UK standard unit of alcohol = 8 g). Applied to cannabis, this framework would label cannabis-based products according to tetrahydrocannabinol (THC) volume in mg.

Unlike alcohol, however, standardization of plant-based products such as cannabis presents complexities, including the interactive pharmacological effects of other bioactive constituents in cannabis, such as cannabidiol (CBD), as discussed by Freeman & Lorenzetti. Although described as preliminary evidence in support of CBD's protective effects against THC's harms, there is growing recognition of CBD's therapeutic potential independent of THC [2]. Indeed, some US states where THC has remained illegal, such as Texas, have adopted CBD laws for the indication of several medical conditions. In 2018, the Food and Drug Administration (FDA) approved the first CBD drug, Epidiolex, following convincing evidence of seizure control in pediatric epilepsy [3]. Keeping in mind that there are > 100 cannabinoids currently identified in cannabis, the interactive synergy between these compounds, referred to as the 'entourage effect', might also be critical for symptom relief in medical conditions beyond the isolated effects of THC or CBD [4]. It is, therefore, necessary to consider standardized units of cannabis compounds not only from a risk prevention perspective, but also from a therapeutic perspective, as new cannabis strains continue to emerge that narrow the gap between THC and CBD profiles.

Freeman & Lorenzetti recommended a standard unit of 5 mg THC, the lowest dose associated with subjective intoxication effects common across different modes of use (oral, inhalation, etc.). In addition to the rationale that a low standard dose may promote lower levels of average consumption, some studies suggest a paradoxical effect of THC, where positive effects at low doses result in negative effects in high doses. For example, a 2017 study showed that in comparison to placebo, 7.5 mg of THC significantly reduced self-reported subjective distress whereas 12.5 mg THC increased negative mood, impaired task performance and attenuated blood pressure reactivity to a stressor [5]. Similar effects have been noted in the treatment of pain where the lowest dosage of cannabinoids was associated with greatest relief from pain, while higher doses exacerbated pain [6]. These paradoxical effects have led to the recognition of a condition referred to as cannabinoid hyperemesis syndrome—severe, and uncontrollable vomiting—resulting from high THC cannabis use, whereas low-dose THC provides nausea relief in cancer patients [7]. These studies demonstrate that the therapeutic effect of THC can be optimal at lower doses. Low-dose THC also minimizes the potential for its intoxicating effects and the development of tolerance, and therefore could be beneficial for drug maintenance therapies.

In closing, given evidence that the effects of cannabis are dose-related, a standard unit system will allow cannabis dosage information to be communicated clearly to consumers and caregivers. It is critical, however, to address current and future impediments that might limit the utility of a standard unit.

Declaration of interests

None.

Keywords Cannabinoids, cannabis, CBD, marijuana, potency, THC.

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IMPORTANCE OF A STANDARD UNIT DOSE FOR CANNABIS RESEARCH

A standardized measure for 9-tetrahydrocannabinol (THC) content in cannabis products is necessary to advance research both on the adverse effects of cannabis (e.g. risks for brain development, mental illness and addiction) and on the drug's potential medical uses

Recognizing the increasing diversity of cannabis products and their expanded use, Freeman & Lorenzetti propose a

standard unit dose of 5 mg 9-tetrahydrocannabinol (THC) to be used for all cannabis products, regardless of method of administration [1]. They argue that a standard dose would help to guide consumers towards safer patterns of cannabis use. The National Institute on Drug Abuse (NIDA) strongly supports the need for a standardized measure to facilitate research, and this was a key recommendation from NIDA's Cannabis Policy Research Council Workgroup [2].

However, as discussed by Freeman & Lorenzetti, the development of such a measure has been challenging, due to concerns that the effects of any standardized dose would differ on the basis of mode of consumption or, possibly, how it is combined with other cannabinoids such as cannabidiol (CBD) [3].

These complexities hardly negate the value of having a standardized measure of THC, irrespective of product type. In fact, having and using such a standard is a prerequisite for comparing the effects of various cannabis products on THC bioavailability, pharmacokinetics and pharmacological effects [3], which is knowledge fundamental to studies pertaining to medical use of cannabis.

A standardized measure will also be essential for advancing our understanding of some of the major concerns related to cannabis use, especially its influence on brain development, and the risk for cannabis use disorders and psychoses [4,5]. Current and past studies evaluating the effects of cannabis on brain development and cognition, whether focused prenatally or during childhood or adolescence, are limited to rough estimates on the basis of reported frequency of use (life-time, past year, past month or regular use) and there is no information on the THC content of the product(s) consumed [6].

This lack of information on THC content probably contributes to discrepancies among investigators, with some reporting adverse effects even after single cannabis exposure [7] and others showing no differences with regular exposures during adolescence [8]. The Adolescent Brain and Cognitive Development (ABCD) study will prospectively investigate close to 12 000 children as they transition from childhood into adulthood with a variety of measures, including brain imaging, neurocognitive and behavioral tests, educational achievement and patterns of drug use [9]. This study and others like it would benefit enormously from a standardized measure of THC, as would pre-clinical studies aiming to mimic clinical exposures.

It is widely believed that the increase in THC content of cannabis (which almost tripled in the past 2 decades) [10,11] is responsible for greater adverse effects associated with cannabis consumption [12]. Evidence already points to a higher risk for cannabis use disorder and for psychoses with consumption of cannabis with high vs. low THC content, but these associations have been based on estimates of the THC content of cannabis in the region studied [13,14], and research on the influence of THC content on adverse outcomes is very limited. One of the main challenges for conducting such research has been the multiplicity of issues that influence the dose of THC a user is exposed to, e.g. the ability to titrate the dose of an inhaled product. A standard dose will not, by itself, be able to address all of the various complexities noted, but it will move us towards greater precision in our measures.

Although cannabis remains an illicit substance in the United States, the expanded legalization by states requires us to develop the knowledge base that can help states develop policies to minimize risk from cannabis exposures, such as limits on the THC content of cannabis products.

Regarding what a standard THC dose should be, Freeman & Lorenzetti propose a unit dose of 5 mg THC for all cannabis products and methods of administration. Their rationale is that this dose has psychoactive effects regardless of route of administration, but is mostly devoid of adverse effects. This is a reasonable justification based on our current knowledge, although future research will help to determine its usefulness and whether there is a need to further refine the measure. Further research will also be necessary to develop a concomitant standard dose for CBD. Despite the multiple caveats and complexities, the use of a standard unit dose of THC in research is an important step for improving our ability to understand the effects of cannabis in the population.

Declaration of interests

None.

Keywords Brain development, cannabidiol, cannabis use disorders, marijuana, psychotic disorders, tetrahydrocannabinol.

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STANDARD TETRAHYDROCANNABINOL UNITS: AN IDEA WHOSE TIME HAS COME

The increasing diversity of cannabis products represents a challenge for measuring and reporting potency. Freeman & Lorenzetti's proposal for a standard tetrahydrocannabinol (THC) unit has considerable potential as a tool for reporting potency with respect to market surveillance and sales data, as well as in research studies. Although no standard unit can fully capture the qualitative differences across modes of administration, a 5-mg THC unit represents an appropriate threshold for communicating the potency of cannabis products.

This commentary discusses a proposal from Freeman & Lorenzetti on the use of standard units of tetrahydrocannabinol (THC) for cannabis products [1]. With the advent of legal cannabis markets, regulatory authorities and the industry have a shared responsibility to ensure that consumers have adequate information regarding the potency and appropriate dose of products [2]. Effective consumer guidance is particularly important, given the proliferation of cannabis products and the wide range of tetrahydrocannabinol (THC) levels, which range from less than 1% to more than 90% [3]. Within this context, there is a need to standardize how cannabis potency is reported.

Freeman & Lorenzetti propose a 'standard THC unit' of 5 mg of THC for all cannabis products. The authors point to the use of standard alcohol units as a framework; however, the nicotine market provides a more appropriate reference point given the diverse modes of administration for both cannabis and nicotine products, which include transdermal, oral ingestion, vaporized aerosol and smoke inhalation. A key question raised by Freeman & Lorenzetti is whether a 5-mg THC unit has the same meaning among these modes of administration, given inherently different pharmacological effects. Ultimately, there may be no way of reconciling these differences within a standard quantitative unit: modes of cannabis use differ not only with respect to the onset and duration of 'peak' THC effects, but also in the qualitative effects of THC. Nevertheless, even an imperfect standard unit would represent a considerable improvement on the *status quo*, in which consumers typically depend upon word of mouth and references to cannabis 'strains', which are unreliable indicators of cannabis potency [4,5].

HOW WOULD STANDARD THC UNITS BE USED IN PRACTICE?

Standard THC units have the potential to serve as a common metric for reporting market-based data among different product categories, such as sales volumes and prices paid per unit. Standard THC units could also be integrated into product labelling as a consumer information tool. Currently, few consumers understand the THC numbers that serve as the basis of potency labelling in legal cannabis markets, in part because THC numbers are communicated using different units among different products, including dried herb, oils and edibles [1]. Although these practices are technically sound, consumers have little idea of how to interpret and apply these numbers to guide consumption levels. Alternatively, regulators could label the number of standard THC units in a particular product, such as a joint, edible or unit of oil, which is likely to be more intuitive for consumers [6]. Standard units could also enhance the way cannabis consumption is reported in epidemiological and clinical studies, most of which rely upon crude measures of frequency of use,