

A crisis of opioids and the limits of prescription control: United States

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ABSTRACT

A rise in addiction and overdose deaths involving opioids in the United States has spurred a series of initiatives focused on reducing opioid risks, including several related to prescription of opioids in care of pain. Policy analytical scholarship provides a conceptual framework to assist in understanding this response. Prior to 2011, a 'policy monopoly' of regulators and pharmaceutical manufacturers allowed and encouraged high levels of opioid prescribing. This permissive policy fell apart in the face of adverse outcomes brought to public attention by an 'advocacy coalition' consisting of officials, thought leaders, journalists and interest groups who shared common beliefs. This coalition has generated a more cautious prescribing regimen that has incentivized involuntary termination of opioids in otherwise stable patients, with resultant reports of harm. Its emphasis on dose reduction, regardless of outcomes, mirrors in some ways the prior focus on minimizing pain scores, regardless of outcomes. Central to the present analysis is that policies cannot be comprehensively rational; rather, they emerge from a range of actors and agencies constrained in their ability to assimilate complex data, evaluate the data objectively and to command necessary resources in an iterative, rapid response fashion. The imbalance between strong prescription control and weak pain and addiction treatment expansion exemplifies the policy scholar's notion of 'bounded rationality'. Results have been suboptimum: opioid prescriptions have fallen, but harms to pain patients and overdose deaths have risen. US policymakers could revise the course through a more thoroughgoing engagement with patients, families and communities now coping with both pain and addiction.

Keywords Health care, health-care policy, opioids, overdose, policy, policy analysis, prescription drug monitoring, prescriptions, rationality.

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A CRISIS OF OPIOIDS AND THE LIMITS OF PRESCRIPTION CONTROL: UNITED STATES, 2017

In 2017, the United States faced a rising tide of opioid-related deaths: overdoses accounted for 63 600 deaths in 2016 [1], with approximately two-thirds involving opioids. The years 2016–17 saw a proliferation of policies, initiatives and regulations discouraging initial and continuous opioid prescriptions for pain. Coming from a range of agencies, encompassing professional boards, public and private payers, law enforcement and more, they reflected a re-calibration of policy compared to the prior decade, when powerful commercial, regulatory and legal initiatives

embraced opioids as a cardinal, underappreciated asset for treatment of pain [2,3].

The shift in public attention could seem, from one point of view, to flow inevitably from a rise in both addiction and overdose [4,5]. However, policies do not shift automatically in response to objective data. Policy analysis studies focus upon how a given set of facts, interpretations and values comes to structure public priorities [6]. This paper applies policy analysis to interpret ongoing shifts in US policy regarding opioids, pain and addiction. We will suggest that US policy reflects an imbalance that threatens efforts to address pain and addiction, while endangering patients whose receipt of opioids for pain represents a key part of their care.

In structure, this manuscript first lays out a framework of policy concepts, drawing upon a summary review by Cairney [6]. As these policy concepts are not familiar to all, they are introduced preliminarily in the form of a brief narrative framing how they apply to US policy. Rhetorically, this involves offering an interpretive narrative first, before factual review. We ask readers to treat that narrative with the skepticism that any policy argument deserves. It is our hope that the data that follow, covering historical events, public information and scientific findings, will allow readers to decide if they find our narrative a credible one.

FRAMEWORK: CORE CONCEPTS IN POLICY SCHOLARSHIP

Bounded rationality

The policy scholars' notion of bounded rationality recognizes that policies emerge from competing actors and agencies acting simultaneously, only some of whom are governmental or central [6]. Rationality is always constrained by the limited degree to which leaders can assimilate complex data, and by the reality that they have multiple problems to fix with limited resources. The result is that they are subject to influence by highly informed advocates who can sway policy by predigesting data in ways that often reflect their own interests. Bounded rationality does not explain why one policy approach wins or loses, or why a given policy paradigm controls public allegiance until it is replaced. Whatever party wishes to criticize shortfalls of the current US arrangement (or the prior one) as insufficiently rational, or as insufficiently humane, should confess to a degree of wishful thinking.

Policy monopoly

A policy monopoly is a collection of agents who control the definition of problems that deserve to be solved, voices that deserve to be heard and methods that deserve to be considered. Our view is that from 1995 until approximately 2010, control of pain was prominent in the ladder of rhetorically emphasized priorities [7], although resource-intensive multi-disciplinary programs of pain care never had strong support from payers and health-care organizations. Instead, opioids were advanced optimistically, based in part on a few excessively cited studies [8,9], pharmaceutical marketing [3], high-stakes quality metrics [10] and reckless distribution [11]. The policy monopoly included health providers, some pharmaceutical companies, the US Food and Drug Administration (FDA) and health-care regulatory agencies [2]. Notably, the agenda would not have survived without concessions: law enforcement retained power to prosecute physicians, and detractors spoke out. Interventional pain physicians (who saw opioids' downsides and had financial interest in alternatives)

protested [12], as did clinicians who saw aberrant behaviors and addiction [13–18]. These detractors had the weaker hand, and the stability of the prescribing environment depended upon members of the policy monopoly blaming a few bad doctors and patients for whatever harms emerged.

Punctuated equilibrium

The rapid change in US opioid policy, from pill promotion to restriction, is an example of punctuated equilibrium [6,19]. Punctuated equilibrium proposes that a set of stable relationships between interest groups and officials fixes the definition of a problem and its management. However, equilibria can be altered (i.e. 'punctuated') by crisis, if new parties advance a different view.

Advocacy coalition

Such punctuations depend upon the emergence of what Sabatier termed an advocacy coalition, 'people from a variety of positions (elected and agency officials, interest group leaders, journalists, researchers) who share a particular belief system—i.e. a set of basic values, causal assumptions, and problem perceptions—and who show a non-trivial degree of coordinated activity over time' [20,21]. Advocacy coalitions share core beliefs (e.g. 'pain is unavoidable and we should not overmedicalize it') and policy beliefs ('prescribing should be more strictly governed'). Successful coalitions build beliefs into policy.

All four concepts help to explain a transition in the United States regarding opioids, addiction and pain.

THE OPIOID LANDSCAPE

US epidemiological data from 2003 to 2017 show a rise in opioid use disorder (OUD) and overdose deaths. The percentage of US adults with OUD rose between 2001–02 and 2012–13, from 0.4 to 0.8% for prescription OUD [22] and from 0.2 to 0.7% for heroin OUD [5]. Approximately 2.1 million Americans qualified as having OUD in 2016, according to another survey [23].

Opioid medications obtainable via prescription (but often diverted) probably played a role in addiction involving opioids and other illicit substances. Among people aged 12–49 years reporting at least one past-year episode of heroin use in the National Survey on Drug Use and Health (2002–11), 80% reported at least one prior non-medical use of prescription pain relievers [24]. This observation turbocharges arguments that centralize prescription control as a key policy response [25].

However, some evidentiary wrinkles raise questions about the anticipated impact of prescription control. First, people who misuse opioid medications usually report they

were not obtained for care of themselves [26]. Such reports buttress a concern that many were prescribed unnecessarily [27]. Secondly, heroin addiction may not begin with medication. Among people with heroin OUD in the 2012–13 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), the percentage who started with non-medical use of prescription-type medication was 53% for whites and 26% for non-whites [5]. Similarly, among people entering opioid treatment programs, the percentage who reported first using heroin (as opposed to pain medication) for getting high rose from 8.7% in 2005 to 33.3% in 2015 [28]. Most people in this sample reported psychiatric disorders predating opioid use and described having sought opioids to manage their emotions [29].

Other indicators suggest that prescription control may have contributed to a reduction in some prescription opioid problems, without clearly stunting the growth in heroin use. From 2012 to 2017 the number of opioid prescriptions fell 18%, from 81.2 to 66.5 per 100 people [30,31]. Similarly, data from law enforcement, poison center reports and surveys indicate a rise in prescription opioid misuse from 2002 to 2010, but then a decline, except for a rise in prescription opioid misuse by college students to 2013 [32]. Additionally, the US National Survey on Drug Use and Health (NSDUH) reported a 19% relative reduction in past-year prescription opioid misuse from 2012 (4.8%) to 2014 (3.9%) [33] and a further 8.7% drop from 2015 (4.7%) to 2016 (4.3%) [23]. A rise in heroin has transpired during the same time-frame. The NSDUH depicts a continuous increase in people with heroin use disorder (rising 121%, from 283 000 to 626 000 in the 2008 to 2016 [23]. The NESARC also reports a rise in prevalence of heroin use disorder from 2001–02 to 2012–13 [5].

These indicators invite questions regarding the efficacy of pill control [34]. Viable counter-arguments note that opioid prescribing remains higher than in 1999, and that prescriptions are a common avenue to addiction [35–37]. Undergirding such debates lie disagreements about the causes of addiction, and the competing roles of drug supply, human demand and the tractability of either as a policy solution.

Such debates cannot obscure a catastrophic rise in overdose [4]. Since 2013, illicitly manufactured synthetic opioids such as fentanyl have played a rising role in these deaths [38,39], perhaps reflecting changes in the market. Prescribed opioids have declined among drugs found in legal seizures since 2012. Long-standing shortfalls in testing by coroners and in tabulations by the Centers for Disease Control (CDC) have tended to obscure aspects of the crisis. For example, in detailed studies, poisoning events with licit and illicit opioids often involve multiple other substances and low doses of prescription opioids [40,41]. However, coroners tend not to test broadly. Problematically, the CDC's reports tabulate by single drugs [4], with each

death potentially counted in multiple drug categories, obscuring polydrug deaths. Despite these ambiguities synthetic opioids, predominantly illicit in source, contributed to nearly 20 000 deaths in 2016, up from 5544 in 2014 [4]. Even this figure probably underestimates their role, as testing for them remains costly and non-standard [34].

THE POLICY RESPONSE: BOUNDED RATIONALITY

The parallel rises in overdose, in addiction and in prescriptions (to 2011) defined a crisis [17,24]. An advocacy coalition emerged that included advocacy groups, academics and officials such as the former Director of the CDC, Dr Thomas Frieden, who wrote: 'few medications are so consistently lethal as opioids for pain' [42]. Pain patients who took opioids chronically (and their doctors) found their position undermined by a series of emerging arguments that had some merit, even if they offered far from comprehensive understandings of pain, of addiction or of how to treat either problem. Opioids, it was noted, lacked trial evidence of greater than a year's duration [43], although few acknowledged that the same critique characterized most alternatives [44] and that efficacy for any of single pain treatment modality was modest. Reducing pain, it was argued, was an unduly narrow care metric that incentivized pharmaceutical numbing rather than more comprehensive care [45]; and opioids incur risks, as does overdose [46].

It was also proposed that opioid physical dependence among pain patients was not meaningfully distinct from addiction [14]. 'A false dichotomy' had been erected between two groups of patients [47]. In an analysis that did not assess therapeutic intent or outcomes, longer initial prescriptions were associated with likelihood of opioid receipt at later time [48]. Accordingly, some regulators proposed that turning 10-day prescriptions into 3-day prescriptions would stop addiction from happening [48–50]. As one advocate wrote in 2013, public health depended heavily, although not exclusively, upon controlling the causal agent, 'the pill': 'To bring an epidemic under control, we must prevent new individuals from developing the disease (opioid addiction) and we must ensure that individuals already suffering from the disease have access to effective treatment' [47].

Amid tragedy, a narrative focus on 'the pills' dominated. In fact, opioids had been promoted aggressively [3], pain scores treated as a high-stakes quality metric [2] and opioid risks downplayed systematically. Such a narrative implied simple solutions. 'This is not a hard problem to solve', said the Governor of the state of Vermont. 'We didn't have a heroin crisis in America before OxyContin was approved and started being handed out like candy... we could fix the majority of this problem with a click of our fingers'

[51]. The same narrative apportioned blame in ways that were comforting to Americans. Blame fell first upon unscrupulous pharmaceutical companies and distributors, and secondarily on well-intentioned but naive health-care providers who had been duped into serving as drug dealers for innocent victims [52–54] who had neither agency nor responsibility. The doctors could and would be redeemed with training on opioid prescribing. Fundamental gaps in training on addiction, pain and rehabilitation were ignored [25,55]. The policies that followed epitomize bounded rationality. Given a tragedy to solve but limited information, time and resources, leaders embraced prescription control and stumbled in treating addiction or protecting pain patients who had been stable on opioids, and might not be after medications were taken away.

THE CDC GUIDELINE AND PRIOR EFFORTS

There were initiatives and efforts to remediate opioid prescribing risks from 2011 onwards [56,57]. They included re-formulation of long-acting oxycodone to be less susceptible to crushing in 2010 [58], influential state guidelines [59] and early reports from the CDC [60]. Illicit distribution of prescription drugs declined, as reflected in data showing downward trends in law enforcement seizures of oxycodone, hydrocodone and morphine, paralleled by upward trends for heroin and fentanyl [61].

In this context, the CDC Guideline on Prescribing Opioids for Chronic Pain of 2016 [62] stands as a point of inflection, largely because of how it was enshrined in a range of governmental and non-governmental policies, all of which tended to accelerate a shift in prescribing. The CDC Guideline was characterized by nuance in its language [62] and secrecy in its development [63]. Many regulatory initiatives invoked the Guideline's cautionary language on dose and duration as differentiating acceptable versus irresponsible care [64–66].

Broadly, the Guideline reflected a consensus view that non-pharmacological and non-opioid treatments are preferred in chronic pain, given that trials do not suggest that opioids are, on average, routinely superior to other options [43,67]. It urged cautious re-evaluation when considering doses above thresholds of 50 and 90 morphine milligram equivalents. It suggested 3- and 7-day restrictions on opioids for acute pain. Importantly, for patients receiving opioids, the Guideline advocated neither involuntary discontinuation nor forced taper. Instead, it called on clinicians to balance observable harms and benefits. This approach was sensible, as no data support forced opioid reductions as safe or effective [68], and doing so failed in a randomized trial among patients with prescription opioid use disorder [69]. As general principles, the Guideline's holdings were probably acceptable to many audiences.

The Guideline is not perfect. The absence of evidence stronger than observational for all but one recommendation (medications to treat OUD) was sobering. Also, it emphasized relative, rather than absolute, risk calculations as the basis for clinical management, an approach susceptible to framing bias [70,71], particularly when what matters for a patient is the absolute risk of a medication versus alternatives for a condition that involves relentless suffering.

Additionally, the Guideline's emphasis on opioid dose [milligram morphine equivalents (MME)], as the core driver of opioid risk was unduly narrow. The dose–risk correlation in observational studies [72,73] obscures the independent impact of risk factors that correlate with dose escalation. These include psychological vulnerabilities, race and polypharmacy [46,74–76] which, in turn, multiply (or, in their absence, reduce) overdose risk by factors of 2 to 20 [46,75]. Among overdose events in prescription opioid recipients, as with heroin overdose, most occur at low drug levels [41,73]. In a 2018 paper, opioid dose did not predict overdose deaths after controlling for other factors (such as mental health) [77]. In short, dose restriction, the centerpiece of today's initiatives, ignores most of the prescription recipients' risk for opioid related morbidity [73].

Despite limitations, the Guideline was written in a way that should have mitigated the risk of calamitous care decisions and, just in case, the CDC's Opioid Guideline Workgroup formally demanded that the agency watch for implementation mishaps [78].

A WEAPONIZED GUIDELINE

In practice, most nuances of the Guideline were lost on the public, on regulators and on physicians. The document was 'weaponized'. Weaponization was evident in regulations requiring extensive documentation or testing to justify continuation of opioids, along with a plethora of restrictions on the number of dose units, the MME dosage, number of days covered or the prerequisites for coverage [79,80]. By mid-2017, 23 states had passed laws limiting prescription duration or dose or authorizing other entities to set limits with effective legal force [80]. The state of Maine mandated that patients on opioids have doses reduced to < 100 MME save for narrow exceptions, the nature of which must be reported on every prescription [81]. Private insurers also restricted coverage to force doses down [82].

In the summer of 2017, two pharmacy firms announced plans to restrict first-time opioid prescriptions to 7 days [66,83]. As if to highlight its lack of interest in treating addiction, one announced donations of 0.02% of its \$10 billion profits (\$2 million) for treatment [66], 16 times less than what it spent lobbying the US Congress to

limit drug regulations [11]. Private insurers applied payment restrictions to push doses down [82]. An insurer announced proudly that it had lowered prescribing by 25%, ‘one year ahead of goal’, and publicized donations to addiction-related community programs that amounted to only 1/100 of 1% of its profits [84].

Similarly, the National Committee for Quality Assurance (NCQA) and two other agencies imposed metrics in which the number of patients receiving > 120 MME would count against doctors [85], regardless of patient outcomes, even death (which reduces the number of patients on opioids). In so doing, they rejected a petition claiming that a binary dose standard incentivized involuntary tapers and endangered patients, violating the CDC Guideline itself [86].

At the same time, the US Departments of Veterans Affairs and Defense published a graphic algorithm demanding dose reduction for all patients at > 90 MME, regardless of the physician’s benefit–risk assessment, although Guideline text recommended otherwise [87]. In December 2017, the Commissioner for the Food and Drug Administration (FDA) announced plans to make physicians jump through ‘additional hoops’ to prescribe opioids [88]. Two months later, eight US Senators unveiled a bill to restrict all first-time opioid prescriptions to 3 days [89].

This plethora of initiatives and regulations following the Guideline should not obscure policy changes that predated it. Pharmacists had been urged to refuse to dispense based on ‘red flags’ [90], including signs of withdrawal or distance from the patient’s home to the pharmacy. For legitimate patients to travel to a second pharmacy after one rejection is itself a ‘red flag’ [56].

Also, over several years, the US Department of Justice promoted Prescription Drug Monitoring Programs (PDMPs) [91]. Although providers can use PDMPs clinically, the data are also accessible to law enforcement without warrants. At the end of 2017 the Department of Justice explained it would combine PDMPs with other indicators, including the distance patients traveled to see their doctors, to target investigations. This, according to a federal prosecutor, would ‘put (doctors) on notice that we have new tools’ [64].

In sum, opioid prescribing is now subject to an array of conflicting, high-stakes imperatives from an alphabet soup of regulators, employers and payers.

Unsurprisingly, doctors have cut prescriptions, even when so doing risked rupturing care relationships. Nationally, high-dose (i.e. > 90 MME) prescribing fell 48% over 8 years [31]. Similarly, the Veterans Health Administration reported a 37% decline in out-patient opioid prescriptions since 2011 [92]. The period of late 2016 to 2017 included reports of pain patients subject to opioid termination who committed suicide, attacked physicians, died in withdrawal, suffered medical decline or overdosed on illicit

opioids [93–99]. Despite a proliferation of such events, with many documented online, no agency or insurer has agreed to track or count these maloccurrences [99]. Some authorities avowed that patient deaths, if regrettable, were necessary. One said: ‘we knew that this was going to be an issue, that we were going to push addicts in a direction that was going to be more deadly... but you have to start somewhere’ [100].

The *zeitgeist* might be phrased: ‘do something, anything, and we’ll discuss the consequences later’.

As this unfolded, a transition in the American tide of opioid-related mortality towards heroin, fentanyl and its derivatives was noted [34,35,101,102]. Whether this reflected falling availability of prescription-type opioids remained unsettled. A late 2017 Presidential Commission condemned a ‘lack of foresight of unintended consequences’ from prescribing controls [55,102], but federal officials had already rebutted such concerns.

In mid-2017, the CDC’s Director wrote that prescription controls had been ‘shown to reduce the amount of opioids prescribed, prescription opioid-involved overdose deaths, and all opioid-involved deaths’ [103].

Her citation [104] used correlational models from 38 states to suggest that US states mandating use of prescription drug monitoring from 2006 to 2013 reduced prescription deaths, without heroin overdoses rising [104]. The data, however, predated the prescribing downturns and fentanyl emergence of 2014–17. Overdose etiologies were poorly captured, as more than one-third of states failed to report substances in $\geq 25\%$ of overdoses [105]. Equally worrisomely, a graphic of the raw death totals showed results contradicting the paper’s conclusion, raising concerns about its statistics. Mandatory prescription monitoring transpired in only four states near the end of the study period, inviting questions as to how well the models fitted end-of-observation variance with just 312 observations and 86 degrees of freedom. Finally, the models imposed linear assumptions on non-linear data, including the assumption that policy interventions exert effects at a single moment, neither growing nor shrinking thereafter, which was contradicted by another paper in that journal [106].

Setting aside methodological shortfalls, the question of whether PDMPs confer benefit is unresolved [25,55,62,87]. The year 2017 saw papers draw contradictory conclusions [107–110], none of which assessed whether PDMPs improved patient outcomes [111]. For now, it is plausible that PDMPs help some clinicians.

THE LESS POPULAR ELEMENTS OF A POLICY RESPONSE

The vigor evident in pill control initiatives has not been evident in regard to two other components of optimum

policy. Those include (a) treatment for OUD and other addictions and (b) addressing the social conditions that tend to drive demand and are prevalent in communities and neighborhoods where opioids, other drugs and alcohol have taken hold [112]. About the latter, little will be said here, save to note that OUD has spared no tranche of society, although popular descriptions focus on rural white communities [112,113]. Concentrated forms of disadvantage, sometimes geographic and local, make drug-related rewards more salient to some individuals, even when the long-term harms are substantial [114]. No US plan to remediate such conditions has any momentum [115].

Regarding treatment, no prominent US advocate denies its value [25]; but that advocacy has not been honored with commensurate action, and the unmet needs in addiction care are profound.

Addiction care in the United States is hindered by the low quality of its treatment infrastructure [116], a lack of training [117] and regulatory restrictions. A 2016 national survey of treatment programs found that just 27% offered buprenorphine and 8.1% offered methadone for OUD [118]. When medication is offered, follow-up care including mental health treatment and urine drug screens is lacking [119]. With taxpayers subsidizing inertia, there is little incentive to change.

Additionally, private payer barriers are substantial. Despite a US law mandating parity in the treatment of physical and mental health [120], insurers continue to limit the duration of care for persons with OUD or duration of pharmacotherapy (e.g. 3 months only for buprenorphine, or challenging prior authorization procedures) [121].

The 2016 National Survey on Drug Use and Health cites 6.7 million Americans as needing treatment for an illicit OUD, but not receiving it [23]. Treatment funding expansions remain limited [122]. In late 2016, Congress budgeted \$1 billion in temporary treatment funds, while more than \$45 billion may be necessary [123].

Dramatizing a political stasis, a 2017 bipartisan Presidential Commission offered 21 recommendations to reduce barriers to treatment, but failed to urge treatment funding expansion [55]. In recommendations from two of the most influential voices on opioids in the United States, four focused on restricting opioids for pain, three on prescription drug monitoring, two on facilitating treatment through regulatory change and none sought new treatment funds [25].

That said, the American treatment response is not ignorable. It includes public health initiatives focused on opioid reversal agents (e.g. naloxone) [124,125] and some community-based efforts to increase capacity for addiction treatment [126–128]. Whether such efforts will stall or grow is unknown.

In describing the weakness of the US addiction treatment infrastructure, a range of explanations could apply. These include poor public perceptions of treatment, stigmatization of people with addiction and entrustment of addiction care to informal, often residential programs focused on moral rehabilitation [129], as well as a history of underinvestment in mental health care generally [116,130,131]. In the end, treatment remains the ugly stepchild of US addiction policy, not excluded from family photos yet never fully embraced.

POLICY ANALYSES THAT BOUND RATIONALITY

In summarizing how policy has evolved in the United States, a stipulation is offered: we do not contest claims that excess prescribing contributed to opioid misuse. It strikes us as likely that some people will be protected if they never touch opioids. Whether the ongoing reduction in prescribing will yield a future reduction in addiction or overdose remains to be seen. The overdose deaths involving potentially prescribed opioids (i.e. natural and semisynthetic, excluding methadone, fentanyl or heroin) remain constant at approximately 10000 yearly since 2010, according to a query from the US National Vital Statistics System, suggesting a lack of return on investment where prescription reduction should have had some effect. In our view, the rise of prescription control with harms to some pain patients (notably, suicides), coupled with stuttering commitment to addiction or pain treatment, reflects an imbalance. Concepts from policy analytical scholarship show how this imbalance happened, if not why.

A pre-2011 policy monopoly buffered pharmaceutical profits and allowed some to claim a mantle of virtue by prioritizing a simplistic approach to pain in a way that did not require much expense on patients with complex needs, save for drugs. In certain ways, the aggressive promotion of opioids echoed a late 19th-century distribution of many substances [132].

That stasis broke, due in part to an undeniable crisis of overdose and addiction [17,133,134], causing many to revisit prior assumptions. A functional advocacy coalition of professionals and organizations of people affected by addiction was joined by key officials and corporate interests (such as pharmacy chains) who needed to contain their liabilities. The rise of prescription control, however, reflects not just coalitional strength but narrative power. A narrative emphasizing pills as the cause of an ‘opioid epidemic’ fits the US time-line to 2011, and delivers a digestible story for policymakers [135]. It assigns blame in ways that are politically easy. It implies steps by which insurers and pharmacy chains can contain their liabilities without much expense. It provides easily measured results,

provided one is satisfied with prescription reductions rather than human health outcomes, and billions of dollars in legal damages will be easier to recover if this narrative remains pristine.

However, the new prescription control framework is a funhouse mirror image of the prior monopoly. What was virtuous under the prior regime was to chase a number—the pain score—using opioid prescriptions, even as naysayers pointed out that people were being harmed. What is virtuous under the new regime is to chase new numbers (opioids prescribed), even as naysayers point out other people harmed.

Neglected, as always, are the social conditions that tend to lead people to use opioids and other illicit substances [115]. Neglected, mainly, is the work of fixing shortfalls in treating patients with multi-system needs, including addiction, pain and complex forms of dependence [136]. These neglected problems would require resources and community effort. The aching question of whether cutting prescriptions saves lives, or harms innocents, has been deferred by pointing to observational correlations between prescribed dose and overdose risk [72]. That addiction might well emerge in the absence of prescription opioids, and that most people with opioid addiction did not start as pain patients, are facts [26,27]. However, they are facts with no purchase on the public imagination because they do not fit the current moment.

The US response may not be fully rational, but from the perspective of policy scholarship, it exemplifies ‘bounded rationality’ in which policy decisions embody the political and economic constraints of the moment.

WAYS FORWARD: OUR SUGGESTION

Coalitions can learn, core beliefs can be revised: so, we hope. We suggest that the conditions favoring revision are present. Namely, the US addiction crisis of 2018 is worse than that of 7 years earlier, when prescriptions began falling. A tide of anecdotes details suicides, health decline, broken health care relationships and—occasionally at least—overdose among abandoned pain patients who have resorted to the illicit market. We do not believe that anyone would approve sacrificing innocent lives in the service of addressing addiction.

We suggest that a way forward requires revisiting prior commitments, with renewed emphasis on systems of care for vulnerable populations. High-dose opioids have accrued historically to patients with complex combinations of physical and mental morbidity [137], embodying a legacy favoring prescriptions and procedures over multidisciplinary care. Payers and health systems could correct course to serve these patients more effectively, without demanding non-consensual dose reductions that, to date, lack any scientific evidence [68].

Restraint in starting opioids is desirable, particularly for typical musculoskeletal pain, where a 2018 trial found them no more effective than systematic non-opioid interventions, with a low-potency opioid in reserve [67]. This approach, however, cannot deliver the rapid prescribing reductions that insurers tout [84] and officials demand [138], due to an arithmetic problem. A small minority of ill people (10%) account for 70% of opioids prescribed [139]. Sparing these disabled patients the trauma of non-consensual dose reduction and protracted abstinence syndrome [140] limits the magnitude of achievable prescribing reductions. A more individualized paradigm, however, would honor a moral tradition that protects the vulnerable, rather than upending their lives as ‘opioid refugees’ [141].

Going forward, policy plans should engage all stakeholders, notably the people affected by pain and by addiction and their families. Their voices, more than ours, can help the US to chart a better path.

Declaration of interests

The views expressed in this paper are those of the authors and do not represent positions of the US Department of Veterans Affairs or any other federal or state agency. S.G. K. attests to ownership of stock in Abbot Pharmaceuticals and Merck, amounting to less than 3% of his assets, sold in calendar year 2017. No other consultancies, honoraria or relationship to industry exists now or in the past.

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References

1. Ahmad E., Rossen L., Spencer M., Warner M., Sutton P. Provisional drug overdose death counts. Atlanta, GA: National Center for Health Statistics; 2017. 2017. Available at: <https://www.cdc.gov/nchs/products/vsrr/drug-overdose-data.htm> (accessed 27 September 2017) (Archived at <http://www.webcitation.org/6xwRsSX8h> on 15 March 2018).
2. Baker D. W. History of the joint Commission’s pain standards: lessons for yoday’s prescription opioid epidemic. *JAMA* 2017; 317: 1117–8.
3. Van Zee A. The promotion and marketing of oxycontin: commercial triumph, public health tragedy. *Am J Public Health* 2009; 99: 221–7.
4. Hedegaard H., Warner M., Miniño A. M. Drug overdose deaths in the United States, 1999–2016. Atlanta, GA: Centers for Disease Control and Prevention. 2017. Available at: <https://www.cdc.gov/nchs/products/databriefs/db294.htm>

- (accessed 11 March 2018) (Archived at <http://www.webcitation.org/6xwQ9IPCB> on 15 March 2018).
5. Martins S. S., Sarvet A., Santaella-Tenorio J., Saha T., Grant B. F., Hasin D. S. Changes in US lifetime heroin use and heroin use disorder: prevalence from the 2001–2002 to 2012–2013 National Epidemiologic Survey on alcohol and related conditions. *JAMA Psychiatry* 2017; **74**: 445–55.
 6. Cairney P. *Understanding Public Policy: Theories and Issues*. Basingstoke, UK/New York: Palgrave Macmillan; 2012.
 7. Quality improvement guidelines for the treatment of acute pain and cancer pain. American Pain Society Quality of Care Committee. *JAMA* 1995; **274**: 1874–80.
 8. Leung P. T. M., Macdonald E. M., Stanbrook M. B., Dhalla I. A., Juurlink D. N. A 1980 letter on the risk of opioid addiction. *N Engl J Med* 2017; **376**: 2194–5.
 9. Porter J., Jick H. Addiction rare in patients treated with narcotics. *N Engl J Med* 1980; **302**: 123.
 10. Phillips D. M. JCAHO pain management standards are unveiled. *JAMA* 2000; **284**: 428–9.
 11. Higham S, Bernstein L. The drug industry's triumph over the DEA. Washington Post. Washington, DC. 2017. Available at: https://www.washingtonpost.com/graphics/2017/investigations/dea-drug-industry-congress/?utm_term=.67608ae43619 (accessed 1 November 2017) (Archived at <http://www.webcitation.org/70OeyJ6Dp> on 23 June 2018).
 12. Manchikanti L., Manchukonda R., Pampati V., Damron K. S. Evaluation of abuse of prescription and illicit drugs in chronic pain patients receiving short-acting (hydrocodone) or long-acting (methadone) opioids. *Pain Physician* 2005; **8**: 257–61.
 13. Banta-Green C. J., Merrill J. O., Doyle S. R., Boudreau D. M., Calsyn D. A. Opioid use behaviors, mental health and pain—development of a typology of chronic pain patients. *Drug Alcohol Depend* 2009; **104**: 34–42.
 14. Ballantyne J. C., Sullivan M. D., Kolodny A. Opioid dependence vs addiction: a distinction without a difference? *Arch Intern Med* 2012; **172**: 1342–3.
 15. Kirsh K. L., Whitcomb L. A., Donaghy K., Passik S. D. Abuse and addiction issues in medically ill patients with pain: attempts at clarification of terms and empirical study. *Clin J Pain* 2002; **18**: S52–S60.
 16. Pletcher M. J., Kertesz S. G., Sidney S., Kiefe C. I., Hulley S. B. Incidence and antecedents of nonmedical prescription opioid use in four US communities the coronary artery risk development in young adults (CARDIA) prospective cohort study. *Drug Alcohol Depend* 2006; **85**: 171–6.
 17. Kolodny A., Courtwright D. T., Hwang C. S., Kreiner P., Eadie J. L., Clark T. W. *et al.* The prescription opioid and heroin crisis: a public health approach to an epidemic of addiction. *Annu Rev Public Health* 2015; **36**: 559–74.
 18. Passik S. D. Issues in long-term opioid therapy: unmet needs, risks, and solutions. *Mayo Clin Proc* 2009; **84**: 593–601.
 19. True J. L., Jones B. D., Baumgartner F. R. Punctuated equilibrium theory. In: Sabatier P. A., editor. *Theories of the Policy Process*, 2nd edn. Cambridge: Cambridge University Press; 2007, pp. 155–88.
 20. Sabatier P. A., Jenkins-Smith H. C. *Policy Change and Learning: an Advocacy Coalition Approach*. Boulder, CO: Westview Press; 1993.
 21. Sabatier P. A. An advocacy coalition framework of policy change and the role of policy-oriented learning therein. *Pol Sci* 1988; **21**: 129–68.
 22. Saha T. D., Kerridge B. T., Goldstein R. B., Chou S. P., Zhang H., Jung J. *et al.* Nonmedical prescription opioid use and DSM-5 nonmedical prescription opioid use disorder in the United States. *J Clin Psychiatry* 2016; **77**: 772–80.
 23. Center for Behavioral Health Statistics and Quality. 2016 National Survey on Drug Use and Health: Detailed Tables. Rockville, MD: United States Department of Health and Human Services; 2017. Available at: [https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf](https://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015/NSDUH-DetTabs-2015.pdf) (accessed 7 January 2017) (Archived at <http://www.webcitation.org/6yAtLFfhe> on 25 March 2018).
 24. Muhuri P. K., Gfroerer J. C., Davies M. C. Associations of non-medical pain reliever use and initiation of heroin use in the United States. Washington, DC: Center for Behavioral Health Statistics and Quality; 2013. Available at: <https://archive.samhsa.gov/data/2k13/DataReview/DR006/nonmedical-pain-reliever-use-2013.pdf> (accessed 23 December 2017) (Archived at <http://www.webcitation.org/6yAtb2oIV> on 25 March 2018).
 25. Kolodny A., Frieden T. R. Ten steps the federal government should take now to reverse the opioid addiction epidemic. *JAMA* 2017; **318**: 1537–8.
 26. Lipari R. N., Hughes A. How people obtain the prescription pain relievers they misuse: Center for Behavioral Health Statistics and Quality. Substance Abuse and Mental Health Services Administration; 2017. Available at: https://www.samhsa.gov/data/sites/default/files/report_2686/ShortReport-2686.html (accessed 1 November 2017) (Archived at <http://www.webcitation.org/70OfMuJp5> on 23 June 2018).
 27. Carise D., Dugosh K. L., McLellan A. T., Camilleri A., Woody G. E., Lynch K. G. Prescription OxyContin abuse among patients entering addiction treatment. *Am J Psychiatry* 2007; **164**: 1750–6.
 28. Cicero T. J., Ellis M. S., Kasper Z. A. Increased use of heroin as an initiating opioid of abuse. *Addict Behav* 2017; **74**: 63–6.
 29. Cicero T. J., Ellis M. S. Understanding the demand side of the prescription opioid epidemic: does the initial source of opioids matter? *Drug Alcohol Depend* 2017; **173**: S4–S10.
 30. Centers for Disease Control and Prevention (CDC). US prescribing rate maps. Atlanta, GA; 2017. Available at: <https://www.cdc.gov/drugoverdose/maps/rxrate-maps.html> (accessed 2 January 2018) (Archived at <http://www.webcitation.org/6xwSKDWYN> on 23 June 2018).
 31. CDC National Center for Injury Prevention and Control. Annual surveillance report of drug-reported risks and outcomes. Atlanta, GA: Centers for Disease Control and Prevention; 2017. Available at: <https://www.cdc.gov/drugoverdose/pdf/pubs/2017-cdc-drug-surveillance-report.pdf> (accessed 23 December 2017) (Archived at <http://www.webcitation.org/6yAtooHuM> on 15 March 2018).
 32. Dart R. C., Severtson S. G., Bucher-Bartelson B. Trends in opioid analgesic abuse and mortality in the United States. *N Engl J Med* 2015; **372**: 1573–4.
 33. Office of Applied Studies Substance Abuse and Mental Health Services Administration. Results from the 2014 National Survey on drug use and health: detailed tables. Rockville, MD: United States Department of Health and Human Services; 2015. Available at: <http://www.samhsa.gov/data/sites/default/files/NSDUH-DetTabs2014/NSDUH-DetTabs2014.pdf> (accessed 2 October 2016)

- (Archived at <http://www.webcitation.org/700fnr1Pe> on 23 June 2018).
34. Kertesz S. G. Turning the tide or riptide? The changing opioid epidemic. *Subst Abuse* 2017; **38**: 3–8.
 35. Dowell D., Noonan R. K., Houry D. Underlying factors in drug overdose deaths. *JAMA* 2017; **318**: 2295–6.
 36. Schuchat A., Houry D., Guy G. P. Jr. New data on opioid use and prescribing in the United States. *JAMA* 2017; **318**: 425–6.
 37. Compton W. M., Jones C. M., Baldwin G. T. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med* 2016; **374**: 154–63.
 38. Gladden R. M., Martinez P., Seth P. Fentanyl law enforcement submissions and increases in synthetic opioid-involved overdose deaths—27 states, 2013–2014. *Morb Mortal Wkly Rep* 2016; **65**: 837–43.
 39. Bharel M. An assessment of opioid-related deaths in Massachusetts (2013–2014). Boston: Massachusetts Department of Public Health; 2016. Available at: <http://www.mass.gov/eohhs/gov/departments/dph/stop-addiction/chapter-55-overdose-assessment.html> (accessed 2 October 2016) (Archived at <http://www.webcitation.org/700gEBb6f> on 23 June 2018).
 40. Hannah H. A., Arambula K., Ereman R., Harris D., Torres A., Willis M. Using local toxicology data for drug overdose mortality surveillance. *Online J Public Health Inform* 2017; **9**: e143.
 41. Darke S. Heroin overdose. *Addiction* 2016; **111**: 2060–3.
 42. Frieden T. R., Houry D. Reducing the risks of relief—the CDC opioid-prescribing guideline. *N Engl J Med* 2016; **374**: 1501–4.
 43. Chou R., Turner J. A., Devine E. B., Hansen R. N., Sullivan S. D., Blazina I. *et al.* The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health pathways to prevention workshop. *Ann Intern Med* 2015; **162**: 276–86.
 44. Tayeb B. O., Barreiro A. E., Bradshaw Y. S., Chui K. K., Carr D. B. Durations of opioid, nonopioid drug, and behavioral clinical trials for chronic pain: adequate or inadequate? *Pain Med* 2016; **17**: 2036–46.
 45. Ballantyne J. C., Sullivan M. D. Intensity of chronic pain—the wrong metric? *N Engl J Med* 2015; **373**: 2098–9.
 46. Bohnert A. S. B., Valenstein M., Bair M. J., Ganoczy D., McCarthy J. E., Ilgen M. A. *et al.* Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA* 2011; **305**: 1315–21.
 47. Kolodny A. Better late than never: time to up-schedule hydrocodone combination products. *Pain Med* 2013; **14**: 1627–8.
 48. Shah A., Hayes C. J., Martin B. C. Characteristics of initial prescription episodes and likelihood of long-term opioid use—United States, 2006–2015. *Morb Mortal Wkly Rep* 2017; **66**: 265–9.
 49. Mundkur M. L., Gordon A. J., Kertesz S. G. Will strict limits on opioid prescription duration prevent addiction? Advocating for evidence-based policymaking. *Subst Abuse* 2017; **38**: 237–8.
 50. Frostenson S. The risk of a single 5-day opioid prescription, in one chart: limiting the length of opioid prescriptions isn't inhumane. It could save lives. 2017. Available at: <https://www.vox.com/2017/3/18/14954626/one-simple-way-to-curb-opioid-overuse-prescribe-them-for-3-days-or-less> (accessed 11 May 2017) (Archived at <http://www.webcitation.org/6xwSksXej> on 23 June 2018).
 51. Bromwich J. E. Vermont governor proposes limits on painkiller prescriptions. New York Times New York: Institution; October 19, 2016. Available at: <https://www.nytimes.com/2016/10/20/us/vermont-governor-proposes-limits-on-painkiller-prescriptions.html?mcubz=0&r=0> (accessed 23 June 2018).
 52. Lembke A. *Drug dealer, MD: How Doctors Were Duped, Patients Got Hooked, and Why It's So Hard to Stop*. Baltimore: Johns Hopkins University Press; 2016.
 53. Becker W. C., Fiellin D. A. Limited evidence, faulty reasoning, and potential for a global opioid crisis. *BMJ* 2017; **358**: j3115.
 54. Kolodny A. Crooked doctors are not fueling the opioid epidemic. New York Times. 5 October 2016. Available at: <http://www.nytimes.com/roomfordebate/2016/02/17/prosecuting-doctors-in-prescription-drug-overdose-deaths/crooked-doctors-are-not-fueling-the-opioid-epidemic> (accessed 2 October 2016) (Archived at <http://www.webcitation.org/700gmgHgI> on 23 June 2018).
 55. Christie C., Baker C., Cooper R., Kennedy P. J., Madras B., Bondi P. The President's commission on combating drug addiction and the opioid crisis. Washington, DC: The White House; 2017. Available at: <https://www.whitehouse.gov/oncdp/presidents-commission/> (accessed 22 June 2018) (Archived at <http://www.webcitation.org/700gzyAnG> on 23 June 2018).
 56. Coalition of Sixteen Stakeholder Organizations. Stakeholders' challenges and red flag warning signs related to prescribing and dispensing controlled substances. Mount Prospect: National Association of Boards of Pharmacy; 2015. Available at: <https://nabp.pharmacy/wp-content/uploads/2016/07/Red-Flags-Controlled-Substances-03-2015.pdf> (accessed 15 June 2018) (Archived at <http://www.webcitation.org/6yAu8VXR6> 25 March 2018).
 57. Federation of State Medical Boards. Guidelines for the chronic use of opioid analgesics 2017. Available at: https://www.fsmb.org/Media/Default/PDF/Advocacy/Opioid-Guidelines-As-Adopted-April-2017_FINAL.pdf (accessed 25 December 2017) (Archived at <http://www.webcitation.org/6yAu5Swch> on 25 March 2018).
 58. Alpert A., Powell D., Pacula R. Supply-side drug policy in the presence of substitutes: evidence from the introduction of abuse-deterrent opioids (Working Paper 23031). National Bureau of Economic Research 2017. Available at: <http://www.nber.org/papers/w23031> (accessed 23 June 2018) (Archived at <http://www.webcitation.org/700hacSIK> on 23 June 2018).
 59. Franklin G. M., Mai J., Turner J., Sullivan M., Wickizer T., Fulton-Kehoe D. Bending the prescription opioid dosing and mortality curves: impact of the Washington state opioid dosing guideline. *Am J Ind Med* 2012; **55**: 325–31.
 60. Paulozzi L. J., Jones C. M., Mack K. A., Rudd R. A. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. *Morb Mortal Wkly Rep* 2011; **60**: 1487–92.
 61. U.S. Drug Enforcement Administration Office of Diversion Control. National Forensic Laboratory Information System: year 2016 annual report. July 2016. Springfield, VA: U S Drug Enforcement Administration; 2016. Available at: <https://www.nflis.deadiversion.usdoj.gov/DesktopModules/ReportDownloads/Reports/NFLIS2016AR.pdf> (accessed 15 October 2017) (Archived at <http://www.webcitation.org/6yAuCr4GK> on 25 March 2018).

62. Dowell D., Haegerich T. M., Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *Morb Mortal Wkly Rep* 2016; **65**: 1–49.
63. Ziegler S., Schatman M. Pain management, prescription opioid mortality, and the CDC: is the devil in the data? *J Pain Res* 2017; **24**: 489–95.
64. Gurman S. Feds employ data-driven early warning system in opioid fight 2018. Available at: https://www.washingtonpost.com/national/armed-with-new-data-officials-target-drug-dealing-doctors/2018/01/01/75033c6c-ef01-11e7-95e3-eff284e71c8d_story.html?utm_term=.53a4b7316fb2 (accessed 1 January 2018) (Archived at <http://www.webcitation.org/6xwTSh83B> on 15 March 2018).
65. Centers for Medicare and Medicaid Services. Advance notice of methodological changes for calendar year (CY) 2018 for Medicare advantage (MA) capitation rates, part C and part D payment policies and 2018 call letter. Washington, DC: United States Department of Health and Human Services; 2017. Available at: <https://www.cms.gov/Medicare/Health-Plans/MedicareAdvtgSpecRateStats/Downloads/Advance2018.pdf> (accessed 21 February 2017).
66. CVS Health. CVS health responds to Nation's opioid crisis 2017. Available at: <https://cvshhealth.com/thought-leadership/cvs-health-enterprise-response-opioid-epidemic/cvs-health-responds-to-nations-opioid-crisis> (accessed 23 October 2017) (Archived at <http://www.webcitation.org/6xwTsvy06> 15 March 2018).
67. Krebs E. E., Gravelly A., Nugent S., Jensen A. C., DeRonne B., Goldsmith E. S. *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. *JAMA* 2018; **319**: 872–82.
68. Frank J. W., Lovejoy T. I., Becker W. C., Morasco B. J., Koenig C. J., Hoffecker L. *et al.* Patient outcomes in dose reduction or discontinuation of long-term opioid therapy: a systematic review. *Ann Intern Med* 2017; **167**: 181–91.
69. Weiss R. D., Potter J. S., Fiellin D. A., Byrne M., Connery H. S., Dickinson W. *et al.* Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence: a 2-phase randomized controlled trial. *Arch Gen Psychiatry* 2011; **68**: 1238–46.
70. Wilson M. C., Hayward R. S., Tunis S. R., Bass E. B., Guyatt G. Users' guides to the medical literature. VIII. How to use clinical practice guidelines. B. What are the recommendations and will they help you in caring for your patients? The evidence-based medicine working group. *JAMA* 1995; **274**: 1630–2.
71. Bucher H. C., Weinbacher M., Gyr K. Influence of method of reporting study results on decision of physicians to prescribe drugs to lower cholesterol concentration. *BMJ* 1994; **309**: 761–4.
72. Gomes T., Mamdani M. M., Dhalla I. A., Paterson J. M., Juurlink D. N. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med* 2011; **171**: 686–91.
73. Bohnert A. S., Logan J. E., Ganoczy D., Dowell D. A detailed exploration into the association of prescribed opioid dosage and overdose deaths among patients with chronic pain. *Med Care* 2016; **54**: 435–41.
74. Park T. W., Saitz R., Ganoczy D., Ilgen M. A., Bohnert A. S. Benzodiazepine prescribing patterns and deaths from drug overdose among US veterans receiving opioid analgesics: case-cohort study. *BMJ* 2015; **350**: h2698.
75. Oliva E. M., Bowe T., Tavakoli S., Martins S., Lewis E. T., Paik M. *et al.* Development and applications of the Veterans Health Administration's stratification tool for opioid risk mitigation (STORM) to improve opioid safety and prevent overdose and suicide. *Psychol Serv* 2017; **14**: 34–49.
76. Kobus A. M., Smith D. H., Morasco B. J., Johnson E. S., Yang X., Petrik A. F. *et al.* Correlates of higher-dose opioid medication use for low back pain in primary care. *J Pain* 2012; **13**: 1131–8.
77. Glanz J. M., Narwaney K. J., Mueller S. R., Gardner E. M., Calcaterra S. L., Xu S. *et al.* Prediction model for two-year risk of opioid overdose among patients prescribed chronic opioid therapy. *J Gen Intern Med* 2018; <https://doi.org/10.1007/s11606-017-4288-3>.
78. Opioid Guideline Workgroup. Observations presented to the National Center for Injury Prevention and Control's Board of Scientific Counselors. Atlanta: Centers for Disease Control and Prevention; 2016. Available at: https://www.cdc.gov/injury/pdfs/bsc/bsc_summary.pdf (accessed 25 December 2017) (Archived at <http://www.webcitation.org/6yAuNx8SL> on 25 March 2018).
79. Zezima K. With drug overdoses soaring, states limit the length of painkiller prescriptions. Washington Post. Washington, DC: Institution. 2017. Available at: https://www.washingtonpost.com/politics/with-drug-overdoses-soaring-states-limit-the-length-of-painkiller-prescriptions/2017/08/09/4d5d7e0c-7d0f-11e7-83c7-5bd5460f0d7e_story.html?utm_term=.da2261f1c0cf (accessed 7 November 2017).
80. National Conference of State Legislatures. Prescribing policies: states confront opioid overdose epidemic. Washington, DC; 2017. Available at: http://www.ncsl.org/Portals/1/Documents/Health/prescribingOpioids_final01-web.pdf (accessed 25 December 2017) (Archived at <http://www.webcitation.org/6yAuSjSSQ> on 25 March 2018).
81. St. Amour M. Central Maine patients fear weaning off opioids as they struggle with chronic pain 2017. Available at: <http://www.centralmaine.com/2017/01/21/central-maine-patients-fear-medication-weaning-as-they-struggle-with-chronic-pain/> (accessed 4 May 2017) (Archived at <http://www.webcitation.org/6xwT9NYXr> on 15 March 2018).
82. Kertesz S. G., Gordon A. J. Strict limits on opioid prescribing risk the 'inhumane treatment' of pain patients: STATNews; 2017. Available at: <https://www.statnews.com/2017/02/24/opioids-prescribing-limits-pain-patients/> (accessed 11 May 2017) (Archived at <http://www.webcitation.org/6xwTcd86i> on 15 March 2018).
83. Salter J. Express Scripts to limit opioids; doctors concerned. *US News and World Report*. 16 August 2017. Available at: <https://www.usnews.com/news/us/articles/2017-08-16/express-scripts-to-limit-opioids-doctors-concerned> (accessed 23 October 2017).
84. Cigna. Cigna's partnership with physicians successfully reduces opioid use by 25 percent—one year ahead of goal. Bloomfield, 2018. Available at: <https://www.cigna.com/newsroom/news-releases/2018/cignas-partnership-with-physicians-successfully-reduces-opioid-use-by-25-percent-one-year-ahead-of-goal> (accessed 13 June 2018) (Archived at <http://www.webcitation.org/70P1gg08K> on 23 June 2018).
85. National Committee for Quality Assurance. NCQA updates quality measures for HEDIS 2018. Washington, DC: National Committee for Quality Assurance; 2017. Available at: <http://www.ncqa.org/newsroom/details/ncqa-updates-quality-measures-for-hedis-2018?ArtMID=>

- 11280&ArticleID=85&tabid=2659 (accessed 23 June 2018) (Archived at <http://www.webcitation.org/70P29le5v> on 23 June 2018).
86. Kertesz SG. An opioid quality metric based on dose alone? 80 Professionals Respond to NCQA. Medium.com 2017. Available at: <https://medium.com/@StefanKertesz/an-opioid-quality-metric-based-on-dose-alone-80-professionals-respond-to-ncqa-6f9fbaa2338> (accessed 10 June 2017) (Archived at <http://www.webcitation.org/6xwUewVV6> on 15 March 2018).
 87. Opioid Therapy for Chronic Pain Work Group. VA/DoD clinical practice guideline for opioid therapy for chronic pain. Washington, DC: Department of Veterans Affairs Department of Defense; 2017. Available at: <https://www.healthquality.va.gov/guidelines/pain/cot/> (accessed 10 June 2017) (Archived at <http://www.webcitation.org/70NovuNBH> on 23 June 2018).
 88. Crow D. FDA plans to curb prescriptions to fight opioid epidemic. Financial Times Washington; December 11, 2017. Available at: <https://www.ft.com/content/3685b678-dc68-11e7-a039-c64b1c09b482> (accessed 14 December 2017).
 89. Facher L. New opioid bill would impose sweeping limits on some prescriptions, boost funding: STATNews; 27 February 2018. Available at: <https://www.statnews.com/2018/02/27/cara-opioid-crisis-bill/> (accessed 11 March 2018) (Archived at <http://www.webcitation.org/70P5tFKuY> on 24 June 2018).
 90. Office for Diversion Control. Pharmacist's manual: an informational outline of the controlled substances act. Washington, DC: United States Drug Enforcement Agency; 2010. Available at: https://www.deadiversion.usdoj.gov/pubs/manuals/pharm2/pharm_manual.pdf (accessed 25 December 2017) (Archived at <http://www.webcitation.org/6yAuhvZp6> on 25 March 2018).
 91. United States Drug Enforcement Agency. State prescription drug monitoring programs: questions & answers. Washington, DC. 2016. Available at: https://www.deadiversion.usdoj.gov/faq/rx_monitor.htm - 2 (accessed 23 June 2018) (Archived at <http://www.webcitation.org/70P2mVvXW> on 24 June 2018).
 92. Grasso M. A., Grasso C. T., Jerrard D. A. Prescriptions written for opioid pain medication in the veterans health administration between 2000 and 2016. *J Addict Med* 2017; 11: 483–8.
 93. Kertesz S. G., Satel S. S. Some people still need opioids 2017. Available at: http://www.slate.com/articles/health_and_science/medical_examiner/2017/08/cutting_down_on_opioids_has_made_life_miserable_for_chronic_pain_patients.html (accessed 15 March 2018) (Archived at <http://www.webcitation.org/6xwVY4tJ6> on 15 March 2018).
 94. Weeks W. B. Hailey. *JAMA* 2016; 316: 1975–6.
 95. Hawryluk M. Opioid crisis: pain patients pushed to the brink. Bend Bulletin 2017. Available at: <http://www.bendbulletin.com/topics/5342867-151/opioid-crisis-pain-patients-pushed-to-the-brink> (accessed 28 August 2017) (Archived at <http://www.webcitation.org/70P5eRMke> on 14 June 2018).
 96. Szalavitz M. Cracking down on opioids hurts people with chronic pain. 2017. Available at: https://tonic.vice.com/en_us/article/8x5m7g/opioid-crackdown-chronic-pain-patients-suicide (accessed 7 November 2017) (Archived at <http://www.webcitation.org/6xwVmleMx> on 15 March 2018).
 97. Haney B. The personal side of pain: Meredith Lawrence. Television Report: KLAS-TV 6 November 2017. Available at: <http://www.lasvegasnow.com/news/the-personal-side-of-pain-meredith-lawrence/852306426> (accessed 7 November 2017) (Archived at <http://www.webcitation.org/70P4lonqU> on 24 June 2018).
 98. Kline T. #OpioidCrisis: pain related suicides associated with forced tapers. 2018. Available at: <https://medium.com/@ThomasKlineMD/opioidcrisis-pain-related-suicides-associated-with-forced-tapers-c68c79ecf84d> (accessed 23 June 2018) (Archived at <http://www.webcitation.org/70P5M0mfX> on 24 June 2018).
 99. Kertesz S. G., Satel S. L., Gordon A. J. Opioid prescription control: when the corrective goes too far: health affairs; 2018. Available at: <https://www.healthaffairs.org/action/showDoPubSecure?doi=10.1377%2Fhblog20180117.832392&format=full&> (accessed 2 June 2018) (Archived at <http://www.webcitation.org/70P6BtyHO> on 24 June 2018).
 100. Vaughn J. 2016 Crime review: heroin deaths rise as prescription policies go into effect. The Sentinel 12 February 2017. Available at: http://cumberlink.com/news/local/closer_look/digital_data/review-heroin-deaths-rise-as-prescription-policies-go-into-effect/article_fcde5d45-676a-54d4-873e-aac9a79b2cb0.html (accessed 28 August 2017) (Archived at <http://www.webcitation.org/700jPVui2> on 23 June 2018).
 101. Fentanyl: the next wave of the opioid crisis (testimony of Debra Houry, Centers for Disease Control and Prevention). Energy and Commerce Committee, Oversight and Investigations Subcommittee. March 21, 2017. Available at: <https://energycommerce.house.gov/hearings/fentanyl-next-wave-opioid-crisis-2/> (accessed 23 June 2018) (Archived at <http://www.webcitation.org/70P6Olw2k> on 24 June 2018).
 102. Beletsky L., Davis C. S. Today's fentanyl crisis: Prohibition's iron law, revisited. *Int J Drug Policy* 2017; 46: 156–9.
 103. Schuchat A., Houry D., Guy G. P. Jr. New data on opioid use and prescribing in the United States. *JAMA* 2017; 318: 425–6.
 104. Dowell D., Zhang K., Noonan R. K., Hockenberry J. M. Mandatory provider review and pain clinic Laws reduce the amounts of opioids prescribed and overdose death rates. *Health Aff* 2016; 35: 1876–83.
 105. National Center for Health Statistics. Percent of drug poisoning deaths that mention the type of drug (s) involved, by state: 2013–2014. Atlanta: Centers for Disease Control and Prevention; 2014. Available at: http://www.cdc.gov/nchs/data/health_policy/unspecified_drugs_by_state_2013-2014.pdf (accessed 17 September 2016) (Archived at <http://www.webcitation.org/6yAvK6gzX> on 25 March 2018 (accessed 17 September 2016).
 106. Patrick S. W., Fry C. E., Jones T. F., Buntin M. B. Implementation of prescription drug monitoring programs associated with reductions in opioid-related death rates. *Health Aff* 2016; 35: 1324–32.
 107. Nam Y. H., Shea D. G., Shi Y., Moran J. R. State prescription drug monitoring programs and fatal drug overdoses. *Am J Manag Care* 2017; 23: 297–303.
 108. Pardo B. Do more robust prescription drug monitoring programs reduce prescription opioid overdose? *Addiction* 2017; 112: 1773–83.
 109. Lin H. C., Wang Z., Boyd C., Simoni-Wastila L., Buu A. Associations between statewide prescription drug monitoring program (PDMP) requirement and physician patterns of prescribing opioid analgesics for patients with non-cancer chronic pain. *Addict Behav* 2018; 76: 348–54.
 110. Lin D. H., Lucas E., Murimi I. B., Jackson K., Baier M., Frattaroli S. *et al.* Physician attitudes and experiences with Maryland's prescription drug monitoring program (PDMP). *Addiction* 2017; 112: 311–9.

111. Donabedian A. Evaluating the quality of medical care. *Milbank Mem Fund Q* 1996; **83**: 166–203.
112. Case A, Deaton A. Mortality and morbidity in the 21st century. Washington, DC: Brookings Institution; 2017. Available at: <https://www.brookings.edu/bpea-articles/mortality-and-morbidity-in-the-21st-century/> (accessed 25 March 2018) (Archived at <http://www.webcitation.org/6yAsij9uq> on 25 March 2018).
113. Quinones S. *Dreamland: the True Tale of America's Opiate Epidemic, Paperback edn*. New York: Bloomsbury Press; 2016.
114. Mennis J., Stahler G. J., Mason M. J. Risky substance use environments and addiction: a new frontier for environmental justice research. *Int J Environ Res Public Health* 2016; **13**: 607.
115. Dasgupta N., Beletsky L., Ciccarone D. Opioid crisis: no easy fix to its social and economic determinants. *Am J Public Health* 2017; **108**: e1–e5.
116. McLellan A. T., Carise D., Kleber H. D. Can the national addiction treatment infrastructure support the public's demand for quality care? *J Subst Abuse Treat* 2003; **25**: 117–21.
117. Wood E., Samet J. H., Volkow N. D. Physician education in addiction medicine. *JAMA* 2013; **310**: 1673–4.
118. Substance Abuse and Mental Health Services Administration. National Survey of substance abuse treatment services (N-SSATS): 2016 data on substance abuse treatment facilities. Rockville, MD 2017. Available at: https://www.dasis.samhsa.gov/dasis2/nssats/2016_nssats_rpt.pdf (accessed 25 March 2018) (Archived at <http://www.webcitation.org/6yAvn2LGO> on 25 March 2018).
119. Gordon A. J., Lo-Ciganic W. H., Cochran G., Gellad W. F., Cathers T., Kelley D. *et al.* Patterns and quality of buprenorphine opioid agonist treatment in a large Medicaid program. *J Addict Med* 2015; **9**: 470–7.
120. Federal Register Final rule of the Paul Wellstone and Pete Domenici mental health parity and addiction equity act of 2008. Final rules. *Fed Regist* 2013; **78**: 68239–96.
121. Burns R. M., Pacula R. L., Bauhoff S., Gordon A. J., Hendrikson H., Leslie D. L. *et al.* Policies related to opioid agonist therapy for opioid use disorders: the evolution of state policies from 2004 to 2013. *Subst Abuse* 2016; **37**: 63–9.
122. National Association of State Alcohol and Drug Abuse Directors. FY 2018 Appropriations August 2017. Update 2008. Available at: <http://nasadad.org/wp-content/uploads/2017/08/FY-2018-House-Approps-August-2017.pdf> (accessed 29 October 2017) (Archived at <http://www.webcitation.org/6yAvPGMAj> on 25 March 2018).
123. Goodnough A. \$45 billion to fight opioid abuse? That's much too little, experts say. *New York Times* 30 June 2017. Available at: https://www.nytimes.com/2017/06/30/health/drug-treatment-opioid-abuse-heroin-medicaid.html?_r=0 (accessed 22 October 2017).
124. Oliva E. M., Christopher M. L., Wells D., Bounthavong M., Harvey M., Himstreet J. *et al.* Opioid overdose education and naloxone distribution: development of the Veterans Health Administration's national program. *J Am Pharm Assoc (2003)* 2017; **57**: S168–S179; e4.
125. Walley A. Y., Xuan Z., Hackman H. H., Quinn E., Doe-Simkins M., Sorensen-Alawad A. *et al.* Opioid overdose rates and implementation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. *BMJ* 2013; **346**: f174.
126. Tierney M., Finnell D. S., Naegle M. A., LaBelle C., Gordon A. J. Advanced practice nurses: increasing access to opioid treatment by expanding the pool of qualified buprenorphine prescribers. *Subst Abuse* 2015; **36**: 389–92.
127. Comprehensive addiction and recovery act of 2016. P. L. no: 114–198 §130 STAT 695.
128. Lopez G. I looked for a state that's taken the opioid epidemic seriously. I found Vermont: *Vox.com*. 2017. Available at: <https://www.vox.com/policy-and-politics/2017/10/30/16339672/opioid-epidemic-vermont-hub-spoke> (accessed 25 March 2018) (Archived at <http://www.webcitation.org/6yAvbRCYi> on 25 March 2018).
129. McGinty E., Pescosolido B., Kennedy-Hendricks A., Barry C. L. Communication strategies to counter stigma and improve mental illness and substance use disorder policy. *Psychiatr Serv* 2018; **69**: 136–46.
130. US Department of Health and Human Services (HHS) OotSG. Facing addiction in America: the surgeon General's report on alcohol, drugs and health. Washington, DC: Department of Health And Human Services; 2016. Available at: <https://addiction.surgeongeneral.gov/> (accessed 25 March 2018) (Archived at <http://www.webcitation.org/6xwWmzVWm> 15 March 2018).
131. Friedmann P. D., Andrews C. M., Humphreys K. How ACA repeal would worsen the opioid epidemic. *N Engl J Med* 2017; **376**: e16.
132. Courtwright D. T. *Dark Paradise: a History of Opiate Addiction in America*. Cambridge, MA: Harvard University Press; 2001.
133. Paulozzi L. J., Kilbourne E. M., Shah N. G., Nolte K. B., Desai H. A., Landen M. G. *et al.* A history of being prescribed controlled substances and risk of drug overdose death. *Pain Med* 2012; **13**: 87–95.
134. Paulozzi L. J., Budnitz D. S., Xi Y. Increasing deaths from opioid analgesics in the United States. *Pharmacoepidemiol Drug Saf* 2006; **15**: 618–27.
135. Lopez G. The opioid epidemic, explained: *Vox.com*: 2017. Available at: <https://www.vox.com/science-and-health/2017/8/3/16079772/opioid-epidemic-drug-overdoses> (accessed 3 August 2017) (Archived at <http://www.webcitation.org/6xwWuvHh2> on 15 March 2018).
136. Manhapra A., Arias A. J., Ballantyne J. C. The conundrum of opioid tapering in long-term opioid therapy for chronic pain: a commentary. *Subst Abuse* 2017; **1**–10; <https://doi.org/10.1080/08897077.2017.1381663>.
137. Morasco B. J., Duckart J. P., Carr T. P., Deyo R. A., Dobscha S. K. Clinical characteristics of veterans prescribed high doses of opioid medications for chronic non-cancer pain. *Pain* 2010; **151**: 625–32.
138. Haberman M., Goodnough A., Seelye K. Q. Trump offers tough talk but few details in unveiling plan to combat opioids. *New York Times*, 19 March 2018. Available at: <https://www.nytimes.com/2018/03/19/us/politics/trump-new-hampshire-opioid-plan.html> (accessed 22 June 2018) (Archived at <http://www.webcitation.org/700ilk8ve> on 23 June 2018).
139. Sun E. C., Jena A. B. Distribution of prescription opioid use among privately insured adults without cancer: United States, 2001 to 2013. *Ann Intern Med* 2017; **167**: 684–6.
140. Shurman J., Koob G. F., Gutstein H. B. Opioids, pain, the brain, and hyperkatifeia: a framework for the rational use of opioids for pain. *Pain Med* 2010; **11**: 1092–8.
141. Gladstone B. The pain refugees: the forgotten victims of America's opioid crisis. *Harper's Magazine* 1 April 2018: 53–61.