**ASSESSING THE PUBLIC HEALTH EFFECTS OF CANNABIS USE: CAN LEGALISATION IMPROVE THE EVIDENCE BASE?**

Hall and Lynskey1 elegantly review evidence on the effects of legalization of recreational cannabis. The trouble is – as they conclude – that it is too early to tell. So, what matters going forwards is whether there will be sufficient investment in generating evidence and conducting research into both the association of cannabis use with health and social harms and the impact of alternative methods of legislating cannabis consumption on the prevention of those harms.

As Hall predicted in earlier reviews of cannabis policy and health, permitting “medical use” of cannabis, especially in an under-regulated commercially driven health system, was the thin edge of the wedge to promoting “de-criminalization” and full legalization. This was illustrated in some US states – prior to legalization – by the growth in young people requiring and obtaining cannabis prescription to manage idiopathic neuropathic complications.

Permitting medical use and legalization of cannabis importantly also challenges the *stance of many politicians and policy makers in other countries – such as the UK – for not removing criminal sanction on cannabis possession due to a “precautionary principle”. That is – that there remain sufficient reasons and uncertainties over the risks of cannabis to peoples’ health – especially in relation to psychosis/schizophrenia – that cannabis should continue to be controlled as a harmful illegal substance. With legalization* v cannabis has not become risk free as Hall and Lynskey argue – but the experiment of using legal sanction to control use and prevent harm is no longer out of the question.

Cannabis exposure is associated with poor school performance (underemphasized in Hall and Lynskey’s review),4, drug dependence, mental health and physical morbidity. *There is little trial or observational evidence that criminal sanction prevented cannabis use in the population, and for a significant minority of people – often the most vulnerable in society – being penalised through drug law offences decreases future employment opportunities and may increase social and health inequalities.* However, we now have an opportunity to assess properly what strategies are more likely to reduce cannabis related harm. Here we focus on two areas – potency and natural experiments.

There is evidence that use of higher potency cannabis is associated with higher risks for mental health outcomes and dependence5. The observed increase in tetrahydrocannabinol content in legalized states is of concern, but legalization does provide consumers with access to accurate information about the potency of the product they are using. The resultant increase in accuracy in assessments of cannabis potency in legal markets will be vital for improving our understanding of the relationship between cannabis potency and mental health.

One effect of the legalization of cannabis in the US is the proliferation of different products, such as edible cannabis (e.g., gummy bears, candy and chocolates) and high-potency cannabis extracts (wax, shatter). Such products allow cannabis consumption without the need for combustion. In the absence of these products, cannabis is commonly consumed in combination with tobacco, which may confound the relationship between cannabis and mental health6. However, given that factors such as the route of administration will affect the bioavailability of the drug, and there will be variation in amount contained in self-rolled joints amongst those not using edibles, *there is a need to develop a standard unit of cannabis exposure – similar to alcohol – so that we can better understand and measure the acute and long-term effects of cannabis exposure7*.

Hall and Lynskey suggest that legalization provides opportunities to minimize adolescent access to cannabis. However, as noted above there has been a rise in cannabis products (chocolates and candy) that may be attractive to children, and little evidence for a fall in adolescent cannabis use in states where cannabis is legalized. Additionally, adolescents will also be exposed to increased marketing and perceived societal acceptability of cannabis use. Given restrictions on purchase age (21 years and over), adolescents are excluded from legal purchase, but will still have access to an illicit market which may now include diverted products.

We know that risks for dependence, mental health problems and negative socioeconomic outcomes are associated with initiation of drug use during adolescence – and that progression to cannabis dependence occurs as part of a profile of other drug dependencies and mental health issues8. Cannabis regulation provides new opportunities to instigate public health interventions and information campaigns related to cannabis and monitor the effect of these on preventing harms amongst adolescents who are most vulnerable to developing problem use.

Furthermore, there are research opportunities afforded by changes in legislation and policy that can enable us to generate better evidence as to the causal nature of some of the associations between cannabis and negative outcomes, such as poor mental health and memory impairment. For example, within the US, where neighbouring states can have vastly different policies in place, the conditions making it possible to conduct a natural experiment have arisen. This could be conceptualized as a cross-contextual study, whereby the demographics (or other potential confounding factors) of individuals choosing to use cannabis in the different regions may differ due to these policy differences.

If associations seen between cannabis and health outcomes remain the same under these different conditions, this is stronger evidence that the associations seen are causal. If, conversely, associations are seen only in conditions where prohibition is in place, this could provide evidence that some of these associations are likely to be confounded by factors either related to prohibition, such as an increased risk of punishments for use, or factors related to the demographics of who is likely to use cannabis under these different circumstances.

We have argued before that there needs to be better use of alternative methods to establish causal association between cannabis and health and other harms – *such as the use of Mendelian randomization studies that identify and use genetic instruments of specific exposures – such as alcohol, tobacco, cannabis, high BMI, folate or Vitamin D exposure 9. Genetic variants or markers can be shown to be not confounded by other exposures or subject to selection bias or reverse causation. We do not yet have robust genetic instruments of cannabis dependence and/or hazardous use – moving beyond measures of early first or lifetime use10*  but with legalisation there is an opportunity to generate larger studies of richer phenotypes of levels of cannabis exposure.

Given the research and public debate around the strength of evidence for public health risks from cannabis use, the research community can now capitalize on the unique opportunity that these changes in legislation present to us, and use the findings to inform evidence-based policy changes throughout the rest of the world.

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