US Opioid Policy is "Looking for Love In All The Wrong Places"

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"…I was lookin' for love in all the wrong places,
Lookin' for love in too many faces,
searchin' their eyes and lookin' for traces
of what I'm dreamin' of…"

Song lyrics, Johnny Lee, 1980

In a strangely ironic way, US Federal and State government efforts to "do something" about the widely hyped "opioid crisis" fit these lyrics perfectly. Government at all levels seems determined to do exactly the wrong things with the wrong people in its search for citizen approval. Dreams of easy solutions have turned into nightmares for millions of pain patients.

We've all heard media stories of young people who quickly become addicted on minimal exposure to medically managed opioids, descending into a spiral of drug-seeking, life failure and eventual overdose death. Such stories are tragedies for the families that actually experience them.

Families grieve. They demand that government "do something." Their stories are very influential in our public conversation about substance abuse and overdose deaths. It is small wonder that government policy has focused centrally on reducing the availability of medical opioids.

However, is the present focus on reduction of medical supply appropriate? Almost certainly not. No matter how tragic these stories are, they are neither typical nor representative. We now know that "unlike tolerance and physical dependence, addiction is not a predictable result of opioid prescribing. Addiction occurs in only a small percentage of persons who are exposed to opioids — even among those with preexisting vulnerabilities... The molecular mechanisms underlying addiction are distinct from those responsible for tolerance and physical dependence." [i]

Addiction growing out of managed medical exposure is rare. Government policy based upon such narratives is doomed to failure. [ii] [iii] [iv]

Emerging Science on Substance Abuse versus Medical Exposure to Opioids

Pain is the number one reason why people see a doctor. The American Academies of Medicine estimate that over 100 million people in the US have moderate to severe pain every year -- of whom, perhaps 30 million have pain severe enough to disrupt life. Estimates of the number of Americans prescribed opioids every year vary widely between sources. Regardless of source, millions of people are certainly exposed.[v]

If millions of people are exposed to medical opioids, what we hear from news and from politicians would lead us to expect millions to fall victim to addiction from prescriptions that doctors write for them. But this is clearly not the case. Millions undergo surgery every year. Yet two recent large scale studies show how unusual it is for post-surgical patients to "get hooked" on pain relievers or to continue taking these drugs long after surgery.

A 2018 study investigated 565,000 patients prescribed opioids for the first time after surgery. [vi] Less than one percent continued renewing their prescriptions longer than 13 weeks. Less than one percent were diagnosed with opioid abuse during follow-up periods averaging 2.6 years between 2008 and 2016. Likelihood of diagnosis increased with the length of prescriptions, but increased only weakly with higher doses.

For several reasons, estimated risk of opioid abuse in surgical patients should be understood as a maximum figure. Many doctors who diagnose patients with abuse are general practitioners who lack deep training in addiction and have little experience evaluating the behaviors which actually define addiction. Likewise, doctors are increasingly concerned with being sanctioned by the US Drug Enforcement Agency or State authorities; thus they may diagnose drug abuse to protect themselves – not the patient. Finally, some physicians mistake patient reports of continuing pain – caused by failed surgery -- for potential opioid abuse.

A second study [vii] tracked long term opioid prescriptions in 642,000 post-surgical patients versus prescriptions in patients who did not receive surgery. Renewed opioid prescriptions were defined as "chronic" when 10 or more scripts were written in one year or a prescription was renewed continuously for more than 120 days.

In this study, the rate for chronic prescriptions of opioid analgesics among millions of non-surgical patients was estimated at 0.136 percent. For 11 common surgical procedures, the same rate occurred after surgery for four. In the seven remaining procedures, long-term opioid prescriptions rose by factors from 1.28 for caesarean delivery, up to five (0.69%) for total knee replacement.

The highest rate of chronic prescriptions occurred for total knee replacement – a procedure known to cause lingering pain in many who undergo it. [viii] [ix] It is likely that many ongoing prescriptions after knee replacement reflect chronic post-surgical pain

rather than issues of opioid misuse. This may also be true of other procedures where chronic prescribing was observed.

These studies demonstrate that managed medical exposure doesn't significantly raise risks of opioid abuse in surgical patients who are properly screened for previous opioid use. This outcome directly contradicts the poster boy model that claims addiction may start with just a few Percocet.

Problems in the 2016 CDC Opioid Prescription Guidelines

Much of the controversy surrounding government policy on opioid addiction in America traces directly from March 2016 opioid prescription guidelines of the US Centers for Disease Control and Prevention. [x] Published critiques of these guidelines by medical professionals and informed laymen have revealed biased or weak scientific evidence [xi] and errors. [xii] [xiii] [xiv] Indeed, the guidelines appear to have violated the research standards of the CDC itself, by improperly confusing a scarcity of long-term double blind trials of opioid effectiveness with an asserted but unproven lack of effectiveness for opioids themselves. The two are not the same thing at all.

The CDC also ignored significant research. [xv] [xvi] Particularly of concern was failure to address the implications of genetics in the ways that the body metabolizes (breaks down) opioids into forms which pass into the brain to provide pain relief. [xvii] Because of natural genetic variations, millions of people either poorly metabolize or "hyper" metabolize some of the opioids used in pain management. In these people, low doses either do not reach a useful level in the bloodstream, or reach it so rapidly that they pass out of the body in minutes rather than hours.

Many poor- or hyper-metabolizers can benefit from opioid therapy – but only at doses greatly exceeding the threshold of risk where the CDC recommended that physicians do a risk-versus-benefits analysis before prescribing more. Thus it is clear that there can never be a one-size-fits-all patient or opioid therapy plan. For CDC to specify a dose rate at which it is simply *assumed* that risk of drug abuse rises is inappropriate. But this is exactly what happened. [xviii]

Treatment must be tailored to the individual by their doctor(s), balancing undesired side effects against pain relief. There is no medical evidence for reducing or tapering opioid doses among otherwise stable patients if such therapy has been successful in supporting a better quality of life. To the contrary, coerced tapering creates significant medical risk to the patient.

Horrific Unintended Outcomes

CDC prescribing guidelines were originally written as "voluntary" recommendations for

General Practitioners. However, three months before publication, Federal legislation transformed the guidelines into a mandatory practice standard for the US Department of Veterans Affairs. Despite protests of some of the guideline writers themselves,[xix] thousands of hospitals and medical practices have imposed severe limitations on opioid prescribing, interpreting the CDC document as a legal standard of care. The impact of these limitations on doctors and patients has been horrendous. [xx] [xxi]

The good intentions of CDC writers seem to have fallen afoul of a basic principle of policy writing: simple clarity is not enough. Writing must be so definitive that biased readers cannot reasonably claim ambiguity. Failure to adhere to this principle in the CDC Guidelines has created horrific unintended outcomes for millions of pain patients. [xxii]

Throughout North America, doctors are leaving pain management practice, fearing sanction from State authorities or the DEA if they continue prescribing opioid analgesics at effective levels. Some doctors are coercing their patients to taper down or go off opioids altogether. Many pain management centers have closed. There are thousands of reports in social media and popular press from patients being discharged and falling into disability. Some are committing suicide. This is particularly true among Veterans denied effective pain treatment. [xxiii] [xxiv] [xxv]

Current Opioid Policy Has Failed

Despite these clearly unacceptable outcomes, Federal and State opioid regulation is now focused almost entirely on reducing medical supply. Comparison of CDC statistics for opioid prescribing versus drug-overdose deaths demonstrates that such a policy has already failed (Figure 1). As medical supply has dropped to a ten-year low, drug-related overdose deaths continue to rise. Deaths involving prescription opioids have been stable at approximately 15,000/year since 2011 but deaths from illicit opioids -- primarily heroin and fentanyl -- have risen exponentially from 7,000 in 2011 to 35,000 in 2016 (Figure 2).

Physicians do not prescribe heroin. Fentanyl that is either injectable or orally available is not prescribed for the management of chronic non-malignant pain. 15,000 deaths from prescription opioids (most of them diverted) translate to an annual risk of death for an individual patient of less than 1%. This is a risk that nearly all patients with chronic moderate to severe pain are quite willing to accept.

A substantial portion of deaths related to illicit opioid use may be occurring among patients so desperate for pain relief that they are turning to the opioid black market. To the extent that this is true, current misguided efforts to stem the crisis by limiting

physician prescription of opioids are actually having the opposite effect: they are *fueling* the crisis.

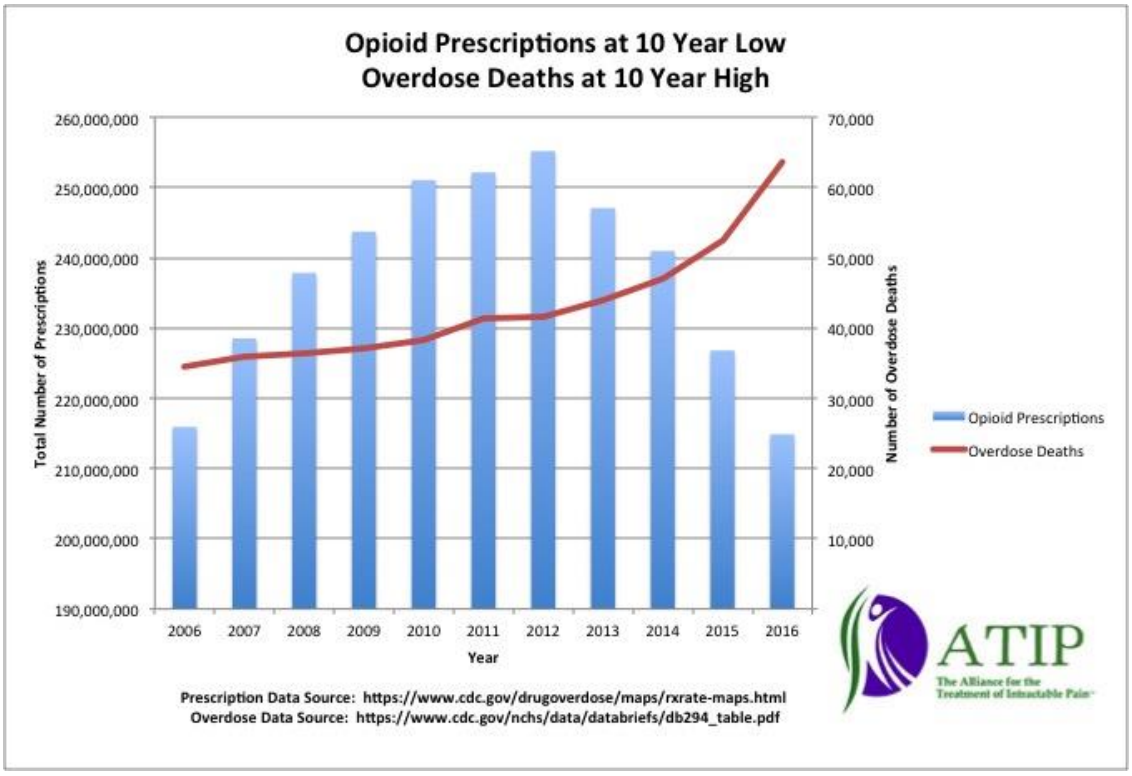

Figure 1: Opioid Prescriptions vs. Overdose Deaths -10 Year Trends

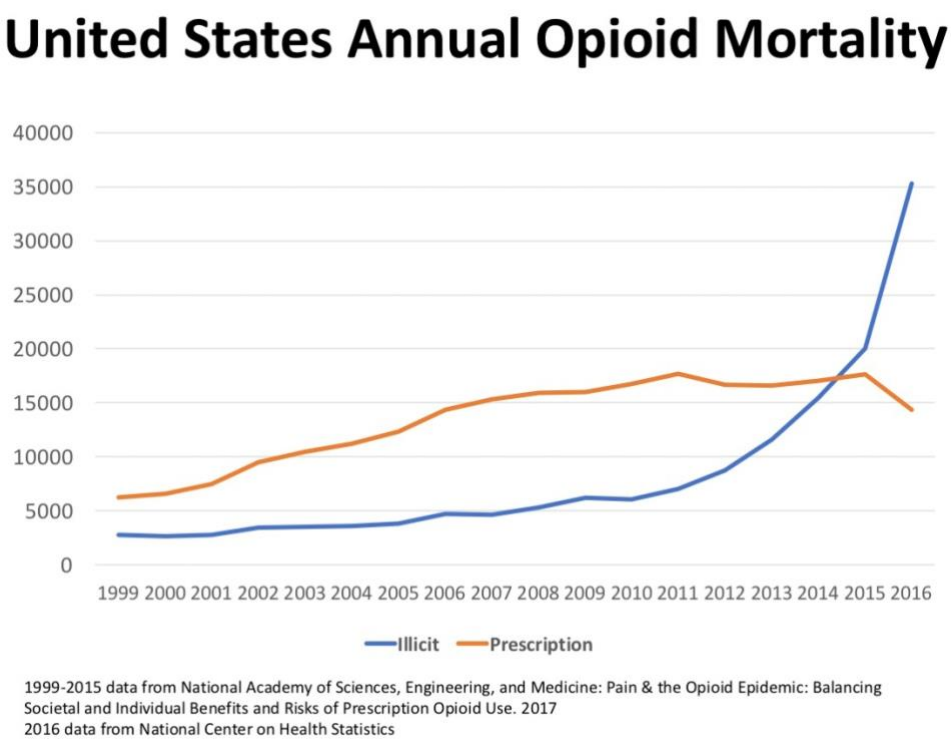

Figure 2: United States Annual Opiod Mortality

Doubling Down on Failure

Multiple US Agencies have undertaken initiatives intended to address the "opioid crisis." One such measure recently proposed by US FDA in its Opioid Risk Estimation and Mitigation Strategy is to "specify threshold drug amounts for opioid analgesic prescriptions above which prescribers would be required to provide additional documentation of medical necessity." [xxvi] In public hearings on January 30, 2018, the American Association for Pain Medicine (AAPM) advocated against such a step. Many pain patients agreed emphatically, for reasons discussed above.

The US Department of Health and Human Services Centers for Medicare and Medicaid also proposed major rule changes for Medicare Part D, based on the CDC Guidelines:

> "All sponsors [are] to implement hard formulary-level cumulative opioid safety edits at point-of-sale (POS) at the pharmacy (which can only be overridden by the sponsor) at 90 morphine milligram equivalent (MME), with a 7 days supply allowance." [xxvii]

90 MME is a modest dose that will likely enable adequate pain control for only a minority of patients. CMS estimated that their proposed "safety audit" will directly impact 1.6 Million patients who are prescribed higher levels. The predictable outcome

of these rule changes will be to deny or seriously delay pain relief to Medicare patients and many others treated under private insurance.[xxviii]

In a third effort to suppress opioids, a "citizen petition" to the FDA seeks "the removal of certain opioid analgesics from the market, deemed 'Ultra High Dosage Unit'". Medical professionals have responded in opposition, asserting that the proposed restriction puts patients at risk and comprises a misreading of CDC guidelines. [xxix]

Needed Changes of Policy Direction

There is no doubt that America faces a public health crisis in the addiction of millions of people and in thousands of overdose-related deaths. But as CDC statistics demonstrate, these real problems are dominated by street drugs, not prescriptions given by doctors to people in pain.

Addiction is primarily a disorder of social and economic disintegration, in which medication diversion or theft play a starting role for some, particularly young people. However, further restriction of medical opioid supply will harm millions of people in pain while doing *nothing* to address much more important causes of addiction. [xxx] [xxxi] [xxxii]

US and State governments are under great public pressure to "do something" – even when it is the wrong thing – to abate the crisis. As subject matter experts and medical professionals, the authors would assert that any policy correction in more constructive directions must begin with three essential first steps:

- The CDC must withdraw its 2016 guidelines for a major rewrite to correct multiple biases, errors, and omissions. The effort should led by Board certified pain management specialists with experience in ongoing opioid therapy for patients seen in community practice. Patient advocates must be voting members of the core writers group. The process must be both fully transparent to public review and supported by enough staff to read, process and integrate outside input into the rewritten guidelines.

- The Veterans Administration must be directed by Congress to stand down from efforts to eliminate opioids from patient treatment plans. Present policy is killing Veterans by forcing them off opioid analgesics when no adequately tested alternative therapies exist.[xxxiii]

- State legislatures and regulators must halt in place before imposing new regulations or restrictions on medical opioid therapy, pending completion of the CDC re-write.

With these steps taken, we can begin to deal with the real magnitude and directions of constructive change. As long as the CDC opioid guidelines continue as official policy and doctors continue to coerce patients to taper off opioids, people will continue to be disabled and to die as doctors desert them or they are forced to reduce opioid therapy to ineffective levels.

Note: Contents of this paper do not represent the views of the U.S. Department of Veterans Affairs, the United States Government, or the University of Florida

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