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3 **Title: Standard Units for cannabis dose: Why is it important to standardize cannabis dose for**
4 **drug policy and how can we enhance its place on the public health agenda?**

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

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34 Cannabis is the third most used psychoactive substance globally. An estimated 192 million
35 people used cannabis during 2018 (3.9% of the global population aged 15– 64) (United Nations
36 Office on Drugs and Crime, 2020b). Legislative frameworks relevant to cannabis are evolving
37 globally. In 2020 the United Nations removed cannabis from Schedule IV of the Single
38 Convention on Narcotic Drugs but retained it in Schedule I (potential therapeutic but significant
39 public health risk) (United Nations Office on Drugs and Crime, 2020a). This represents a
40 moment of opportunity for deeper evaluation of how to manage such rapidly evolving changes.

41 Recreational cannabis use is increasing across many regions worldwide (European Monitoring
42 Centre for Drugs and Drug Addiction (EMCDDA), 2020; Hasin et al., 2015; United Nations
43 Office on Drugs and Crime, 2020b), while the perception of risks associated with cannabis
44 seems to be declining, at least in high income countries (Barrett & Bradley, 2016; Carliner et
45 al., 2017). Yet multiple health related harms associated with frequent cannabis use have been
46 documented in the scientific literature, including respiratory problems, cardiovascular effects,
47 gastrointestinal disorders and detrimental impacts on mental health, cognition, and behaviour,
48 the latter of which increases the risk of injury (Campeny et al., 2020). Changes in cannabis
49 policy will align cannabis use more closely with alcohol, benzodiazepines, prescribed opioids
50 and tobacco rather than with currently illegal drugs. Diverse approaches can be taken in a
51 transition to legal and regulated access which will present new challenges for implementing
52 prevention and harm reduction strategies (Kilmer, 2019) as cannabis products become more
53 widely available. Although the quantity used per occasion (dose) has shown to influence
54 cannabis-related outcomes (Freeman & Lorenzetti, 2019), up to this point cannabis use had been
55 mainly assessed by frequency of use. Based on experiences with other drugs such as alcohol or
56 tobacco, frequency alone may lead to a biased estimation of the risks and harms. For instance,

57 frequency does not capture variations of quantity per day of use in frequent use (European
58 Monitoring Centre for Drugs and Drug Addiction, 2013). As such, reliable data on quantity of
59 cannabis use is required to improve assessment for epidemiological and clinical analysis.
60 Consequently we propose the establishment of a Standard Cannabis Unit (SCU) based on
61 quantity of 9-Tetrahydrocannabinol (9-THC), the primary psychoactive component of cannabis
62 (Casajuana Kogel et al., 2016). Most cannabis related harms seem to show a dose-response
63 relationship with THC exposure, as extensively reported in the literature. For instance, evidence
64 points to increased risk of developing psychosis symptoms (Di Forti et al., 2019) and increased
65 risk of psychiatric hospitalization (Schubart et al., 2011) with higher levels of THC. The US
66 National Institute on Drug Abuse along with prominent scientists (Volkow, 2020) has called for
67 standard units of dose for cannabis, similar to those used for alcohol.

68 In establishing a standardized unit for cannabis dose, learning from the experiences of alcohol
69 and tobacco could prevent errors from being repeated. For instance, during the 1980s and 1990s,
70 several countries reached national consensus on defining a Standard Drink (SD) for alcohol.
71 However, there is wide variation in country definitions of a SD (Kalinowski & Humphreys,
72 2016) due to cultural differences and the fact that some are based on national consensus while
73 others were derived from empirical research. This makes cross-country comparisons, policy
74 analysis and prevention efforts more difficult. Importantly, although different definitions of a
75 SD exist, they are all based on the same unit of measurement (grams of pure alcohol) and thus
76 can be converted. As a result, the concept of a SD represents an important advance for the
77 alcohol public health field. It provides clinicians, public health specialists, policy makers, and
78 researchers with a useful tool when implementing programs ranging from early identification to
79 harm-reduction. Efforts to establish standard units have also been made with other drugs, for
80 example, Morphine Milligram Equivalents (MME) or diazepam equivalents which allow
81 standardization of opioid and benzodiazepine dosing respectively. These examples of standard
82 units, similar to the desired SCU, enable calculating equivalent total dosing for different drugs
83 in the same substance family and with different routes of administration, permitting an

84 estimation of the risk of adverse health consequences. With cannabis both the possible routes of
85 administration and continuing changes in potency are not standardized or systematically
86 registered and thus are not taken into account.

87 The implementation of cannabis policy aimed at reducing the adverse health impact of
88 recreational cannabis use must be grounded in evidence. As the SD has proven to be an
89 important vehicle for reducing alcohol-attributable harm through interventions across the
90 spectrum, ranging from prevention and therapy to harm-reduction, a SCU could similarly be
91 used in evidence-based interventions that guide and transform health policy targeting cannabis
92 use and related harms. A SCU has the potential to become a critical tool for universal
93 prevention, akin to SD for alcohol. For example, a SCU will help determine what level of
94 cannabis exposure constitutes high risk use. Consequently, consumers could make better
95 informed choices regarding their own use, and healthcare providers could more assuredly
96 prevent potential harms. The development and refining of a SCU can also inform targeted
97 prevention and harm-reduction strategies, through the development of guidelines for low-risk
98 use (Fischer et al., 2017). Additionally, information on patterns of use as measured by SCUs
99 (dose and frequency) can be used to inform screening and brief interventions, in conjunction
100 with short standardized screening instruments. Use of a SCU in prevention, treatment and public
101 health strategies holds promise for reducing morbidity, mortality and costs related to cannabis
102 use. This is based on the demonstrated benefits of the standard alcohol unit (i.e. standard drink
103 (SD)) in Screening and Brief Intervention (SBI), which has been shown to be cost-effective and
104 cost-saving for alcohol use (<I\$150 and <I\$1,500 in low- and high-income settings,
105 respectively) (Chisholm et al., 2018).

106 Importantly, steps have been made towards achieving an international consensus around what
107 could constitute a SCU. During a workshop with 32 experts (including authors of this paper)
108 from different disciplines (sociology, psychology, public health, basic and clinical research,
109 psychiatry) at the Lisbon Addictions Conference 2019, a back-casting exercise was used to
110 address challenges and achieve consensus in developing a SCU. Participants in back-casting

111 exercises do not predict the future, but rather choose a desired future and work backwards to
112 define the steps needed to achieve that goal. During this exercise, several characteristics of a
113 SCU (divided into three domains to facilitate discussion and reaching consensus) were
114 identified and agreed: 1) core values: easy-to-use, universal, focused on THC, accurate, and
115 accessible; 2) key challenges: sudden changes in patterns of use, heterogeneity of cannabis
116 compounds (diversity in content/composition e.g. quantities/proportions of THC, CBD, other
117 cannabinoids, etc.) as well as in administration routes, variations over time in THC
118 concentrations, and of laws that regulate the legal status of recreational and medical cannabis
119 use; and, 3) facilitators: previous experience with standardized measurements, funding
120 opportunities, multi-stakeholder support, high prevalence of cannabis users, and widespread
121 changes in legislation (López-Pelayo et al., 2021)..

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

134 Another important challenge to consider is recent changes in cannabis potency. Changes in
135 potency in recent years have been well-documented internationally (T. Freeman et al., 2020),
136 and high potency is associated with increased psychosis risk (Di Forti et al., 2019) and first-time
137 cannabis admissions to drug treatment (T. Freeman et al., 2018). More data on THC levels per
138 joint in different settings and countries are needed. Easily and rapidly reproducible methods of

139 analysis are required in order to adapt a future SCU (based on milligrams of THC) to changes in
140 potency that can impact dosing (Fischer et al., 2017).

141 Previous research in Spain (a naturalistic study in which adults, reporting cannabis use in the
142 last 60 days, answered a questionnaire on cannabis use and were asked to donate a joint to
143 further determine their 9-THC and Cannabidiol (CBD) content) found the Standard Joint Unit
144 (SJU) to be 7mg of THC for the population 18 years or older (Casajuana Kögel et al., 2017), but
145 empirical data from other countries are less consistent. Generalization of the results of this study
146 is not warranted. The impact of changes in the levels of cannabis potency on use behaviour or
147 more specifically, on dose, remains a challenge to tackle for standardizing the SCU. Another
148 issue is that cannabis is not exclusively used in joints (it is also used for example in bong, pipes,
149 edibles and drinks). A standard unit is the fixed content of milligrams of THC in each
150 unit of consumption. The definition of dose is the quantity of milligrams of THC per occasion
151 of use and through a standard unit the dose could be measured taking into account different
152 routes of administration and potency (e.g., an individual who consumes 1 joint and 1 edible is
153 self-administering 2 Standard Units, which means 10 milligrams of THC). As some of the
154 authors previously proposed, a complementary strategy might be to apply a fixed standard unit
155 of THC (5mg THC per unit) to all cannabis products (T. Freeman & Lorenzetti, 2019). A
156 standard THC unit of 5mg is a low dose with minimal risk of adverse events, and is compatible
157 with existing policies in the USA and Canada such as a maximum dose of 5mg or 10mg per
158 serving size (T. Freeman & Lorenzetti, 2019).

159 The previously described Standard THC Unit and Standard Joint Unit could be complementary
160 tools. A SJU, based on a fieldwork that measured composition of handmade joints (Casajuana
161 Kögel et al., 2017), would account for the most frequent route of administration in Europe
162 (Hindocha et al., 2016) and might provide a useful framework for both legal and illegal markets
163 when the route of administration is smoking. On the other hand, a Standard THC Unit, based on
164 a revision of several research studies focused on cannabis doses (T. Freeman & Lorenzetti,
165 2019), might be most useful for medical uses of cannabis, within regulated legal markets, and in

166 contexts where more diverse routes of administration are available, such as the USA (Hindocha
167 et al., 2016). Further work is needed to explore the application of SCUs in diverse cannabis
168 markets and for different cannabis products, consumers and applications ranging from public
169 health policy to clinical practice. For instance, a possible future direction in the research agenda
170 could be an internationally coordinated effort to find a region specific SJU which could enable
171 comparison of research study findings based on samples using joints, as one of the most typical
172 routes of administration globally. Previous efforts to standardize units of other psychoactive
173 substance doses (such as alcohol) suggest that local differences in typical doses might appear.
174 For example, a SD in Spain is 10 grams of alcohol, but a SD in the United Kingdom is 8 grams
175 and in the United States is 14 grams (Kalinowski & Humphreys, 2016).

176

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

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