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Cannabis liberalisation and the US opioid crisis

Too early to tell whether cannabis liberalisation reduces opioid deaths

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The United States is in the midst of an unprecedented opioid crisis, partly worsened by the novel coronavirus disease pandemic.¹ Approximately 10 million people misused prescription opioids, 808 000 people misused heroin, and two million people met the criteria for an opioid use disorder in 2018.² In that same timeframe, 46 800 people died of an opioid overdose, with two thirds of the deaths involving synthetic opioids (including fentanyl and fentanyl analogues).³ In response to the rising burden of disease, a range of opioid related policies have been implemented, which have been geared towards reducing high risk opioid prescribing, improving access to treatment, and expanding overdose prevention efforts.⁴

One perspective points to the co-occurring cannabis liberalisation as a potential means of reducing opioid related harms. Increased availability of cannabis has been suggested to result in the partial substitution of opioids for cannabis in managing pain.⁴ In a linked paper, Hsu and colleagues (doi:10.1136/bmj.m4957) contribute to this area of research by using an ecological design paired with county data from 2014 to 2018.⁵ Specifically, they examine the association between average counts of cannabis dispensaries—stores authorised to sell cannabis—and opioid overdose deaths among US states with medicinal or recreational cannabis legalisation. Additional controls for county population characteristics, state provision of recreational cannabis sales, and opioid related policies are included in the models.

Hsu and colleagues show that increases in average counts of medicinal and recreational cannabis dispensaries are jointly and independently associated with reduced deaths from opioid overdose, especially synthetic opioid overdose. Three methodological enhancements are noteworthy. Firstly, counties are modelled as the unit of analysis to enable within state differences to be considered. Secondly, average counts of cannabis dispensaries are modelled as the explanatory variable to achieve a closer approximation of the availability of cannabis.⁶ Thirdly, states without medicinal or recreational cannabis legalisation are excluded from the main analyses to exercise better control over broader differences in the social and legal environments.⁷

Hsu and colleagues' findings join an overall mixed evidence base,^{6 8 -11} which makes firm conclusions difficult. Although some authors might interpret their findings as evidence supporting cannabis liberalisation to address the opioid crisis, such conclusions are currently premature without evidence of causality. Two considerations merit further discussion. Firstly, the mechanism of action

underlying the association remains unclear. In the context of medicinal cannabis legalisation, reduced deaths from opioid overdose do not coincide with reduced non-medicinal use of pain relievers or with opioid distribution—defined as the flow of substances from the manufacturers to retail distributors.^{6 11} The absence of concurrent changes in such opioid related outcomes questions the premise of substitution.¹¹

Secondly, the ecological design used in many studies confers the risk of ecological fallacy—an epidemiological principle that prohibits inferences at the individual level on the basis of associations observed at the aggregate level. Indeed, an aggregate level relationship might not hold, or even reverse in direction, at the individual level. Harmful and beneficial associations are evident between opioids and cannabis at the individual level. On the one hand, cannabis use is associated with increases in non-medicinal use of prescription opioids and opioid use disorder in population studies.¹² Additionally, medicinal cannabis use has been associated with increases in use of prescription pain relievers for medicinal and non-medicinal purposes.¹³ On the other hand, emerging evidence from studies of people at high risk of opioid overdose indicate that regular cannabis use is associated with increases in injection opioid cessation, retention in opioid agonist treatment programmes, and decreases in illicit opioid use.^{14 -16}

These considerations are better addressed by experimental designs. In particular, cannabis liberalisation in the US offers unique opportunities to prospectively randomise counties within states to legalisation of either medicinal or recreational cannabis. Comparing individual level data of participants with use of prescription opioids and illicit opioids within these designs would inform a more nuanced understanding of the substitution between opioids and cannabis. Such an endeavour would require consensus between county and state authorities, which should be possible given the current magnitude of the opioid crisis burdening both types of jurisdictions. Cannabis liberalisation cannot be regarded as a remedy to the opioid crisis until a robust evidence base is available.

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