

## Medical Marijuana and the Opioid Epidemic

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**O**n November 1, 2011, the Centers for Disease Control and Prevention declared overdoses involving prescription opioid analgesics to be an “epidemic.” In the decades prior, the concerted efforts of federal agencies, accreditation organizations, specialty societies, state medical boards, and the pharmaceutical industry had driven a massive increase in opioid analgesic prescribing for pain.<sup>1,5</sup> By 2007, the United States consumed 83% of the world’s oxycodone and more than 99% of the world’s hydrocodone.<sup>6</sup> In parallel to this increase in supply, morbidity and mortality have escalated. Between 2002 and 2012, the number of addiction treatment admissions involving opioid analgesics more than tripled.<sup>7</sup> By 2013, overdoses involving opioid analgesics had become a leading cause of injury and accidental death in the United States, killing 16,235 individuals in that year alone.<sup>8</sup>

While concerns over the safety of opioid analgesics have been mounting, access to medical marijuana has been exploding across the United States. As of January 2015, 23 states and the District of Columbia had legalized marijuana for medical use. While not all states specify chronic pain as a qualifying indication, in states that do, this is by far the most common condition reported. In Michigan, for example, 93.7% of people who registered with the medical marijuana program cited severe and chronic pain.<sup>9</sup>

Despite their increasingly common intersection, the relationship between medical marijuana and opioid analgesic use is not well understood. In surveys from medical marijuana states, a majority of people attending medical marijuana assessment clinics or dispensaries report substituting marijuana for prescription drugs.<sup>10-13</sup> Furthermore, many attendees report

interest in alternatives to chronic opioid analgesic therapy.<sup>13</sup> In one clinical study, patients taking opioid analgesics chronically had decreased pain with the addition of vaporized marijuana.<sup>14</sup> However, patients in the treatment arms of two clinical trials (i.e. smoked marijuana for HIV neuropathy and a cannabinoid spray for cancer pain) did not have decreased opioid analgesic use, though the studies were not specifically designed or powered to detect a difference in this outcome.<sup>15,16</sup> Furthermore, the role of marijuana in potentially causing the use of other illicit drugs remains hotly debated.

Given these potential connections between medical marijuana and opioid analgesic use, I co-authored a study in 2014 seeking to estimate the impact of medical marijuana laws on fatal overdoses involving opioid analgesics.<sup>17</sup> Using death certificate data from the Centers for Disease Control and Prevention from 1999 to 2010, the study team and I found that the presence of a medical marijuana law was associated with a 24.8% lower rate of fatal overdoses involving opioid analgesics relative to pre-law trends and trends in non-law states. A recent follow-up study incorporating more years of data and using more complex methods found similar results but reported this association to be limited only to states allowing dispensaries (versus those allowing only home cultivation).<sup>18</sup>

While the results of these studies are compelling, they should be interpreted in light of certain limitations. As we and others have noted, these are ecological studies at the state level, and inferences about individual outcomes or the precise mechanisms underlying our findings cannot be made. Fundamentally, they also

rely on observational data, with the attendant risks of confounding.

While policy research can guide policymakers, clinical research is needed to guide clinicians. The overwhelming consensus among health care providers is that more research is needed on the safety and efficacy of medical marijuana. In particular, information on the safety and efficacy of marijuana relative to opioid analgesics would be useful. While many have noted that chronic marijuana use has a host of risks, these are risks of marijuana relative to using nothing. Perhaps a more relevant question for many patients is: What are the risks of marijuana relative to the risks of opioid analgesics? While many aspects of this question are uncertain, few would dispute that the overdose fatality risk of marijuana by itself is essentially nil.

Given federal and state limitations, many have found such clinical research to be exceedingly challenging. But this may be changing. Colorado’s statute legalizing marijuana included a provision to fund medical marijuana research. Currently approved projects include a comparative effectiveness trial of marijuana versus oxycodone for pain—an incredibly timely study.

In view of the overwhelming support for medical marijuana among the American public, it seems likely that the number of states legalizing it will continue to increase in the coming years. Therefore, providers will be increasingly asked to make difficult clinical decisions about medical marijuana, either by itself or in combination with other medications. Some have advocated that refusing to recommend medical marijuana is the “safest” route, but what if receiving

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medical marijuana prevents a patient from being prescribed opioid analgesics chronically? Or what if medical marijuana allows a patient to lower the dose or discontinue opioid analgesics altogether?

Many health care providers remain skeptical about marijuana as medicine. While it is too early to know if marijuana will ultimately fulfill this role, we can all agree on the clear need to expand the number of non-opioid options for the millions of Americans with chronic pain.

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