially strong incentive to promote habit-forming products—perhaps by initially charging below-marginal-cost prices—if they anticipate that they can maintain a medium- to long-term monopoly over that product. When the habit-forming-nature of a product generates negative externalities, as is the case for medical addiction, the combination of this effect with the more general demand-creation incentives can have devastating social consequences. It is possible that this misalignment of IP rewards with social welfare could be addressed by reforms internal to IP. For example, Michael Risch has called for a revitalization of patent law’s utility requirement to deny patents on inventions from which society reaps no benefit (even if the innovator can reap significant profits).³²⁴ Margo Bagley has suggested legislative restrictions on patentable subject matter to revive moral utility doctrine and move away from the United States’s current (and distinctively American) “patent first, ask questions later” approach.³²⁵ As another example, Ted Sichelman suggests that patent law remedies should be reformed to better reflect the social value, not market value, of an invention.³²⁶ But non-IP innovation institutions also have an important—and perhaps paramount—role to play in correcting the IP system’s biases.³²⁷

A fourth lesson from the opioid crisis for other areas of innovation policy is that the notion that government subsidies can promote access to IP-protected products turns out to be less than clear-cut. Medicaid’s best-price mandate incentivizes pharmaceutical firms to charge *higher* prices to the private sector, and as the number of patients covered by Medicaid increases, so too does the

³²² See generally Bradley T. Shapiro, *Positive Spillovers and Free Riding in Advertising of Prescription Pharmaceuticals: The Case of Antidepressants*, 126 J. POL. ECON. 381 (2018).

³²³ See generally John Bronsteen, Christopher Buccafusco & Jonathan S. Masur, *Well-Being Analysis vs. Cost-Benefit Analysis*, 62 DUKE L.J. 1603, 1665–66 (2013) (discussing and critiquing the conventional view that consumption equates to welfare).

³²⁴ See Michael Risch, *Reinventing Usefulness*, 2010 B.Y.U. L. REV. 1195 (2010); Michael Risch, *A Surprisingly Useful Requirement*, 19 GEO. MASON L. REV. 57 (2011). Effectively addressing social problems would likely require a more dynamic utility requirement because many social downsides do not surface until long after patent filing.

³²⁵ Margo A. Bagley, *Patent First, Ask Questions Later: Morality and Biotechnology in Patent Law*, 45 WM. & MARY L. REV. 469 (2003). Bagley’s focus is social concerns with patents grounded in morality rather than negative externalities, but some hybrid of these concerns has in fact driven judicial changes in patentable subject matter. See Lisa Larrimore Ouellette, *Patentable Subject Matter and Nonpatent Innovation Incentives*, 5 UC IRVINE L. REV. 1115, 1118–25 (2015).

³²⁶ Ted Sichelman, *Purging Patent Law of “Private Law” Remedies*, 92 TEX. L. REV. 517 (2014).

³²⁷ Using validity doctrines such as utility to weed out socially harmful patents would be both administratively challenging for patent examiners and would not help with inventions that create negative externalities but have a net social benefit. And tailoring remedies may be difficult as well; for example, Mark Lemley called Sichelman’s proposal “a perfectly correct statement of aspirations, but nothing that could ever be operationalized without perfect knowledge.” Mark Lemley, *Taking the Regulatory Nature of IP Seriously*, 92 TEX. L. REV. SEE ALSO 107, 112 (2014).

incentive for firms to set private-sector prices with Medicaid in mind. This is not an argument against Medicaid expansion, and removing the best-price mandate without creating an alternative means to control government drug spending would lead to different (and perhaps worse) pathologies. But it does suggest that government subsidies should be designed with attention to their impact on private pharmaceutical pricing.

Indeed, in a world without Medicaid's best-price mandate or other limits on incentives to offer discounts to some purchasers, pharmaceutical firms might seek to maximize profits through price discrimination (i.e., seeking to ensure that every consumer who values a product at more than its marginal cost will be charged her willingness to pay and no more). Perfect price discrimination entails no deadweight loss. Medicaid changes the incentive to engage in price discrimination, however, because the lowest price charged to other purchasers becomes the ceiling for Medicaid reimbursement. The limit on charging CMS more than the "usual and customary charges to the general public" has a similar effect.³²⁸ In such cases, IP does lead to serious allocative inefficiencies, but the inefficiencies are because of the way IP interacts with other government policies. To be sure, perfect price discrimination will almost never be possible, and deadweight loss in the IP system is inevitable. But the opioid crisis illustrates that subsidies can do as much to increase deadweight loss as to reduce it.

Finally, and notwithstanding our criticisms of the IP system, we again emphasize that non-IP innovation incentives and allocation mechanisms are imperfect. In the case of the opioid epidemic, CMS created powerful non-IP incentives for hospitals to prescribe more opioids.³²⁹ That turned out to be a disaster. The root causes of this particular policy failure are unclear, but we should be cognizant in our critique of certain aspects of market-based IP policies that the grass is not always greener on the non-market side.

Conclusion

The opioid epidemic is not the first public health crisis that has exposed flaws in innovation institutions. The global AIDS crisis drew the world's eyes toward high prices for patented antiretroviral therapies (ARTs) and highlighted ways in which international IP law limited the ability of low-income countries to respond to health emergencies. The episode resulted in the World Trade Organization issuing its Doha Declaration in 2001, which in turn led to the loosening of restrictions in low- and middle-income countries on access to generic versions of lifesaving drugs.³³⁰ Around the same time as the Doha Declaration, the anthrax attacks in the United States also placed a spotlight on patent law's allocative inefficiencies and resulted in Bayer A.G., the

³²⁸ See *supra* notes 207–208 and accompanying text.

³²⁹ See *supra* notes 220–226 and accompanying text.

³³⁰ See Ellen 't Hoen et al., *Driving a Decade of Change: HIV/AIDS, Patents and Access to Medicines for All*, 14 J. INT'L AIDS SOC'Y 15 (2011); Amy Kapczynski, *The Access to Knowledge Mobilization and the New Politics of Intellectual Property*, 117 YALE L.J. 804, 828–29 (2008).

manufacturer of the anthrax medicine Cipro, cutting prices steeply.³³¹ A crisis—as Nobel laureate economist Paul Romer once said—is a terrible thing to waste,³³² and innovation policy scholars and reformers did not let these earlier crises meet that fate.

Crisis-based policymaking raises the obvious concern that lawmakers and bureaucrats will sacrifice sense for speed. Yet the opioid epidemic, like AIDS but unlike the anthrax scare, is a crisis whose timeline is marked in months and years rather than hours or days. An optimistic scenario is that the crisis's comparatively slow movement will allow for the sort of careful contemplation that crisis-based policymaking often lacks, while the crisis's magnitude will overcome the legislative inertia that often stands in the way of innovation policy change. We ourselves lack the political predictive powers to say whether institutional reform will be the ultimate outcome or whether instead legislative interest in the subject will wane.

What we can say with confidence is that close consideration of the interaction between innovation institutions and the opioid epidemic has the potential to reveal important aspects of each. This is not to say that the opioid epidemic is entirely attributable to innovation policy or that the flaws of the innovation system are all at work in the opioid crisis. It is to say, however, that one cannot fully comprehend the causes of the opioid epidemic without understanding the role that innovation institutions played in it, and one's understanding of innovation institutions will almost certainly be enhanced by attention to opioid problem. The epidemic already has wasted far too many lives and laid waste to communities across the country. Hopefully the opportunities for reflection and reform that can come from the crisis will not be squandered as well.

³³¹ See Brennan et al., *supra* note 299, at 303 (describing the government's threat of importing generic versions of the drug under 28 U.S.C. § 1498, which led to Bayer's price reduction); Keith Bradsher with Edmund L Andrews, *U.S. Says Bayer Will Cut Cost of Its Anthrax Drug*, N.Y. TIMES (Oct. 24, 2001), <https://www.nytimes.com/2001/10/24/business/a-nation-challenged-cipro-us-says-bayer-will-cut-cost-of-its-anthrax-drug.html>.

³³² See Jack Rosenthal, *On Language: A Terrible Thing to Waste*, N.Y. TIMES MAG. (June 31, 2009), <https://www.nytimes.com/2009/08/02/magazine/02FOB-onlanguage-t.html>.