

**Dear Esteemed Elected Officials:**

As a physician who prescribes Suboxone, I find there are many misconceptions regarding this important medication. As we are, in the midst, of an opiate epidemic, I know we can improve on our ability to protect our constituents from overdose. By and large, we are losing healthy young men and women, the taxpayers and future of our state.

Many think that Suboxone is a medication to get high from, this is not the case. As Suboxone is a partial agonist of the mu receptor, it prevents withdrawal symptoms without providing a sense of euphoria (or high). Most people who have an opiate use disorder, fear withdrawal symptoms. They don't want to feel "sick". So Suboxone provides relief from withdrawal symptoms. It is not a medication that produces euphoria in opiate dependent individuals.

As it binds to the opiate receptors, it blocks other opiates. So, if someone uses heroin, while on Suboxone, the high is blocked, as is the risk of overdose. As one of my patients noted "it feels like you just wasted 100.00 dollars" The risk of overdose is reduced substantially when the stronger opioids cannot bind to the receptor.

Suboxone is a very safe medication. Many experts in the field of addiction medication, have called for it's declassification as a controlled substance. The naloxone portion is present to prevent euphoria from intravenous use. It is not absorbed well in the sublingual form.

"As a full agonist, methadone has more than 4 times the risk of overdose than buprenorphine." "Buprenorphine has rarely been linked to overdoses outside of concurrent alcohol or other sedative abuse and lacks the QTc prolongation and drug-drug interactions of methadone."

The concerns about this medication as a gateway drug are unfounded. No one with a substance use disorder has ever told me that they began their history of substance use disorder by using Suboxone.

Many of my patients report using Suboxone "from the street" so they stave of withdrawal and don't use a life threatening fentanyl product. Opiate withdrawal has been described to me as having your face wrapped in saran wrap and attempting to breathe. You do whatever you can to get air.

I note nearly 100% of my patients using "heroin" are in fact using deadly fentanyl. Their urine screens show fentanyl, sometimes exclusively.

Allowing Suboxone to be exempt from prosecution is necessary right now, in the midst of this epidemic, we need every tool available. Increasing MAT availability, increasing Narcan availability, fentanyl test strips and discouraging prosecution for possession of buprenorphine are all essential components.

My son died from a fentanyl overdose. The amount of fentanyl was actually quite small. I am certain, that had he been on suboxone he would not have had a fatal overdose.

Excerpts from:

## **Suboxone: Rationale, Science, Misconceptions**

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Buprenorphine is a long-acting, high-affinity partial agonist at the mu-opioid receptor. As a long-acting agonist, buprenorphine prevents withdrawal and craving and stabilizes opioid receptors. As a high-affinity agonist, buprenorphine blocks other opioids from binding, preventing abuse of other opioids. As a partial agonist, it has a smaller effect with a ceiling, a low overdose risk, and no intoxication in the opioid dependent. Buprenorphine is available in many formulations (Table 1). The most common formulation is buprenorphine and naloxone (Suboxone) in a 4:1 ratio.<sup>17</sup> As an opioid antagonist with high first-pass hepatic metabolism, naloxone has no effect on sublingual use of buprenorphine but blocks intravenous or intranasal abuse of buprenorphine. In contrast, naltrexone is another opioid antagonist with greater oral bioavailability that blocks all opioids regardless of delivery method and is also US Food and Drug Administration (FDA) approved for treatment of opioid use disorder. Buprenorphine without naloxone is used for pain management and can be prescribed for opioid use disorder in sublingual film or tablet form. Except in the case of severe hepatic impairment or pregnancy, prescription of isolated buprenorphine is discouraged given the potential for intravenous abuse.

### **EVIDENCE FOR USE OF BUPRENORPHINE**

As elaborated below, current evidence shows buprenorphine is superior to methadone for tolerability but equivalent for treatment retention and other outcomes. The data also indicate that buprenorphine is equal or superior to antagonist-based treatment (depot intramuscular and oral naltrexone). US Department of Veterans Affairs guidelines currently recommend either buprenorphine or methadone vs depot intramuscular naltrexone, oral naltrexone, or abstinence-based treatment.<sup>19</sup>

Several placebo-controlled studies document the general efficacy of buprenorphine for opioid use disorder. Patients in a Swedish treatment program randomized to buprenorphine had 1-year retention of 75% and negative urine drug tests in 75% of patients compared to 0% of patients randomized to placebo.<sup>20</sup> One major randomized placebo-controlled trial was terminated early because of the clear superiority of buprenorphine to placebo, with 4 times the rate of negative urine drug tests and significantly less craving in patients on buprenorphine.<sup>21</sup> The follow-up open-label study showed continued benefit and no increase in adverse events compared to placebo.<sup>21</sup> In another study of 110 patients initiated on buprenorphine, those who remained on buprenorphine after 18 months were more likely to be sober, employed, and involved in 12-step groups.<sup>22</sup>

Buprenorphine significantly lowers the risk of mortality and adverse outcomes. In a metaanalysis, both methadone and buprenorphine maintenance were found to be superior to detoxification alone in terms of treatment retention, adverse outcomes, and relapse rates<sup>6</sup> Studies have also shown a reduction in all-cause and overdose mortality and significantly improved quality-of-life ratings with maintenance buprenorphine.<sup>23,24</sup> Patients on buprenorphine had reduced rates of HIV and hepatitis C transmission compared to abstinence-based therapy or detoxification alone.<sup>13,14</sup> Maintenance buprenorphine is also associated with better hepatitis C treatment outcomes.<sup>25</sup>

Suboxone has been shown to have similar efficacy to methadone when treatment conditions are similar and when patients take higher doses of Suboxone. One early study suggested that methadone was associated with better treatment retention and more negative urine drug tests than buprenorphine.<sup>26</sup> These findings were hypothesized to be attributable to increased dependence on the medication because of the full agonist activity and the support provided by the daily visits required for methadone treatment.<sup>27,28</sup> However, this study and other early studies typically underdosed buprenorphine, prescribing only 8 mg to many participants. When the subgroups on lower doses were excluded in later analyses, the outcomes between buprenorphine and methadone were the same.<sup>26,29</sup> This equipoise argues for buprenorphine instead of methadone, given the better safety profile of the former. As a full agonist, methadone has more than 4 times the risk of overdose than buprenorphine.<sup>30</sup> Buprenorphine has rarely been linked to overdoses outside of concurrent alcohol or other sedative abuse and lacks the QTc prolongation and drug-drug interactions of methadone.<sup>31</sup>

Oral naltrexone has been established as inferior to the extended-release depot form of naltrexone (Vivitrol) and to buprenorphine. Rates of relapse for oral naltrexone and placebo at 6 months were similar, and both were 3 times higher than the relapse rate for patients on buprenorphine maintenance.<sup>32</sup> Several recent studies indicate that buprenorphine and extended-release naltrexone are equally efficacious. Two naturalistic studies showed better treatment retention for buprenorphine products compared to extended-release naltrexone.<sup>33,34</sup> An outpatient-based randomized open-label study in Norway showed similar treatment retention and rates of negative urine drug screens between extended-release naltrexone and buprenorphine-naloxone, with significantly fewer days of heroin and illicit opioid use.<sup>35</sup> This study was limited in that it only followed patients for 12 weeks. A 2017 randomized controlled study of buprenorphine and extended-release naltrexone conducted for 6 months found both medications to be equally efficacious in the per-protocol analysis.<sup>36</sup> However, the intention-to-treat sample showed buprenorphine to be superior to extended-release naltrexone because of the relative difficulty of induction on antagonist-based therapy, which carries a higher probability of eliciting withdrawal symptoms even weeks after the last illicit opioid use. Of the 283 patients randomized to extended-release naltrexone, 79 failed induction and ultimately relapsed.<sup>36</sup> Buprenorphine may also be a safer option than antagonist-based treatment. A longitudinal study showed 8 times the risk of overdose after patients left naltrexone treatment compared to agonist treatment.<sup>37</sup>

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