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REVIEW ARTICLE



Patterns of recreational cannabis use in Aotearoa-New Zealand and their consequences: evidence to inform voters in the 2020 referendum

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ABSTRACT

The majority of New Zealanders (approximately 80%) born in the 1970s report using cannabis at least once, despite its illegal status. Four-10% of past-year users were at risk of developing a cannabis dependence syndrome that impaired psychological, social and/or occupational functioning. There were negative psychiatric consequences for a subset of the population who began using cannabis in early/mid-adolescence, particularly in terms of developing psychosis (the risk appeared to be highest for those with a genetic predisposition), and to a lesser degree for depression. There was a consistent dose-response relation between increasing levels of, and/or persistence of cannabis use and a range of deleterious health outcomes including loss of cognitive capacity, increased respiratory symptoms and impaired lung function, periodontal disease, compromised educational achievement and employment history, as well as a host of negative social outcomes (e.g. criminal convictions, relationship difficulties, driving impairment). No discernable impacts upon cardiovascular function were observed. The majority of cannabis users did so with little or no harm. In contrast, a non-trivial minority of the population (approximately 5%-10%) were at heightened risk because they: (i) used cannabis on more days than not; (ii) had become cannabis dependent; or (iii) began using cannabis during mid-adolescence and persisted well into adulthood. Implications are discussed with respect to the 2020 referendum.

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Cannabis use; cannabis dependence; cannabisrelated harms; referendum; legalisation

A leading international authority on cannabis use and abuse recently noted that New Zealand was blessed with two of the world's richest sources of information about the natural history of cannabis use. The Dunedin and Christchurch cohort studies have both studied approximately 1000 people from birth into their 40's, capturing in detail key developmental periods and patterns of cannabis use. According to Professor Wayne Hall when discussing the state-of-the-science in 2015,

The best designed and most informative of these [epidemiological] studies have been two New Zealand birth cohort studies whose members lived through a historical period during which a large proportion used cannabis during adolescence and young adulthood; sufficient numbers of these had used cannabis often enough, and for long enough, to provide information about the adverse effects of regular and sustained cannabis use. Confidence in the results of the New Zealand studies has been increased by the replication of their results in cohort studies in Australia (e.g. Swift, Coffey, Carlin, Degenhardt, & Patton, 2008), Germany (Wittchen, Frohlich, Behrendt, Gunter, Rehm, Zimmermann et al, 2007) and the Netherlands (van Os, Bak, Hanssen, Bijl, de Graaf, Verdoux, 2002). The fact that cannabis dependence and some of these adverse effects have also been reported in the Netherlands (where cannabis has been decriminalized for nearly 40 years) makes it unlikely that these adverse psychosocial effects can be attributed to legal policies towards cannabis. (Hall 2015, pp. 19–20)

Given that New Zealand has world-class information on cannabis use and its consequences we sought to draw together in one place relevant information to inform the voting public ahead of the cannabis referendum in 2020. In providing this overview we are acutely aware that there are hotly contested views and opinions about cannabis use among the public, and even differing views within the scientific community itself. Our aim is to provide a 'cool-headed', agnostic view on what the best (i.e. most reliable and robust) evidence can tell us.

We begin by describing in some detail the credibility of the sources of the information – the Dunedin and Christchurch studies. To help the non-expert reader we provide a short tutorial on design features that produce strong, robust information, laying out the case for why the voting public can have confidence in our findings. We acknowledge the difference between correlation and causation, and explain how we try to strengthen our causal inferences. The value of general population samples over selected samples (e.g. those attending clinics for treatment, those in the judicial system, or tertiary students as samples of convenience) will be touched upon, as well as the importance of maintaining sample integrity in cohort studies via high retention/follow-up over many years. Finally, we will reflect on the importance of making careful judgments about the strength of reported associations and how this should guide interpretation.

Technically our two studies are known as longitudinal or lifecourse studies. They have obtained a large amount of information about Study participants (and their families) beginning at birth and then via detailed assessments conducted at regular intervals as people have grown up and grow older. During the childhood years, assessments occurred regularly (every 1-2 years) due to the rapidity of development during this period; in the adult years, the assessments have occurred less frequently (every 5-7 years) due to the more gradual change characterising this stage of development (20 to 50 years, noting that the gap between assessments is likely to shorten with advancing age).

The research projects

The Dunedin Study, formally known as the Dunedin Multidisciplinary Health and Development Study (DMHDS), is a longitudinal investigation of health and behaviour in a population-representative birth cohort of 1,037 individuals (91% of eligible births; 52% male) born between 1 April 1972 and 31 March 1973 in Dunedin, New Zealand. The longitudinal study was established at age 3 years based on residence in the greater Dunedin metropolitan area (Poulton et al. 2015). Assessments have been conducted at birth and at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, 38, and most recently at age 45, when 94% of the 997 living participants took part. As at previous assessments, each study member was brought to the research unit for a fullday of interviews and direct examinations, regardless of their location in the world. For the first time at age 45, 93% of eligible participants also completed MRI scanning in a second half-day assessment. The cohort represents the full range of socioeconomic status on NZ's South Island, and as adults match the NZ National Health and Nutrition Survey on adult health indicators e.g. BMI, smoking, and GP visits (Poulton et al. 2006). Study participants are primarily of New Zealand European ethnicity. Written informed consent was obtained from participants, and the study was approved by the New Zealand Health and Disability Ethics Committee (NZ-HDEC).

The Christchurch Study, formally known as Christchurch Health and Development Study (CHDS), is a birth cohort of 1,265 children (635 boys, 630 girls), representing 97% of births in the Christchurch urban region of New Zealand between April and August 1977. The cohort has been studied at birth, 4 months, 1 year, annually to age 16, and at ages 18, 21, 25, 30, 35, and 40 years. All study information was collected following signed consent from study participants, is confidential, and was approved by the regional Health and Disability Ethics Committee. Unlike the Dunedin study, assessments have normally been undertaken in the homes of participants, or in locations in which participants are comfortable being interviewed, with interviews lasting between two and five hours (normally two to three hours). Participants based overseas are generally interviewed via phone or Skype. CHDS participants are also primarily European, but about 13% report Maori or Pacific ethnicity.

Both Studies use a prospective-longitudinal correlational design. This enables several different types of research including: (1) prediction studies of the childhood antecedents of later health, behaviour and wellbeing; (2) developmental studies about onset, course, continuity and change in health, behaviour and wellbeing; (3) epidemiological studies of the prevalence and incidence of health, behavioural problems, and variations in wellbeing and the associations among problem types; and (4) methodological studies of reliability and sampling biases.

The main strategy of both Studies involves testing for causal relations within this correlational design. Typically we adopt a stepwise approach. First, we document that a basic association between two constructs exists, striving for gold-standard measurement (of the time). Second, we document temporal sequence; whether the putative causal variable precedes the outcome variable. Third, we look for a dose-response contingency between the putative cause and outcome. Fourth, we attempt to rule out as many rival causal explanations as possible by introducing control variables into the analyses from our extensive databases (i.e. adjusting for potential confounders). Fifth, we test whether putative causal experiences are associated with within (intra-) individual change. Sixth, we try to establish specificity by substituting alternative dependent (outcome), then independent (predictor) variables. Finally, we posit a plausible explanatory process and test this using mediation analyses. By following this general approach we seek to maximise the robustness of our

research findings. Ultimately how 'true' a finding is will be determined by independent replication. However, this general approach - augmented by multiple standard checks such as sensitivity analyses - will increase the likelihood of successful replication.

Some notable strengths of the studies

Prospective versus retrospective designs

Human memory is fallible. Research that relies upon people's memory for events occurring over a long period (i.e. retrospective recall) can be very inaccurate due to forgetting, event modification, and the influence of current circumstances and mood states (Rueben et al. 2016). The main appeal of this type of approach is that it can be done quickly and at lower cost compared to prospective studies because you don't have to follow people over long periods, nor do you have to administer multiple measures on multiple occasions. Retrospective designs are also very good if you wish to study rare events or disorders that are hard to sample in the general population, but this is not the case for cannabis use. Clearly interviewing a sample just once, and working with that data has appeal, especially when set against the more expensive and time-consuming prospective approach which involves measuring as you go. This can be especially challenging when you wish to study the unfolding of peoples' lives in a wide variety of contexts. It is not surprising then that the number of studies using this gold-standard design is relatively small compared to retrospective study designs.

So what does this mean? Boiled down, the key message is that findings from prospective-longitudinal designs should carry more weight than those from retrospective studies. Both studies reviewed here adhere to this gold-standard approach.

Samples capture all walks of life, not just narrow bands of the population

It is also well recognised that if you wish to draw conclusions that impact upon the whole population, then your study sample should be representative of that whole population. Only then can you be assured that your findings faithfully capture the full range of life experiences and the many potential outcomes associated with those experiences or exposures. More concretely, studying a sample of drug clinic attendees may be convenient (particularly if you work at that clinic) but the findings can only ever apply to (or be generalised to) people attending clinics for treatment. This is particularly problematic in the case of cannabis research because the majority of people with substance dependence problems do not seek treatment (Andrews and Henderson 2000). The same generic problem applies to volunteer samples (e.g. those responding to media advertisements or university students - these groups differ in important ways from people who don't interact with media or from those who don't attend university). Both Studies avoid these problems because they recruited representative (of the general population at the time) samples at foundation. Thus, they are not subject to sampling biases.

High enrolment and retention

One of the major challenges facing prospective-longitudinal research is non-random loss to follow up. In lay terms this means that the people who quickly drift away from the study, and are hardest to find and re-enrol in future assessments, are not a random group. In fact, they are individuals within whom multiple difficulties tend to aggregate.

For example, they may be in and out of institutions, they might be on the run from the law, they may be homeless, they might be abusing substances, or living on the margins of society. Clearly these people are very important to retain in studies that purport to include all walks of life! To provide a specific example of the potential impact of failing to keep these people involved, the prevalence of a cannabis dependence diagnosis in the Dunedin study at age 26 - the age at which use was at its highest - was 8.4% among the easiest to recruit 80% of the cohort, whereas it was almost double that (14.0%) among the hardest to recruit 20%. Six years later at age 32 years, and despite the overall rates of annual use and dependence declining, the same picture emerged. Specifically, the prevalence of cannabis dependence was 4.5% among the easiest to recruit 80% whereas it more than doubled among the hardest to reach 20% group (with the prevalence of cannabis dependence at 9.6%). Thankfully neither Study has suffered from significant sample loss to follow up, suggesting that their findings are not influenced by selective sample attrition.

Covers the period of onset, peak usage, and gradual decline in prevalence through to mid-life

The period of life covered by both studies is ideal for understanding the natural history of cannabis use and its consequences precisely because it has measured people during the key stages of use including: initiation, rise, peak and decline. If data were missing during any of these periods we would have less certainty about both the short- and longer term consequences of cannabis use on a range of life outcomes.

Broad measurement

Both studies have measured many outcomes of relevance over almost ½ a century. The Dunedin study began as a multidisciplinary study by assessing a broad range of development indicators including biological, physiological, psychological and social aspects of peoples' lives. The Christchurch Study has specialised in social and psychological aspects of people's lives, with less focus on physical health. The combined value of these studies cannot be underestimated for the purposes of informing the public about cannabis use, misuse and its consequences. In particular, both Studies are able to adjust for the potential impact of multiple confounding variables simply because they have these in their datasets. Confounding is a technical term that describes the situation where other factors can better explain the association between cannabis and a specific outcome. To give an unrelated, but local example: if you researched the correlation between drinking Speights beer and supporting the Highlanders rugby team you would find a significant correlation but could erroneously conclude that drinking Speights beer 'caused' Highlander support. The confounder, in this case, would be regional location. That is, living in Otago can better explain both drinking Speights and supporting the Highlanders.

Some limitations of these two studies

Underpowered in terms of analytic sample size for Pasifika

Any study is a product of its time and our two studies are no different. This almost inevitably brings some limitations related to the nature of the population at foundation. Perhaps most significantly both Studies enrolled very few Pasifika families due to the low numbers living in the South Island in the 1970s. Both studies have slightly lower rates than the national average for Maori, but because the Christchurch study began with a slightly larger sample, it has been able to report on some Maori-specific outcomes related to cannabis use (see more below).

A lack of detailed qualitative information around the time of use

Our studies are not able to provide enormous depth around what was happening at the time of cannabis use. This would require controlled experimental conditions, more invasive assessment, and a longer period of uninterrupted observation, and this was just not feasible (or desirable) in our case.

Lack of information about the THC content of the cannabis used

Given the illegality and lack of regulation in the underground cannabis market we were unable to determine the strength of the cannabis ingested. That is, the level of THC, where THC is the psychoactive component of cannabis that gives the user a 'high'. Concretely this means that two individuals reporting cannabis use three times in the previous week would appear to be the same in our data, but they could differ in terms of how much THC they were exposed to. What is known is that the THC content of cannabis has increased over the period of time in which members of both cohorts have been using cannabis. Strictly speaking, we can never know if the lifecourse patterns of use and associated consequence reported here (from the 1980s to the present day) would change had more potent (modern) forms of cannabis had been used during the whole of this period, but it is possible that at least some effects might have strengthened.

Some pointers for the non-researcher to aid understanding and interpretation

All the findings reported below have been replicated by independent research groups. This is a basic prerequisite for treating research results as 'scientific fact'. The more times a finding is replicated the more confidence an observer can have that it is a real or true finding. The corollary, of course, is that failures to replicate call into question the robustness of the original finding. Failures to replicate can come in two broad forms: (i) failure to replicate, using the same or similar designs. For example, if the Dunedin and Christchurch studies had captured similar data at the same point in the lifecourse, using similar methods then it would raise serious questions about why the finding was found in one study and not the other. In other words, if the finding is trustworthy it should be impervious to small differences in approach. The second type of replication is when different approaches e.g. longitudinal, cross-sectional, clinical, biological and animal models converge to point to the same conclusion. In the current context, early research using mice suggested changes in brain structure occurred after exposure to cannabis during the mouse-equivalent of adolescence. This was followed by findings from cohort studies like ours showing a vulnerability to the effects of cannabis use in human adolescence (this is known as construct replication). Both forms of replicability have been taken into account in what follows.

Finally, all data reported here were obtained during a period when use of cannabis was illegal in Aotearoa–New Zealand. We are not able, nor do we attempt to comment on patterns of use, and their consequences, under different legal settings.

How many people use cannabis?

Both the Dunedin and Christchurch Studies (Poulton et al. 1997; Fergusson and Horwood 2001) converge to show that cannabis use began relatively early among a small section of the population (approximately 15% by age 15 years) and that rates of use increased rapidly as people moved into their 20's – by the mid-twenties 71% of the Dunedin Study population and almost 80% of the Christchurch sample had used cannabis at least once. Prevalence of *any* past year use in the 20's was consistent across both cohorts (approximately 45%–50% of the total population).

Yearly rates of use and dependence began to decrease in both studies from the early 30's and continued to decline into the forties, such that at the Dunedin Study Age-32-Assesment, past-year rates were: Use = 37.2%, Regular Use = 8.8%, and Dependence = 5.4%; at the Age-38-Assessment past-year rates were: Use = 25.8%, Regular Use = 6.1%, Dependence = 4.1%, and by the Age-45-Assessment, past year rates were: Use = 24.5%, Regular Use = 6.1%, Dependence = 2.1%. Comparable figures were observed in the Christchurch Study: At the Age-30-Assessment past-year rates were: Use = 33.4%, Regular Use = 11.0%, and Dependence = 2.5%, by the Age-35-Assesment, rates were: Use = 22.4%, Regular Use = 7.8%, Dependence = 1.6%; and at the Age-40-Assessment, rates were: Use = 23.0%, Regular Use = 8.9%, Dependence = 1.4%.

Mental health problems

Substance dependence diagnosis

Focusing on the twenties when use was highest, levels of problematic usage resulting in a DSM cannabis dependence diagnosis (based on past year use) were around 4%–10% of the whole population, or 9%–20% of those who had used cannabis. Cannabis dependence is a term that describes a maladaptive pattern of behaviour induced by frequent (daily or almost daily) use of cannabis. Study participants were asked questions relating time spent using, obtaining, or recovering from cannabis use; impairment of ability to control cannabis use; tolerance; continued use despite social, psychological or physical health problems caused or exacerbated by cannabis use; use of cannabis in hazardous situations, and whether cannabis usehas led them to neglect any of their usual responsibilities or to give up any of their usual social, occupational or recreational activities. In order to be diagnosed as dependent, our participants had to respond to 'yes, definitely' to questions in the last three of the above areas and to indicate that for at least one of these, the problem had endured for at least a month or had recurred over a longer period of time.

Interestingly the snapshot of use patterns among our samples when they were in their twenties appears to capture most if not all of those who will ever use cannabis. Specifically, life-time rates up to age 45 in the Dunedin Study (73.3%) and by age 40 in the

Christchurch study (80%) had increased only marginally from those twenty years prior. The equivalent rates for ever using alcohol for the Dunedin Study in the midtwenties were 95.8%, and by 45 are 98.4%, and for the Christchurch study were 98% in the mid-twenties, remaining stable to age 40. It is unclear whether the current legal status of cannabis use contributes to decline in use over time.

Cannabis use as a gateway to harder drug use

Longitudinal findings to date suggest that there is a relationship between cannabis and other illicit drug use. For example, Fergusson and Horwood (2001) found that by age 21 years, 70% of their participants had used cannabis and 26% had used other illicit drugs. Heavier cannabis users (>50 occasions a year) were much more likely to use other illicit drugs. The study found that nearly all individuals who had tried both cannabis and other drugs, had tried cannabis first. It is important to note, however, that the majority of cannabis users (63%) did not go on to use other illicit drugs by 21 years of age. In a more recent study, Fergusson, Boden, et al. (2006) found that the association between cannabis use and the use of other illicit drugs was particularly strong among those using during adolescence but that the strength of this relation declined thereafter. A study by Silins et al. (2014) gathered data from the Christchurch study along with data from two other Australian cohorts and reported that daily use of cannabis before 17 years was associated with a much higher chance (an 8-fold increase) of using other illicit drug use (e.g. hallucinogens, amphetamines, cocaine) by 30 years of age. They found that the association between cannabis and other drug use remained significant after controlling for a number of potential confounders (e.g. alcohol use, socio-economic status). Cannabis users may be more likely to try other drugs because of their relationships with other substance-using peers or through contact with drug dealers (Fergusson and Horwood 2001). There may also be neurobiological effects from cannabis that lead to other illicit drug use (Realini et al. 2009; Fergusson et al. 2015).

Psychiatric consequences

Both studies have shown that the chances of experiencing psychotic symptoms and/or psychotic disorders are elevated, especially if use began during adolescence and continued into adulthood. For example, the risk for having a psychotic disorder by age 26 in the Dunedin Study among early-onset cannabis users approximately doubled compared to non-users (Arseneault et al. 2002); in the Christchurch study rates of psychotic symptoms were approximately 1.5 times greater than for non-users (Fergusson et al. 2003). The effects were still present after adjustment for (i.e. ruling out the influence of) tobacco, alcohol and other drug use. We have also been able to rule out reverse causation whereby early emerging psychotic symptoms led to cannabis use, perhaps because of short-term 'self-medication' benefits (Fergusson et al. 2005). Perhaps most critically, the size of the risk relation between cannabis use during adolescence and adult psychosis is not large at the population level, appearing to be strongest among a sub-group of users who possess a genetic vulnerability and begin using during their adolescent years (Caspi et al. 2005). This explains why you wouldn't expect to see a huge increase in psychosis as a result of increasing rates of cannabis abuse. We concluded 15 years ago that on

the balance of evidence available at the time, that there was likely to be a causal association between cannabis use and risk for psychosis, but this risk was not large at a whole of population scale, rather it manifested among a smaller subset of users who had a predisposing genetic make-up (Fergusson, Poulton, et al. 2006). Subsequent studies and reviews have not changed our view (e.g. Hall et al. 2019).

The relation between cannabis use and other more common psychiatric disorders such as anxiety and depression is less consistent. However, a 2012 report from the Christchurch Study along with three other Australasian cohort studies showed that increasing amounts of cannabis use were associated with increasing depressive symptoms and that the association was strongest among adolescents (Horwood et al. 2012). The authors noted that they were unable to determine whether the direction of the relationship was likely to be from cannabis use to depression or whether depression led to cannabis use. Earlier Fergusson et al. (2002) found a modest relation between depression and weekly cannabis use in adolescence and young adulthood (1.7 times greater among weekly users versus never-users), even when other factors were taken into account (e.g. alcohol abuse/dependence, life circumstances) and this association did not vary with age. A more recent trajectory analysis showed evidence of a depression association for those who used regularly/heavily that persisted into mid-adulthood (Boden et al. 2019). The Christchurch Study also examined the association between weekly cannabis use and suicidal ideation or suicide attempts. They found that the association was strongest at ages 14-15 years, but cannabis use was found to have little or no association with suicidal behaviours at 20-21 years, again suggesting that the risk seems to decline with increasing age. Consistent with this common picture of high risk stemming from use beginning in early to mid-adolescence, a later paper from the Christchurch study found that the earlier that frequent (i.e. several times per week) cannabis use occurred, the earlier individuals began having suicidal thoughts, although this association was only found among males (van Ours et al. 2013).

Physical health problems

Respiratory consequences

The Dunedin Study has consistently shown impacts of regular cannabis use on lung function. By age 21 a diagnosis of cannabis dependence was associated with elevated rates of respiratory symptoms including: wheezing apart from colds, exercise-induced shortness of breath, nocturnal wakening with chest tightness and early morning sputum production. The proportion of cannabis dependent study members with an FEV1/FVC ratio of <80% (a clinical threshold denoting poor lung function) was 36% versus 20% for nonusers - a small but statistically significant difference even though cannabis smoking history was of relatively short duration (Taylor et al. 2000). Five years later the negative impact of cannabis use on lung function remained, and the association followed a dose-response pattern. That is, the more cannabis consumed, the stronger the association with poor lung function (Taylor et al. 2002). More recently the Dunedin Study showed that long-term cannabis use (measured as joint-years since age 17, and modelled after pack-years for tobacco) had detrimental effects on a set of standard physiological measures of lung function, although it was noted that the mechanism mediating this effect did not appear to be the same as for tobacco smoking. Importantly, the associations reported were shown to be independent (or over and above) any damage attributable to tobacco use (Hancox et al. 2010). This was important as some people who smoke cigarettes also smoke cannabis and vice versa.

More recently still, a report from the Dunedin Study showed that by age 38 cannabis use at least weekly was associated with an approximate doubling of risk for morning cough and excess sputum production, and a 50% increase in wheeze. Perhaps more interesting was the observation that reducing or quitting cannabis use was associated with a reduction in the prevalence of cough, sputum and wheeze to levels similar to those of non-users. The latter suggestive evidence for reversibility of negative affects following cessation of cannabis use is akin to the types of benefits that accrue following stopping tobacco smoking (Hancox et al. 2015).

Oral health consequences

The Dunedin Study has demonstrated an association between increasing levels of cannabis use and increased likelihood of being diagnosed with periodontal (gum) disease by age 32. The oral health measures were obtained via direct examination of study members by trained dentists (see Hong et al. 2020 for an overview of the oral health programme of research in the Dunedin study). This association was observed even after controlling for tobacco, the most well-established behavioural risk factor for periodontal disease, as well as other potential influences such as sex, irregular use of dental services and dental plaque. To convey a sense of the strength of this association, compared to non-users, regular cannabis users had a two to threefold increased risk of developing gum disease between the age of 26 and 32 years, depending on the threshold used to define disease (Thomson et al. 2008). This initial report has been confirmed using data collected up to and including age 38 years in the Dunedin Study. The strength of the association was of a similar size to that of other recognised risk factors in the oral health field (Meier et al. 2016).

Cardiovascular consequences

The aforementioned paper from the Dunedin Study also investigated the impact of longterm cannabis use on a number of clinical biomarkers indicating risk for cardiovascular disease and diabetes (Meier et al. 2016). These analyses included measures of metabolic health (e.g. overweight and obesity, high blood pressure, cholesterol levels), elevated levels of inflammation, and self-reported health, and included relevant adjustments (e.g. tobacco usage). Using cannabis joint-years as the risk exposure measure, we observed elevated risk for periodontal disease by age 38 years, after controlling for the above factors in childhood and adjusting for levels of gum disease 12 years earlier at age 26, and tobacco smoking. No other risks were observed for cannabis use suggesting that by early mid-life cannabis use was unrelated to risk for cardiovascular disease and diabetes. However some caution should be applied when interpreting this null finding as this could change as cohort members age. In contrast, tobacco pack-years were associated with worse lung function, systemic inflammation and poor metabolic health at age 38, as well as with deterioration in individual's health between age 26 and 38 years.



Cognitive (brain) problems

The Dunedin Study reported a relationship between cannabis use and loss of cognitive ability across the first four decades of life. The largest loss of 8 IQ points was found among study members who began using cannabis during adolescence and who continued using cannabis up to the age 38 assessment. Like all risk factor studies from Dunedin and Christchurch, appropriate adjustments were made to rule out alterative explanations for the findings observed, in this case: (i) past 24-hour cannabis use; (ii) past-week cannabis use; (iii) persistent tobacco dependence; (iv) persistent hard drug dependence; persistent alcohol dependence; and schizophrenia. Further, among the group of early-onset, persistent users the evidence suggested that some of this cognitive loss might be irreversible (Meier et al. 2012). Both animal and human studies have found that cannabis may affect both brain structure and functioning (e.g. Zalesky et al. 2012). Based on these findings, researchers have recommended that prevention and policy-making should concentrate on delaying the onset of cannabis use until adulthood and that education programmes should be used to target adolescents with messages about how cannabis can affect their brain development (Meier et al. 2012).

Since publication of this paper, a number of studies have also attempted to examine this association, but have fallen short of the desirable criteria for casual inference. For example, the clear temporal ordering made possible by good measures of cognition obtained in the Dunedin study well before people began using cannabis has not always been possible (e.g. Giancola and Tarter 1999; Ersche et al. 2012), nor have there been sufficient periods of exposure (cf. 20 years in our case) to allow a dose-response relation to emerge (e.g. Fried et al. 2005). Finally, the ability to adjust for multiple potential confounders has been limited in other studies, or simply misunderstood (see for example Daly 2013; Moffitt et al. 2013; Rogeberg 2013).

Social problems

Educational consequences

In a study combining data from the Christchurch study and two Australian cohort studies, Horwood et al. (2010) found that young people who had not used cannabis before 18 years of age had twice the odds of completing high school compared to early cannabis users (i.e. <15 years of age). Early use was also associated with not attending university and not getting a university degree. By using three different studies with different methods and controlling for a number of confounders (e.g. socioeconomic status, other substance use, problems at school) the researchers were able to demonstrate a robust association between early cannabis use and later educational underachievement. Moreover, they found that the more cannabis that was used, the stronger the effects (a dose-response relation). Studies have also found that the association between cannabis use and not completing high school was not the result of reverse causal association. That is, leaving school early does not result in increased cannabis use (Fergusson et al. 2003). There are a number of reasons why early and heavy cannabis use may be related to educational underachievement. Cannabis may affect developing brains influencing motivation and cognition (Lynskey and Hall 2000). Young people who use cannabis may also be exposed to a number of social situations that might encourage non-conventional

behaviours and discourage educational achieverment (Fergusson et al. 2003). In this regard, a very recent paper from the Christchurch study found that the relationship between cannabis use and later socioeconomic outcomes including educational underachievement remained significant even after adjusting for childhood and adolescent factors like adolescent problem behaviours and affiliations with other substance using peers (Boden et al. 2019). Long-term chronic cannabis users were found to earn on average NZD\$273/week less than non-users, after adjustment for confounding.

Employment consequences

In the Dunedin study persistent cannabis use was characterised by downward social mobility and arange of social problems (Cerda et al. 2016). Those with a longer history of cannabis dependence (or of regular cannabis use) reported financial difficulties, debt and cash flow problems (e.g. failing on credit card or loan repayments), an inability to cover basic living costs such as food and rent, welfare dependence, and a lower credit rating. Persistent dependence and regular cannabis use was also linked to antisocial behaviour at work and to higher rates of intimate relationship conflict. These findings were observed after controlling for potential confounders including familial substance-dependence, socioeconomic adversity, low self-control, low IQ during childhood, adolescent mental health problems and low achievement orientation. The associations were robust to adjustments for sex, ethnicity and adult family structure, thereby ruling out these as alternative explanations for the associations between cannabis dependence, regular cannabis use and poor psychosocial outcomes. In contrast associations were not related to higher rates criminal conviction among cannabis users, earlier age of onset among those using persistently over time, or to alcohol or hard drug dependence. Finally, we saw a dose-response relation such that the longer the period of use and/or dependence the worse the economic and social outcomes.

Interestingly, cannabis dependence was more strongly associated with financial difficulties than alcohol dependence, but looked very similar to alcohol with respect to downward mobility, antisocial behaviour at work and relationship conflict. This runs counter to conventional wisdom. However, we noted a dearth of studies that had actually compared the effects of alcohol and cannabis on such awide range of social outcomes in the same people, over many years. Where this had been done, the findings were similar to ours. However, it is important to acknowledge that our analyses only addressed economic and social outcomes - it remains possible that for a other outcomes (like those reviewed above) the results might differ. Also, it is important to acknowledge that the rates of alcohol dependence tend to be higher than cannabis dependence in the population. This suggests that the overall burden associated with alcohol use and misuse is probably higher. However, this could change if cannabis use increased significantly post-legalisation.

Consistent with the Dunedin Study, findings from the Christchurch study have shown that increasing levels of cannabis use from ages 14-21 years was related to higher levels of unemployment and welfare dependence and lower income by 25 years of age (Fergusson and Boden 2008). After adjustment for confounding factors and comorbid mental health disorders and substance use, those who used cannabis more than 400 times prior to age 21 (approximately weekly during that period) had odds of completing a tertiary degree that were 74% lower than those who did not use cannabis prior to age 21. In addition,

those using cannabis 400 or more times had odds of welfare dependence that were 4.9 times higher than those who had not used cannabis, and odds of unemployment that were 3.3 times higher. Finally, those who had used cannabis 400 or more times earned only 76% of the mean income reported by those who had not used cannabis prior to age 21.

Driving consequences

The Christchurch Study examined rates of driving under the influence of cannabis and alcohol between ages 21 and 25, and rates of motor vehicle collisions (MVC) during that period (Fergusson et al. 2008). MVC were limited to those in which the driver could have been deemed to have been 'at fault'. One of the most striking findings was that self-reported rates of driving under the influence of cannabis were 2.5 times higher than self-reported rates of drink driving in the cohort. Before adjustment, those reporting driving under the influence of cannabis had rates of collisions that were 2.25 times higher than those who had reported no driving under the influence of cannabis. After adjustment for confounding factors, this association decreased to 1.4 times the rates of those not driving under the influence of cannabis. This analysis showed that, for young adults, driving under the influence of cannabis was clearly a more serious issue than driving under the influence of alcohol, and that those who did so were more likely to have been involved in accidents.

Bias in the application of the law

Issues about cannabis use among Mãori from a lifecourse perspective are summarised in a sister paper (Theodore et al. 2020). In that paper, as well as here, biases in the application of the cannabis law are considered. Specifically, the Christchurch study found that by the age of 21 years, 5% of their participants had been arrested for a cannabis-related offence and 3.6% were convicted (Fergusson et al. 2003). Moreover, 25% of heavy users (those who had used cannabis on more than 400 occasions) had been arrested or convicted on a cannabis-related offence. When the researchers examined conviction rates for Māori they found that Māori were more likely to be arrested or convicted for cannabis-related offences than non-Māori who had the same level of cannabis use. Māori rates of arrest and conviction were three times higher than non-Māori even when other factors (e.g. having a previous police record) were taken into account. Based on these findings, they argued that the administration of cannabis law was biased and was not being enforced in an equitable manner. The researchers also found that arrest or convictions for cannabis offences did not result in a reduction of cannabis use. Nearly all (95%) of those arrested or convicted either continued using cannabis at a similar rate or increased their use, postarrest. That is, arresting or convicting people for cannabis use did not stop them from using.

Findings that Māori youth are treated differently to their non-Māori peers by the police are concerning, but they align with earlier Christchurch study findings. Researchers found that Māori children (up to age 15 years) were more likely than non-Māori children to come into contact with the police (based on official records) for any type of offence. This ethnic bias remained even when Māori and non-Māori children had similar levels of self or parent reported offending (Fergusson and Horwood 1993). These findings

suggest that from very young ages, Māori are affected by biases resulting in them being subject to increased police attention compared to non-Māori. Further, the 2007 Department of Corrections report on the over-representation of Māori in the criminal justice system noted that the stopping and checking of certain ethnic groups within a population as compared to others, was a known issue both nationally and internationally (Department of Corrections 2007). These findings from the Christchurch Study raise some questions about the likely effectiveness of the recent law changes requiring that public interest concerns be met before proceeding down a legal pathway.

Conclusions

The majority of New Zealanders who are now entering middle-age have used cannabis at some point in their life, most often in their late teenage years or during emerging adulthood (19-29 years, Arnett 2000). In their youth most perceived very few social sanctions were it known they had used cannabis (Poulton et al. 2001). The majority of cannabis users appear to do so with relative impunity, escaping serious health and/or social consequences. The major risks associated with cannabis use appear confined to those who begin using in early to mid-adolescence and/or use frequently, and/or are dependent. This comparatively small group of the population experience non-trivial negative outcomes that range from impairment in psychological function, loss of cognitive capacity, poorer respiratory and gum health, and a range of negative psychosocial outcomes such as early school leaving and academic underachievement, failure in employment and the workplace, dependence on social benefits, and risk of criminal conviction or incarceration. It is important to note that all these harms have come about at a time when cannabis use was illegal. The illegal status of marijuana does not prevent some people from using, and arrests and convictions do not lead to a reduction in use. Further, criminalising drug use can deter individuals from seeking or getting appropriate help (Human Rights Council 2015). Drug users in countries with prohibition laws report they would be more likely to engage with health services if drug policies were liberalised (Human Rights Council 2015; Benfer et al. 2018). Moreover, as shown in the current reviews, cannabis law in New Zealand can been forced inequitably, with a racial bias towards arresting and convicting Māori, compared to non-Māori. One of us (RP) has been giving evidence to various health select committees about cannabis use and harms for almost a quarter of a century and the same point has been made each time: harms associated with cannabis use should be treated as a health issue, not as a legal issue, with a strong preference for evidence-informed preventive and early intervention approaches. This approach would include age-appropriate educative efforts, but these are significantly hampered by the (il) legal status of cannabis.

Moving to a fully integrated health response to cannabis use begs several inter-related questions: how should this be done, in what form, and over what time period? The government has established the upcoming referendum as a simple two-option vote: retain the status quo versus full legalisation. In this context the draft Cannabis Legalisation and Control Bill has been designed to deter the illegal supply of cannabis; protect young people through a minimum purchase and use age of 20; license the supply chain to ensure legal cannabis is quality-controlled, including controls on potency, marketing and advertising; protect the public through public health messages about the health risks associated with cannabis; and improve access to social and health services for those with issues linked to cannabis use. The draft Bill meets suggested policies drawn from other policy areas, for instance, including a cap on potency and protection from corporate interest (e.g. Shover and Humphreys 2019), although the extent to which it addresses areas such as pricing policies or expunging existing criminal records is unclear. At a minimum, we encourage voters to carefully reflect upon the pros and cons of the option that removes the legal penalties associated with use. This is because such consequences can significantly reduce a persons life opportunities, impact on their employability and severely curtail their freedom of movement in a global twenty-firstcentury world. A criminal record also portends ongoing punishment or discrimination and stigma (Ispa-Landa and Loeffler 2016; National Inventory of Collateral Consequences of Conviction 2018). In theory, a minimalist position would have included a third option: decriminalisation of use as opposed to complete legalisation. This might have had several advantages. It could have: (a) removed the possibility of life-limiting criminal conviction and/or incarceration for normative behaviour, noting that despite recent legislative changes there remains a possibility of bias in the interpretation and/or application of the Act similar to past practice (e.g. Fergusson et al. 2003; Theodore et al., 2020); (b) provided more time to observe and consider the impact of different approaches to legalisation underway in jurisdictions such as Canada, some U.S. states like Colorado, and South American countries like Uruguay; (c) recognised what some had speculated but now appears to be the case: legalisation can be followed by small increases in the rates of use and misuse (Cerda et al. 2019; Hall et al. 2019); (d) allowed NewZealand to anticipate and plan for mitigation of risks resulting from increased usage; (e) informed further discussion about the details of the regulations required to minimise harm, viewing other countries as natural experiments, whilst protecting the rights of citizens to use cannabis without fear of legal sanction; and finally more generally (f) provided time to sort myths from reality, distortion from fact; and polemic from evidence (e.g. Humphreys and Hall 2019).

Given that the referendum process does not allow for a more graduated, evidenceinformed move towards legalisation, we urge the government to establish clear expectations for a careful, deliberative roll out of a new legislative framework if voters select this option. Systematic ongoing evaluation of the impacts of, and concerns about, harmful use will be important. The plan should be flexible in order to consider real-world commercial imperatives and profit-making activities. The parallels are obvious with the alcohol industry, such that identification of new markets (e.g. youth) resulted in the emergence of alco-pop products. In this regard, it is reassuring that the 'rules of engagement' published in 2019 (and summarised above) appear thorough and well-considered. One thing is very clear from the research - and thankfully it appears to be a message that has been widely understood and accepted - regulations that restrict access to use by children and adolescents must be prioritised and enforced.

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