

The 'Grass Ceiling': Limitations in the Literature Hinder our Understanding of Cannabis Use and its Consequences.

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ABSTRACT

Aim: To illustrate how limitations in the cannabis literature undermine our ability to understand cannabis-related harms and problems experienced by users and identify users at increased risk of experiencing adverse outcomes of use. **Method & Results:**

Limitations have been organized into three overarching themes. The first relates to the classification systems employed by researchers to categorize cannabis users, their cannabis use and the assumptions on which these systems are based. The second theme encompasses methodological and reporting issues, including differences between studies, inadequate statistical control of potential confounders, the under-reporting of effect sizes, and the lack of consideration of clinical significance. The final theme covers differing approaches to studying cannabis use, including recruitment methods. Limitations related to the nature of the data collected by researchers are discussed throughout with a focus on how they affect our understanding of cannabis use and users. **Conclusions:** These limitations must be addressed to facilitate the development of effective and appropriately targeted evidence-based public health campaigns, treatment programs, and preventative, early intervention and harm minimization strategies, and to inform cannabis-related policy and legislation.

KEYWORDS: Cannabis, dependence, literature review, marijuana, confounding, risk factors.

INTRODUCTION

It is estimated that \$7.7 billion is expended annually on the enforcement of cannabis prohibition in the United States of America alone [1] with presumably several more billions spent across the globe. This spending is ineffectual at best, with an estimated 143-

190 million people using cannabis each year (3.3-4.4% of 15-64 years olds globally) [2]. The vast majority of these cannabis users will not experience adverse effects of use [3-5], nevertheless, the illegal status of cannabis implies that all use is harmful [6]. This divergence between policy and evidence has a long history [5,7] and is unlikely to change in the short-term [8].

However, this does not mean that we should not push for evidence-based policies, strategies, interventions, and treatments. These elements should be based on the actual harms of the substance [9-11] and appropriately targeted to those most at risk of experiencing adverse outcomes of cannabis use [6].

Movement toward an evidence-based approach is hampered by limitations in the literature. These limitations have been organized into three overarching themes: the classification of cannabis use and cannabis users; methodological and reporting issues; and, approaches to studying cannabis use. Limitations of the data currently collected by researchers are discussed in each section as well as avenues for future research being suggested.

LIMITATIONS ASSOCIATED WITH THE CLASSIFICATION OF CANNABIS USERS AND CANNABIS USE

Several limitations in the cannabis use literature relate to cannabis use/user classification systems employed by researchers, including the assumptions on which these systems are based. For example, studies investigating the effects and outcomes of cannabis use tend to categorize participants solely on the basis of dependency status or frequency of use (with age of onset employed occasionally). This results in a lack of detailed knowledge about

overall patterns of use and contributes to a failure to explain the differences between cannabis users that are evident in society. This situation is related to the validity of dependence criteria and diagnoses, the manner in which frequency of use variables are utilized for categorization (including current frequency of use, and past year and lifetime usage rates), and the assumption that dependent and/or frequent use equates to problematic or harmful use.

A diagnosis of cannabis dependence requires that an individual meet a minimum of only three of six of the World Health Organization's *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) criteria [12] or three of seven of the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) criteria [13]. Although these two diagnostic systems are often used interchangeably by researchers, they are not directly equivalent systems, and can lead to divergent diagnoses [14]. When either of these diagnostic systems is employed in the classification of research participants it is generally based on the assumption that the relevant dependence criteria relate to actual harms of use, with dependent users, therefore, assumed to encounter more use-related harm than non-dependent users. However, none of the ICD-10 and DSM-IV-TR dependence criteria directly assesses harms of use. Rather, they focus on physical effects of use (e.g., tolerance, withdrawal) or behaviours associated with use (e.g., increased time spent on use-related activities). As such, a diagnosis of cannabis dependence does not necessarily equate to harmful or problematic use of the substance [15-17].

Further, because the nature of the diagnostic criteria increases the likelihood of some cannabis users receiving a diagnosis while others with similar usage patterns do not

[18,19], there is increasing concern that these diagnostic systems may not be valid [4,18]. The lack of assessment of the magnitude of cannabis used by an individual (i.e., quantity consumed, frequency of use) and the lack of weighting of dependence criteria also means that those diagnosed as dependent may actually experience no symptoms of physiological dependence [4]. For example, research participants have been reported as meeting dependence criteria when using cannabis less than monthly [20] or only once or twice in their lifetime [21].

The classification of cannabis users on the basis of frequency of use also has a number of drawbacks, impacting on our understanding of cannabis use. First, the comparability of study findings is hampered by researchers employing different frequency of use related classification systems. For example, there is no consensus among researchers regarding the definition of '*regular users*', '*heavy users*' or even '*non-users*' [e.g., 15 vs.17; 22 vs. 23]. Consensus is also lacking with regard to how to segment frequency of cannabis use into time-related categories. For example, current use may be categorised as: '*not at all*', '*once or twice*' or '*three or more times*' in the last 30 days [24] or as '*never used*', '*less than weekly*', '*at least weekly*', or '*daily*' [25]. This lack of consensus means that a particular individual may be arbitrarily classified as either a high or low level user based solely on the classification strategy employed in a given study. This affects the external validity of findings and means that readers have to be extremely careful when comparing and interpreting findings from different studies.

Second, given the dose-dependent nature of cannabinoids [26], it is concerning that there is an implicit assumption that more frequent consumption equates to higher dose, with minimal consideration given to the actual quantity or quality (potency) of the cannabis

consumed [21]. This is particularly worrisome when the classification systems employed do not even adequately distinguish between users who consume cannabis once a week, once a day, or multiple times a day. Validity is also questionable where researchers are not specific in relation to what a ‘use’ of cannabis means (i.e., is it one joint/cone, or one session of use in which many joints/cones are consumed? And, is a cone equivalent to a joint?). To illustrate, according to current published criteria, someone who is classified as a ‘*daily user*’ may have shared one joint of bush leaf with a number of people on most days of the past week (at one extreme), or pulled 20 cones of hydroponic buds each day (at the other).

Finally, frequency of use classification systems are based on the assumption that frequent use equates to harmful or problematic use. However, it is evident in the literature that daily cannabis use does not necessarily equate to dependence on the substance (as the usual measure of problematic/harmful use) and, conversely, non-daily use does not necessarily equate to a lack of dependency [15,17]. Additionally, there are indications in the literature that individuals who use cannabis frequently (i.e., daily or near daily) are not an homogenous group, with only some engaging in use that could, plausibly, be defined as problematic [27-29]. Thus, it is apparent that factors beyond frequency of use and dependence must play a role in problematic or harmful use [30,31]. These factors may include the social and physical context of use, methods of administration, motivations for using cannabis, and subjective effects of intoxication [26, 29-33].

LIMITATIONS RELATED TO METHODOLOGICAL AND REPORTING ISSUES

Methodological issues are responsible for a number of limitations in the cannabis use literature, including a lack of correspondence between studies and potential confounding. The manner in which cannabis research is reported has also hampered our understanding of cannabis use, with the lack attention paid to effect sizes and clinical significance affecting our ability to interpret findings.

Inability to Control for Confounding Factors

Of particular concern is the finding that it is not possible to complete a meta-analysis exploring the relationships between cannabis use and psychological and social issues because: “...*although some measures were similar across studies, no two studies measured either illicit drug exposure or psychosocial outcome in the same way. Additionally, potential confounding factors were inconsistently assessed across studies...*” [9][p. 1582]. Importantly, when studies do statistically control for potentially confounding factors, such adjustments have led to the attenuation and sometimes elimination of the associations between cannabis use and adverse outcomes, such as affective disorders [9,22,34,35]. This is pertinent because substance use and psychopathology both share common antecedents, such as childhood adversity. Thus, it is essential that common risk factors and concomitant substance use are measured and accounted for appropriately.

Similarly, some inconsistencies evident in the literature investigating the effects of cannabis use on cognitive function appear to be due to methodological differences between studies [36,37], although confounding may also be an issue. For example, impaired cognitive functioning is typically evident in people experiencing psychotic symptoms/disorders (e.g., schizotypy, schizophrenia, psychosis) and also in people with mood disorders [38,39], who are often over-represented within cannabis using

populations. Consequently, it is not clear whether the deficits in cognitive functioning seen in these individuals are related to their comorbid diagnoses, cannabis use, or both.

Effect Sizes

Another issue of concern is that most researchers base interpretations of their findings on levels of statistical significance, often without reporting effect sizes. This is particularly troublesome in relation to large general population-based studies with many thousand participants where statistically significant results may be more a reflection of statistical power than an indication of the actual strength of the association between variables. For example, without effect sizes to guide readers, it is possible that an inappropriate level of importance will be attached to variables that are only weakly associated with cannabis use, simply because the relationship was reported as being statistically significant.

Clinical Significance

Similarly, studies that report statistical significance and not clinical significance, also only tell one part of the story. Inexplicably, while a few researchers have reported that their statistically significant results were not actually clinically relevant [e.g., 36,40], it is rare for authors to discuss clinical significance at all. Thus, while the cannabis literature contains many reports of statistically significant differences between cannabis users and non-users or between light and heavy users, it is possible that these group differences may not be clinically significant. For example, a deficit in reaction time or verbal memory measured within a laboratory setting may have no impact on an individual's performance at work, ability to fulfill role responsibilities, or social competence, and as such, may not represent use-related harms or problems. The lack of consideration and discussion of

clinical significance in the literature has, therefore, left us with limited understanding of the impact of cannabis use on the day-to-day lives of users.

LIMITATIONS ASSOCIATED WITH APPROACHES TO STUDYING CANNABIS USE

Ultimately, what is known and unknown about cannabis users and cannabis use is largely due to the approaches employed by researchers to study this phenomenon. Studies investigating cannabis use typically follow one of two approaches: either non-users/never used vs. current users; or infrequent/light/non-dependent use vs. frequent/heavy/dependent use. The former approaches are typically employed to investigate cannabis use in the general population, commonly recruiting university students or being based on a subset of items from large general population household or school-based surveys [41]. In contrast, the latter approaches generally include more rigorous assessments of cannabis use, and typically recruit treatment-seeking/referred users.

There are several drawbacks associated with these approaches to investigating cannabis use. For example, studies comparing non-users/never used and current users often assess only a limited range of cannabis use factors, such as frequency of use, onset of use, or dependence, and ignore the fact that individuals who have never used cannabis are likely to differ from users in numerous ways beyond just their use or non-use [42]. These differences may be particularly apparent for younger cohorts, where not using cannabis may be considered almost an abnormal behaviour [29,43]. Studies comparing different levels of current cannabis use are similarly affected by typically overlooking the likelihood that individuals engaging in different patterns of cannabis use are likely to also differ in other ways. Additionally, because treatment-seeking/referred users are more

likely to be dependent and experience more adverse use-related problems than non-treatment seeking users [41,44], studies that recruit from this population of users do not necessarily inform us about the larger (and relatively under-researched) hidden population of cannabis users who do not experience difficulties of a magnitude that would lead them to seek treatment [44]. As such, both of these approaches to investigating cannabis use can lead to studies which lack appropriate control groups and are typically limited by inadequate data collection and/or through the recruitment of non-representative cannabis users.

Both of these approaches are predominantly employed in the identification of cannabis use-related risk factors and, therefore, may have contributed to the large number of inconsistencies present in the literature [9]. For example, conflicting findings have been reported regarding whether increased risk is associated with: male gender [e.g., 45 vs. 46]; use of tobacco [e.g., 24 vs. 45], alcohol [e.g., 17 vs. 46], or other illicit drugs [e.g., 15 vs. 47]; history of conduct [e.g., 24 vs. 46] or internalizing [e.g., 48 vs. 49] disorders; exposure to parental conflict [e.g., 46 vs. 48] or a socio-economically disadvantaged childhood [e.g., 24 vs. 46]. It is also evident that identifying possible risk factors has not been an effective tool in the prevention or reduction of cannabis use in Western societies [50].

In aiming to identify individuals at risk of cannabis use, there is an implicit assumption that all use will lead to problematic patterns of use and all use is harmful [41]. However, as cannabis use has become relatively normalized amongst young people in Western cultures, many potential users do not now fit the stereotypical profile of users alluded to by a summary overview of identified risk factors (i.e., young, male, dysfunctional and/or

disadvantaged background, with delinquent/antisocial behaviour) [29,43]. This type of risk factor informed stereotypical profile is evident in the depiction of cannabis users in public health campaigns, which typically show only adolescent users. It is possible that such campaigns decrease the likelihood of identification of ‘non-typical’ users by health professionals, because these cannabis users do not fit the expected profile. As such, we need to ensure that the use of risk factors does not blind us to the heterogeneity of cannabis users. Specifically, there is a tendency for a ‘one-size-fits-all’ approach in the literature, with some researchers seeking a single solution that suits all (or at least most) users, rather than acknowledging that it is likely to be more complex with different subgroups of users having different experiences and outcomes of use.

Non-Holistic Studies

A related issue is the tendency for researchers to view cannabis users through the prism of their use, rather than to take a more holistic approach, where research participants are viewed as individuals who happen to use cannabis. Non-holistic approaches lead to research that focuses on cannabis use/dependence as the primary negative outcome of risk-factor studies, or on cannabis use/dependence as the primary contributor to adverse life experiences in outcome studies. By focusing on cannabis use as the key ‘adverse’ factor in an individual’s life, researchers might overlook important environmental or individual factors that may contribute to adverse life circumstances. Thus, although the findings from these studies make an important contribution, it is important to acknowledge that this represents only part of the story. Non-holistic studies only provide a limited contribution to our overall understanding of people who use cannabis, their use of the substance, and the consequences of such use.

AVENUES FOR FUTURE RESEARCH

Several issues covered in this paper are unfortunate by-products of the time and financial constraints associated with large population-based cohort and cross-sectional studies where cannabis use is just one of many variables under investigation. Nevertheless, the quality of the cannabis use-related literature can be improved through the routine measurement and control of potentially confounding factors and the publication of effect sizes. It is also necessary to broaden our sampling populations in cannabis research to incorporate both treatment-seeking/referred and non-treatment seeking users, or at least acknowledge that the findings of studies related to treatment-seeking/referred users may not be generalizable to non-treatment-seeking user populations. It is worth noting that ‘snowballing’ [e.g., 15,51] and the Internet [e.g., 27,41,52] have been employed successfully for the recruitment of samples of non-treatment seeking cannabis users. Additionally, greater consideration needs to be given to the clinical significance of research findings so that they can be understood in relation to ‘real world’ differences and the true impact of cannabis use on an individual’s ability to function in daily-life can be ascertained.

Overcoming methodological differences between studies may be more difficult and it is worth noting that some benefit is gained in terms of information about the generalisability and general robustness of findings when a broad range of valid measures are employed by different researchers. However, it would be useful to have some consensus among researchers regarding how substance use, psychosocial and even demographic variables are assessed to increase comparability of findings and enable meta-analytic studies. Specifically, some of the problems associated with frequency measures could be rectified if researchers incorporated a broader range of use-criteria into their assessments. For

example, in terms of consumption, it would be useful to assess the typical number of days per week/month/year on which cannabis was used and the typical number of joints/cones consumed on each day of use. This more detailed consumption data, if supplemented with information about other aspects of use, such as the quantity (including cannabis to tobacco ratio of joints/cones) and quality (type of cannabis, relative potency) of cannabis consumed, may go some way to being valid as a proxy measure for dose, in lieu of measuring THC/CBD (which is difficult to assess in many studies). Further investigation is needed in this area, but it is worth noting the research potential of individual assessments of intoxication level as a proxy measure of dose [53].

Additionally, while some researchers [e.g., 17,27,51,54] have assessed problems associated with cannabis use alongside dependence criteria, more research is required to better understand the types of cannabis use-related problems and harms experienced by users in their daily lives and the prevalence and severity of these adverse outcomes. Further, when dependence is assessed it may be beneficial to examine the specific criteria met by individuals, as well as the total number of criteria endorsed [19]. Importantly, it should not be assumed that dependence necessarily equates to problematic or harmful use. Nor should it be assumed that a diagnosis of dependence informs us about the impact that cannabis use has on an individual's everyday life. In line with this, there is a need for studies that examine a broader range of variables relating to overall patterns of cannabis use (e.g., context of use, method of administration, motives for use, subjective effects) to gain a greater understanding of differing patterns of use and how these use factors may be associated with use-related harms and problems experienced by cannabis users.

A more recent approach to understanding cannabis users and their cannabis use is through the identification of detailed typologies using cluster and/or latent profiling analyses [e.g. 28,29,55,56]. The advantage of using a typology, rather than a simple categorisation approach using risk factors, is the ability to determine group membership on the basis of a larger number of factors. This leads to more detailed descriptions of users, which may, for example, enable a greater understanding of the differences between individuals with similar frequencies of use, and potentially illuminate the basis for the different outcomes of use evident in society. Greater exploration of overall patterns of use will also assist our understanding of cannabis use within the context of an individual's life. This research will be beneficial for the development of appropriately targeted and evidence-based treatment programs and early intervention and harm minimisation strategies.

CONCLUSIONS

The existing body of cannabis use-related research contains a number of limitations that have contributed to our current inability to state definitively: (a) the nature of the association between cannabis use and adverse use-related outcomes; (b) the likelihood of users experiencing these outcomes; (c) the severity with which they might be experienced; and, (d) the 'real world' impact of these outcomes on the ability of users to function in daily life.

As such, the limitations in the literature must be addressed so that service providers, governments, opinion bodies, and individual users can make informed decisions about cannabis use. More detailed characterization of users and a greater understanding of the role cannabis use plays in the context of people's lives are also required so that

appropriately targeted prevention strategies and treatment interventions may be developed. In particular, it is important that public health and education campaigns are as accurate as possible when detailing the outcomes of cannabis use and the likelihood of individuals experiencing use-related problems. Similarly, all interventions need to be evidence-based and appropriately targeted towards individuals who are most likely to encounter use-related harms or problems in their everyday life.

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