

# Opioids, Addiction and Pain: Message Clarity to Prevent Harm and Save Lives

## Briefing for Policy Leaders

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### Key Points:

1. Excessive opioid prescription is a problem and doctors should undertake opioid prescribing as a **solemn** and **serious** responsibility, limiting prescription to persons who require it based on risk & benefit.
2. Well-intended statements by officials laying primary responsibility on physicians to curb the opioid epidemic, coupled with widespread misinterpretation of the recent CDC Guideline, have caused a **pendulum swing** in the care of patients with chronic pain who had previously been stable and functional on opioids.
3. Widespread involuntary opioid dose tapering and termination have caused loss of function and even death in some published reports, in anecdotal observation, and in some unpublished analyses.
4. The pendulum swing reflects a misinterpretation of the CDC Guideline as requiring involuntary tapering or termination, a practice the Guideline did not endorse.
5. Public leaders should explicitly affirm physicians' responsibility to **treat each patient as an individual in decisions regarding pain**, rather than seeing each opioid prescription as a **risk to be eliminated**.
6. Public leaders should challenge the belief that we can **solve the opioid epidemic in the doctor's office alone**, given that most of this epidemic is now mainly attributable to illicitly manufactured and diverted opioids. Most illicit opioid use is not directly tied to doctor's care. Ill-conceived changes to care by doctors can spur illicit consumption.
7. Public leaders must **differentiate clinical addiction from physical dependence**. Not doing so spurs resistance to evidence-based treatment for addiction and harms pain patients.

### Case Examples:

*From a report provided to leaders of a large integrated care system, by a doctor.*

"The situation of chaotic and involuntary tapers was brought home to me by a patient who **shot himself in our parking lot**. I was called to attend and cared for him in our clinic lobby after security relieved him of his gun (he lived). Chart review showed that he had been subject to an erratic and variable taper of long-acting opioids, absent a documented plan, personal counseling about what was happening to him, or even an evaluation that a taper was warranted. His primary care provider numbers among several who had sworn off prescribing opioids and said, incorrectly to most staff, **"the CDC" wants all opioid prescriptions to stop**. She is not the only one in her unit who has that understanding.

*From one expert physician who has advised key federal agencies on opioids and pain:*

"It seems like I'm being called weekly by the patient advocate office expressing their concerns about specific patients and how their pain management, especially their opioids are being handled. In most of these cases (two in the last week), the patient was "doing well" on opioids and working a steady job. The decision to taper to off was made unilaterally and led one patient to set up an appointment with the Chief of Staff to express how poorly the communication was handled. He was irate and in my opinion...justifiably so. In most of the cases referred to me, it seems that the balance towards benefits outweighs the risks. I think we need a validated clinical tool that can help PCPs with this "risk-benefit calculation." This is an understatement, but the current environment is **very concerning** to me."

## Core Scientific Concepts:

1. Overprescribing of opioids for pain has been and likely still remains a major upstream driver for today's opioid epidemic.<sup>1</sup>
2. Opioid prescriptions are in 4-year decline,<sup>2</sup> as is misuse of prescription pain relievers<sup>3</sup>, while opioid overdoses are rising quickly, nationally and locally, driven by illicit fentanyl and heroin.<sup>4,5</sup> In databases where mutually exclusive categories of opioid overdose are designated (Massachusetts, Alabama) overdose deaths related solely to potentially prescribed opioids account for 8-15% of overdoses.<sup>5,6</sup>
3. This does not mean that prescribing is no longer relevant to the epidemic. However, it appears likely that much misuse and addiction is more concentrated in a group of users with more intractable problems, a phenomenon termed "hardening" of the epidemic. The degree to which these individuals rely on doctor's offices, pill diversion versus heroin, is not clear. If identified in doctor's offices, the next step in their care is of cardinal importance. Merely "cutting them off" is frankly dangerous.
4. Addiction's causes, as noted in "Facing Addiction", reflect multiple environmental, social, familial characteristics and age. It is (almost) never due to mere exposure to a drug (the vector-born theory of addiction). The vector theory reinforces stigma and fear for patients with addiction, and for patients with pain who receive a prescription.
5. There are risks to how leaders discuss physician responsibility, because improper communication has fueled three outcomes no one should want:
  - a. A physician stampede or "Scorched Earth" tactic: Widespread involuntary and abrupt tapers of patients who die, commit suicide, or overdose (examples attached, including one from a CDC Guideline peer reviewer). Death of a physician's sister was reported in JAMA.<sup>7</sup>
  - b. Progressive loss of function for patients who have chronic pain, are employed and maintaining family roles, and who are taken off involuntarily (abruptly or gradually), and deteriorate.
  - c. A physician-centered policy tracks doctors as "easy targets" but misses most opioid users. That shortchanges resources to fight **today's** epidemic (i.e. "generals fighting the last war")
6. Terminating opioids in a patient with identified addiction, absent clearly **accessible** treatment, puts the patient's life at risk. It is like terminating any medical treatment with rebound potential (i.e. beta blockers). Physicians often do not perceive that they are accountable for what happens to their patient, and that should change.
7. There remains a pressing problem in the lack of access to medication treatment for opioid use disorder across most of the country. Just 19% of persons with opioid use disorder received treatment in 2015.<sup>8</sup> Buprenorphine prescribing growth has slowed precipitously over the last 3 years.<sup>9</sup>
8. There is excellent language that can communicate clear understanding of the physician role, without encouraging views that precipitate inhumane care, stigmatization of patients with addiction, or harm to patients with pain.

## Well-Intended but Irresponsible Public Statements:

### Opioid pills for pain are "just as addictive as heroin"<sup>10</sup>

Problem: The CDC Guideline reports the incidence of new-onset opioid use disorder after receiving chronic opioids for care of pain ranges from 0.7% at 36 MME to 6.1% (at 120 MME),<sup>11</sup> which seems to contradict the CDC Director's phrase. No one knows the risk of new addiction after chronic heroin, but the phrase implies that persons receiving opioids for pain are like heroin users. It's pejorative in ways that scare clinicians, patients and family members. Cross-sectional prevalence of opioid use disorder in primary care patients receiving opioids is **substantial** (3%-26%, per CDC). This signals an addiction population seeking care in the wrong places. It does not capture risk for emergent addiction in, for example, an arthritis patient lacking prior addiction. The phrase may conflate physiologic dependence with addiction.

### **“One-third of long-term users are hooked on prescription opioids”**

Problem: The statement, based on a Kaiser survey published in the Washington Post, conflates the psychiatric diagnosis of opioid use disorder with self-report of difficulty stopping, which can include physical dependence alone. It is not verifiably true, and it reinforces misunderstandings that the “Facing Addiction” report sought to counter.<sup>12</sup> Confusing physical dependence with addiction, reinforces popular resistance to evidence-based treatment for addiction, as detailed in a paper by Charles O’Brien and Nora Volkow.<sup>13</sup>

### **“We know of no other medication routinely used for a nonfatal condition that kills patients so frequently”<sup>14</sup>**

Problem: The number cited in one New England Journal Perspective is inflated (1:550) through use of Canadian data,<sup>15</sup> reflecting **higher doses and higher rates of benzodiazepine co-prescription** than are typical for the US. In a Group Health Study, median opioid doses were 9.4 mg morphine equivalent (MME) (for lower-dose patients) and 28.6 mg (for higher-dose patients)<sup>16</sup>, versus 43 mg in the Canadian study. Benzodiazepine co-prescription, which increases mortality risk four-fold,<sup>17</sup> was seen in 85% of deaths in a similar Canadian cohort.<sup>18</sup> In the US, benzodiazepine co-prescription is far less common (<5% in US Department of Veterans Affairs, 10% elsewhere<sup>19</sup>). A recognition that prescribed opioids can cause death is extremely appropriate. It should spur risk mitigation aligned with the CDC Guideline. A blanket statement like the one above, however, **implies that stopping opioids for all persons receiving them is inherently protective**, which is entirely **untested**. Anecdotal and some research data are beginning to suggest the opposite may be true.

### **Silence (regarding many aspects of opioid use for pain)**

Problem: Statements not made include acknowledgement that we lack any formal prospective quantitative study of the effects of involuntary termination of opioids in patients who appear to be functioning stably and/or benefiting from them. Many clinicians and health agencies have adopted or encouraged a de facto practice of involuntary withdrawal. This is an untested practice with potentially grave implications for patients, as reported in JAMA, November 2016.<sup>7</sup>

## **Helpful Public Statements**

### **When physicians prescribe, they should see it is a solemn and momentous responsibility**

Value: This underscores the risks to be managed, and honors the work required of health care teams in handling a responsibility (modified from Frieden & Houry<sup>14</sup>).

### **Opioids should be offered and the should be continued when expected benefits for pain and function are likely to outweigh risks**

Value: This statement reinforces the **patient-centered assessment** that should guide all medical practice. It represents the collective wisdom of the writers of the CDC Guideline.<sup>11</sup> It reinforces that clinicians may legitimately judge continuation to be appropriate, as opposed to involuntary termination or taper.

### **We have a tragic lack of accessible treatment for patients with opioid use disorder, with 80% of patients needing treatment not getting it**

Value: This statement points public officials toward a harder but arguably more important problem to confront, which is an enormous lack of accessible, high-quality treatment.<sup>12</sup> It is accurate with respect to large parts of the country where subsidized access to methadone and buprenorphine are absent. The CARA fund allocation is limited to two years, and in many states calls for generation of new systems of care that are currently absent.<sup>20</sup> We lack assurance that medications for addiction treatment can be delivered in states where addiction treatment grant recipients lack prescribers or systems to monitor them.

### **Scientific Background:**

1. **There is every reason to believe that the large increase in opioid prescribing (2000-2010) induced de novo substance use disorder in a significant number of persons.** It also recruited persons with substance use disorder into doctors' offices for what amounted to the most readily obtainable substance. Most persons who use heroin assert they first used pain relievers nonmedically.<sup>1</sup> This does not necessarily support the idea that today's crisis of opioid misuse can be reversed through doctor's offices, given the complexities of the problem.
2. **Among persons who needed treatment for any drug use disorder in 2015, 82% did not obtain it.** An estimated 7.7 million Americans required treatment for a drug use disorder in 2015, with 2.0 million identified as having a drug use disorder involving pain relievers and 591,000 involving heroin (a category that now would include illicit fentanyl, typically sold as an adulterant or substitute without clear designation as such to the purchaser).<sup>21</sup>
3. **Between 5 and 8 million Americans regularly take opioids for care of chronic pain,**<sup>22</sup> according to a National Institutes of Health consensus paper. A larger number, 97.5 million, used prescription pain relievers at least once in the past year, according to the 2015 National Survey on Drug Use and Health.<sup>21</sup>
4. **Not every pain patient is an addiction patient in waiting.** The CDC Guideline summarizes estimates of de novo opioid use disorder among persons receiving opioids for pain and it is tied to dose, 0.7% to 6.1% (the latter applies to dose > 120 MME). Median dose for opioids in the USA is <50 MME, so the estimate of 0.7% is more realistic for persons receiving low doses.
5. **Among the estimated 12.5 million Americans who misuse opioid pain relievers (e.g. hydrocodone, oxycodone) each year,**<sup>23</sup> **most did not obtain them from doctors.** For this reason, physicians offer only a partial and restrictive window on the opioid epidemic. Specifically:
  - a. In the 2014 National Survey on Drug Use and Health, 22% persons of persons misusing pain relievers reported getting them from a doctor.<sup>3</sup> The 2015 National Survey on Drug Use and Health expanded the definition of nonmedical use (now termed "misuse") to include use of one's own prescribed opioid to treat a painful condition other than the one for which the prescription was originally issued (and under this definition, 63% of such misuse was "to treat pain"). Under this expanded definition, 34% of prescription opioid misuse is with opioids secured from one doctor.<sup>23</sup>
  - b. Most persons seeking treatment for opioid use disorder with oxycontin never received oxycontin for pain.<sup>24</sup>
6. **The opioid crisis of 2016-17 involves a well-remarked paradox**<sup>6,25</sup>: a 5-year rollback in opioid prescribing has accompanied a rapid acceleration of overdose.
  - a. The 5-year roll-back in opioid prescribing is reflected in IMS/Symphony prescription (2013-2015)<sup>2</sup>, in Veterans Administration (down 30-40% from 2014-2016<sup>26</sup>) and in individual state reports. Prescription pain reliever misuse by teens and adolescents is at a 2-decade low,<sup>27</sup> as is DEA recovery of prescription opioids. This suggests that drug supply from doctors is drying up.
  - b. Nevertheless, opioid overdoses are at an all-time high. There were 33,091 opioid overdose deaths in 2015 (up from 28,647 in 2014).<sup>4</sup>
7. **The rise in the opioid overdose is driven by synthetic opioids like illicit fentanyl (n=9580, a 72% rise since 2014), and heroin (n=12,898, a 20.6% rise from 2014).**<sup>4</sup> Natural and semisynthetic opioids (which would include hydrocodone, morphine, oxycodone) were identified in 12,727 of opioid overdose deaths in 2015. This is an ostensible rise of 2.6% from 2014. However, failure of coroners to test consistently for synthetic opioids like fentanyl means this figure is a likely overestimate (e.g. if a patient dies with detected hydrocodone and undetected fentanyl, the latter is the medically more probable cause of death). Separate analyses by the CDC show that rising deaths due to synthetic opioids reflect illicitly manufactured fentanyl and not ordinary prescriptions of fentanyl.<sup>28</sup>
8. **Recognized limitations in the CDC's source data for analysis tend to underestimate fentanyl deaths.** Some points:
  - a. CDC's most recent reports do not include 2016, but other data show continued rapid escalation of fentanyl deaths in 2016 (e.g. Cuyahoga County,<sup>29</sup> Massachusetts,<sup>5</sup> Jefferson County, AL<sup>6</sup>).
  - b. For coroners, fentanyl is a costly, optional "send-out" GC/MS test, and thus many jurisdictions do not test for it and do not regularly detect it as a cause of death. If hydrocodone is detected on a standard low cost immunoassay, the coroner may close the case without seeking to determine if fentanyl was present.
  - c. Overdose tabulations by individual substance "sum to greater than the number of deaths recorded" because many people die with multiple drugs taken simultaneously. This can sometimes produce a misunderstanding of which drugs were truly responsible for deaths in overdose cases. Establishing mutually exclusive "most likely" cause of death is only done systematically in Massachusetts.<sup>5</sup>
  - d. In analyses that did seek to determine the mutually exclusive most likely cause of death, the number of overdoses attributable to a nonmedically used pain reliever is 8-15% (King County, Jefferson County, Massachusetts provide examples).
9. **Treatment with maintenance medication for opioid use disorder remains the most underutilized avenue to reverse the opioid epidemic.** It is the foundation for evidence-based care.<sup>30</sup> Medications such as methadone and buprenorphine are effective in randomized controlled trials,<sup>31</sup> and associated with up to a 50% reduction in overall mortality in observational studies.<sup>32,33</sup> However, most persons with opioid use disorder do not receive these foundational medications.<sup>8</sup> Among persons with opioid use disorder in the 2015 National Survey on Drug Use and Health, only 19.4% obtained treatment that was specific to opioid use disorder.<sup>8</sup> Although medications such as buprenorphine have permitted some expansion of treatment access, large parts of the country lack any method to deliver such expansion, in part because Medicaid expansion under the Affordable Care Act was declined by 19 states, and because physicians possessing waivers served a median of just 13 patients in a recently-published review of data from 2010-2013.<sup>34</sup> Analyses of national

pharmacy data conducted by IMS Institute for Healthcare Informatics show that rate of growth in buprenorphine prescribing has slowed precipitously in the last 5 years (just 6.4% for 2016, relative to 2015).<sup>9</sup> This slowdown in medication access from doctors has accompanied an accelerating epidemic. Short-term expansion of grants to state-funded addiction treatment programs, most of which lack physicians, will likely prove insufficient to address underlying barriers to treatment expansion.

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