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Neat, Plausible, and Generally Wrong:

A Response to the CDC Recommendations for Chronic Opioid Use

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Abstract

The American crisis of opioid addiction and overdose compels our strongest eﬀorts toward successful prevention and treatment. Recommendations from the Centers for Disease Control and Prevention (CDC) for chronic opioid use, however, move away from evidence, describing widespread hazards that are not supported by current literature. This description, and its accompanying public commentary, are being used to create guidelines and state-wide policies.

These recommendations are in conﬂict with other independent appraisals of the evidence—or lack thereof—and conﬂate public health goals with individual medical care. The CDC frames the recommendations as being for primary care clinicians and their individual patients. Yet the threat of addiction largely comes from diverted prescription opioids, not from long- term use with a skilled prescriber in a longitudinal clinical relationship. By not acknowledging the role of diversion—and instead focusing on individuals who report functional and pain beneﬁt for their severe chronic pain—the CDC misses the target.

We provide here a review of the evidence regarding long-term opioid use for chronic pain in order to a) better point public health eﬀorts, and b) reduce harm from consequent restriction of these medications for patients who have substantial beneﬁt in their use.

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Introduction

The Centers for Disease Control and Prevention (CDC) has had historical credibility with the medical community, generally making judicious use of evidence for public health beneﬁt. That is why it is disconcerting to read its recommendations [1] on opioids for chronic pain and accompanying descriptions in the media. With these new recommendations concerning the use of opioids, the CDC has taken available data and developed a narrative that H.L. Mencken would generally have described as “neat, plausible, and wrong.” [2]

The narrative is as follows: People in chronic, severe pain are readily provided unproven opioids in ever-increasing doses, get easily addicted and die of overdose either from the opioids prescribed to them or from a switch to lethal heroin.

Neat? Yes. Plausible? Yes. Wrong? Unfortunately, yes.

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People in chronic, severe pain are readily provided unproven opioids in ever- increasing doses …

Patients with chronic, severe pain in 2016 have often tried available ﬁrst-line options of physical therapy, behavioral treatment, NSAIDs, acetaminophen, anticonvulsants, tricyclic antidepressants, etc. prior to beginning an opioid medication. Indeed, the general outcome for many patients in pain is ever- increasing hardship in ﬁnding skilled prescribers who are willing to provide such treatment. [3–6]

Long-term opioid medication is intended to help address intractable suﬀering. Here the CDC makes a striking set of exceptions; its recommendations are exclusive of “active cancer treatment, palliative care, and end-of-life care.” Why is cancer privileged over other debilitating conditions? Sickle cell anemia, severe arthritis, spinal stenosis, inoperable kidney stones, chronic pancreatitis, and other conditions also have high levels of pain that can be successfully mitigated by opioids.

In addition, the exception “palliative care” is notable. In deﬁning people to be served by palliative care, the National Consensus Project notes that “serious or life-threatening illness is assumed to encompass populations of patients at all ages within the broad range of diagnostic categories, living

with a persistent or recurring medical condition that adversely aﬀects their

daily functioning or will predictably reduce life expectancy.” [7] Chronic pain, when controlled for sociodemographic factors, has been found to reduce life expectancy by ten years. [8] It doubles rates of suicidal ideation, attempts, and completion [9] while quadrupling rates of depression and anxiety. [10] When people look for some relief of chronic suﬀering, they are doing so relative to a situation of misery. Given the impact of chronic severe pain, it appears to meet the deﬁnition for palliative care itself.

Can people in chronic pain expect meaningful relief from long-term opioid use? Not according to the CDC. The recommendations state there is no evidence for such use and only evidence of harm. While it is certainly true there is an absence of longer-term data, the CDC deﬁned chronic pain as lasting longer than three months, but included only studies that lasted over one year. An independent systematic review [11] ﬁnding evidence of beneﬁt was thus excluded.

Absence of evidence is not evidence of absence, and the CDC’s claim is also belied by direct reports from patients using long-term opioid treatment who report substantial pain and functional improvements. The CDC, in telling patients that “the beneﬁts are transient and generally unproven,” [12] is essentially telling patients they are wrong about their pain and function.

When conventional evidence is limited and suﬀering is high, use of clinical ethics for individual patients has been proposed as a worthwhile decision- making model. [13]

Another model is ﬁnding what safely works for each patient. [14] While acknowledging the limitations of current evidence, the 2014 National Institutes of Health “Pathways to Prevention Workshop: The Role of Opioids in the Treatment of Chronic Pain” concluded that:

Patients, providers, and advocates all agree that there is a subset of patients for whom opioids are an eﬀective treatment method for their chronic pain, and that limiting or denying access to opioids for these patients can be harmful.

[O]ur consensus was that management of chronic pain should be individualized and should be based on a comprehensive clinical assessment that is conducted with dignity and respect and without value judgments or stigmatization of the patient. [15]

… Biased media reports on opioids also aﬀect patients. Stories that focus on

opioid misuse and fatalities related to opioid overdose may increase anxiety and fear among some stable, treated patients that their medications could be tapered or discontinued to “prevent addiction.” [16]

The CDC, in contrast, highlights that prescription opioids are “really dangerous medications which carry the risk of addiction and death.” [12]

Though it found, as did the CDC, a lack of long-term evidence for opioid use, the American Geriatrics Society still determined them to be a potentially “indispensable” treatment for selected patients. [17] British geriatric guidelines are similar. [18] While advocating their judicious use, Canadian guidelines note that “opioids can be an eﬀective treatment for chronic non-cancer pain (CNCP) and should be considered.” [19] In the month preceding the CDC recommendations, the Lancet published an editorial titled “Increasing worldwide access to medical opioids,” describing how 80% of the world’s population lack access to morphine, part of the World Health Organization’s essential medicine list since its inception. [20] Disproportionate use of opioids in the US is an expression not only of American supply and demand, but near-complete restriction on opioid access for 5 billion people. [21]

Potential side eﬀects from appropriately-dosed opioids include constipation, fatigue, and lower libido. As with other medication side eﬀects, patients and their clinicians can develop ways to ameliorate them or discontinue treatment should the side eﬀects be too troublesome. Much has been made of opioid-induced hyperalgesia. But even the most recent reviews of this phenomenon are unable to determine its prevalence, and studies have generally been experimental in nature or with unusual administration of opioids (e.g., intrathecal). [22,23] Whether it is clinically important for patients with chronic pain on standard opioid medication is unclear. [24] As to concern for dose escalation, a recent cohort study found it occurred in fewer than one in ten opioid-naïve patients. [25]

First-line interventions advised by the CDC are limited in their eﬀectiveness. Acetaminophen was recently found to have no impact on osteoarthritis pain.

[26] NSAIDs had their FDA warning strengthened in 2015 regarding heart attacks or strokes [27] and their risks of kidney injury and gastrointestinal bleeding have long been recognized. [28,29] Anticonvulsants or tricyclic medications for neuropathic pain have a number needed to treat of 5, meaning 4 patients do not have a beneﬁt. [30] Perhaps “multidisciplinary biopsychosocial care with a prominent component of self-management,

generally accepted as the gold standard of care for chronic pain”? According

to a pain specialist, its availability has “all but disappeared in the United States.” [31]

Ultimately, for the individual patient, the choice to use opioids is not made in a vacuum. The decision is made in comparison with the status quo of chronic, intractable pain despite other medical interventions. As a comparison, chemotherapy for cancer treatment also has severe side eﬀects, even toxicity. People make the choice to use such treatments because they are choosing against the alternative.

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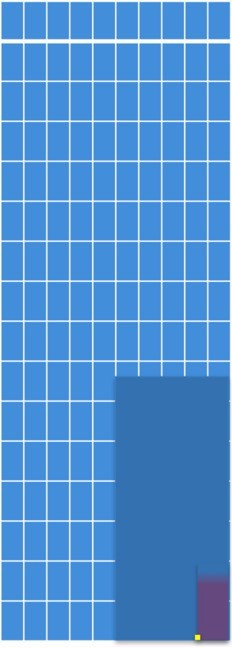
… get readily addicted and die of overdose of either the opioids prescribed to them or from a switch to lethal heroin.

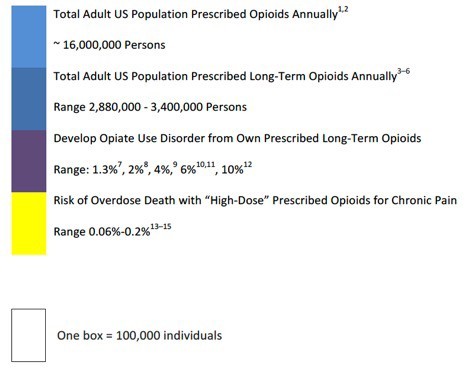
The CDC states that “prescription opioids are just as addictive as heroin.”

[[32] Others call them “heroin pills.” [33] But a full year after after major](http://archsurg.jamanetwork.com/article.aspx?articleid=2542665) surgery, only “0.4% of older opioid-naive patients continued to receive ongoing opioid therapy.” For chronic opioid treatment, studies show rates of developing an opiate use disorder to be in the range of 2% to 10% (Figure 1a). Even then, as others [34] have noted, the complexities of chronic pain and addiction behaviors make the outright diagnosis of opiate use disorder a challenge. Unfortunately, recent publications have included “pooled studies with widely diﬀering deﬁnitions, outcome variables, and populations,” which detract from their conclusions. [35] Concerns about such misleading data and deﬁnitions come from a wide variety of sources. [36–38] The term “prescription opioids” itself is problematic as the adjective does not distinguish how the drug was actually obtained by the user.

# Figure 1a

Annual Total and Long-Term Prescriptions of Opioids, with Risks of Opiate Use Disorder and Overdose Death





Among those who take opioids long-term for chronic pain, the CDC

highlights the potential for overdose (“overdose” is mentioned 144 times in the recommendations) and death. [1] This is certainly an outcome to be feared. The study cited in the CDC’s own telebrieﬁng [12], however, found “opiate-related” death to occur in 59 of 32,449 (0.2%) patients taking opioids for more than three months. [39] The context of these deaths was unknown (e.g., whether medications were taken as prescribed or from intentional overdose) and there was no corresponding control cohort of patients in chronic pain without opioid use. The senior author noted that the “generalizability of these ﬁndings to other patients is uncertain.” A prior study by the same authors put the rate of overdose death at less than 1%, even for “high dose” prescriptions (Figure 1a). [40,41] In its review of a Citizen’s Petition to limit doses of chronic opioids, the FDA found that “the scientiﬁc literature does not support establishing a maximum recommended daily dose of 100 mg MED [morphine equivalent dose].” [42]

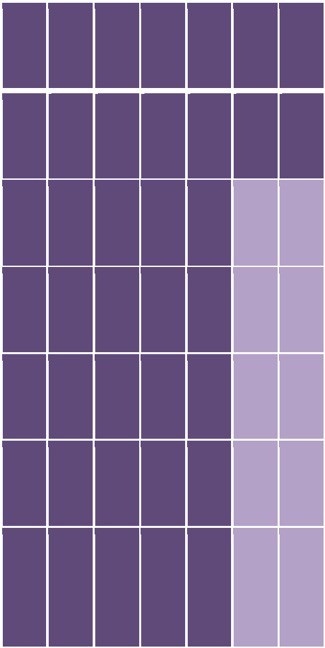
Opioid overdose deaths are generally the result of diverted medications (“diversion” is mentioned 2 times in the recommendations) (Figure 1b), heroin, fentanyl, or a combination of these. Diversion is most often from prescriptions for acute, not chronic, pain. [43] Most West Virginia overdose deaths were associated with diversion. [44] Among Montana overdose deaths, only a third of those on Medicaid had a claim for an opioid prescription during the month before their death. [45] Analysis of recent Massachusetts overdose deaths found “evidence to support an emerging

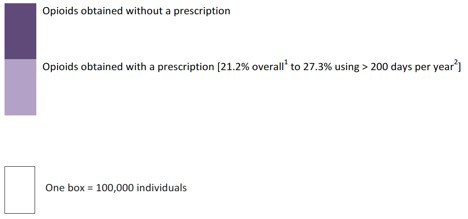
hypothesis that illegally-obtained substances are the driving force behind

opioid-related deaths.” [46] Prescription opioids accounted for a minority of 2014 Massachusetts fatal overdoses [47,48], a trend that has also been found nationally. [49] Should prescription opioids be used prior to initiating heroin, the CDC has found that use to be “nonmedical.” [50] Heroin is currently the most lethal opioid in terms of people aﬀected (though [fentanyl, with or without heroin, is also having an increasingly grave](http://emergency.cdc.gov/han/han00395.asp) impact). 94% of people in treatment for opioid addiction said they chose to use heroin because prescription opioids were “far more expensive and harder to obtain.” [51] The National Institute on Drug Abuse estimates that fewer than half of young people injecting heroin report abusing prescription opioids beforehand. These crucial details are unacknowledged in the CDC recommendations.

# Figure 1b

Sources of Nonmedical Opiate Use





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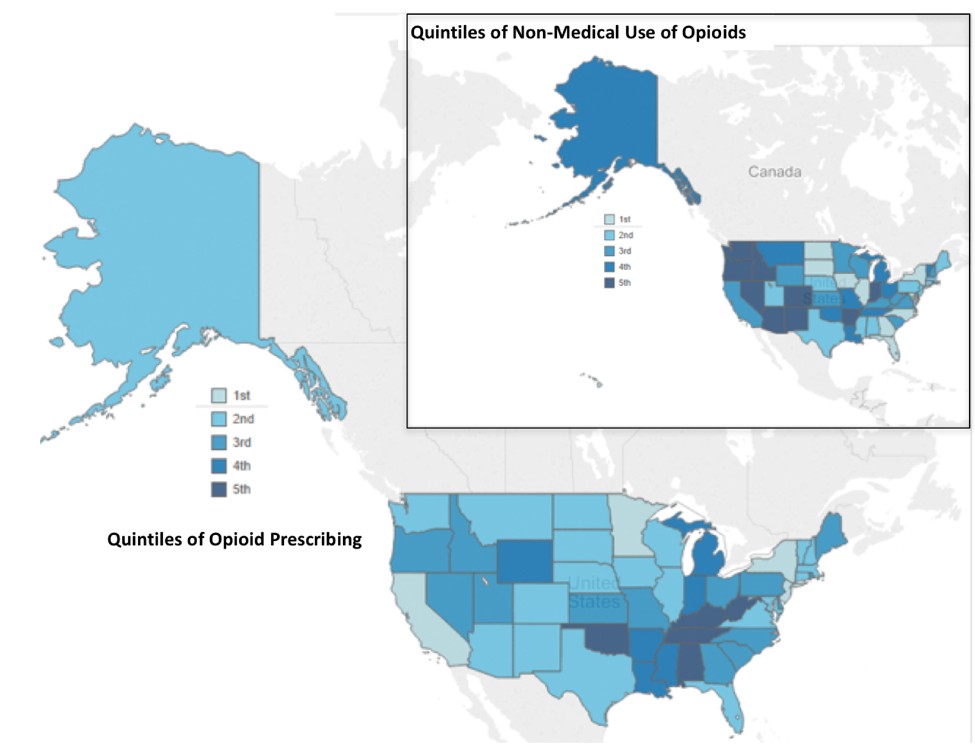
Examining this Narrative

Public health interventions are diﬀerent than clinical interventions. The former are scaled, diﬀuse and unilateral. The latter are individualized and shared. The CDC recommendations are more focused on public health concerns (such as non-medical use of prescribed drugs) rather than the individual risks and beneﬁts of opioids for actual patients. These guidelines may have, in some form, been helpful in the late 1990s or early 2000s when OxyContin’s faulty, criminal formulation made for tragic outcomes for patients and communities alike. [52] In 2016, many regions and prescribers have already taken steps to improve clinical education and prescription monitoring. [53,54] The added constraints of the CDC recommendations and hyperbole that surrounds them serves neither public health nor individual care well.

The CDC recommendations describe a linear relationship between opioid prescribing and nonmedical use. But data on opioid prescribing [55,56] and nonmedical use [57], state by state, tell a more complicated story [Figure 2]. As shown in Figure 2, Colorado is in the lowest quintile of opioid prescribing but the highest quintile of nonmedical use. North Carolina is in the middle quintile of opioid prescribing but the lowest quintile of nonmedical use. CDC data from 2012 shows Florida with the second-lowest quartile of opioid prescribing. But in 2010 Florida physicians bought nearly 90% of all Oxycodone sold in the United States to distribute in more than 1,000 pain clinic “pill mills” [58]; at the time, Floridians themselves were in the lowest quintile of nonmedical use. Just four states—Kentucky, Alabama, Georgia and Arkansas—have 41 of the 50 cities with the highest prevalence of opioid use nationwide [59]; yet these states straddle four quintiles of nonmedical use.

# Figure 2

State Comparison of Opioid Prescription Intensity with Nonmedical Use



An international comparison also belies a linear relationship. Between 1997

and 2010, the UK has had a similar trend in increased opioid prescriptions— though at a lower absolute level—but without an increase in overdose deaths. This outcome does not comport with overdose being an inevitable outcome of opioid prescription. [60] Rather than a straightforward infectious model of an epidemic, we need to acknowledge the data show something more complicated, often regional. When it comes to this epidemic, place matters, as the CDC itself reminds us [61], though its new recommendations do not.

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A Diﬀerent Narrative

Our concern for individual patients is that recommendations and regulatory changes [62] concerning prescribed opioids are increasingly being developed not through evidence, but by a ﬂawed narrative of how addiction develops and overdose occurs. [63,64] The CDC was provided with descriptions of these ﬂaws in the period of public comment, but chose to make only minor revisions. Our concern for public health is that these recommendations do nothing explicitly to address the major source of prescription opioids used in substance use disorders in the United States: diversion. [65] If the actual goal is to reduce the overall reservoir of prescription opioids in order to

reduce diversion, that would be a worthy one. The continued use of graphs

that track kilograms of prescription opioids and overdose deaths, however, misleads when many of those “prescriptions” are taking place outside of a skilled, longitudinal, patient-clinician relationship. [66,67]

The data we provide here describe a more accurate narrative: Should other treatments not succeed, people suﬀering from intractable chronic pain may ﬁnd that carefully monitored long-term opioids, in combination with other modalities, can help reduce their suﬀering and improve their function. The evidence indicates they can do so with a low risk of developing opiate use disorder and an exceedingly low risk of overdose death. As with all treatments, the decision to use and continue long-term opioids should be one of ongoing shared decision-making.

Overall, the new recommendations sacriﬁce accuracy for a fabricated sense of clarity. We support eﬀorts to reduce the scourge of opioid addiction and harm. Indeed, this is much of our own clinical work in primary care. But this goal is better addressed by recommendations that consider both individual patient choice and the impact of prescribed opioids on public health through diversion, two very distinct issues. The outcome might be less neat—yet still plausible—and have the added advantage of being beneﬁcial to the many people struggling with chronic pain.

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Authors

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