Reframing the Opioid Epidemic into its Proper Context

With results from survey taken in March 2018

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Abstract

In this essay, I will address the imperative nature of relieving pain due to its physiological consequences. I will also reference sources that illustrate comprehensively how to do this. I also recommend measure that can be taken to reduce the diversion (particularly by theft, which is responsible for most prescription drugs that end up on the black market) substantially and effectively without reducing patient access to them. I will also elucidate the differences between dependence and addiction, and explain why opioids are essential for the management of severe (or intractable) pain.

The American Society of Interventional Pain Physicians (ASIPP) are by far the most recent, comprehensive, detailed, thorough, and useful guidelines formulated on opioid prescribing in light of the national crisis of overdose deaths. Utilizing the ASIPP guidelines in place of the older, and far less comprehensive CDC guidelines would be advisable, and beneficial to millions suffering from chronic pain, and steps that can be taken to reduce the number of deaths resulting from illicit fentanyl analogues such as carfentanil that are driving these deaths. Taking "high dose" –an arbitrary distinction (Kroenke and Cheville, 2017)–opioids off of the market will only cause suffering and death at worst, and inconvenience and suffering at best without reducing overdose deaths. This is especially true when one considers how the vast majority of "overdose" deaths involved illicit carfentanil and its analogues, not drugs prescribed by doctors, and as such there is no rational reason to remove these lifesaving drugs from the market or restrict access in any other manner as has been proposed by the FDA, and enacted via the CDC's guidelines for opioid prescribing (2016), which have indisputably resulted in a great deal of pain and suffering (Kline and Lamb, 2017) The gaps and inconsistencies left in the management of pain have been profound; in every state in the U.S. since the implementation of the VA Department of Defense guidelines and the CDC guidelines, patients have been expressing disturbing amounts of suicidal ideation on social media sites such as Twitter, Facebook, and on comment threads of news articles. Their complaints and reasons for expressing such sentiments are always in relation to inadequate pain relief, typically because their doctors forcefully, involuntarily, tapered them, a practice with no research showing benefit, and plenty of research showing profound harms, as well as an abundance of testimonials.

Survey results:

Recent research that I conducted (with 385 respondents from multiple chronic pain support groups on Facebook, especially those associated with the most severe, pain such as arachnoiditis, Ehlers Danlos Syndrome, and CRPS/RSD) has shown that over half of patients with severe intractable pain surveyed were involuntarily tapered, and 60% of them after being tapered considered the adequacy of their care to be 4 or less on a 1-10 scale. These are the preliminary results of the study, and haven't yet been published, but the data speaks volumes nonetheless. Of the respondents, 83% noticed changes in their treatment regimens since the passage of the CDC guidelines, over half of whom had had difficulties actually filling prescriptions at the pharmacy that had not been issues before,

When asked, "Does the current medical system facilitate access to the medications/treatments that reduce your pain to a level at which you can function (basic self care, work, etc.)?" nearly 70% of respondents said no. This is a profound issue in the medical system that has been grossly exacerbated by the CDC guidelines and state laws passed in their image. Over 73% of respondents said that their average level of pain was 6 or greater, which constitutes as severe pain, and since all of the respondents have had pain for multiple years, they would all be classified as severe intractable pain patients. As such, the data clearly indicate that this population has been seriously harmed by the CDC guidelines' provisions encouraging involuntary tapering and prescription MME limits and the state laws passed encouraging the same. 26.7% of respondents rated their quality of life as 1 on a 1-10 scale. That is appalling. And over 65% of respondents' quality of life was rated at a 4 or lower. Furthermore, their quality of life before the guidelines were passed and state laws implemented, was significantly better.

Over 41% of respondents said their current treatment was less than a 4 out of 10 in terms of helpfulness and how adequately it treated their pain. Furthermore, few, if any of these individuals were receiving opioid analgesics, and in fact they largely seem to have been the individuals who had been involuntarily tapered. When asked whether or not they had experienced discrimination in a medical setting due to their chronic pain, over 80% said yes, and the stories largely revolved around being denied care, being denied any kind of pain relief, being summarily dismissed with little or no reason give, though when reasons were given, they most commonly fell into the categories "the CDC guidelines," "State Law based on the CDC guidelines," and "I don't want to lose my license." Over 89% of the sample were receiving long term opioid therapy prior to the CDC guidelines. Nearly 55% of them were involuntarily tapered after the passage of the CDC guidelines, and only two respondents regarded the event in a positive manner. The rest shared experiences of losing their jobs, homes, marriages, and being bedbound, unable to play with their grandkids, living lives bereft of meaning and happiness, and that before they were tapered they were functional individuals (to varying extents) able to live meaningful lives. The vast majority of respondents are now bedridden. A minimum of 65% are bedridden. And 90+% of the respondents indicated that their doctors were virtually completely unwilling to increase their dosages under any circumstances, even if they were now bedbound

due to their dosage reductions. In fact, of the patients adversely affected by their dosage reductions (the vast majority) 91.2% of their doctors were unwilling to revert their dosages back to what they were before, that is reevaluate whether long term opioid therapy was beneficial for them (in all of these cases it was, and even so, they did not do what was best for the patient). These results clearly indicate that placing public health concerns above the welfare of the individual patient causes immense harm.

Any committee or task force must include both people actively advocating for the adequate treatment of individuals such as these (severe, intractable pain patients who either currently or formerly benefitted a great deal from opioid analgesics), in addition to people who currently suffer and are not treated, and whose function has been severely impaired, in addition to physicians who are still maintaining individuals on long term opioid therapy because of the profound benefits that these patients receive from the therapy.

A specific insurance and ICD code should be given for severe intractable pain, and within the definition of this code should be the frequent necessity of opioid analgesics in their treatment regimens, and doctors treating severe intractable pain should be given more money than they are given for the average patient by insurance companies, because people with severe intractable pain are highly complex patients requiring specific, specialized forms of care that require a lot of skill and precision. Further, because these patients will likely require lifelong care, and regular doctor's visits, this should be taken into account. Payers should be required to pay for these patients as well, given the fact that this is one of the most vulnerable populations in all of medical care, since without treatment they are unable to participate in the daily requirements of life and society without being adequately treated which will frequently include dosages of opioid analgesics above 90MME. The MME metric was never intended to be used by anyone other than trained physicians due to its dangers in converting dosages, and its known flaws and imperfect conversions that vary substantially from drug to drug, and as such any kind of MME based metric should be removed from any and all policy, since this flawed measurement tool was never meant for this purpose (Schatman et al., 2016). Furthermore, as Schatman et al.'s research shows, there is only very low quality evidence suggesting any kind of dose-dependent risk for opioid analgesics, and the issue lies more with the number of medications the individual is on, and other research clearly shows that non opioids such as NSAIDs are every bit as harmful as opioids, but particularly when they are mixed with other drugs, which is why opioid "overdoses" should really be classified as polydrug toxicity deaths, as the mixture of the drugs is what makes drugs deadly far more so than any one drug itself (excluding illicit carfentanil and other analogues, whose potency is responsible for the continued rise in deaths, not to be confused with therapeutically beneficial, physician prescribed transdermal fentanyl patches, which are a mainstay for severe intractable pain treatment), given the compelling results of studies looking at the topic (Labianca et al., 2012).

Efforts at clinical innovation in the treatment of addiction should be focused on the drug known as ibogaine, which is used elsewhere in the world, such as in Mexico and New Zealand, to great effect, and given the limited toolbox for treating addiction, the continued classification

of ibogaine as a schedule one substance is preventing strides from being made in this area. If the welfare of people suffering from addiction is a concern, the immediate instigation of this drug to be reclassified as (at worst) a schedule two drug, and the beginning of research into its utility in treating addiction (though there is an abundance already) (Alper et al., 2001) (Carnicella et al., 2010) (French et al., 1996) (Rodger, 2011) (Stern, 2015) (Mash, 2005) (Leal et al., 2017) (Vastag, 2005).

All of the above issues are explored further in this paper, and I implore you to take them all into consideration.

Section 1: Curtailing Abuse and Understanding the Nature, Scope, and Complexity of the Problem

Section 1.1 Addiction and the Controlled Substances Act

There are several approaches that can be taken to effectively curtail opioid abuse and overdose in the United States; some are more effective and desirable than others. The approach of criminalizing drug use (the people who tend to be using illegal drugs such as opioids, are not typically legitimate patients, and typically did not obtain them from a legitimate prescription), has failed miserably in every country in which it has been implemented.

Increases in the past of opioid use should not be alarming, in fact they should be encouraging, because worldwide, pain is undertreated, and people suffer and die in agony needlessly (Seya, 2011). The United States has an opportunity to be an example of how to properly treat pain while making addiction treatment (both attachment-based group therapy for addiction, and methadone and suboxone maintenance) available, and exploring the potential of ibogaine to *cure* addiction, as other countries are currently doing. If we continue the prohibition of drugs that were labeled years ago as having no medical uses such as ibogaine and marijuana, and do not allow research into their potential therapeutic benefits, then the American public will suffer as a result, and the U.S. will fall behind as a leader in high-quality medical care.

Reconsideration of the structure of the Controlled Substances Act is necessary to stop impeding scientific and medical advancements in regards to pharmacological treatments for a variety of currently "incurable" conditions such as addiction, by creating a simpler legal path for drugs to be rescheduled as having medical uses and to study whether drugs have therapeutic effects with no limit on how many trials can be conducted, allowing drugs such as marijuana and ibogaine to be researched adequately and potentially rescheduled, on account of both showing the potential to curb opioid abuse and overdose, is imperative if the United States is to improve its current state of affairs and solve both the problem of the undertreatment of chronic pain and the problem of addiction and overdose. Removing the "potential for physical dependence" from the requirements for being scheduled drugs would be a more useful categorization, as drugs themselves are not in and of themselves addictive, but rather they sometimes cause dependence, which, only means that withdrawal happens upon abrupt cessation, which happens to every coffee

drinker in the morning before they have had their coffee. Every coffee drinker in America is not an addict, and the very idea is ludicrous. It is time to stop conflating dependence and addiction, as it contributes to the undertreatment of pain, and mischaracterizes addiction (Morgan and Christie, 2011). Also of note is that many SSNRI cause dependence and withdrawal, and literature regarding this topic abounds (Cymbalta, which causes "brain zaps" a form of neuropathic pain that is poorly understood and remarkably difficult to treat is one notable example). These drugs are not classified as controlled substances, and it is absurd to list "physical dependence" as a reason to prohibit the use of a drug, as it is a potential side-effect that the benefits must be weighed against. Needing to take a drug daily or every two or three days is worth the quality of life the drug provides in many cases, so drugs that have this property should not be so inaccessible. Doctors and patients should be allowed to decide if the benefits outweigh the risks in the privacy of the doctor patient relationship without interference from groups such as the DEA. Right now, this is not the case. Doctors are routinely being targeted by the DEA rather than working with them to reduce patient diversion (Szalavitz, 2004).

If addiction is reconceptualized as a disturbance of early life attachments to caregivers wherein the addict uses drugs (or engages in activities that are especially rewarding to the individual such as gambling or sex addiction) to replace the love, safety, support, and care they did not receive as an infant, so that the drug replaces the bonding chemicals released in the brain (oxytocin) during pair bonding, then it becomes clear that the aim should not be to restrict drugs that save lives, but to instead heal the individuals with disrupted attachment styles. The criminalization of drugs and addiction has been ineffective, and in order to heal these people, we must treat those with substance use problems with compassion. (Flores, 2001) If combined with evidence that addiction requires the genetic predisposition of having mu receptor polymorphisms (Kreek and LaForge, 2007), and are associated with abnormal attachment behaviors (Barr et al., 2008), it becomes clear that restricting drugs is not the solution to this problem, removing high dose opioids is not the solution, and criminalizing the medical ailment of addiction is not the solution. Similarly, restricting the medications that are used to treat severe intractable pain (opioid analgesics in many cases, relatively frequently at high doses) is not the solution to any of the problems of addiction. It is not about exposure to a drug; it is about the intergenerational transmission of trauma.

We need to divert the money going into the criminalization of drug use into the treatment of addiction, as the toll has grown high enough. The way to do this is **not** by restricting the prescribing of opioids, as these are lifesaving drugs to people suffering from moderate and severe chronic pain. In these recommendations, a strategy will be outlined as to how balance can be achieved between adequate pain relief and adequate addiction treatment with the result of reduced opioid-related mortality.

Including provisions in the controlled substances act that allow a drug to be researched *exhaustively* by multiple researchers, in order to determine if they can be used medically would save millions of lives, add to the country's revenue by utilizing cures to conditions that other countries have had success treating conditions such as addiction using drugs that are illegal here,

such as ibogaine, which has shown the definite potential to cure addiction, not just treat it, but cure it (Leal et al., 2017) (Vastag, 2005). Allowing research on such a substance without having as many research barriers (because it is listed as having 'no medical uses' in an outdated, and unscientific classification system, that is still used today) as currently exist, the problems of addiction, and overdoses would have the potential to dissipate completely, with a single administration of this drug, repeated as little as once every 3 months by some reports (Alper et al., 2001) (Carnicella et al., 2010) (French et al., 1996) (Rodger, 2011) (Stern, 2015) (Vastag, 2005). England has been researching this, and we are falling behind as a nation, but removing institutional barriers (other than safety, ethics, and other mandatory research standards) from research on pharmacological agents would increase the quality of care people receive in the healthcare system, but only if the government allows science, and licensed medical practitioners to determine what is safe for an individual, on an individual basis, as is necessary for chronic pain.

Not everyone with chronic pain will benefit from opioids, but many will. On the other hand, virtually everyone with acute pain benefits from opioids (with 95% of people *not* becoming addicted), and **contrary to myths in the media about addiction, it *cannot* happen to everyone who takes an opioid, and in fact, it *does not happen* to 99.81% of people with chronic pain** who have been preselected to not have a history of substance abuse and **96.73% of the time, it *does not happen* to chronic pain patients who have not been preselected to not have a history of substance abuse** (Fishbain et al., 2008). This finding has been replicated multiple times. (Cowan et al., 2003)

And if the barriers to research on ibogaine were removed, addiction could potentially be an entirely curable ailment (Leal et al., 2017) (Vastag, 2005). Further, much of the research on addiction up to this point has been of low quality, conflated dependence and addiction, and did not specify their definitions for addiction, which when the body of evidence is analyzed with this in mind, things such as family history of substance abuse is no longer predictive of addiction risk. (Wu, et al., 2006)

As it stands now, the regulations already passed have restricted patients' abilities to obtain adequate care, and in states such as Kentucky, where they passed a strict acute pain prescribing limit for opioids some time ago, even the state legislators and their family members were affected. As a result, changes were made to make the limits more flexible due to the immediate and adverse consequences of this kind of legislation. The situation remains that adequate treatment for chronic pain in this state is not available to the vast majority of people who need care. This is dangerous.

Section 1.2 The Consequences of Unrelieved Pain

Chronic pain reduces the lifespan substantially. As Grol-Prokopcyzk, 2016 noted, "...higher pain at baseline predicts death even 10 to 12 years later. Pain serves as a long-term mortality risk," causes heart conditions, accelerated cellular aging, and death from said heart conditions along with suicide. So to prevent unnecessary death, opioids are necessary for many patients because the pain is what causes these problems, and **opioids are the only effective**

remedy that exists for pain for many people and the only true analgesics available–especially for many people with chronic pain–both in terminal and non-terminal (non-malignant) conditions, because the pain is what causes death in the latter, as it is arguably the most severe type of stress the body experiences (Blackburn, 2001). Opioids are the only known acceptable treatment for severe pain.

Chronic stress has a well defined set long-term of consequences: "impaired immunity, atherosclerosis, obesity, bone demineralization, and atrophy of nerve cells in the brain. Many of these processes are seen in major depressive illness and may be expressed also in other chronic anxiety disorders." (Mcewen, 2004)

The severity of the effects of inadequately relieved chronic pain are bolstered by way of pain's status as a form of stress, and these consequences include, but are not limited to memory impairment, decreases in brain volume that are reversible with adequate treatment, (Seminowicz, 2011) as well as any and all of the aforementioned consequences of chronic stress.

The prevalence of chronic pain varies, but some estimates are as high as 36.6% of the population as of 2016 (Grol-Prokopcyzk, 2016), and this is disturbing when the seriousness of this condition is reflected upon. *Depriving people of life-saving medications by instituting more regulations on the use of opioids is effectively leading to the death of these people*. Why are we demonizing medications when a huge portion of the population would die if medications were outlawed and/or so heavily regulated that nobody had access to the medications?

No other condition is A.) deprived life-saving treatment B.) No other condition has its treatment, and in effect the person's life contingent on the result of faulty drug tests, as is the case for CPP C.) No other condition is left untreated (adversely affecting health and life expectancy) for as many years as chronic pain is after diagnosis and D.) No condition has what is often its only effective treatment avenue (especially for moderate and severe pain) completely cut off and inaccessible as severe chronic, intractable pain's only effective treatment avenue for many patients is E.) No other condition is forced to first explore interventions empirically shown to be ineffective, such as mindfulness training, which has no effect on pain intensity (Skaer, 2015).

The only comparable situation is that of those suffering from addiction who by and large lack adequate access to the medications they need, and since this is unjust, and has lead to deaths, and considering that evidence cited herein supports this assertion, the same is true for those suffering from chronic intractable pain.

Chronic pain affects 116 million Americans, and all it takes for the majority of these people to become functional again is the adequate pain relief wrought by using opioid analgesics, which would relieve the majority of the $560-$635 billion disease burden, the largest disease burden of any one disease entity (Institute of Medicine, 2011). We need more research into alternatives yes, but until there is an affordable, and safe alternative, it is unethical to let these people die slowly in ear-splitting agony in the decade leading to their death. Especially considering that everybody has a 1/3 chance of developing it at some point in their life (Institute of Medicine, 2011). The result of the proposal at hand would be precisely this.

If insulin were so heavily regulated and criminalized that doctors treating diabetes were driven out of practice (which is happening with doctors that prescribe these lifesaving medications), the public backlash would be massive, but much of this population is too disabled, in pain, and in complete despair due to how the medical system and the government has abandoned them that they can only cry out in agony, not form cohesive arguments.

Using a risk of addiction as an excuse not to treat pain is invalid, because pain interferes with the intrinsically rewarding nature of opioids (Inturrisi, 2002), and the rate of addiction in people with no history of addiction is 0.19% and in populations not preselected, it's 3.27%, (Fishbain, 2008) both of which are substantially lower than the population average. The Cochrane review on the topic comes to a similar conclusion (Noble et al., 2008). These people are not addicts, they are potentially functional members of society if their treatment is no longer denied to them. The number of opioids prescribed dropping is not a good thing. It should alarm all of you, telling you that next time you're in pain, it won't be relieved. The number of posts on social media like Facebook and Twitter of chronic pain patients expressing suicidal ideation has skyrocketed, and the number of people saying that when they or a loved one had a surgery that they woke up in horrific agony has skyrocketed, as has the number of people saying that their pain continued to be unrelieved after they woke up from their surgery. This is a disturbing fact that should factor into your decision in regards to removing "high dose" opioids from the market; this would also result in me no longer being able to attend college due to the severe pain-causing condition I was born with called Ehlers Danlos Syndrome.

No other condition has their treatment denied to them on the basis of risk for another condition. Further no other condition has relief from agony contingent upon faulty, inherently flawed drug tests that do not have a place in the practice of medicine, where they can do a great deal of harm. (Hansen et al., 1985) (Seitman et al., 2014) (Pesce et al. 2012) (DePriest et al., 2010) (Reisfield and Maschke, 2014) Further, "No current screening test is close enough to perfect, and as close to perfect as possible is necessary in these circumstances… Discharging a patient from a medical practice is virtually never an acceptable response to an inappropriate drug test." (Reisfield and Maschke, 2014) Yet, this happens a great deal, and no disciplinary action is ever taken against the physician doing this.

"[Chronic Opioid Analgesic Therapy] COAT is associated with moderate side effects but a low risk of abuse or drug addiction. COAT was not associated with adverse long-term sequelae… **There is a place for the use of chronic oral or transdermal opioid analgesics in the treatment of some patients with [Chronic Low Back Pain].**" (Bartleston, 2002) This simple fact seems to have been forgotten in the rhetoric about opioids that has excluded people with chronic pain and doctors treating people in chronic pain, the only two parties that are indispensable to a debate on whether opioids are helpful, from the discussion.

Further, "An addiction disorder occurs in about 5 percent of people who take these pain relievers as directed over the period of a year for *acute or chronic pain*," (NIH MedlinePlus) which shows that 95% of people who take opioids for pain do not become addicted to their medications. It also demonstrates that drugs are **not inherently addictive, as no drug is**.

Conceiving of drugs as being addictive is simply saying that some drugs form dependence, such as caffeine, some antidepressants, and opioids. Dependence is simply the presence of withdrawal symptoms upon abrupt cessation of a drug. (Morgan and Christie, 2011) Addiction on the other hand is far more complex, a neurological disease, and an attachment disorder, and will be addressed in some detail throughout this proposal.

There are countless immensely painful afflictions that the human body can manifest. Listing all of the painful conditions would be a lengthy, laborious, and ultimately pointless task. One would be left at the end with dozens or even hundreds of pages of medical terminology. Yet one fact could be extracted from such a pointless exercise: pain affects well over a third of the United States population (Institute of Medicine, 2011) (Grol-Prokopcyzk, 2016). This figure should be startling, and disturbing. Estimates vary somewhat, but they cluster around the number of 100,000,000 million people in the U.S., which means that you and each of your loved ones has a ⅓ (33%) chance of developing chronic pain at some point in their lifetime.

When this inevitably happens to you or a loved one, the availability of opioids through medical providers will be a pertinent and immensely important issue to you and your loved ones. If things remain as they are and/or the current proposal is implemented, the availability of opioids will be reduced dramatically, and the situation in the United States will resemble that of India, who made morphine and other opioid analgesics almost completely unavailable to the entire population, which resulted in unspeakable suffering of people with routine acute pain from injuries, and the unending agony of those with chronic pain because doctors could not and would not provide opioids for pain due to fear of regulatory scrutiny, who were already not given the care they needed in order to be able to live productive lives. Many people with cancer pain died in horrible, needless pain. In a report on the availability of opioids in India, the authors went on to say:

> "The Pain and Policy Studies Group at Madison Wisconsin has been collaborating with many Indian palliative care workers and government officials to improve availability of opioids to those who need them for pain relief. As a result of this collaborative effort, the Government of India asked all state governments to modify the narcotic regulations following a model given to them." (Rajagopal, 2007)

In India, doctors prescribing these lifesaving drugs have been subjected to criminal prosecution, long prison sentences, and similar situations have arisen here in the United States with the prosecution of legitimate prescribers relieving the acute and chronic agony (Szalavitz, 2004) caused by the endless number of painful conditions that exist. This creates a fear of regulatory scrutiny that is one of the largest barriers to adequate management of chronic pain (Rich, 2000). By painting pain management doctors as the reason for the opioid epidemic, the issue is left poorly understood, and flawed notions become common "knowledge." This is highly counterproductive. The media and the CDC's flawed guidelines have had no problem publicizing this view, that at its core is completely divorced from reality. This misleads the public, doctors, and government officials into believing that treating acute and chronic pain is not a priority, when the opposite is true. Pain is lethal when left unrelieved.

Chronic pain is a form of chronic stress. (Blackburn, 2001) The consequences of chronic pain when left untreated or undertreated includes, but are not limited to:

- "Stress could potentially lead to oxidative stress by means of chronic activation of the autonomic and neuroendocrine stress responses." This leads to **accelerated DNA damage and aging** (Epel, 2004) (Mcewen, 2004)
- So called chronic *non-malignant* pain predicted **death** within 10 years (Grol-Prokopczyk, 2016)
- "Increased protein breakdown leads to a negative nitrogen balance, resulting in reduced wound healing (Marieb, 2000)." (Middleton, 2003)
- **Cognitive issues**, (brain fog) and **memory problems** (Porta et al. 2015)
- "Atrophy of nerve cells in the brain" (Mcewen, 2004)
- "Involuntary responses to noxious stimuli can cause reflex muscle spasm at the site of tissue damage (McCaffery and Pasero, 1999). Impaired muscle function and muscle fatigue can also lead to immobility, causing venous stasis, increased blood coagulability," (Middleton, 2003) commensurately increasing risk for deep vein thrombosis.
- **Changes in DNA** (Massart et al., 2016)
- "Hyperglycemia, impaired glucose tolerance," (Middleton, 2003)
- "Impaired immunity" (Mcewen, 2004) (Middleton, 2003) meaning, **the shutting down of your immune system, which can and does often result in death.** This puts individuals at risk of infections, pneumonia, and sepsis (Marmo and D'Arcy, 2013)
- "Major depressive illness and may be expressed also in other chronic anxiety disorders" (Mcewen, 2004) **Untreated chronic pain results in depression and anxiety disorders.**
- Strain on interpersonal relationships (WHO, 2000)
- Hypoxia secondary to respiratory pressures which "can cause cardiac complications, disorientation and confusion, and delayed wound healing..." (Middleton, 2003)
- Sodium and water retention, (along with many other factors) contributing to high blood pressure (Middleton, 2003)
- "Therefore, the stressor effects of unrelieved pain have the potential to increase anxiety levels further and interfere with activities of daily living, such as diet, exercise, work or leisure activities and to interrupt normal sleep patterns causing varying degrees of insomnia (Macintyre and Ready, 2001)." (Middleton, 2003)
- Pneumonia secondary to the respiratory dysfunction caused by unrelieved pain (Middleton, 2003)
- Obesity (Mcewen, 2004)
- Disruption of the neuro-endocrine system, whose purpose is to adequately maintain homeostasis in a changing environment (Middleton, 2003)
- Reduced appetite and self-esteem (WHO, 2000)
- "Bone demineralization" (Mcewen, 2004)
- Inhibition of digestion (Middleton, 2003)

- **Disability** (Lohman et al., 2010)
- **Suicide** and/or a desire for death (WHO, 2000)

"Unrelieved pain can impair all aspects of a person's life, including appetite, mood, self-esteem, relationships with others, and even the ability to move. In some countries, it has been reported that unrelieved pain can lead to the wish for death and inquiries about euthanasia and assisted suicide. Relief of pain has been demonstrated to improve quality of life." (WHO, 2000) Chronic pain has adverse effects on the "cardiovascular, gastrointestinal, respiratory, genitourinary, musculoskeletal and immune systems." (Middleton, 2003)

All of these physiological consequences have their own price tag (monetarily and to the individual and their loved ones) to go along with pain's 500-600 million-dollar price tag, and the bill totals up to be unmanageably large, so in order to reduce this price to the government, and to hospitals, and those within the healthcare profession.

Section 2 The Use of Opioids in Chronic Pain

Section 2.1 Rationale and Importance of Treating Chronic Noncancer Pain

As if these consequences were not enough, "Chronic pain is a one of the most significant causes of suffering and disability worldwide," (Lohman, 2010). Yet, people in chronic pain have little-to-no access to adequate treatment in the U.S.. Adequate treatment for chronic pain shall be defined as, "Treatment that controls a patient's pain such that the patient has the minimum possible interference of pain with their daily life, pain is minimally disrupting homeostatic balance in the body, and the patient has as great of quality of life as that individual can achieve within the limits of medical science."

For a comprehensive, empirical, exhaustive analysis of literature on the topic of the usage of opioids in chronic noncancer pain, the American Society of Interventional Pain Physicians (ASIPP) created an excellent guideline (Manchikanti et al., 2017) that is superior to in every way the CDC's guidelines, and provides evidence based guidelines that are far more empirically rigorous than any other current guidelines on the topic. If policy were to be based on anything, it should be based on these.

No patient will gain the same amount of pain relief and function from the same set of interventions. Pain management is a very individualized process. As such, patients must have access to all modalities available so that they and their pain management physician may determine what is best for that patient, without the government dictating what a doctor can or cannot prescribe (or at what dosage they may prescribe) a patient. This includes the potentially highly effective (and impossible to abuse) topical formulations of opioids such as morphine which have been shown to be effective in reducing the overall consumption of systemic opioids, and to serve as a useful adjunct to the treatment of severe, intractable chronic pain (Tennant, 2008). Insurance

currently is able to avoid covering topical opioid formulations and formulations combining lidocaine and morphine as well as a variety of other topical therapeutic agents. This must be addressed, but is beyond the scope of this essay.

"However, if the stress response is allowed to continue, a variety of harmful effects may ensue that involve multiple systems of the body and are potentially life-threatening." (Middleton, 2003) Middleton goes on to state, "The physiological responses that take place via the sympathetic nervous system and the neuro-endocrine system are numerous and intrinsically linked," which is to say that when moderate-severe pain (a major stressor) is experienced, that it begins a cascade of physiological responses that are inextricably linked, and are known to cause disease and death, particularly when the response is sustained for a long period of time. "Although the initial effects of the sympathetic nervous system allow survival of an individual...in the long term it is disruptive and harmful." (Middleton, 2003)

Establishing a legal right to adequate and effective treatment for pain that reduces their pain and suffering, which includes opioids in many cases, as a human right, is imperative to reducing opioid related mortality, needless suffering, and the overdose deaths from patients driven to illegal drugs due to inadequate pain relief (Lohman, 2010). It is also a part of a person's right to life in the U.S. Constitution, and their right not to be subjected to inhumane treatment. (Office of the United Nations High Commissioner for Human Rights, 2002)

Opioids are rarely a first line treatment for chronic pain. So *when* measures such as physical therapy (specifically manual therapies) and nonopioid medications have failed, as they do for very significant numbers of patients, only then are opioids even considered. Getting the government involved in healthcare and dictating how your doctor can treat you, is and will never be a good idea, because **a doctor's job** is to deal with *each* patient *individually*, and do what is best for *specific* patients, so instituting dosage limits, or blanket policies as the CDC guidelines suggest, will have deadly consequences, and decrease the quality of care throughout the medical profession. It is best to leave health care decisions to trained healthcare professionals, and not chase after them for "drug trafficking" when they attempt to alleviate suffering, as only a miniscule percentage of doctors could or even are considered guilty of this, seeing as chronic pain patients need their medications to function, and as such cannot afford to sell them.

If this profoundly dangerous proposal to remove opioids above an arbitrarily selected dose off of the market, it will deeply infringe on doctors' ability to adequately treat their patients with chronic pain and it will increase the cost of care to those with pain, in addition to further restricting access to needed treatments. It would also make doctors less willing to prescribe these medications, which would even further restrict access to treatments people with severe intractable pain require in order to continue being alive, meaning they will die, but only after their loved ones and family watch them suffer in profound agony for potentially months, unable to find care elsewhere, their immune system will shut down, and they will die. This is if the individual does not end their own life before then, but regardless, these individuals' blood will be on your hands. This population constitutes between 10 and 25 million people, who would die as a result of this proposal. Be very careful how you go about dealing with this proposal, as it could result in the

deaths of a little under 3% of the population of the United States of America if dealt without the utmost of care and precision.

Between 96.73%-99.81% of chronic pain patients do not become addicted to opioids when being treated with long term opioid therapy. It is nonsensical to target this population when the majority of patients do not abuse or sell their lifesaving medications, because they are interested in preserving their quality of life. In a separate, well-structured study, the rate of addiction in long term opioid therapy (LTOT) was 2.8%, again well below the population average; it even noted that, "**72.5% of all patients derived benefit from opioids**." (Cowan et al. 2003).

Regardless, neglecting to treat chronic pain is unjustifiable when considering that there are no alternatives to opioids that have been proven to be as effective, and they are safe and lifesaving drugs when taken as directed under the guidance and monitoring of adequately trained physicians. (Monitoring being defined in this context as checking prescription drug monitoring programs, as this is an effective, noninvasive, reasonable course of action.) While there are no true alternatives, there are many adjunctive therapies, most of which have not been studied as much as opioids. Manual therapy techniques such as myofascial release seem to be an effective adjunct to opioids (Altindag, 2014). The reason it and virtually all other interventions are adjunctive and not alternatives to opioids is because one cannot reasonably expect to have any real measure of control of their pain if it constant by spending all of their income (people with chronic pain often have very little or none) seeing specialists and attempting to control their pain. It is not possible. It would also be a life lived with very little quality of life, and in essence it prevents the sufferer from functioning properly in society, whereas when these are used as adjuncts to opioids, the patient often benefits immensely.

Section 2.2 Treating Chronic Noncancer Pain

The key to the effective treatment of pain is **individualized care, not instituting unscientific ceiling doses that have no basis in science, medicine, or ethics**. (Schneider, 2009) (Inturrisi, 2002)

"We call the legal barriers ''fundamental'' because where laws forbid access to pain relief, that prohibition trumps all other reasons for the inequity." (Nickerson and Attaran, 2012)

The solution to addiction is not about controlling a substance, but about healing a person, which is why prohibition didn't work, created drug crime, and caused more problems than it solved. The difference here and now with opioids is that the prohibition or even more severe restriction of opioids will cause widespread suffering as the direct result, many, many chronic pain patients will die either from the malignance that is severe intractable pain, or from suicide, and it will compromise even further the trust all patients have in their physicians to do what is best for them, because the government would be preventing patients from receiving the proper treatment and the physicians from administering it. The similarities between these situations are many, but the most prominent could be said to be that in both situations, restrictions will not help anyone, will not reduce mortality, and will increase it.

This proposal would lead to situations where a patient receiving 75mcg/hr Duragesic patches every 48 hours would be forced to instead of buying 15 75mcg/hr patches, they would instead be forced to purchase (their insurance company would likely not pay for all of it) buy 45 25mcg/hr patches, which would cost in the upwards of $300-500. This would put an immense financial burden on patient with severe, intractable pain, as well as those with cancer for whom the Duragesic patch at 75mcg/hr is often prescribed. Do not contribute to the profound suffering of those with cancer and other conditions causing severe intractable pain.

Section 3: The Nature of the "Opioids Epidemic" and the Diversion of Controlled Substances

Section 3.1 The Sources of Controlled Substances that are Sold on the Black Market

The myth that doctor shopping is common and has been perpetuated for far too long: "On average, patients in the extreme outlying population (0.7% of purchasers), presumed to be doctor shoppers, obtained 32 opioid prescriptions from 10 different prescribers. They bought 1.9% of all opioid prescriptions, constituting 4% of weighed amounts dispensed," (Mcdonald and Carlson, 2013) This is a miniscule number of prescriptions and potentially diverted drugs when weighed against the DEA's figures of the quantities stolen: The following are the quantities of various opioids stolen and diverted to the black market from 2000-2003 alone: "The total number of dosage units for the six opioids is as follows:

- 4,434,731 for oxycodone
- 1,026,184 for morphine
- 454,503 for methadone
- 325,921 for hydromorphone
- 132,950 for meperidine
- 81,371 for fentanyl" (Joranson and Gilson, 2005)

It is not possible to match this volume of diversion on an individual patient level, the provider level, or even from so called "pill mills," considering the actual numbers of prescriptions being dispensed for legitimate patients who are closely monitored, so rather than limiting prescriptions, which are not the source of diverted opioid analgesics, it is more logical to protect these points in the chain of distribution. And as Human Rights Watch notes, diversion of medical opioids is rare. Morgan and Christie's 2011 piece states:

> "Drug addiction is defined as an uncontrolled craving for a substance and is manifested in drug-seeking behaviours. Opioid addiction, heroin addiction in particular, has been well characterized scientifically (Rosenberg, 2009) and portrayed to the public in graphic detail in movies such as *Trainspotting* and *Requiem for a Dream*. The power of opioids to motivate behaviour is clearly evident in both cases. **The one exception is the relatively low incidence of**

> **addiction to opioids in chronic pain patients** (Fishbain *et al.*, 1992; Noble *et al.*, 2010). **The lack of addiction in this case could be caused by pain interfering with the rewarding properties of opioids**, limited liability as a result of the type of opioid and route of administration used to treat pain (e.g. fentanyl patch vs. intravenous heroin), or restraint in dosing because of the fear of addiction." (Morgan and Christie, 2011) [emphasis added]

Given that most "ovedose" deaths, 85% in fact (Kertesz, 2016), are from illicitly manufactured fentanyl and fentanyl analogues in lethal concentrations, not drugs prescribed by doctors, which are given in small, small, quantities, that are arbitrarily being called "High dose" opioids, when in reality, saying that something is a high dose has little meaning, because each person has different needs given their various concentrations of liver enzmes that govern the metabolism of all drugs (the CYP 450 enzyme family).

Chronic pain patients often hide their pain, suffer in silence, because they are quiet, and do not wish to deal with the stigma against chronic pain, whereas addicts use others to obtain a fix due to deficits in empathy and overall psychological structure (Flores, 2001, 2012).

There are marked differences between people these groups, and as such there is no excuse for lumping these two populations together by conflating dependence and addiction.

Section 3.2 Death as a Result of Chronic Pain

The body of literature on chronic noncancer pain agrees that "prevalence among US adults is high: 11% to 47%..." (Grol-Prokopczyk, 2016) and the author goes on to note, "The ratio of mild to moderate to severe pain remained fairly constant across the 7 waves, at approximately 3:6:2…" which underscores how much of the cost of chronic pain could be mitigated with adequate treatment, often involving opioids. Mild pain is not frequently disabling, but moderate and severe pain is. So the individuals who are on social security and not making money because they are unable to obtain adequate treatment could have their function restored, and no longer need social security benefits, and alleviate well over half of the aforementioned 560-635 billion-dollar disease burden of chronic pain, as well as the serious consequences of untreated chronic pain.

Hanna Grol-Prokopcyzk goes on to note that pain continues to worsen with age, and individuals who died during the survey period had 31% higher pain on average than those who lived, and those who died "were 48% more likely to deem the pain severe…those with moderate pain had on average 0.72 the odds of surviving until the next survey wave, and those with severe pain had 0.50 the odds." The author concludes that chronic noncancer pain of a high intensity predicts death within the subsequent 10-12 years. (Grol-Prokopczyk, 2016)

As Middleton notes in "Understanding the physiological effects of unrelieved pain,"

> "The cardiovascular system responds to the stress of unrelieved pain by increasing sympathetic nervous system activity which, in turn, increases heart rate, blood pressure and peripheral vascular resistance. As the workload and stress of the heart increase, owing to hypertension and tachycardia, the oxygen consumption of the

> myocardium also increases. When oxygen consumption is greater than oxygen supply, myocardial ischaemia and, potentially, myocardial infarction, occur. The myocardial oxygen supply may be further compromised by the presence of any pre-existing cardiac or respiratory disease or by hypoxaemia due to impaired respiratory function (Macintyre and Ready, 2001)." (Middleton, 2003)

Chronic pain, when left untreated, or undertreated, comes with substantially increased risk of fatal cardiovascular events such as heart attacks, pulmonary embolism, and deep vein thrombosis (Middleton, 2003). Thus, it may be prudent to consider the condition (if left untreated) a terminal condition, as it does result in death. As such, removing these dosages from the market for palliative and long-term care in addition to for acute care, would result in numerous deaths, and undue suffering for people with intractable pain and other sources of pain such as cancer.

Section 3.3 The Nature of the "Opioid Epidemic" and Mitigation Strategies to Reduce Harm

The nature of the so called "opioid epidemic" has been misunderstood, and as a result the responses have been directed at the wrong targets. "Heroin and fentanyl have come to dominate an escalating epidemic of lethal opioid overdose, whereas **opioids commonly obtained by prescription play a minor role, accounting for no more than 15% of reported deaths in 2015**." (Kertesz, 2016) [emphasis added] This means that restricting opioid prescribing will not reduce overdoses, and will only serve to cause suffering and death, which is supported by other experts in the field (Gilson et al., 2007), as well as the data we currently have on the lack of efficacy of these restrictions on overdose deaths. In Alabama, a trend seen throughout the U.S. of restricting opioid prescribing having no effect on overdose deaths, is clearly evident (Yurkanin, 2017). Even the CDC's own data states that overdose deaths have continued to increase despite reductions in the prescribing opioids. (Gery et al., 2017) They of course did not mention the vast and numerous examples of public suicidality that has resulted from the reductions in opioid prescribing as well as the many, many anecdotal reports of suicides that have resulted directly from forced opioid tapering that occurs to reduce opioid prescribing.

Kertesz gos on to say:

> "The observed changes in the opioid epidemic are particularly remarkable because they have emerged despite sustained reductions in opioid prescribing and sustained reductions in prescription opioid misuse. Among US adults, past-year prescription opioid misuse is at its lowest level since 2002. Among 12th graders it is at its lowest level in 20 years**. A credible epidemiologic account of the opioid epidemic is as follows: although opioid prescribing by physicians appears to have unleashed the epidemic prior to 2012, physician prescribing no longer plays a major role in sustaining it. The accelerating pace of the opioid epidemic in 2015–2016 requires a serious reconsideration of governmental policy initiatives that continue to focus on reductions in opioid prescribing**. **The dominant priority should be the assurance of subsidized access to**

> **evidence-based medication-assisted treatment for opioid use disorder**. Such treatment is lacking across much of the United States at this time. **Further aggressive focus on prescription reduction is likely to obtain diminishing returns while creating significant risks for patients**." [emphasis added]

This is of course notwithstanding the fact that the majority of "opioid overdoses" involved multiple drugs, making them drug interaction deaths resulting from additive toxicity, most frequently the combination of alcohol, benzodiazepines, and opioids, all of which are central nervous system depressants, so it is unsurprising that these individuals died from respiratory depression. (Warner et al., 2016)

Section 3.4 Postmortem Toxicology, Additive Drug Toxicity, and Data Collection

If one takes a look at the NCHS drug poisoning statistics, less than half of drug poisoning deaths are from opioid analgesics. The vast majority of overdose deaths were not prescribed opioid analgesics (Kertesz, 2016) This means that there is a clear drug poisoning problem in the United States that restricting the prescribing of opioids does not address. Further, as Kertesz notes above, **physician prescribing is not the primary source of the problem**. Also of note is that suicide misclassification is frequent (due to the highly variable data collection practices across the country), so **many of the deaths involving opioids could have been suicides** (Rockett et al., 2015), even as much as 40% of opioid "overdoses" could be suicides as the suicide prevention coordinator in Montana noted (Benoit, 2015) and as I will note in the next paragraph, opioids were likely not responsible for death in the majority of the deaths classified as opioid overdoses.

Making matters worse, **postmortem toxicology data is highly unreliable to to variable data collection** (Warner et al., 2016). Coroners nationwide must be encouraged to consider drug interactions in the cause of death rather than focusing on single drugs, must create standards to follow that also require consistently testing BAC, acetaminophen concentrations, along with other NSAIDs, as well as benzodiazepines whenever an opioid is detected, because the data would suggest that the vast majority of "overdose" deaths involved multiple drugs which clearly indicates that they are not overdoses as most people conceptualize them, but instead are drug interactions that created an additive toxicity effect. This is precisely the reason that restricting opioids will have no effect on "opioid related" mortality, because the majority of "opioid related" mortality involved more than just opioids. Further, **the data being cited about the "opioid epidemic" is of extremely low quality and should not be the basis of public policy due to the heterogeneity of the data collection practices and the multitude of pitfalls and problems in postmortem toxicology. They include but are not limited to: an unacceptably high number of false positives and false negatives, the cross reactivity of drugs** (heroin might show up as morphine and hydrocodone, even if neither was ingested, and suboxone will show up as oxycodone nearly 70% of the time), **and a lack of focus on drug interactions**. (Jenkins et al., 2009) (Saitman et al., 2014) (Reisfield, 2014)

These all work together to create *extremely unreliable data* that *cannot, and should not be used for policy making decisions, as low-quality data leads to dangerously poor decisions when making strong recommendations*. This is perhaps the greatest fallacy of the CDC's guidelines for opioid prescribing which have done nothing to reduce opioid related mortality while simultaneously legitimizing the stigmatization and denial of care to chronic pain patients that has likely contributed to the rise in suicides, and has certainly reduced the quality of life of at minimum a million people thus far, as the number of people being prescribed opioids long-term has dropped significantly (Kertesz, 2016) which should cause a great deal of alarm considering that the problem of pain has not changed, and it still affects approximately one third of the United States population (Grol-Prokopczyk, 2016).

I am immensely disturbed and unsettled by the reduction of opioid prescriptions being branded as a positive event, because it heralds inadequate pain relief the next time you have a major or minor surgery–as is already the case in many emergency rooms around the United States. (Anson, 2016)

Section 4: Correcting Misconceptions

Section 4.1 The significance of Pain

Because pain is the most common reason people seek medical care (Fishman, 2007), and it reeks havoc on the human body physiologically as well as psychologically, and costs $560-$650 billion in lost productivity every year (Institute of Medicine, 2011) (Gilson et al., 2007), the adequate treatment of chronic pain would stimulate our economy in addition to being the ethically acceptable thing to do.

> "Pain is one of the most common physical complaints on a person's admission into the health care system, and moderate to severe pain is frequently reported to be experienced throughout hospitalization, during treatment, and even after discharge. The costs of pain, both emotional and financial, can be enormous. Unrelieved severe pain at any stage of the disease can limit a person's functioning, productivity, and ability to interact socially; sometimes pain destroys the will to live. When the quality of pain relief provided is inadequate, it is usually the result of failures to apply existing knowledge about pain and its treatment, including the appropriate use of opioids. But pain relief also can be affected by the regulatory environment and fear of being investigated for excessive prescribing. The importance of evaluating and improving policies governing pain management has been recognized by national and international authorities, including the Institute of Medicine and the World Health Organization." (Gilson et al., 2007)

I recommend that anyone working on drafting any guidelines about the use of opioids read the following article, (and guides such as the Institute of Medicine's "National Pain Strategy A Comprehensive Population Health-Level Strategy for Pain about making an adequate national plan to treat pain"), as the Gilson et al. article details policies that will impede and facilitate

adequate treatment of chronic pain (Gilson et al., 2003) They go on to say, "With increased misuse of opioid pain medications and associated media coverage, **efforts to address drug abuse and diversion must not interfere with the use of these drugs for pain management**." [emphasis added] The CDC's recent guidelines are doing precisely that, as the laws and resolutions currently in the senate have the potential to do. The results of taking such drastic action will be the unspeakable suffering of millions of Americans in an ineffective effort to save a miniscule minority of people who use these medications (almost entirely illegally), (Fishbain et al., 2008) which is profoundly unethical (Rich, 2000). I also recommend reading the ASIPP Opioid Prescribing guidelines cited earlier.

The narrative of people getting addicted to opioids in 5-7 days is blatantly false, as it conflates dependence with addiction, cites little-to-no evidence, and is designed to misinform people who are not well educated about the matter. (Lawhern, 2016) It is deeply troubling that I must point this out, as it is blatantly false, and an absurd proposition at that.

Section 4.2 Opioids are the Last Resort Treatment Already

People who may be on opioids are people who are at the end of the road in terms of finding effective interventions for their pain. Doctors are so cautious about prescribing opioids for chronic pain that most are reticent to prescribe opioids to people who desperately need them (Institute of Medicine, 2015), so if a person manages to find a physician who is willing to prescribe them, they work for that individual, and they show no signs of addiction, these medications will likely give them quality of life, and restore function in many individuals.

Taking away the only effective treatments we have for pain, opioids, is effectively ending individuals' lives who are on long term opioid therapy. When pain becomes so great, and all of the avenues of treatment have failed many patients opt to stop feeling any and every kind of sensation through suicide (Baumeister, 1990). The risk of suicide in chronic pain, as mentioned earlier, is substantially higher than most other illnesses, independent of depression (Webster, 2014) (Racine et al., 2016) It is generally accepted that pain is associated with depression, and likely causes it. (Middleton, 2003) (Blackburn-Munro, 2001)

If these restrictive policies pass, then the hardships regularly endured by chronic pain patients when they must see doctors in person in order to receive a prescription to relieve their pain, despite often being in terrible agony, this will happen to everyone receiving opioids for acute pain, and will be especially problematic for more major surgeries with longer recovery times. If you have a hip surgery or any kind of major surgery, you will need to drive to your surgeon to get pain medication every 5-7 days, (depending upon whether there are refills allowed) and after that all you will only have over the counter pain medications, and ibuprofen and other nonopioids that are equally if not more dangerous than opioids. (Giummarra, 2015) This is both inhumane and detrimental to the healing process. (Middleton, 2003)

> "Collaboration between Human Rights Watch and the international palliative care community to highlight the need for opioid use for medical purposes with the Narcotic Drugs Committee at the United Nation. The committee overseeing the ICESCR is

> preparing a general comment on the issue of discrimination. A submission has been made to the committee by the IAHPC, the WPCA, and the IASP describing discrimination in the provision of, and access to, both pain management and palliative care. The submission argued that draconian domestic opioid laws, policies, and practices that restrict opioid availability, accessibility, and affordability constitute a significant discrimination against patients in pain and the dying. Other examples of de facto discrimination in the provision of pain management and palliative care are laws, policies, and practices that fail to provide adequate health care services in rural and remote areas or fail to provide adequate health care services for children, patients with HIV/ AIDS, indigenous persons, persons with disabilities, prisoners, women, refugees, and stateless persons." (Gwyther et al., 2009)

One of the most compelling reasons that opioids are necessary for chronic pain (both from cancer and from other, often more painful conditions, such as a variety of connective tissue disorders) is the aforementioned long-term *consequences of untreated pain*. "Far more than just a symptom, chronic pain can be a disease in its own right—the biggest health problem facing America today." (Foreman, 2016) This combined with the lack of alternatives that are equally as effective (Inturrisi, 2002) (Lohman et al., 2010) makes it unethical to restrict the prescribing of opioids any further.

> "However, many countries have regulations that go well beyond these restrictions, creating complex procedures for procurement, stocking and dispensing of controlled medications, including: restrictive licensing requirements for health care providers prescribing medicines; cumbersome dispensing procedures; and limitations on the formulation and quantity of medicine that can be prescribed [55]. In some cases, drug control authorities or health systems adopt even more restrictive measures than those required in the formal regulations. Although the diversion of medical opiods from its proper use is frequently cited as the explanation for such policies, the INCB has noted that, in practice, diversion is relatively rare [56] and the WHO has observed that 'this right [to impose additional requirements] must be continually balanced against the responsibility to ensure opioid availability for medical purposes' [46]." (Lohman et al., 2010) [1]

One of the biggest misconceptions floating around in the media is that effective alternatives to opioids exist. Most chronic pain patients tend to be poor because doctors refuse to treat their pain, they are fired from their job as a result when they miss too many days because they are laying at home in agony, and they end up in poverty and unable to work. Nearly all of the treatment "alternatives" doctors recommend are not financially feasible, and they do not reduce pain or increase functionality by an appreciable amount for people in moderate to severe pain. (Skaer, 2015) Alternative medicine is alternative because the evidence base for its effectiveness is severely limited, even more so than opioids' use long term, as there are in fact studies of long term opioid therapy's efficacy in a patient population, but not for these so-called alternatives. The reason that exercise (one of the many recommended therapies for chronic pain

that often does not work) is not an effective way to relieve pain in a variety of chronic pain syndromes has to do with the nature of the underlying illness (for example, people with EDS HT will re-injure their already lax ligaments if they exercise vigorously after dislocating a bone, which happens daily, and will cause increased pain as well as accelerate their disease progression), and the mechanism by which exercise can produce analgesia is the production of endogenous opioids, but "Unfortunately endogenous opioids degrade too quickly to be considered as useful analgesics (McCaffery and Pasero, 1999)." (Middleton, 2003) This is why yoga is abysmally ineffective in relieving pain in a variety of pain-related conditions. In fact, I have not seen a single well-controlled randomized controlled study that shows that yoga is even remotely comparable in efficacy to opioids for treating moderate to severe pain.

Most patients are already self-managing their pain to the greatest extent that is possible for them, they are also exploring all of the alternative treatments available, almost all of which are abysmally ineffective, and extremely expensive. Many CPPs become poor because they pursued "alternative treatments," and they did not work, as they should should never have been expected to because there is no evidence suggesting that they do (inherent to the definition of alternative medicine), nor are they covered by insurance. This is contrary to the myth that patients take a passive role in their treatment and want to just "pop a pill and make the pain disappear." I have heard this phrase and derivatives of it dozens of times, and it is a gross misrepresentation of chronic pain. Chronic pain disrupters the homeostatic balance of the sufferer and opioids only relieve enough pain to allow them to function. They do not eliminate pain, and patients do not expect treatment to do so.

If a patient is in moderate to severe acute pain, they must be given opioids, or else the likelihood that the pain becomes permanent increases (Hashmi et al., 2013), it drains them financially (Gilson et al., 2007), and they become poor and apply for disability, as they are unable to work. If they were given opioids initially, they may have only needed them for a short time, but by allowing pain to continue untreated, the body is being damaged on a cellular level, on a hormonal level, a psychological level, and a functional level, as cited throughout (Middleton, 2003).

"Poorly controlled acute pain can lead to debilitating chronic pain syndromes. Appropriate aggressive acute pain management is essential to prevent this from occurring (McCaffery and Pasero, 1999)... Good acute pain management, including an expert knowledge of analgesic drugs and an understanding of the physiological effects of pain, is an essential element of holistic nursing care." (Middleton, 2003) This highlights the immense importance of adequately relieving both acute and chronic pain. Doctors must be educated as to the severely damaging effects of unrelieved pain.

Section 4.3 Opioids are Safe When Used Appropriately

"Animal studies suggest that the reinforcing and rewarding properties of opioids (e.g., euphoria) that are associated with opioid abuse involve the mesolimbic dopamine system and appear to be distinct from those supraspinal systems involved in the production of analgesia and

physical dependence," (Inturussi, 2002) This has been reiterated multiple times (Morgan and Christie, 2011) by many different researchers. This means that having your pain relieved does not stimulate the neural circuitry involved with addiction, unless an individual is already predisposed.

Opioid induced hyperalgesia has not been adequately documented in humans to confirm its existence. If it occurs at all, it occurs even less frequently than addiction (Schneider, 2009) (Romo, 2011), and it is a risk most patients in severe chronic pain are willing to take. A chance at relief is worth potentially continuing to live in agonizing pain every day. (Webster, 2014)

Mandating the CDC's methodologically and ethically questionable guidelines would result in the unbridled suffering of millions, and the continuation of the violation of these people's rights to have their pain relieved. We are a supposedly developed country, yet animals that research is conducted using are arguably treated better than most people in chronic pain in terms of humane treatment and adequate pain relief.

The limited number of people on LTOT (appx. 5-10 million Americans) are terrified that the government will pass a regulation that will plunge them back into agony, and unless you would like to have the cries of unbridled agony fill the streets, hospitals, homes, and eventually the senate chambers, then implementing a ceiling dose on or anymore regulations of opioid analgesics, then more people will suffer worse agony that many people can comprehend every day until any policies of this sort are repealed, as has happened in India. (Murthy, 2010)

The myth of options that work in regards to reducing moderate and severe pain to any appreciable extent is precisely that–a myth–and has been perpetuated for far too long. It's especially harmful for the millions with severe pain because these "alternatives" do virtually nothing for them, and these measures of "pain control" have very limited efficacy (which is in a controlled, not a real world environment, whereas effectiveness is how well it works in the real world), and the research on most of these questionable interventions point to their lack of efficacy (especially for moderate and severe pain), do not report pain levels, which defeats the purpose, or only had mild pain participants. The body of research for these "alternatives" is in many cases more limited than the body of research for opioids. For opioids, we know they're safe if administered and prescribed by an educated physician. According to the CDC's data, 99% of people treated with opioids will not overdose. (Warner et al., 2016) We also know that the rate of addiction is quite low, even lower than might be expected in CPPs (Fishbain et al., 2008). They are the best analgesics available. As Inturrisi 2002 notes, the pharmacological properties of opioids in cancer pain "can be safely extended to patients with noncancer pain."

Further, non-opioid analgesics are associated with their own serious side effects:

> "...cyclooxygenase (COX) inhibitors, carry an increased risk of serious upper gastrointestinal complications, including ulcers, perforation and bleeding. The introduction of COX-2 inhibitors provided a NSAID-based option with improved gastrointestinal safety, but increased risk of cardiovascular effects. Opioids are powerful analgesic agents used to treat moderate to severe chronic pain… Balanced against the adverse effects of pain management medications, there is a need to be mindful of the widespread, often serious, adverse consequences of

> poorly managed pain itself… Adequate analgesia is one of the primary goals of chronic pain management, together with ensuring improvements in the physical and mental functioning of patients." (Labianca et al., 2012)

Drug interactions are the primary danger that chronic pain patients encounter due to the severe restriction of opioids, and practice of using off-label medications for pain, as a patient may end up taking 8 medications, and have little to no relief in pain, have very low functionality, and later when seeing a different doctor who is willing to prescribe opioids, be on 1 or two medications, and have a very high functionality. In one study, it was concluded that the number of medications, not whether they were taking opioids, was what determined whether the participants were in danger of serious adverse events (such as death). (Giummarra et al., 2015)

With this in mind, ludicrous ideas of reducing suffering without reducing pain intensity, such as the CDC guideline's authors stating, "willingness to accept pain and engagement in life activities despite pain, may reduce suffering and disability without necessarily reducing pain intensity," cannot be allowed to persist, as this statement has no basis in science or morality. It is directly contrary to the goals of pain management, and ignores the lethal consequences of untreated pain.

If you require a spinal fusion, and a surgical error is made (as happened to a close friend of mine), you may wake up in horrific agony, be denied medication, dismissed as faking it, and then told that you must accept the most excruciating pain you've ever experienced as your reality for the rest of your days… it has happened, and it was morally and professionally unacceptable, so statements like these must be refuted outright, because pain, especially more intense pain predicts death within 10-12 years (Grol-Prokopczyk, 2016), and is associated with the aforementioned adverse health effects. Some experts, such as Dr. Forrest Tennant have suggested that severe intractable pain if left untreated can kill the person within days through cardiovascular complications and stroke.

Mandating pain curriculum that includes at least 40 hours on pain, at least 24 of which should be on the safe and effective use of opioids would have immensely positive effects on both the treatment of pain, and overdose mortality, as it would keep desperate people in pain from turning to street drugs. Mandating opioid pharmacology and anesthesiology training for any and all physicians who could conceivably be prescribing for pain would improve quality of care in every discipline of medicine, and reduce accidental overdose in the few cases that do have their origin in the prescriber's behavior. "Comprehensive guidelines for goal-directed and patient-friendly chronic opiate therapy potentially will enhance the outlook for future chronic pain management. The improvement of pain education in undergraduate and postgraduate training will benefit patients and clinicians." (Manijani, 2014) Training physicians on the use of topical opioids would also likely prove quite beneficial and reduce overall consumption of oral opioids. Topical opioids are known to have little-to-no abuse potential because they do not enter the central nervous system.

On a separate note, the MME (morphine milligram equivalent) is an immensely complex measure, with limited clinical usefulness, so its use in both faulty research and in proposing a

dosage ceiling for opioids is outrageous, due to the imprecise nature of the conversions (Inturrisi, 2002), and the fact that opioids pharmacologically speaking, have no ceiling dose. "The analgesic efficacy of the opioids does not appear to have a conventional dose-related ceiling, rather dose escalation is usually limited by the incidence and severity of adverse effects. Therefore, individual titration of the dose combined with measures to reduce the adverse effects is key to optimizing the management of pain with these drugs." (Inturussi, 2002) (Kroenke and Cheville, 2017) The MME measure has no place in putting regulations on prescribers due to its questionable scientific basis, complex conversion metrics, and the necessity of individualized approaches to the treatment of pain.

Any actions based on MME to remove opioids from the market are founded on an unscientific and faulty basis that will have profound consequences for people suffering from chronic intractable pain.

Section 4.4 Further Steps the FDA Could Take

Ensuring that physicians and policy experts on these topics such as Aaron Gilson, Lynn Webster, Daniel Carr, and chronic pain patients themselves are included would vastly improve the quality of any recommendations made by the FDA, and reduce the potential harm and unintended consequences of such guidance. The abundant media coverage has already done an ample amount to disseminate information about the *possible* public health effects of opioid prescribing, has scared physicians to such a degree that numerous people have been forcefully tapered, and resulted in loss of function and/or death (Kertesz, 2017), and given how profoundly unlikely the *possible* effects are, that is less than a fraction of a percent of people who are prescribed opioids ever overdose (CDC, 2016), the FDA should not any further changes to opioid-related regulatory decisions unless they are to make them more available for people with intractable chronic pain.

If the FDA insists upon promulgating some kind of mandatory education, then it should follow the ASIPP guidelines for prescribing opioid analgesics. It should also take the following resources into account, which essentially illustrate precisely how such a thing should be done, and the people who made it are scholars on these topics:

https://www.ncbi.nlm.nih.gov/books/NBK92522/ Particularly, chapter 4

The ways in which an individual suffering from an addiction differs from a person with intractable chronic pain must be included and fully explicated in the education module if one is made. Things such as the fact that the presence of pain actually decreases the likelihood of addiction (Betourne et al, 2008), because as Inturissi (2002) noted, pain interferes with the intrinsically rewarding properties of opioids, and that the rates of addiction in chronic pain are well beneath 1% (0.19%) when the individual doesn't have a previous history of addiction, but even when individuals are not screened for previous history of addiction, then rate only increases to 3.27% (Fishbain, et al., 2008), and further, "72.5% of all patients derived benefit from opioids." (Cowan et al. 2003). With this in mind, and the anecdotal evidence from the numerous individuals receiving long term opioid therapy, that opioids are in fact effective long-term, especially when

opioid rotations are implemented. Opioid rotations must also be covered in any education required of physicians treating pain. The details of the physiological consequences of pain (concisely summarized earlier) are requisite material for any educational requirement of physicians, as are the vast number of people with chronic pain, and its profoundly negative sequela that occur if the pain is left unrelieved.

In addition to this, physicians would need to be educated about the nature of addiction, which is immensely complex, and I will summarize briefly what a physician would benefit most from knowing about it. Firstly, a physician must know the difference between dependence, addiction, and tolerance, and be able to differentiate them effectively and easily, as they are completely distinct clinical entities.

Dependence, the presence of withdrawal symptoms upon abrupt cessation of a drug, is distinct from addiction (Morgan and Christie, 2011) (ASAM, 2001), which is compulsive use despite harm, and involves a genetic predisposition (Shi et al., 2001), environmental factors, and involves attachment disturbances (Barr et al., 2008), requires an early life trauma in order for it to occur (Flores, 2001) (Perroud et al., 2011) (Barr et al., 2007). Drugs themselves are not necessarily the problem (otherwise gambling, sex, and shopping addictions would make little sense, nor would they exist), but rather the individuals' relationship with the drug or activity is the relevant process underlying addiction (Flores, 2012). Dependence is natural and occurs in a large proportion of the population with most drugs, including antidepressants, caffeine, benzodiazepines, and is an expected part of long term opioid therapy (Inturrisi, 2002). If the pain is expected to continue the rest of the individuals' life, or for a very long time, dependence is expected, and natural, as it is simple habituation, the natural adaptation to the presence of a substance in the body (Inturrisi, 2002).

Dependence is a clinical choice, and many people choose to rely on insulin to live as close to an ordinary life as they can, and people with intractable pain utilizing opioid analgesics find themselves in an analogous situation, and when the pain is severe enough to kill the person, they are left with only one reasonable choice, and the same is true of the physician prescribing the medication: to be dependent upon opioid analgesics, when the alternative is agony and eventually death, is a rational and clinically justifiable choice, but recall, this is an entirely different clinical phenomena from addiction (ASAM, 2001). This report from the American Society of Addiction Medicine is an excellent, short, concise, and required reading for any effort to educate physicians about addiction, and the use of opioid analgesics. From various surveys on the subject, it is clear that dependence for people suffering from intractable pain is not a clinically significant issue (Cowan et al., 2003), and the benefits outweigh the side effects. Further, opioids have been shown to be both safe and effective long term:

> "Patients reported here are functioning quite well after 10 or more years in opioid treatment. The vast majority can care for themselves and even drive. Opioid dosages have generally remained stable for long periods without significant escalation. Given the findings here, there is no obvious reason to discourage opioid use or encourage pain patients to cease opioids." (Tennant, 2011)

In addition to the aforementioned information, noting that the standard of care for the treatment of addiction at this stage is medication assisted treatment, involving the continuous administration of methadone or buprenorphine-naloxone, and counseling with a trained mental health professional. Attachment-based group therapy for addiction (Flores, 2001) may also be of great help in treating addiction, and has been included in numerous books, and integrated into a great many practices, and has been shown to have a substantial efficacy, which is noted in Parolin and Simonelli (2016).

Physicians must also be educated about urine drug testing, its lack of utility in chronic pain compliance monitoring (Snyder et al., 2017), the profound lack of evidence supporting the use of urine drug testing and opioid contracts in people with chronic pain receiving long term opioid therapy (Collen, 2009) (Hansen, 1985) (Saitman et al., 2014), and discouraged from using it, as the problems are numerous, and the causes of false positives and negatives endless. Further, they can cause significant harm (Reisfield and Maschke, 2014)

The following is a reasonably good resource to look into on this topic, but all of the articles I cite on this topic must be considered when creating an education module: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3550258/

Given that the aforementioned information (and more) would be included, and effectively taught, (particularly, the physicians must be able to differentiate addiction, dependence, and tolerance, know the physiological consequences of pain, and know the standard of care for addiction treatment) then the implementation of mandatory education may not cause horrific consequences, but if not all of these requirements are met, it would be profoundly dangerous, and produce a large number of bitter, indignant physicians who did not trust the FDA, and would not respect the FDA, in addition to the needless suffering of people suffering from chronic pain who would be the most adversely affected by this.

The FDA would be profoundly helpful if they were to investigate the unintended consequences of the promulgation of the CDC guidelines, because they have led to numerous suicides (Kline and Lamb, 2017), and numerous cases of public suicidal ideation among people suffering from chronic pain who frequently have been tapered forcefully from their previously stable regimen, (Kertesz, 2017) and the CDC has failed to do so, despite noting that they would do so, and as such the responsibility should fall to the FDA.

Section 5 Conclusion and Discussion

Section 5.1 Moving Forward/Areas of Focus when Constructing Policy

In regards to telling addiction apart from chronic pain, "The psychopathology seen among adult users is certainly consistent with the model. More importantly, however, are the extraordinarily high levels of childhood trauma and psychopathology that occur typically well before the initiation of heroin use. In contrast, the postulate of drug specificity appears less supported by the polydrug use patterns typical of heroin users, and does not appear to be a necessary corollary of the model." (Darke, 2012) *If any regulations are being designed in regards*

to drugs or addiction prevention, this is imperative to consider. **This states that particular drugs are not the cause of addiction, but that mental illness is the cause of addiction, not the use of drugs that represent an attempt to compensate for the love and compassion they did not receive as infants.** Doctors are already adequately skilled at telling substance users from people suffering, and further most pain physicians prescribing opioids monitor patient's prescription filling behavior already, which serves as an adequate low-mid risk monitoring strategy.

I will reiterate where funds must be diverted to in order to curb drug abuse of illegal drugs and reduce addiction and overdose: direct the DEA's efforts towards filling a security role in guarding pharmacies and funding security upgrades in pharmacies (or requiring the companies who own pharmacies that are frequently robbed to do so) that are direct, like bulletproof glass, and speakers, similar to those seen in prison visiting booths would be adequate, and determining the most frequently robbed locations that have prescription drugs, and having the DEA simply there defending the drug distribution centers, manufacturers, etc. from theft. Diverting funds to researching attachment based therapies for addiction, and ibogaine research, as well as developing more pharmaceutical options in terms of opioids and other analgesics must be a priority, and the primary way in which illicit use of pharmaceuticals is reduced.

An important goal that must be adequately funded is researching new analgesic medications, but **until new medications are discovered, and are entirely affordable, it is unethical to excessively restrict opioids**. (Rich, 2000)

Another measure that would reduce overdose is dispensing naloxone with opioid prescriptions (at an affordable price), and making it over-the-counter. Other opioid analgesics being rescheduled to make prescribing easier and less subject to potential criminal charges in situations where it was medically appropriate would encourage doctors to more adequately treat pain as well as reduce overdose deaths, because people in pain would not be forced to use dangerous illicitly manufactured drugs for their pain relief. Letting scientists research potential therapeutic avenues, because some day when they or a loved one is ill, one of the drugs labeled as having "no accepted medical use" could have held the key to treating their condition, such as ibogaine for people suffering from addiction (Mash, 2005). In the case of drugs having high abuse potentials, oxycodone being more pharmacologically abusable than morphine (due to oxycodone's euphoria-inducing effects), fentanyl, etc. is a scientifically acknowledged phenomenon (Inturrisi, 2002). Taking a more pragmatic approach of reinforcing physical security is the only thing that could possibly have any positive impact without adversely affecting CPPs, and is nothing short of imperative in this day and age.

Making the focus of the DEA be protection of the drugs at their source: pharmacies, and manufacturers, where most illicit drugs that cause overdoses are **stolen** from, increasing security in the form of bulletproof glass partitions and bins that can be slid through the glass for exchanging prescriptions and money while protecting them from theft, and substantially reducing costs of drug enforcement would be prudent. It will also allow them to focus on illegal trafficking and manufacturing of drugs like illicitly manufactured fentanyl (to be distinguished from prescription fentanyl which is for pain patients with moderate-to severe chronic pain).

A potentially beneficial measure to curb opioid overdoses is to make naloxone over the counter, or distribute it at clean needle clinics, as many cities in the U.S. are doing. It seems to be a relatively effective measure, but this will only be effective if chronic pain patients can receive adequate treatment through legitimate medical channels. Only then will the overdoses subside, as this is a multifactorial problem that requires precise, multifaceted solutions meant to minimize harm to the 116 million chronic pain patients' lives who are already having huge difficulties receiving adequate care to allow them to live a long and healthy life. So instead of choking a weak point in the supply line, why not buttress it instead? Decreasing pressure on physicians will increase quality of care nationwide.

Another potential measure to reduce opioid associated mortality is to give anyone filling a prescription for opioids a naloxone syringe (and they will have one until it expires or they ask the pharmacy for another), so that in the event of an overdose, their life can be saved. Rescheduling naloxone would go a long way to reducing overdose deaths. If safer opioids such as morphine and hydromorphone, were moved to schedule 3, and more abusable opioids–specifically oxycodone–(because oxycodone causes more euphoria, and has greater abuse liability, whereas drugs such as morphine cause a great deal less euphoria, and have fewer overdoses associated with them) moved to schedule 2, which would increase the frequency of prescription of safer opioids such as morphine, and reduce the prescription of oxycodone, but this would only be an acceptable option if those currently maintained on oxycodone were allowed to continue on it if it is effective for them, or rotate to a different opioid at a physician-determined equianalgesic dose. If patients are abruptly cut off from opioids, as has been happening since the CDC guidelines were issued, painful withdrawal, which is associated independently with suicide risk, would occur, and these people would be plunged into horrific agony. This would also occur if the current proposition to take the majority of opioid analgesics off of the market. This is an undesirable outcome, as some would turn to illegal drugs, and others commit suicide due to the already excessively high risk for suicide people in chronic pain demonstrate.

In the 2011 Seya et al. study, "A First Comparison Between the Consumption of and the Need for Opioid Analgesics at Country, Regional, and Global Levels" they note:

> Despite a century of medical chemistry, suitable alternatives to strong opioids for treatment of moderate to severe pain have not been found…Indeed, several barriers contribute to the insufficient utilization of opioid analgesics. Most of these barriers trace back to fears of abuse and [addiction] of opioids, particularly the fear of prescribed opioids being diverted to illicit circuits (2, 3). Therefore, many laws and government policies primarily focus on rendering opioids unavailable, without acknowledging that their rational medical use is beneficial to patients in pain (2, 4, 5). Still today, in many countries, patient access to opioids for cancer pain is profoundly restricted through legislation (6). However, for terminal patients [addiction] is irrelevant. Moreover, during treatment of chronic noncancer pain, [addiction] rarely results (7)... Reports from India and Malaysia show that diversion by patients is rare or nonexistent (9, 10). When patients cannot access

> pain relief, this may result in excruciating suffering, suicide, or the use of street-bought heroin (11)... United Nations (UN) bodies, including the World Health Assembly, the Economic, Social and Cultural Council, the Commission on Narcotic Drugs, and the International Narcotics Control Board (INCB), declared that access should improve (9, 12–15)... There is recognition now that pain relief is part of the human right to the highest attainable standard of mental and physical health, or is even a human right on its own (20–22). (Seya et al., 2011) (Excerpted citations noted below[2])

Seya et al. notes that the WHO Access to Controlled Medications Programme (ACMP) is a good model to follow. Having a board of stakeholders that reflects accurately the people involved in this issue whose meetings are broadcast publicly, and can be attended by anyone who so desires, either by calling in via telephone, online commenting, or in person, unlike the process of the formation of the CDC guidelines, which was almost entirely closed off. (Pergolizzi, 2016) Such a panel would necessarily include: Multiple anesthesiologists with extensive experience treating patients in pain, such as Dr. Forrest Tennant, leaders of patient advocacy groups, DEA representatives, FDA representatives, and an addiction specialist who understands the trauma-based nature of addiction, and preferably is familiar with the use pharmacological nature of Ibogaine.

The WHO "Achieving Balance in National Opioids Control Policy" is a good template for action. In it they note, "Unrelieved pain can impair all aspects of a person's life, including appetite, mood, self-esteem, relationships with others, and even the ability to move. In some countries, it has been reported that unrelieved pain can lead to the wish for death and inquiries about euthanasia and assisted suicide. Relief of pain has been demonstrated to improve quality of life." (WHO, 2000)

The CDC guidelines are not based on well-constructed, methodologically sound research (Pergolizzi, 2016) (Martin et al., 2016), which should be very concerning to everyone, as a very large body of research highlights the major health problems (including death) that result directly and indirectly from chronic pain being inadequately relieved; the CDC's guidelines, which are flawed in their inception, were written behind closed doors, and ignored all of the input from the many pain patients, pain physicians, and patient advocacy groups who submitted their concerns, publishing the guidelines virtually unchanged (Pergolizzi, 2016) (Martin et al., 2016); this guideline is "voluntary," and meant only for primary care providers, so basing any policy upon it will codify inherently flawed, empirically incorrect guidelines as a mandate for all healthcare professionals, taking away their ability to choose what is best for their patient, which the CDC did not intend with their guidelines, as they were, "optional." So aligning with such poorly thought out, empirically flawed guidelines is not in the American public's best interest, and adopting guidelines where collusion has been publicly reported on by a variety of news outlets is not a way to advance the health of the people of the U.S.

There are **116 million** other **people in chronic pain in the U.S. alone** (Institute of Medicine, 2011). Rates of chronic pain continue to increase. (Grol-Prokopcyzk, 2016) The odds

of you, or a loved one developing chronic pain at some point in their lives are very high: the odds are more than a one in three chance, which means that policy decisions regarding this delicate issue could very well affect you or your loved ones in ways that inflict profound, indescribable amounts of pain on them needlessly.

Addiction affects approximately 20 million people in the U.S. (NIDA, 2017) as opposed to 116 million in chronic pain. This simple difference in numbers should put in perspective who is being affected the most by these policies. It is not those with addiction problems who will be affected, as they will continue obtaining stolen or illicitly manufactured drugs, unless something is done to protect pharmacies and manufacturers. As Joranson and Gilson (2005) noted, "The Controlled Substances Act makes thefts of controlled substances from Drug Enforcement Administration (DEA) registrants a federal crime, and requires pharmacists, manufacturers, and distributors to report significant thefts and losses… Theft/losses were primarily from pharmacies (89.3%), with smaller portions from medical practitioners, manufacturers, distributors, and some addiction treatment programs that reported theft/losses of methadone." More recent estimates are consistent with this figure.

It is not possible to match the volume of diversion on an individual patient level, so it is only logical to protect these points in the chain of distribution.

It makes no sense to inflict untold suffering–adding insult to injury (in more than one sense)–upon 116 million people, 33% of the population, a third of everyone in America. Suicide rates have increased with governmental drug regulation, many of whom are chronic pain patients whose quality of life has already been greatly diminished by pain, and couldn't receive adequate treatment. Many of these people couldn't stand the agony any longer, and decided to end their suffering and their lives. This will be the fate of hundreds of thousands if not millions more upstanding, American citizens who did nothing wrong if doctor prescribing is further targeted.

Consider, also, that most non-opioid pain management medications and therapies are ineffective for severe chronic pain in the 6-10 range (WHO, 2000). Of the extremely limited effective non-opioid therapies, their benefits do not last more than an hour after the treatment the vast majority of the time, as is the case for people with Ehlers Danlos Syndrome Hypermobility Type, which involves frequent dislocations of all the bones in the body, which causes fibrosis in the myofascial tissue (Pavan, 2014), which allows unusually large forces to be transmitted through the fascia (a connective tissue that goes all throughout your body, housing your nerves that allows for smooth gliding movement of the muscles), which puts unusual strain and shear forces on the fascia, which contains many nerve endings that these shear forces are tearing apart on a cellular level. Needless to say, this is very painful, and many people with chronic pain already do manual therapy techniques, like myofascial release which can be helpful, yet the results are not permanent, and the simple act of driving home could cause an individual with EDS HT (a fairly common, often devastating condition) to dislocate their collar bones and hips, which causes the benefits of the therapy to go away completely within a day, and the individual is left in terrible pain, as the dislocation and subluxation of the rest of the bones in their body ensues.

There are similarly complex mechanisms underlying all chronic pain syndromes, and until our medical science advances another 100 years, it is unethical to pass a policy that would even further decrease the access to opioid pain medications (Lohman et al., 2010).

The government simply doesn't have the necessary expertise to be qualified to limit the options for doctors and their patients. Each American citizen should have the right to have their serious health conditions treated *within the privacy and sanctity* of their trusted physician's office. No one wants a government panel dictating anyone's treatments. That should be left to the relationship between the patient and their private, trusted, well-trained physicians. Government panels do not have any business in physicians' offices. If the government insists upon implementing more regulations, consulting the sources I've cited, and the resources cited in Lohman et al., 2010 would be a wise decision.

Much of the stigma against opioids that is driving restrictive prescribing policies is based in doctors' lack of knowledge about pain (and subsequently the public's misconceptions), about how to treat it, and about the difference between dependence and addiction (Rich, 2000). These issues can be resolved by simply educating doctors more effectively. Dependence is simply the presence of withdrawal symptoms upon the cessation of a drug, (Inturrisi, 2002) which happens every morning to much of America as they make coffee. The grogginess, headache, and nausea are withdrawal symptoms of caffeine, and these are ordinary citizens, not addicts–addiction, which is something that a person must be genetically predisposed to in order to develop–is an entirely different condition that is a neurological disease (Morgan and Christie, 2011). In order to have the capability of developing an addiction, a person must have disturbed caregiver attachment bonds, caused by trauma at an early age, and it involves widespread alterations to the reward system in the brain that you simply do not see in chronic pain patients, as well as continuing to obtain the drug despite harm to others, a hallmark of addiction (Flores, 2004). The literature also suggests that mu receptor polymorphisms are also necessary. (Barr et al., 2008) (Kreeke and LaForge, 2007) (Shi et al., 2002)

On the other hand, in chronic pain, although the patients require their medication to avoid withdrawal (dependence) and to avoid severe pain; they are not addicted, and there is no indication that simply being dependent on a drug is equivalent to being addicted to a drug. Chronic pain interferes with the intrinsically rewarding tendencies of opioids (Inurrisi, 2002) (Fields, 2011) (, meaning that because the medicine is being used properly under proper supervision, that in appx. 98% of chronic pain patients receiving opioids long-term, addiction doesn't occur (Fishbain, et al., 2008) (Burgess et al., 2014). The last conflated term, tolerance simply means that the body is habituating to its environment, the way the human body is designed to (Inurrisi, 2002). There is nothing inherently wrong with this, as it is an important survival mechanism built into the human body. It is expected, and a non-issue as an opioid rotation can be implemented.

Another author noted the usefulness of long term opioid therapy in chronic noncancer pain, and the outlandishness of using addiction as the rationale to not to treat pain:

> "A Cochrane Review on long-term opioid management for chronic noncancer pain published in 2010 reported similar findings, with an estimate of opioid addiction

> of 0.27%, leading the authors to conclude that the risk of iatrogenic opioid addiction is low. [Hojsted, 2007]" Burgess et al., 2014 went on to summarize Boscarino's 2010 study stating,: "One of the most consistent risk factors predicting opioid abuse/addiction, is a history of opioid abuse (odds ratio of 3.81).[Boscarino, 2010] Patients with a history of severe [psychological] dependence or abuse had an odds ratio of 56 for developing abuse/addiction. [Boscarino, 2010] Weisner *et al* surveyed patients receiving long-term opioids in two large group health plans and found that patients with a history of opioid abuse had a prevalence rate of opioid use approaching 50%, compared to patients without a prior opioid abuse history of 2–3%." (Burgess et al., 2014)

The nature of the so called "opioid epidemic" has been misunderstood. "Heroin and fentanyl have come to dominate an escalating epidemic of lethal opioid overdose, whereas opioids commonly obtained by prescription play a minor role, accounting for no more than 15% of reported deaths in 2015." (Kertesz, 2016)

Also of note is that suboxone, a drug used to treat addiction may very well be a rising cause of opioid overdose, and even more troubling it shows up as oxycodone, or not at all in a drug test (Jenkins et al., 2009) (Anson, 2013). Its combination with other drugs is what could make it potentially toxic, as with all "overdoses" which as discussed earlier are mostly additive drug toxicity deaths.

Drug testing technology has not improved, and is still prohibitively expensive and untenably inaccurate. (Depriest et al., 2010) (Pesce et al., 2012) (Reisfield, 2014) Consequently, it has no place in the practice of medicine, the collection of data, or the evaluation of anything that is classified as objective. (Reisfield, 2014) The use of post mortem toxicological data is subject to the same issues as urine drug testing, and even more egregious issues that make it even less accurate. As such data collected using these methods has no place in policy decisions, as policy should not be based upon such useless data that does not reflect reality.

"It is commonly thought that opioid dependence often begins through an initial, possibly chance, exposure to a physician-prescribed opioid, although data from studies to empirically evaluate this claim are lacking." (Barnett et al., 2017) In other words, people **do not simply become addicted by being exposed to opioids**, and **there is *no* evidence to support this outrageous claim**. There is however limited evidence to suggest that chronic pain patients receiving long term opioid therapy have extremely low rates of addiction (Fishbain et al. 2008) (Burgess et al., 2014) (Hojsted, 2007) and many derive greatly enhanced health, wellness, quality of life, and function from long term opioid therapy (Furlan et al., 2006).

When addiction is looked at as an attachment disorder that also happens to be neurological disease, and requires a genetic predisposition, it becomes much clearer why some people suffer from addiction upon exposure to drugs and others do not. Those that do are using a drug (it could be nearly any drug) to replace the comfort that social interaction and healthy peer bonding provides to non-addicted individuals (Flores, 2004). The mu receptor abnormality seems to

mediate this difference (Shi et al., 2002). This is markedly different from chronic pain patients who are able to socialize because of opioid medications.

The Furlan et al. literature review on the efficacy and safety of long term opioid therapy for chronic noncancer pain concludes that while the studies are limited, there is sufficient evidence that opioids are beneficial for some individuals with chronic noncancer pain, and considering the complete lack of similarly effective alternative treatments, there is no rational reason to deny treatment to these individuals, especially considering the deadly consequences of doing so. Leaving pain untreated, as restricting pain medication further tends to do, is condemning the well over 25 million people with severe and intractable chronic pain to a slow, agonizingly painful death, feeling betrayed by their government, their physicians, and life itself. (Grol-Prokopcyzk, 2016) (Epel, 2004) (Mcewen, 2004) (Lohman, 2010) (WHO, 2000)

Restricting opioid prescribing as the CDC *recommended* for primary care physicians *only* would have dire consequences if it were implemented as a policy of any kind. It would disable people currently on long term opioid therapy who are able to live a normal life because of these medications. Those who are not currently on medication have either already been stripped of their dignity and quality of life by needless suffering, due to the immense difficulty involved in finding a physician who is willing to treat their pain. So much so that many are driven to the point where they are totally disabled (many of whom re receiving social security benefits), who could be made able to work again if they were given adequate treatment that such a policy would completely prevent, because of their pain, and are causing a totally unnecessary financial drain on the U.S. government in the order of **$560-635 Billion** per year (Institute of Medicine, 2011). The cost of this could be almost entirely eliminated (or at the least greatly reduced) if the availability of opioids were to increase substantially (Seya et al., 2011) (Sessle, 2012).

Please consider the points I have brought up, as you have millions of lives in your hands. Thank you for taking the time to read this.

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