



## Viewpoint

## Standard units for cannabis dose: Why is it important to standardize cannabis dose for drug policy and how can we enhance its place on the public health agenda?



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Cannabis is the third most used psychoactive substance globally. An estimated 192 million people used cannabis during 2018 (3.9% of the global population aged 15–64) (United Nations Office on Drugs & Crime, 2020b). Legislative frameworks relevant to cannabis are evolving globally. In 2020 the United Nations removed cannabis from Schedule IV of the Single Convention on Narcotic Drugs but retained it in Schedule I (potential therapeutic but significant public health risk) (United Nations Office on Drugs & Crime, 2020a). This represents a moment of op-

portunity for deeper evaluation of how to manage such rapidly evolving changes.

Recreational cannabis use is increasing across many regions worldwide (European Monitoring Centre for Drugs and Drug Addiction EM-CDDA, 2020; Hasin et al., 2015; United Nations Office on Drugs & Crime, 2020b), while the perception of risks associated with cannabis seems to be declining, at least in high income countries (Barrett & Bradley, 2016; Carliner, Brown, Sarvet, & Hasin, 2017). Yet multi-

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ple health related harms associated with frequent cannabis use have been documented in the scientific literature, including respiratory problems, cardiovascular effects, gastrointestinal disorders and detrimental impacts on mental health, cognition, and behaviour, the latter of which increases the risk of injury (Campeny et al., 2020). Changes in cannabis policy will align cannabis use more closely with alcohol, benzodiazepines, prescribed opioids and tobacco rather than with currently illegal drugs. Diverse approaches can be taken in a transition to legal and regulated access which will present new challenges for implementing prevention and harm reduction strategies (Kilmer, 2019) as cannabis products become more widely available. Although the quantity used per occasion (dose) has shown to influence cannabis-related outcomes (Freeman & Lorenzetti, 2019), up to this point cannabis use had been mainly assessed by frequency of use. Based on experiences with other drugs such as alcohol or tobacco, frequency alone may lead to a biased estimation of the risks and harms. For instance, frequency does not capture variations of quantity per day of use in frequent use (European Monitoring Centre for Drugs and Drug Addiction, 2013). As such, reliable data on quantity of cannabis use is required to improve assessment for epidemiological and clinical analysis. Consequently we propose the establishment of a Standard Cannabis Unit (SCU) based on quantity of 9-Tetrahydrocannabinol (9-THC), the primary psychoactive component of cannabis (Casajuana Kogel, López-Pelayo, Balcells-Olivero, Colom, & Gual, 2016). Most cannabis related harms seem to show a dose-response relationship with THC exposure, as extensively reported in the literature. For instance, evidence points to increased risk of developing psychosis symptoms (Di Forti et al., 2019) and increased risk of psychiatric hospitalization (Schubart et al., 2011) with higher levels of THC. The US National Institute on Drug Abuse along with prominent scientists (Volkow, 2020) has called for standard units of dose for cannabis, similar to those used for alcohol.

In establishing a standardized unit for cannabis dose, learning from the experiences of alcohol and tobacco could prevent errors from being repeated. For instance, during the 1980s and 1990s, several countries reached national consensus on defining a Standard Drink (SD) for alcohol. However, there is wide variation in country definitions of a SD (Kalinowski & Humphreys, 2016) due to cultural differences and the fact that some are based on national consensus while others were derived from empirical research. This makes cross-country comparisons, policy analysis and prevention efforts more difficult. Importantly, although different definitions of a SD exist, they are all based on the same unit of measurement (grams of pure alcohol) and thus can be converted. As a result, the concept of a SD represents an important advance for the alcohol public health field. It provides clinicians, public health specialists, policy makers, and researchers with a useful tool when implementing programs ranging from early identification to harm-reduction. Efforts to establish standard units have also been made with other drugs, for example, Morphine Milligram Equivalents (MME) or diazepam equivalents which allow standardization of opioid and benzodiazepine dosing respectively. These examples of standard units, similar to the desired SCU, enable calculating equivalent total dosing for different drugs in the same substance family and with different routes of administration, permitting an estimation of the risk of adverse health consequences. With cannabis both the possible routes of administration and continuing changes in potency are not standardized or systematically registered and thus are not taken into account.

The implementation of cannabis policy aimed at reducing the adverse health impact of recreational cannabis use must be grounded in evidence. As the SD has proven to be an important vehicle for reducing alcohol-attributable harm through interventions across the spectrum, ranging from prevention and therapy to harm-reduction, a SCU could similarly be used in evidence-based interventions that guide and transform health policy targeting cannabis use and related harms. A SCU has the potential to become a critical tool for universal prevention, akin to SD for alcohol. For example, a SCU will help determine what level of cannabis exposure constitutes high risk use. Consequently, consumers

could make better informed choices regarding their own use, and health-care providers could more assuredly prevent potential harms. The development and refining of a SCU can also inform targeted prevention and harm-reduction strategies, through the development of guidelines for low-risk use (Fischer et al., 2017). Additionally, information on patterns of use as measured by SCUs (dose and frequency) can be used to inform screening and brief interventions, in conjunction with short standardized screening instruments. Use of a SCU in prevention, treatment and public health strategies holds promise for reducing morbidity, mortality and costs related to cannabis use. This is based on the demonstrated benefits of the standard alcohol unit (i.e. standard drink (SD)) in Screening and Brief Intervention (SBI), which has been shown to be cost-effective and cost-saving for alcohol use (<I\$150 and <I\$1500 in low- and high-income settings, respectively) (Chisholm et al., 2018).

Importantly, steps have been made towards achieving an international consensus around what could constitute a SCU. During a workshop with 32 experts (including authors of this paper) from different disciplines (sociology, psychology, public health, basic and clinical research, psychiatry) at the Lisbon Addictions Conference 2019, a back-casting exercise was used to address challenges and achieve consensus in developing a SCU. Participants in back-casting exercises do not predict the future, but rather choose a desired future and work backwards to define the steps needed to achieve that goal. During this exercise, several characteristics of a SCU (divided into three domains to facilitate discussion and reaching consensus) were identified and agreed: 1) core values: easy-to-use, universal, focused on THC, accurate, and accessible; 2) key challenges: sudden changes in patterns of use, heterogeneity of cannabis compounds (diversity in content/composition e.g. quantities/proportions of THC, CBD, other cannabinoids, etc.) as well as in administration routes, variations over time in THC concentrations, and of laws that regulate the legal status of recreational and medical cannabis use; and, 3) facilitators: previous experience with standardized measurements, funding opportunities, multi-stakeholder support, high prevalence of cannabis users, and widespread changes in legislation (López-Pelayo et al., 2021).

Among all the challenges to be faced, diversity of cannabis compounds must be taken into account. For example, levels of CBD are present in cannabis and might influence health consequences. But, as some of the authors have already discussed in previous papers (Freeman & Lorenzetti, 2019), up to this point the effects of CBD have not been consistent throughout all studies and outcomes (Freeman et al., 2019). Not all experimental studies have reported protective effects of CBD (Morgan et al., 2018), and some even indicate that it may potentiate certain effects of THC (Arkell et al., 2019). Additionally, other cannabinoids such as  $\Delta^9$ -tetrahydrocannabivarin (THCV) (Englund et al., 2016) and terpenoids (Russo, 2011) may play a role in moderating the effects of THC. Therefore, evidence into the potential role of CBD as a harm reduction strategy is still progressing, and further evidence is needed to establish how different doses of CBD and other cannabinoids might influence the effects of THC. All in all, we consider that a SCU should still be based on dose of THC.

Another important challenge to consider is recent changes in cannabis potency. Changes in potency in recent years have been well-documented internationally (Freeman et al., 2020), and high potency is associated with increased psychosis risk (Di Forti et al., 2019) and first-time cannabis admissions to drug treatment (Freeman et al., 2018). More data on THC levels per joint in different settings and countries are needed. Easily and rapidly reproducible methods of analysis are required in order to adapt a future SCU (based on milligrams of THC) to changes in potency that can impact dosing (Fischer et al., 2017).

Previous research in Spain (a naturalistic study in which adults, reporting cannabis use in the last 60 days, answered a questionnaire on cannabis use and were asked to donate a joint to further determine their 9-THC and Cannabidiol (CBD) content) found the Standard Joint Unit (SJU) to be 7 mg of THC for the population 18 years or older (Casajuana Kögel et al., 2017), but empirical data from other countries

are less consistent. Generalization of the results of this study is not warranted. The impact of changes in the levels of cannabis potency on use behaviour or more specifically, on dose, remains a challenge to tackle for standardizing the SCU. Another issue is that cannabis is not exclusively used in joints (it is also used for example in bongs, pipes, edibles and drinks). A standard unit is the fixed content of milligrams of THC in each unit of consumption. The definition of dose is the quantity of milligrams of THC per occasion of use and through a standard unit the dose could be measured taking into account different routes of administration and potency (e.g., an individual who consumes 1 joint and 1 edible is self-administering 2 Standard Units, which means 10 mg of THC). As some of the authors previously proposed, a complementary strategy might be to apply a fixed standard unit of THC (5 mg THC per unit) to all cannabis products (Freeman & Lorenzetti, 2019). A standard THC unit of 5 mg is a low dose with minimal risk of adverse events, and is compatible with existing policies in the USA and Canada such as a maximum dose of 5 mg or 10 mg per serving size (Freeman & Lorenzetti, 2019).

The previously described Standard THC Unit and Standard Joint Unit could be complementary tools. A SJU, based on a fieldwork that measured composition of handmade joints (Casajuana Kögel et al., 2017), would account for the most frequent route of administration in Europe (Hindocha, Freeman, Ferris, Lynskey, & Winstock, 2016) and might provide a useful framework for both legal and illegal markets when the route of administration is smoking. On the other hand, a Standard THC Unit, based on a revision of several research studies focused on cannabis doses (Freeman & Lorenzetti, 2019), might be most useful for medical uses of cannabis, within regulated legal markets, and in contexts where more diverse routes of administration are available, such as the USA (Hindocha et al., 2016). Further work is needed to explore the application of SCUs in diverse cannabis markets and for different cannabis products, consumers and applications ranging from public health policy to clinical practice. For instance, a possible future direction in the research agenda could be an internationally coordinated effort to find a region specific SJU which could enable comparison of research study findings based on samples using joints, as one of the most typical routes of administration globally. Previous efforts to standardize units of other psychoactive substance doses (such as alcohol) suggest that local differences in typical doses might appear. For example, a SD in Spain is 10 gs of alcohol, but a SD in the United Kingdom is 8 gs and in the United States is 14 gs (Kalinowski & Humphreys, 2016).

In conclusion, the implementation of a SCU in the years to come is feasible, after overcoming several surmountable barriers and harnessing contextual facilitators. The authors agreed in an interactive workshop that the establishment of a SCU is possible on the basis of the following key steps: 1) building a task force to define, develop and advocate for an evidence-based SCU; 2) reviewing and expanding available national-level data on cannabis use and related risks; and 3) examining how the SCU relates to the concept of 'risky use' of cannabis.

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