

### Chronic Pain

As many as one in five Americans lives with chronic pain.<sup>1</sup> Many of these people suffer from neuropathic pain (nerve-related pain) -- a condition that is associated with numerous diseases, including [diabetes](#), [cancer](#), [multiple sclerosis](#), and [HIV](#). In most cases, the use of standard analgesic medications such as opiates and NSAIDS (non-steroidal anti-inflammatory drugs) is ineffective at relieving neuropathic pain. Further, long-term use of most conventional pain relievers, including acetaminophen, opioids, and NSAIDS, is associated with a host of potential adverse side effects, including dependence, heart-attack, liver damage, and accidental overdose death.

Survey data indicates that the use of cannabis is common among patients with chronic pain<sup>2</sup> and patients who use it for this indication typically report to be an effective treatment.<sup>3</sup> Majorities further report that cannabis possesses fewer side effects than conventional pain medications and that it provides greater symptom management than opioids.<sup>4</sup>

In addition to these anecdotal claims, numerous clinical trials report that inhaled inhaled marijuana alleviates neuropathic pain. A recent review identifies 35 controlled studies specific to the use of cannabis or cannabinoids in pain treatment, involving over 2,000 subjects.<sup>5</sup> These include a pair of randomized, placebo-controlled clinical trials demonstrating that smoking cannabis reduces neuropathy in patients with HIV by more than 30 percent compared to placebo.<sup>6-7</sup> (Additional details on these studies appear in the [HIV](#) section of this publication.) A University of California at San Diego double-blind, placebo-controlled trial reported that inhaled cannabis significantly reduced capsaicin-induced pain in healthy volunteers.<sup>8</sup> A University of California at Davis double-blind, randomized clinical trial reported both high and low doses of inhaled cannabis reduced neuropathic pain of diverse causes in subjects unresponsive to standard pain therapies.<sup>9</sup> A McGill University study reported that smoked cannabis significantly improved measures of pain, sleep quality and anxiety in participants with refractory pain for which conventional therapies had failed.<sup>10</sup> Another clinical trial reported that both inhaled cannabis and oral THC significantly decreased pain sensitivity and increased pain tolerance in healthy subjects exposed to experimental painful stimuli.<sup>11</sup>

Clinical trials also report that vaporized cannabis is effective at mitigating pain. A 2013 FDA-approved trial assessing the impact of vaporized cannabis on neuropathic pain reported that even low doses of THC (1.29 percent) "provided statistically significant 30% reductions in pain intensity when compared to placebo."<sup>12</sup> A 2014 Israeli open-label clinical trial reported that the administration of a single dose of whole-plant cannabis via a thermal-metered inhaler was effective and well tolerated among patients suffering from nerve pain.<sup>13</sup> Placebo-controlled data published in 2015 in *The Journal of Pain* further reported that vaporized cannabis provides "a dose-dependent reduction in diabetic peripheral neuropathy pain in patients with treatment-refractory pain."<sup>14</sup> A 2016 placebo-controlled trial in a cohort of 42 subjects with spinal injury neuropathy reported that vaporizing cannabis low to moderate levels of THC elicited a "significant analgesic response" in study participants.<sup>15</sup>

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A review of these and other trials published in the *British Journal of Clinical Pharmacology* concluded, "[I]t is reasonable to consider cannabinoids as a treatment option for the management of chronic neuropathic pain with evidence of efficacy in other types of chronic pain such as fibromyalgia and rheumatoid arthritis as well."<sup>16</sup> A separate review published in *The Clinical Journal of Pain* further concluded, "Overall, based on the existing clinical trials database, cannabinergic pain medicines have been shown to be modestly effective and safe treatments in patients with a variety of chronic pain conditions. ... Incorporating cannabinergic medicine topics into pain medicine education seems warranted and continuing clinical research and empiric treatment trials are appropriate."<sup>17</sup> Another review of the data similarly reports, "[C]annabinoids are safe [and] demonstrate a modest analgesic effect and provide a reasonable treatment option for treatment chronic non-cancer pain."<sup>18</sup> Most recently, a review of over 10,000 scientific studies by the National Academies of Sciences, Engineering, and Medicine concluded that whole-plant cannabis is effective for the treatment of chronic pain in adults. "In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms," they determined.<sup>19</sup>

Longitudinal trials have also shown cannabis therapy to be safe and effective for pain treatment. A one-year assessment of Canadian chronic pain patients reported that daily use of herbal cannabis was associated with sufficient safety and efficacy. Compared to controls, patients in the cannabis use group experienced a significant reduction in average pain intensity while reporting no increased risk of adverse cognitive or pulmonary events. Authors concluded: "[T]his study suggests that the adverse effects of medical cannabis are modest and comparable quantitatively and qualitatively to prescription cannabinoids. The results suggest that cannabis at average doses of 2.5g/d in current cannabis users may be safe as part of carefully monitored pain management program when conventional treatments have been considered medically inappropriate or inadequate."<sup>20</sup>

Preclinical data indicates that cannabinoids, when administered in concert with one another, are more effective at ameliorating neuropathic pain than the use of a single agent -- a phenomenon sometimes referred to as the entourage [effect](#). Investigators at the University of Milan have reported that the administration of single cannabinoids such as THC or CBD produce limited relief compared to the administration of plant extracts containing multiple cannabinoids, terpenes (oils), and flavonoids (pigments). Researchers concluded: "[T]he use of a standardized extract of *Cannabis sativa* ... evoked a total relief of thermal hyperalgesia, in an experimental model of neuropathic pain, ... ameliorating the effect of single cannabinoids," investigators concluded. ... "Collectively, these findings strongly support the idea that the combination of cannabinoid and non-cannabinoid compounds, as present in [plant-derived] extracts, provide significant advantages in the relief of neuropathic pain compared with pure cannabinoids alone."<sup>21</sup> Other studies have reported similar results.<sup>22</sup>

Cannabis dosing also permits some chronic pain patients to significantly reduce their use of opioids. A 2011 clinical trial assessing the administration of vaporized plant cannabis in chronic pain patients on a daily regimen of morphine or oxycodone reported that inhaled "cannabis augments the analgesic effect of opioids." Authors concluded, "The combination (of opioids and cannabinoids) may allow for opioid treatment at lower doses with fewer side effects."<sup>23</sup> A 2016 Israeli clinical trial

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of intractable pain patients similarly reported that inhaled cannabis reduced symptom severity and also was associated with 44 percent overall reduction in subjects' use of opiates.<sup>24</sup> A separate University of Michigan study of 244 chronic pain subjects similarly reported that cannabis use led to a 64 percent decrease in opioid consumption.<sup>25</sup> Patient survey data published in 2017 reported that 97 percent of respondents "strongly agreed/agreed" that they are able to decrease the amount of opioids they consume when they also use cannabis."<sup>26</sup>

In jurisdictions that permit medical cannabis access, patients are using fewer opioids. According to the findings of a 2015 National Bureau of Economic Research study, "[S]tates permitting medical marijuana dispensaries experience a relative decrease in both opioid addictions and opioid overdose deaths compared to states that do not."<sup>27</sup> The NBER findings are similar to those published in 2014 in the *Journal of the American Medical Association (JAMA) Internal Medicine* which also reported that the enactment of statewide medicinal marijuana laws is associated with a 24.8 percent lower mean annual opioid overdose mortality rate compared with states without medical cannabis laws.<sup>28</sup> A 2016 [study](#) produced by Castlight Health similarly reports that rates of unauthorized opiate use is significantly lower in medical cannabis jurisdictions. Incidences of opioid-related hospitalizations<sup>29</sup> and traffic-related fatalities<sup>30</sup> have also fallen, as have overall prescription drug spending.<sup>31</sup> (For a comprehensive summary of relevant studies finding that legal cannabis access is associated with decreases in opioid use, abuse, hospitalization, and mortality, please NORML's fact-sheet, [Relationship Between Marijuana and Opioids](#).) Consequently, some pain experts are now advising that physicians recommend cannabis therapy in addition to or in lieu of opiate medications to "reduce the morbidity and mortality rates associated with prescription pain medications."<sup>32</sup>

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