Innovation Institutions and the Opioid Crisis

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The United States has recently—and belatedly—come to recognize opioid addiction as a public health crisis. What has gone mostly unrecognized is the role that U.S. innovation institutions played in bringing this crisis about. Innovation institutions—including but not limited to intellectual property law—encouraged the development and commercialization of addictive painkillers, restricted access to opioid antidotes, and 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 policy is deeply implicated in the ongoing epidemic to a degree that so far has been underappreciated.

This Article examines the role that innovation policy played in the proliferation of opioid use and abuse, 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 patent law as a tradeoff between allocative efficiency and dynamic efficiency; it highlights the potentially pernicious role of patent protection for addictive and habit-forming products; and it exposes deep flaws in the structure of federal subsidies for 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.

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Introduction

Opioid overdoses killed more than 47,000 people in the United States in 2017.[3] 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] Or framed differently: The number of Americans who die from opioid overdoses every two months is greater than the number of U.S. servicemembers who have died in the Middle East and Afghanistan since 2001.[6] The economic costs are staggering, likely topping $500 billion annually.[7] Without a doubt, the opioid epidemic is among the primary policy challenges facing the United States today.

The causes of America's opioid crisis are multifactorial, and the effort to contain the epidemic's spread will require interventions that cut across multiple policy domains, including complex litigation.[8] Here, we highlight one factor that has been largely overlooked: failures of American innovation institutions—the legal arrangements that structure incentives for the production and allocation of knowledge goods.[9] First, U.S. innovation institutions produced powerful incentives for pharmaceutical firms to invest in the development and commercialization of highly addictive prescription pain medicines. Second and simultaneously, the innovation ecosystem allowed 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. Third, even while encouraging the rapid diffusion of addictive opioids,

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[3] *See* Lenny Bernstein, *U.S. Life Expectancy Declines Again, a Dismal Trend Not Seen Since World War I*, WASH. POST (Nov. 29, 2018), https://wapo.st/2raYn6P. 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.

[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).

[6] *Cf. Casualty Status*, U.S. DEP'T OF DEF., https://dod.defense.gov/News/Casualty-Status (last updated Mar. 11, 2019) (reporting military casualties).

[7] 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.

[8] 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).

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

innovation institutions failed to sufficiently reward firms for formulating, refining, or popularizing alternative treatments for addiction or for the underlying problem of chronic pain.

All three of these problems can be traced—at least in significant part—to distortions generated by intellectual property (IP) law, including patents, trade secrets, trademarks, and FDA-administered regulatory exclusivity. Some of these distortions are relatively familiar. IP is a market-based innovation institution, and markets will not yield efficient 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 toward patentable technologies like pharmaceuticals,[10] 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 has challenged our understanding of the IP system. Most significantly, this study has caused us to question the conventional view that the fundamental tradeoff in IP policy is between innovation and access, or what economists call dynamic efficiency and allocative efficiency.[11] Patents do create an incentive to raise prices and restrict quantity, which can lead to decreased consumption (the source of allocative inefficiency), but they also have countervailing consumption-expanding effects. For example, patents induce investments in efforts to create demand for products that consumers did not previously believe they wanted.[12] The demand-creation incentive is especially pronounced when the patented product is habit-forming—in which case patent protection may cause patent holders to lower prices for their products in the short term in order to raise consumption in the long term.[13] These effects are important for understanding the welfare impact of the patent system: Although scholars typically view increased use of patented technologies as a welfare gain, the example of prescription opioids makes clear 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

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

[11] *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.").

[12] *See infra* Section I.B.1.

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

example, market-based prizes in the form of insurance reimbursement policies appear to be a particularly promising intervention.[14] 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. [15] Additionally, and paradoxically, the federal government's subsidies for opioid antidotes appear to have *reduced* access to these life-saving products, challenging the view that demand-side subsidies are a solution to patents' downsides.[16]

The proliferation of prescription opioids rather than alternative pain treatments—attributable in part to U.S. patent law and other innovation institutions—fueled the epidemic that now engulfs America. Use of these drugs surged throughout the 2000s,[17] such that by 2015, more than one-third of U.S. adults used prescription opioids,[18] which not only put those individuals at risk of addiction but also unleashed a flood of pills that could be used and abused by family members and friends.[19] Prescription opioids were involved in thirty-six percent of opioid overdose deaths in 2017,[20] and they also fed into the spread of other opioids—including heroin, the use of which increased almost five-fold in a decade.[21] While the share of the U.S. population that uses heroin remains small (less than two percent of all adults at last count),[22] roughly four in five heroin users began by abusing prescription opioids.[23] The laws and policies that led to the presence of prescription opioids in tens of millions of household medicine

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[14] *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).

[15] *See infra* Section I.B.3.

[16] *See infra* Section I.C.

[17] *See* Mark R. Jones et al., *A Brief History of the Opioid Epidemic and Strategies for Pain Medicine*, 7 PAIN & THERAPY 13, 16 (2018).

[18] *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).

[19] 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.

[20] *Opioid Overdose: Data Overview*, CTRS. FOR DISEASE CONTROL & PREVENTION (updated Dec. 19, 2018), https://www.cdc.gov/drugoverdose/data/index.html.

[21] *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).

[22] *Id.*

[23] *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. The eighty percent figure refers to "nonmedical" use of prescription opioids—i.e., "use of drugs that were not prescribed for the respondent or used only for the experience of feeling they caused." *Id.*

cabinets contributed significantly to the sharp rise in illicit opioid use and related deaths.[24]

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 IP-generated incentives 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. [25] 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. [26] At the same time, wider access to existing non-pharmacological pain treatments such as acupuncture, physical therapy and exercise, meditation, and cognitive behavioral therapy may do as much to mitigate the overuse of prescription opioids as any pharmacological leap. [27] Moreover, any comprehensive national strategy to contain the opioid epidemic also will require interventions aimed at individuals already in the throes of addiction.[28] 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.[29]

This Article is an attempt to understand how innovation institutions helped bring about 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 illustrates how innovation institutions contributed to rising rates of opioid use, abuse, and overdose. Part II draws on insights from the study of innovation policy and comparative institutional analysis to evaluate potential responses to the opioid epidemic through innovation institutions. For example,

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[24] In recent years, the synthetic opioid fentanyl has overtaken heroin on the illegal drug market; by 2015, fentanyl and 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.

[25] *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.

[26] *See, e.g.*, *infra* notes 51-53 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).

[27] *See infra* note 163 and accompanying text (describing a call from the National Academies for more research in these areas).

[28] *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).

[29] *See infra* Section II.A.2.

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 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 addiction, and (3) the limited availability of non-pharmacological treatments or studies on new uses of nonaddictive existing drugs for either chronic pain or addiction. This Part highlights the role of America's innovation institutions in fueling these phenomena, while also recognizing the complexity of this history and the influence of other actors and structures.

A. A Tale of Two Drugs

In December 1995, the U.S. Food and Drug Administration (FDA) approved Purdue Pharma's application to market OxyContin, a controlled-release form of an opioid called oxycodone, for treatment of chronic pain.[30] The 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.[31] The number of OxyContin prescriptions dispensed nationwide each year reached six million that year, bringing in over $1 billion in sales.[32] By 2018, Purdue Pharma's all-time total OxyContin revenue topped $35 billion.[33]

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[30] *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).

[31] *See OxyContin Diversion and Abuse*, NAT'L DRUG INTELLIGENCE CTR. (Jan. 2001), https://www.justice.gov/archive/ndic/pubs/651/abuse.htm.

[32] *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); Art Van Zee, *The Promotion and Marketing of OxyContin: Commercial Triumph, Public Health Tragedy*, 99 AM. J. PUB. HEALTH 221, 221 (2009).

[33] *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).

The trajectory of the first naloxone auto-injector, Evzio, was starkly different. Naloxone is an antidote that blocks the effects of opioids and thus can prevent death in the event of overdose. Evzio—a hand-held device that delivers naloxone in much the same way that an EpiPen delivers adrenaline to halt an allergic reaction—debuted in 2014 at a list price of $575 for a two-dose prescription.[34] Evzio's manufacturer, the pharmaceutical company Kaléo, subsequently hiked the price per prescription to $750 in 2015, $3750 in 2016, and $4100 in 2017.[35] For comparison, the manufacturing cost for an Evzio unit is $52.[36] Fewer than 70,000 Evzio prescriptions were filled in the twelve months ending in January 2017.[37]

The tale of these two drugs reflects some familiar aspects of the patent system. Patents rely on markets, and so market failures are likely to result in failures of the patent system 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 cabinets), and Evzio produces positive externalities (including the externality to individuals other than the prescription holder who may nonetheless be saved from overdose by a naloxone injection). Markets tend to spawn socially supraoptimal quantities of products that yield negative externalities and suboptimal quantities of products that create positive externalities, so it is in some ways unsurprising that America ended up with too much OxyContin and not enough Evzio. But as the following sections explain, we think the full story is more nuanced and more interesting—and contains some broader lessons that complicate the conventional understanding of patent law's tradeoffs between dynamic and allocative efficiency.

Of course, these two drugs capture only part of the story of the American opioid epidemic, and it would be an oversimplification to say that the story of the opioid epidemic is one of too much oxycodone and not enough naloxone. For one thing, as we discuss in more detail below, oxycodone is just one of many opioids contributing to the overdose epidemic.[38] For another, treating patients in the middle of an overdose is only one intervention to reduce the costs of opioid addiction; for example, using medication-assisted treatment to limit further

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[34] *See* STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, COMM. ON HOMELAND SEC. & GOV'TL AFFAIRS, 115TH CONG., COMBATTING 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.

[35] *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.

[36] STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, at 37. The "unit cost" is $174, including $29 in overhead and $93 in "obsolescence." *Id.*

[37] *Id.* at 5.

[38] *See infra* Section I.B.4.

abuse is another evidence-supported intervention.[39] Medication-assisted treatment is subject to its own innovation institution failures, such as the abuses of the patent and drug regulation systems represented by the best-selling opioid addiction treatment Suboxone, which we discuss in Section II.A.1.[40]

But we think that examining the histories of OxyContin and Evzio—and connecting these narratives to more systematic studies in the health economics literature—captures an important aspect of why America became awash in prescription opioids but not in the drugs needed to reverse overdose and addiction. The next two sections present these two tales: Section I.B describes how U.S. patent and prescription drug policy helped to contribute to an environment in which Purdue Pharma had strong incentives to aggressively market OxyContin. Section I.C then explores the innovation institutions that generated such strong incentives for Kaléo to hike the price of Evzio.

In Section I.D, we then 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, and the Evzio injector is not the only way to a halt an opioid overdose. Yet American innovation institutions failed to promote the development and commercialization of alternative treatments involving existing drugs or non-pharmacological interventions. This is—if not quite by design—nonetheless a byproduct of the design of innovation institutions, which promote technologies that are amenable to patenting but provide insufficient incentives for technologies that are not. And while non-patent policies potentially can offset some of the patent system's biases, the U.S. federal government's non-patent interventions have often done the opposite—exacerbating rather than mitigating the failures of patent-centric innovation institutions.

B. The $35 Billion Question: How Did OxyContin Become So Prevalent?

At first glance, the claim that patent law contributed to the proliferation of OxyContin might seem puzzling. OxyContin is protected by numerous patents, with expiration dates as late as 2030,[41] so it has faced relatively little competition from generic varieties of controlled-release oxycodone.[42] The

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[39] *See* NAT'L ACADS. OF SCIS., ENG'G, & MED., MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES, at S-1 (2019); *Information About Medication-Assisted Treatment (MAT)*, FOOD & DRUG ADMIN., https://www.fda.gov/Drugs/DrugSafety/InformationbyDrugClass/ucm600092.htm (last updated Oct. 3, 2018).

[40] *See infra* notes 190–201 and accompanying text.

[41] *See 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 Jan. 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).

[42] There were some sales of generic controlled-release oxycodone from 2005 to 2010 before patent settlements with Purdue, but they had a relatively small market share compared with OxyContin. *See infra* notes 65–66 and accompanying text.

conventional view of patent law posits that patent monopolies lead to higher prices and lower quantities of patented products.[43] 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. [44] Generally, this reduction in quantity is considered to be a downside of patent protection,[45] 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"[46]: 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?

As explained in the remainder of this Section, we think at least three factors are likely to have played some role in OxyContin's proliferation: (1) the incentive IP provides to invest in demand creation, (2) the addictive nature of the drug, and (3) demand-side subsidies. To be clear, none of these access-expanding effects are inherently problematic. Because the patent owner should not be able to charge any individual more than he or she values the patented product, the patent reward should still be less than the social value of the invention.[47] But in practice, there are a number of reasons that patent rents can exceed social value, including negative externalities and internalities, [48]

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

[44] *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").

[45] *See* Sampat & Williams, *supra* note 11; Shavell & van Ypersele, *supra* note 43, at 529 ("[T]here is a deadweight loss in social welfare because too little is sold at the monopoly price.").

[46] 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 Horizonal Price-Fixing*, 81 CALIF. L. REV. 243 (1993).

[47] *See* Shavell & van Ypersele, *supra* note 43, at 534.

[48] When consumption of a good creates negative externalities—costs not borne by the consumer—patent law's market-set incentive can provide a payoff greater than the social value of a good. *See* Hemel & Ouellette, *supra* note 9, at 555–56. Similarly, negative internalities—costs to the consumer's own well-being that aren't considered when choosing to consume a good—can cause market rewards to exceed social welfare. *See* Brian Galle, *The Problem of Intra-Personal Cost*, 18 YALE J. HEALTH POL'Y L. & ETHICS 1 (2018). Note that when the negative externalities of overuse harm the future value of the good itself, as in the case of antibiotic resistance, overuse

misinformation, and misaligned government interventions—all of which are present in the case of OxyContin.[49]

1. Demand Creation

Patents create a particularly strong incentive to invest in demand creation in ways that can counteract their access-limiting effect. In order to induce physicians to prescribe—and patients to take—controlled-release oxycodone, Purdue Pharma sought to persuade physicians and patients of two propositions: (1) that oxycodone is a more effective treatment for chronic pain than existing analgesics; and (2) that the addiction risks associated with oxycodone—especially in its controlled-release formulation—are tolerable in light of the benefits it brings.[50] Evidence for both propositions 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.[51] (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. [52] Indeed, the non-opioid

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might be managed more effectively by a single owner who has an incentive to maintain that future value. *See* Hemel & Ouellette, *supra* note 9, at 571–73. But the link between the negative externality of addiction and the future profitability of opioids is far more attenuated.

[49] *See infra* notes 55–59, 74–77, 89–91 and accompanying text.

[50] On Purdue's early marketing efforts, see generally *Purdue and the OxyContin Files*, KAISER HEALTH NEWS (June 13, 2018), https://khn.org/news/purdue-and-the-oxycontin-files.

[51] 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 50 (noting on pages 21–22 of Purdue's 1996 OxyContin budget plan that OxyContin had "[a]ll the analgesic efficacy of immediate-release oxycodone" with "[a]ll the ease of [12-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.

[52] 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).

treatment group fared significantly better on a self-reported pain scale.[53] But of course, Purdue and other opioid manufacturers had little incentive to develop or disclose this kind of negative information about their products.[54] Instead, Purdue promoted OxyContin as a way for patients to "gain control of [their] pain" after over-the-counter analgesics had failed.[55]

The second component of Purdue's demand-creation strategy entailed convincing 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."[56] 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."[57] 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.[58] But even then, Purdue argued that the warning was "more of an exercise in graphic design" and that the real victims were "legitimate patients" who would lose access to pain relief if OxyContin were restricted.[59] OxyContin sales continued to climb.[60]

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[53] *Id.* at 877 tbl.2. Dosages in the Krebs et al. study were significantly higher than in Chang et al., *supra* note 51. The highest dosage of oxycodone was 100 morphine-equivalent milligrams per day, or 67 milligrams of oxycodone. *See* Krebs et al., *supra* note 52, 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).

[54] *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 10, at 1923–27 (describing the lack of incentive to produce negative information about pharmaceuticals).

[55] *See Purdue and the OxyContin Files*, *supra* note 50.

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

[57] *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 32, at 223 (explaining how Purdue misrepresented the risk of addiction for OxyContin).

[58] *See* BETH MACY, DOPESICK 50–51 (2018); *Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, *supra* note 30.

[59] MACY, *supra* note 58, at 51 (quoting a Purdue spokesman).

[60] *See* 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 (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

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.[61] It distributed more than 14,000 videos claiming that less than one percent of patients who took opioids would become addicted.[62] In 2001 alone, Purdue's marketing expenses came to approximately $200 million, including $40 million in incentive bonuses for sales representatives.[63] This kind of direct-to-physician marketing of prescription opioids has been linked to increased prescription rates and opioid-related overdoses.[64]

In the absence of patent protection, would Purdue Pharma have had as strong an incentive to invest in creating demand for controlled-release oxycodone? Almost certainly 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. Thanks to its patent rights, Purdue Pharma controlled the entire controlled-release oxycodone market until 2005.[65] 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.[66] In 2010, Purdue also engaged in "product hopping"[67] by replacing its original OxyContin formulation with a new "abuse-deterrent" formulation, which is

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Pharma in 2003 for misleading advertisements. *See Timeline of Selected FDA Activities and Significant Events Addressing Opioid Misuse and Abuse*, *supra* note 30.

[61] Van Zee, *supra* note 32, at 221; *see also* MACY, *supra* note 58, ch. 2 (detailing OxyContin marketing activities).

[62] 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.

[63] Van Zee, *supra* note 32, at 221–22.

[64] 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.

[65] *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 PHARMACOEPIDEMIOLOGY & 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).

[66] *See* Hwang et al., *supra* note 65, at 199 fig.1.

[67] *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).

protected until 2030 by later-expiring patents.[68] (The new crush-resistant formulation seems to have been only moderately effective at deterring abuse.[69]) 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.[70] Once a generic version of the drug became available in 2017, Pfizer's spending on Viagra ads sharply plummeted.[71] 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.[72]

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

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[68] *See* Hwang et al., *supra* note 65, at 200 tbl.1; *supra* note 41 and accompanying text.

[69] *See* Hwang et al., *supra* note 65, at 200–01.

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

[71] *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.

[72] *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 68 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.

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.[73]

With the benefit of hindsight, it seems safe to conclude that the demand creation that was incentivized by patents on OxyContin falls in the "socially harmful" category. As discussed above, prescription opioids like OxyContin present both the externality of addiction risk to others who might obtain the pills, and the internality of significant addiction risk to oneself.[74] The resulting addiction carries significant social costs, including the costs of health care, criminal justice, and lost productivity. When accounting for all opioids, the annual price tag of these costs is likely over $500 billion.[75] And these costs have only partially been borne by consumers and patent owners.

The tort system is now playing an important role in forcing Purdue and other opioid manufacturers to internalize some of these costs. Purdue pled guilty to felony misbranding in 2007,[76] and while its monetary sanctions so far are only a fraction of the $35 billion in revenue it has earned from OxyContin since the mid-1990s,[77] the legal challenges are far from over and the firm is contemplating filing for bankruptcy to manage its potential liabilities.[78] Most recently, Purdue agreed to pay $270 million to settle claims brought by the state of Oklahoma, which may benchmark the value of the lawsuits it faces in other states.[79]

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[73] 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).

[74] *See supra* notes 18–23 and accompanying text.

[75] *See supra* note 7 and accompanying text.

[76] *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-oxycontin.html

[77] So far, Purdue has faced $630 million in fines and community service for three executives. *See id.*

[78] *See* Mike Spector et al., *Exclusive: OxyContin Maker Purdue Pharma Exploring Bankruptcy*, REUTERS (Mar. 4, 2019), https://www.reuters.com/article/uk-purduepharma-bankruptcy-exclusive/exclusive-oxycontin-maker-purdue-pharma-exploring-bankruptcy-sources-idUSKCN1QL1KP.

[79] *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.

2. Addiction

In addition to creating negative externalities and internalities, the habit-forming nature of OxyContin provides a second explanation for its proliferation. The likelihood 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.[80] 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 can become physically dependent upon it (as in the case of medical addiction or drugs that merely require long-term use) or if physicians can become habituated into prescribing it.[81] 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.[82] 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'

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[80] 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).

[81] *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.").

[82] 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).

behaviors at later points in time.[83] If 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 conforms 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-milligram tablet increased by more than eighty percent.[84] When Purdue's patent exclusivity with respect to OxyContin nears its end, we can expect the price to rise further still. As the end date approaches, Purdue's price calculus changes: The benefit of creating more future consumers (or prescribers) becomes smaller, as those consumers will be able to purchase the product from competitors. The incentive to extract greater profits in the short term comes to dominate.

3. Subsidies

A third element of the story of OxyContin's spread involves demand-side government subsidies.[85] 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.[86] The formula for benefits is complex, but in 2019, Medicare Part D covers seventy-five percent of brand-name costs up to an initial limit of $3,820, after a $415 deductible.[87] Medicaid is a joint federal-state program that provides health care coverage for low-income individuals.

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

[84] *See OxyContin Diversion and Abuse*, *supra* note 31; 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).

[85] *See* Sachs, *supra* note 14.

[86] *See* STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, 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.

[87] *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.

Medicaid beneficiaries receive full coverage for prescription drugs, with some states requiring a small co-pay.[88]

Within these limits, Medicare and Medicaid have generally reimbursed the costs of prescription opioids. Indeed, in 2016, opioids were provided to one-third of Medicare Part D beneficiaries (14.4 million individuals).[89] The nearly 80 million opioid prescriptions cost taxpayers $4.1 billion.[90] From 2011 to 2016, Medicaid reimbursed an average of 30 million opioid prescriptions per year.[91]

Generally, we would expect demand-side subsidies for a product to 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.[92] Subsequent 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.[93]

While Medicare Part D appears to have contributed to the proliferation of prescription opioids, there is not evidence that this was the case for Medicaid. Rather, Medicaid-focused studies have found no statistically significant relationship between Medicaid expansion and opioid use.[94] The contrast

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

[89] 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.

[90] *Id.*

[91] *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).

[92] 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 Ouellette & Rachel E. Sachs, The Medicare Innovation Subsidy (unpublished manuscript) (Apr. 23, 2019) (arguing that access-focused proposals such as "Medicare for All" should recognize how demand-side subsidies are connected to innovation incentives).

[93] *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).

[94] *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

between Medicare Part D and Medicaid presents a puzzle with at least two potential answers.[95]

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.[96] 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.[97] 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 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.[98]

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. Epidemiological studies have found that opioid use decreases as income increases,[99] so it seems plausible that any effect of increased access to opioids was counteracted by the greater social safety net of access to Medicaid.

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).

[95] 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.

[96] *See* Ramsey Baghdadi, *Medicaid Best Price*, HEALTH AFFAIRS (Aug. 10, 2017), https://www.healthaffairs.org/do/10.1377/hpb20171008.000173/full. For an overview of Medicaid pricing, see Sachs, *supra* note 14, at 182, 196.

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

[98] *See* Baicker et al., *supra* note 94.

[99] *See Addressing the Opioid Crisis means Confronting Socioeconomic Disparities*, NAT'L INSTITUTE ON DRUG ABUSE (Oct. 25, 2017), https://www.drugabuse.gov/about-nida/noras-blog/2017/10/addressing-opioid-crisis-means-confronting-socioeconomic-disparities; *see also* Joseph Friedman et al., *Assessment of Racial/Ethnic and Income Disparities in the Prescription of Opioids and Other Controlled Medications in California*, JAMA INTERNAL MED. (forthcoming 2019) (advance online publication at E2), https://doi.org/10.1001/jamainternmed.2018.6721 ("[A]cross the racial/ethnic spectrum, higher overdose rates are observed in lower-income communities."); Hanna Grol-Prokopczyk, *Use and Opinions of Prescription Opioids Among Older American Adults:*

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. 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.

4. A Note on OxyContin's Role

While many accounts of the opioid crisis (including ours) emphasize Purdue Pharma's role in aggressively and misleadingly marketing OxyContin,[100] OxyContin is just one of several prescription opioids contributing to America's overdose epidemic. To be sure, OxyContin was for a time the "drug of choice among abusers,"[101] and it still appears to be the most abused *single-entity* prescription painkiller.[102] Moreover, there is some evidence to suggest that oxycodone is more prone to abuse than other common opioids.[103] But Purdue is not the only opioid producer that has pushed doctors to increase prescription rates in ways that crossed legal and ethical boundaries.[104] Oxycodone,

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Sociodemographic Predictors, J. GERONTOLOGY: SOC. SCI. (forthcoming) (manuscript at 2), https://doi.org/10.1093/geronb/gby093 (finding in a study of older adults, that "[l]ow wealth was a strong, consistent predictor of opioid use); *see generally* Anne Case & Angus Deaton, *Mortality and Morbidity in the 21st Century*, BROOKINGS PAPERS ON ECON. ACTIVITY, Spring 2017, at 397, 398 (highlighting the role of low income in the rise of "deaths of despair" such as drug overdoses).

[100] *See, e.g.*, MACY, *supra* note 58; Van Zee, *supra* note 32, Purdue likely came under particularly critical scrutiny because OxyContin was essentially its only product, and it engaged in promotion and marketing on a greater scale than the pharmaceutical industry had previously seen. *See* Van Zee, *supra* note 32, at 225.

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

[102] *See* SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., *supra* note 19, at 170525 tbl. 1.97A.

[103] *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 19, 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 . . . .").

[104] *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).

moreover, is not the only opioid subject to widespread abuse—indeed, the number of people reporting misuse of hydrocodone is now higher.[105]

The availability of other prescription opioids may have placed constraints on Purdue's ability to ratchet up the price of OxyContin. At the same time, the accessibility of imperfect substitutes may have deterred Purdue from investing even more in demand creation, as the company may have believed that some of the profits generated by its marketing efforts would be captured by manufacturers of competing prescription opioid products. What seems clear enough is that Purdue's patent-conferred market power over controlled-release oxycodone encouraged the company to invest in demand creation—an incentive that oxycodone's addictive qualities arguably augmented. Our emphasis on Purdue should not, however, be misinterpreted as a monocausal explanation for what is in fact an epidemic with multiple and converging root causes.

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

The innovation ecosystem that fostered the proliferation of OxyContin did not lead to a similar growth in opioid antidotes and medically assisted treatment for addiction. Much of the difference is due to politics, as we will discuss in Section II.C. Here, we consider the story of just one product that could reduce the opioid overdose death toll: Evzio, a naloxone auto-injector.

Naloxone is a drug that binds to opioid receptors to block the effects of other opioids, and it was first approved by the FDA in 1971 to reverse opioid overdose.[106] It is widely used for this purpose by medical professionals, but it has been difficult for lay people to use effectively.[107] To address this problem, the pharmaceutical company Kaléo developed an naloxone auto-injector, which was approved by the FDA in 2014.[108] Evzio's delivery mechanism resembles the much more familiar epinephrine auto-injector EpiPen, and the product has been described as "an EpiPen for naloxone."[109] 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—gives Evzio a significant ease-of-use advantage over other naloxone delivery mechanisms.[110]

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[105] *See* SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., *supra* note 19, at 170525 tbl. 1.97A.

[106] *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).

[107] *See id.* at 22.

[108] *See id.*

[109] *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).

[110] *See, e.g.*, Merlin et al., *supra* note 106.

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.[111] The direct costs of these trials are typically tens or hundreds of millions of dollars.[112] 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 adequately deliver naloxone to a dummy using the auto-injector without training or reading the guide.[113] Kaléo claims that it "has invested more than $100 million in the research, development and commercialization" of Evzio,[114] 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.[115]

Yet in spite of—or more likely, *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 twenty-six patents, expiring as late as 2034.[116] We say that this lengthy period of exclusivity is related to 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

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[111] *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).

[112] *See id.* (finding a median estimated direct cost of $19 million).

[113] *See* Merlin et al., *supra* note 106. 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).

[114] 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.

[115] *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).

[116] *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 Feb. 1, 2019). Note that the 2014 Evzio has been discontinued and replaced with a higher strength version in 2016—another example of product hopping. *See supra* note 67 and accompanying text. 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 Feb. 1, 2019).

to consumers.[117] 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.[118] 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.[119]

1. Allocative Inefficiencies

Even if extended patent exclusivity was not needed to incentivize R&D on Evzio, this seems like a case in which the perceived downside of IP in terms of restricting access would not be as much of a downside as conventional models would suggest.[120] Given Evzio's likely positive externalities,[121] the demand-expanding factors described in Section I.B would have a positive social welfare effect. But on first glance, Evzio seems to reflect a more traditional tale of patents leading to high prices and restricted quantities.[122] As noted above, Kaléo increased Evzio's price per two-dose prescription from $575 in 2014 to $4100 in 2017—a more than 600% increase, with a final price nearly eighty times the then $52 unit manufacturing cost.[123] These high prices have generated complaints from a number of potential purchasers, including state and local governments.[124]

The contrast between Evzio's trajectory and OxyContin's is stark and, at first glance, puzzling. Both products enjoy long-lasting patent protection, and

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

[118] *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 creates a distortion in R&D).

[119] 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).

[120] Of course, patents that are unnecessary for incentivizing an innovation still create a downside in terms of an unnecessary transfer—the point is just that this transfer is not always accompanied by quantity restrictions.

[121] There has been some speculation that naloxone might increase crime and high-risk drug use, but we share the skepticism that this argument has met. *See* Richard G. Frank, Keith Humphreys & Harold A. Pollack, *Does Naloxone Availability Increase Opioid Abuse? The Case for Skepticism*, HEALTH AFFAIRS (Mar. 19, 2018), https://www.healthaffairs.org/do/10.1377/hblog20180316.599095/full.

[122] *See supra* note 43 and accompanying text.

[123] *See supra* notes 34–36 and accompanying text.

[124] *See* CHRISTIE ET AL., *supra* note 7, 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.

the three factors behind OxyContin's proliferation described in Section I.B—(1) IP-driven demand creation, (2) habit formation, and (3) subsidies—are present to at least some degree for Evzio.

First, Kaléo's marketing-related expenditures are not as extravagant as Purdue's, but Kaléo still seems to be pouring all its revenues and then some into expanding sales.[125] ProPublica reports that from 2013, Kaléo spent $888,000 on Evzio-related payments to physicians and $1.3 million on naloxone-related lobbying,[126] compared with OxyContin-related payments of $3.86 million to physicians and over $15 million on lobbying.[127] These payments seem like a substantial effort at demand creation, especially considering that Evzio debuted nearly two decades after OxyContin.

Second, even if Evzio does 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. 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, "[b]ut those who've accepted free Evzio devices and have come to rely on it may soon face withdrawal" and be forced to pay higher prices.[128] And physicians may become routinized into prescribing Evzio as instructed by Kaléo's substantial sales force. These forms of "addiction" may help explain Kaléo's decision to distribute a certain number of free devices and then to increase Evzio's price over time.

Third, 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.[129] 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

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[125] *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.

[126] *See Dollars for Docs: Evzio*, PROPUBLICA, https://projects.propublica.org/docdollars/products/drug-evzio (last visited Mar. 3, 2019); *Lobbying Arrangements Results for 'Kaleo,'* PROPUBLICA, https://projects.propublica.org/represent/lobbying/search?search=kaleo (last visited Mar. 3, 2019).

[127] *See Dollars for Docs: OxyContin*, PROPUBLICA, https://projects.propublica.org/docdollars/products/drug-oxycontin (last visited Mar. 3, 2019); *Lobbying Arrangements Results for 'Purdue,'* PROPUBLICA, https://projects.propublica.org/represent/lobbying/search?search=purdue (last visited Mar. 3, 2019).

[128] 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.

[129] STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, at 74–84.

government plans.[130] 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.[131]

Given these similarities, one might expect Kaléo to have followed a similar distribution strategy to the one Purdue followed for OxyContin. The Evzio pricing story, however, is far more complicated.

2. Price Discrimination and Demand-Side Subsidies

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 packet.[132] Another firm advised Kaléo to price its packets in the $300 to $350 range.[133] A third recommended a target price per packet of $575, which is where Evzio started out in 2014.[134]

Two Chicago-based consultants, Todd Smith and Benjamin Bove, were hired in 2015 and offered up a very different strategy, which Kaléo ultimately adopted.[135] Under the distribution model urged by Smith and Bove, Kaléo promised to cover the copays of patients who received Evzio.[136] These patients would receive Evzio in the mail, bypassing the traditional pharmacy channel.[137] 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.[138] The strategy was described to *60 Minutes* journalists by former Kaléo employees as "a legal shell game to bilk insurance companies."[139]

Kaléo's shell game hit a number of roadblocks. Two of the three major U.S. pharmacy benefit managers (PBMs),[140] Express Scripts and CVS, removed Evzio from their drug menus in 2016 and replaced it with the naloxone nasal spray Narcan,[141] which is generally considered to be less user-friendly than

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[130] *Id.* at 4.

[131] *Id.* at 5.

[132] *Id.* at 38.

[133] *Id.*

[134] *Id.* at 39–41.

[135] *Id.* at 47.

[136] *Id.* at 54–55.

[137] *Id.* at 55.

[138] *Id.* at 54–55.

[139] *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.

[140] 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.

[141] STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, at 66–70.

Evzio.[142] Kaléo responded by terminating rebate agreements with the PBMs and with CMS, allowing it to earn a higher profit per device.[143] 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.[144] Meanwhile, state and local governments—which were not the beneficiaries of Kaléo's zero-copay pledge—struggled to afford the $4100 drug.[145] Ultimately—though only after significant pressure from a Senate investigation and critical news articles[146]—Kaléo began offering Evzio to first responders for $180 in April 2018,[147] and in December 2018, Kaléo announced that a subsidiary will sell an authorized generic version for $178.[148]

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.[149] 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.[150] Specifically, Medicaid receives a minimum rebate of 23.1 percent off the Average Manufacturer Price (AMP),

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[142] *See 60 Minutes: Evzio: The Overdose-Reversal Drug with a $4000+ Price Tag*, *supra* note 139 (showing reporter Lesley Stahl struggling to administer Narcan but exclaiming that Evzio is "[r]eally easy").

[143] STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, at 67, 79.

[144] *Id.* at 74.

[145] *See supra* note 124 and accompanying text.

[146] *See* STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34; *see, e.g.*, *60 Minutes: Evzio: The Overdose-Reversal Drug with a $4000+ Price Tag*, *supra* note 139; Luthra, *supra* note 35; 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.

[147] *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.

[148] *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.

[149] *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").

[150] *See* Baghdadi, *supra* note 96.

and if any private purchaser (or some public purchasers, including local governments) receives more than this discount, Medicaid receives that "best price."[151] This mandate made it unattractive for Kaléo to negotiate discounts with individual PBMs.[152] And even after Kaléo ended its rebate agreements, it could (and did) receive Medicaid and Medicare Part D payments when doctors certified Evzio as "medically necessary,"[153] but these payments could not be higher than "usual and customary charges to the general public,"[154] again limiting incentives to negotiate individual discounts.[155]

Under typical accounts of the patent system—including our own—demand-side subsidies like Medicaid are viewed as a *solution* to allocative inefficiencies.[156] 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.[157]

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[151] *Id.*

[152] *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.").

[153] *See* STAFF OF S. PERMANENT SUBCOMM. ON INVESTIGATIONS, *supra* note 34, 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").

[154] 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).

[155] 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 that 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.").

[156] *See* Hemel & Ouellette, *supra* note 9, 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).

[157] 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.

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.

D. Where Were the Alternative Pain and Addiction Treatments?

The previous two Sections illustrated the history of the opioid crisis through a tale of two drugs. But why is it a tale of two *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 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.[158] 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.[159]

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.[160] Negative information—including to correct misinformation about existing drugs—is also difficult to patent or commodify.[161] Recent randomized controlled trials have suggested that certain non-opioids may be as effective as opioids at treating both acute and chronic pain.[162] 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

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[158] *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).

[159] Kapczynski & Syed, *supra* note 10.

[160] *See* Benjamin N. Roin, Solving the Problem of New Uses (Oct. 1, 2013) (unpublished manuscript), https://ssrn.com/abstract=2337821.

[161] *See* Sean B. Seymore, *The Null Patent*, 53 WM. & MARY L. REV. 2041 (2012); *supra* note 54 and accompanying text.

[162] *See supra* notes 51–53 and accompanying text.

significant 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. A 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 therapy, and mindfulness meditation.[163] But even if firms could overcome the legal hurdles to patenting improvements to these methods of pain management,[164] it would be difficult to monitor the dispersed use of these knowledge goods and to enforce these legal rights.[165]

Ideally, these patent law failures could be compensated for 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.[166] 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.[167] Specifically, the Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey—introduced by CMS in 2006 and administered to patients after discharge[168]—asked in its now-controversial Question 14: "How often did the hospital or provider do everything in their power to control your pain?"[169] Providers anecdotally observed that patients who received opioid prescriptions were more likely to provide favorable survey responses. 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

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[163] 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 84–91 (2017).

[164] 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).

[165] 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.

[166] *See* CHRISTIE ET AL., *supra* note 7, at 56–57.

[167] *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).

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

[169] Adams et al., *supra* note 167, at 985.

and submit HCAPHS data, which was then made publicly available.[170] The rewards for high HCAPHS scores increased after the Affordable Care Act explicitly tied hospital reimbursements in part to a hospital's HCAHPS performance.[171] Hospitals were effectively rewarded (or, at least, believed they were being rewarded[172]) for alleviating 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 innovation institutions helped get us into the opioid crisis, they also can play an important role in helping us to 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 discovery. 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.[173] 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

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[170] *HCAHPS Fact Sheet*, *supra* note 168, at 2.

[171] *Id.*

[172] 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. Brummett, *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).

[173] *See* Hemel & Ouellette, *supra* note 9.

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 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. Patents and Market Incentives

Conventionally, innovation scholars have focused on patent law as the main policy tool to increase production of new knowledge goods.[174] 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.[175] 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, [176] abuse-resistant opioids,[177] drugs that can be used to treat addiction,[178] and easier delivery

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[174] *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.").

[175] *See* Hemel & Ouellette, *supra* note 9, at 554–57.

[176] *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 . . . .").

[177] 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).

[178] *See Information About Medication-Assisted Treatment (MAT)*, *supra* note 38 (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).

methods for the overdose antidote naloxone.[179] (Indeed, many firms already have.[180]) There is, to be sure, something unseemly about the very firms that 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 those same people on opioids in the first place.[181] 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 skew research toward treatments which require repeated use—and thus generate steady streams of revenue—rather than preventatives which are effective after a single administration.[182] Patent law may therefore be more effective, for example, at encouraging the development of nonaddictive painkillers than the development of anti-addiction vaccines. [183] 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,[184] informing

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[179] *See supra* note 116 and accompanying text.

[180] *See* CHRISTIE ET AL., *supra* note 7, 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-search-for-the-perfect-painkiller-tens-of-thousands-us-deaths-g-protein-coupled-receptor; Mathias, *supra* note 176. 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).

[181] 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-oxycontin-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/culture-news/oxycontin-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.").

[182] Preventatives also require larger clinical trials with lower tolerance for adverse side effects, making them more expensive to bring to market. *See generally* 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).

[183] 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.

[184] *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).

doctors when their patients overdose,[185] or encouraging the use of alternative pain treatments such as physical or behavioral therapy.[186] Patents are also ineffective incentives for non-pharmaceutical addiction recovery tools such as medical apps,[187] for creative ideas like using reverse-motion detectors in clinic bathrooms to prevent fatal overdoses,[188] and for research on the comparative value of different drug court protocols or streamlined ER-to-outpatient transfers for preventing relapse.[189]

Perhaps the apex example of patent law run awry in the area of addiction treatments involves Indivior, the maker of the best-selling opioid addiction treatment Suboxone. Suboxone is a combination of buprenorphine and naloxone that, according to some studies, is a more effective opioid substitution treatment than buprenorphine alone or the more familiar methadone.[190] Indivior introduced Suboxone to market in 2002 as a sublingual (under the tongue) tablet subject to a seven-year period of exclusivity under the Orphan Drug Act.[191] The approaching end of Indivior's exclusivity period brought another example of product hopping.[192] The company developed and gained FDA approval for a sublingual film version of Suboxone, with patent protection extending until 2030.[193] 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.[194] 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.[195] It priced the film version below the tablet version even though the film version is more expensive to produce.[196] And then in 2012, it announced that it

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

[186] *See supra* notes 163–166 and accompanying text.

[187] *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.

[188] *See* MACY, *supra* note 61, at 288.

[189] *See id.* at 220, 301.

[190] *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.

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

[192] *See supra* notes 67, 72, 116 and accompanying text.

[193] *See id.* 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 Jan. 21, 2019).

[194] *See In re Suboxone*, 2017 WL 3967911, at *4.

[195] *Id.*

[196] *Id.*

would take the tablet form off the market due to a "pediatric exposure safety issue."[197] Indivior also petitioned the FDA to deny approval for generic versions of the Suboxone tablet due to purported safety concerns.[198]

If the states' allegations are correct, then the Suboxone story is a vivid illustration of patent protection encouraging demand creation. Because Indivior believed it would enjoy monopoly power over Suboxone film but would soon face competition from generic tablets,[199] the company apparently sought to cannibalize the tablet market and induce demand for a new, though not necessarily better, product. (The FDA has not found Indivior's claims regarding the dangers of Suboxone tablets to be supported by evidence.[200]) Indivior's efforts to transition patients to the patented film version of Suboxone appear to have borne fruit. By 2013, eighty-five percent of prescriptions for Suboxone were written for the film formulation.[201]

Episodes such as Indivior's effort to undermine the tablet form of Suboxone 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.[202] 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," to use Martin Luther King's words.[203] While patents may play a role in promoting the development and commercialization of opioid alternatives, antidotes, and addiction

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[197] *Id.*

[198] *Id.* at *5. 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 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).

[199] 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).

[200] *In re Suboxone*, 2017 WL 3967911, at *5.

[201] *Id.*

[202] *See, e.g.*, NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 163, 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); 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 (discussing the importance of tort litigation in responding to the crisis); Robin Feldman, *May Your Drug Price Be Evergreen*, J.L. & BIOSCIENCES (forthcoming), https://academic.oup.com/jlb/advance-article/doi/10.1093/jlb/lsy022/5232981 (suggesting legal changes to cabin extensions of exclusivity with limited public health benefits); *infra* notes 287–289 (discussing potential doctrinal changes to patent law's utility requirement and remedies rules to incorporate broader social welfare concerns).

[203] 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).

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 policy 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.[204] Government-set rewards can encourage innovation in areas where patent law fails (e.g., where welfare-enhancing ideas are difficult to commodify).[205] But government-set rewards are, as we discuss below, vulnerable to pathologies of their own.

The United States already does provide direct funding for opioid solutions, 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).[206] In fiscal year 2018, Congress nearly doubled NIH funding for research on opioid addiction with an additional $500 million.[207] Yet these investments, while nontrivial, are on a scale too small for a problem whose economic costs likely top $500 billion annually.[208] For example, opioid-related research funding is less than the $3 billion the NIH provides each year for HIV/AIDS research,[209] even though in 2016, there were over ten times more Americans abusing prescription pain relievers than living with HIV,[210] and more Americans now die from opioid overdoses than died from the AIDS epidemic at its peak.[211]

The 2017 National Academies report recommended that the United States invest more heavily in research on pain and on opioid use disorder.[212] We agree, and we think understanding the failures of innovation institutions that contributed to the present crisis can help policymakers direct this funding to

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[204] *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.

[205] *See* Hemel & Ouellette, *supra* note 9, at 555; W. Nicholson Price II, *Grants*, BERKELEY TECH. L.J. (forthcoming 2019), https://ssrn.com/abstract=3174769.

[206] *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.

[207] 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).

[208] *See supra* note 7 and accompanying text.

[209] *See Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*, *supra* note 206.

[210] *Compare* SUBSTANCE ABUSE & MENTAL HEALTH SERVS. ADMIN., *supra* note 19, at 170525 tbl. 1.97A (eleven million), *with HIV in the United States and Dependent Areas*, CTRS. FOR DISEASE CONTROL & PREVENTION, https://www.cdc.gov/hiv/statistics/overview/ataglance.html (last updated Jan. 29, 2019) (one million).

[211] *See supra* note 5 and accompanying text.

[212] NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 163, at 162–63.

where it is most needed. For example, although patent law is likely to incentivize investment in new non-addictive pain treatments, it is less likely to encourage research on unpatentable pain treatments such as acupuncture, physical therapy and exercise, cognitive behavioral therapy, and mindfulness meditation.[213] 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 treatment [214]). Grantmaking 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 state[215]—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,[216] 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 costs pale in comparison to the costs of patent litigation[217] and seem rather trivial compared with the magnitude of the crisis that opioid-related R&D addresses. That the federal R&D grant process remains far from

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[213] *See supra* note 163 and accompanying text.

[214] Findings on the effectiveness of cognitive behavioral therapy for patients simultaneously receiving medication-assisted treatment for opioid abuse are decidedly mixed. *Compare* David A. Fielin 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 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).

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

[216] *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.

[217] *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).

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."[218] Less well recognized—at least outside the innovation policy literature[219]—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 success, at least as long as researchers can acquire necessary bridge financing until their ideas reach fruition.[220]

Innovation inducement prizes are a small but growing portion of U.S. innovation institutions,[221] 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.[222] 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.[223] 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."[224] And the HHS two-day Opioid Code-a-Thon distributed three $10,000 prizes for "data-driven solutions to

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[218] *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.

[219] 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).

[220] *See* Hemel & Ouellette, *supra* note 9, at 556–57.

[221] *See* Hemel & Ouellette, *supra* note 217, at 317–18.

[222] *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 217, at 317–376.

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

[224] *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).

combat the opioid epidemic."[225] 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.[226] 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.[227]

Many opioid-related prize competitions offer funding at such a small scale that it seems 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.[228] 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."[229] Despite the lack of financial reward, the competition generated significant interest, with 250 applications, from which eight winners were selected.[230] Of course, the absence of a clear counterfactual makes it difficult to draw any strong conclusions about the causal effect of these programs.[231]

Innovation inducement prizes 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

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[225] *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).

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

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

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

[229] 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.*

[230] *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).

[231] *See generally* Heidi Williams, *Innovation Inducement Prizes: Connecting Research to Policy*, 31 J. POL'Y ANALYSIS 752, 768 (2012) (describing this evaluation problem).

fixed prizes and market-set patent rewards.[232] This kind of market-based prize has been used to incentivize distribution of pneumococcal vaccines.[233] 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, bear some similarities to market-based prizes[234] (though they may also introduce new distortions, as discussed above[235]).

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 Food and Drug Administration (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."[236] 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.[237] Indeed, the SAMHSA explicitly include funding for "identify[ing] which system design models will most rapidly and adequately address the gaps in their systems of care."[238] 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.[239] To encourage policy experimentation, federal

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[232] *See* Hemel & Ouellette, *supra* note 9, at 554.

[233] *See generally* Williams, *supra* note 231, at 752, 758–59, 769–70 (describing this pneumococcal prize and the challenges in measuring its effectiveness).

[234] *See* Lemley et al., *supra* note 92; Benjamin N. Roin, *Intellectual Property Versus Prizes: Reframing the Debate*, 81 U. CHI. L. REV. 999, 1011–14 (2014); Sachs, *supra* note 14.

[235] *See supra* Section I.C.2.

[236] 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.

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

[238] *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).

[239] *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.

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.[240] But while this benefit-internalization approach might work for 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.[241]

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.[242] 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."[243] 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

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[240] *See* Hemel & Ouellette, *supra* note 9, at 550 (referring to this combination of innovation policies as "layering," or "the use of different policies at different jurisdictional levels, such as using non-IP innovation incentives and allocation mechanisms at the domestic level within an international legal system oriented around IP").

[241] *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.").

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

[243] *Id.*

does not necessarily imply a decreased reward for the innovator.[244] 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 boost their profits from new products.[245] 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? The downside of moving toward open access allocation mechanisms is the decreased role of price as a screening function to distinguish the most valuable innovations. As Glen Weyl and Jean Tirole have explained, market prices often serve a useful informational 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.[246] 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.[247] These markets have also been plagued with misinformation that further misaligns economic rewards and social value.[248] 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.[249] It is hard for lay people and even doctors[250] to understand the complex and statistical evidence needed to evaluate medical information, and it seems implausible that the choice between two treatment

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[244] *See* Hemel & Ouellette, *supra* note 9.

[245] *See supra* notes 231–236 and accompanying text.

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

[247] *See supra* notes 48–49 and accompanying text.

[248] *See, e.g.*, *supra* notes 55–59 and accompanying text.

[249] *See generally* CHOICE, BEHAVIOURAL ECONOMICS AND ADDICTION (Rudy E. Vuchinich & Nick Heather eds., 2003).

[250] *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).

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. First, the Food and Drug Administration (FDA) plays a key gatekeeper role in setting the relevant market when deciding whether to approve a given drug or device—a decision that does not incorporate public health considerations.[251] Then, as previously discussed, the federal government subsidizes access to new medical technologies through programs like Medicare and Medicaid, which have generally covered prescription opioids.[252]

All of these factors suggest that the value of proprietary pricing is more attenuated in markets for pain and addiction 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.[253] 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.

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 case leading to poor clinical outcomes."[254] 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

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[251] *See* NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 163, at 410–14 (arguing that the FDA should incorporate public health considerations into regulatory decisions); 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).

[252] *See supra* notes 89–91 and accompanying text.

[253] *See supra* notes 150–155 and accompanying text.

[254] 42 U.S.C. § 1315a(b), (d)(1).

plans in the areas hit hardest by the opioid epidemic.[255] 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.[256] 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 appear to be turning a profit from Evzio,[257] it's not crazy to think that they 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 positive externalities and Kaléo's apparent financial struggles. But what if patent rents are predicted to be higher than the social value of the invention? 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.[258] 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.[259] These statutory mechanisms are

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[255] On the scope and limit of the Secretary's authority to waive the best-price mandate, see generally Sachs et al., *supra* note 157, at 14–16.

[256] *See* Hemel & Ouellette, *supra* note 9, 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).

[257] *See supra* note 144 and accompanying text.

[258] 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.

[259] *See* Wang & Kesselheim, *supra* note 115 (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,

important tools when the patent incentive is greater than socially optimal, although the government has shown reluctance to embrace this authority in other contexts.[260]

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.[261] Coverage of non-pharmacological treatments through private insurers has been similarly limited.[262] In addition to incentivizing additional research into these alternative pain treatments,[263] the government should address this bias by requiring or subsidizing coverage for these interventions.

Insufficient coverage is a barrier to access not only for non-opioid pain treatments, but also for addiction treatments such as Suboxone.[264] The 2017 report from the President's opioid commission recommended that all addiction patients have access to medication-assisted treatment including buprenorphine (one of the active ingredients in Suboxone) 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 waiver from the Drug Enforcement Administration prescribe this drug.[265] And even when a physician has received the waiver, insurance requirements often delay access and fail to provide the same level of reimbursement as for other health conditions.[266]

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.[267] 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

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2018), https://www.keionline.org/wp-content/uploads/2018/03/Conway-Carrol-KEI-1498-Evzio-29mar2018.pdf (same).

[260] *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).

[261] *See supra* notes 89–91, 166 and accompanying text.

[262] *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).

[263] *See supra* note 213 and accompanying text.

[264] *See* NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 39, at S-7 ("Most people who could benefit from medication-assisted treatment for opioid use disorder do not receive it, and access is inequitable across subgroups of the population.").

[265] CHRISTIE ET AL., *supra* note 7, at 34, 68.

[266] *Id.* at 70; *see also* NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 39, at S-9 (discussing these and other regulatory barriers such as counseling requirements).

[267] *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.

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 choice 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 unemployment.[268] And the stigma of addiction further limited the political capital of those hardest hit.[269] 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.

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,[270] and the ensuing President's Commission on Combatting Drug Addiction and the Opioid Crisis issued a comprehensive report on addiction prevention and treatment.[271] 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.[272] The difference may reflect racial politics; the

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[268] *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).

[269] *See generally* MACY, *supra* note 58, 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").

[270] *See The Opioid Crisis*, WHITE HOUSE (last visited Mar. 14, 2019), https://www.whitehouse.gov/opioids.

[271] CHRISTIE ET AL., *supra* note 7

[272] *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").

press has typically portrayed opioid users as sympathetic white suburbanites, compared with urban black and Latino heroin users.[273] 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.[274]

Of course, even when opioids began to gain policymakers' attention, government interventions were often too small or were misdirected, as illustrated by the distortions described 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 and crime.[275] 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 science of treating pain and addiction, but also on the science of communicating this knowledge in ways that overcome existing cultural hurdles.[276] 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.[277] Innovations in cancer therapy require not just scientific advances but also the political support to fund those research efforts—compare

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[273] *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). 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* Friedman et al., *supra* note 99. 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).

[274] *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.

[275] *See* MACY, *supra* note 61, at 216, 281, 288; NAT'L ACADS. OF SCIS., ENG'G, & MED., *supra* note 39, 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.

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

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

the amazing success of the pink ribbon movement for breast cancer research[278] with the low funding rates for stigmatized lung cancer,[279] even though lung cancer is the deadliest cancer, killing more Americans than breast cancer, prostate cancer, and colon cancer combined.[280] 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 the patent system run amok, but it is also a narrative in which the pathological politics of pain and addiction infected the non-patent institutions that could have been used to 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.

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 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 and Evzio confirm some truths that we have long known about the patent system. Patents are effective innovation incentives for aggregating dispersed information about consumers' willingness to pay for new knowledge goods—but when markets fail, so too will patent incentives.[281] 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. Evzio is an example of a product that generates positive externalities (the purchaser might not be the person whose life is saved), and—also unsurprisingly—we have ended up with too little Evzio.

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

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[278] *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.

[279] *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.

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

[281] *See generally* Hemel & Ouellette, *supra* note 9, at 555–56.

poorly structured to support the development of processes and practices such as checklists, cognitive behavioral therapy, and alternative medicine.[282]

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 patent strength as a tradeoff between dynamic efficiency and allocative efficiency is less accurate than we once believed.[283] 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.[284] 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 is unlikely to prevent the vast majority of U.S. patients from gaining access.

Second, and relatedly, the fact that patent protection encourages demand creation should affect our view of patent law'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 untreated depression.[285] But we should be aware that the patent system creates incentives for firms to promote products that consumers did not know they needed (and indeed might not have needed).[286]

Third, the interaction between patent protection and addiction is particularly pernicious. As we sought to illustrate in Section I.B.2, 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 patent rewards with social welfare could be addressed by reforms internal to patent law. 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

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[282] *See generally* Kapczynski & Syed, *supra* note 10.

[283] *See supra* notes 11, 43–46 and accompanying text.

[284] *See supra* note 72 and accompanying text.

[285] *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).

[286] *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).

profits).[287] 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.[288] 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.[289] But non-patent innovation institutions also have an important—and perhaps paramount—role to play in correcting the patent system's biases.[290]

A fourth lesson from the opioid crisis for other areas of innovation policy is that the notion that government subsidies can promote access to patented 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 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.[291] In such cases, patent protection does lead to serious allocative inefficiencies, but the inefficiencies are because of the way in which other government policies interact with the patent system. To be sure, perfect price discrimination will almost never be possible, and deadweight loss in the patent

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[287] *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).

[288] 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).

[289] Ted Sichelman, *Purging Patent Law of "Private Law" Remedies*, 92 TEX. L. REV. 517 (2014).

[290] 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).

[291] *See supra* notes 154–155 and accompanying text.

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 patent system, we again emphasize that non-patent innovation incentives and allocation mechanisms are imperfect. In the case of the opioid epidemic, CMS created powerful non-patent-based incentives for hospitals to prescribe more opioids.[292] 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 the patent system 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 intellectual property 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.[293] 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 manufacturer of the anthrax medicine Cipro, cutting prices steeply.[294] A crisis—as Nobel laureate economist Paul Romer once said—is a terrible thing to waste,[295] 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 this will

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[292] *See supra* notes 167–172 and accompanying text.

[293] *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).

[294] *See* Brennan et al., *supra* note 259, 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.

[295] *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.

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 all attributable to innovation policy or that the flaws of the patent 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.