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The need to calibrate standardized cannabis measurements across cultures

The iCann Toolkit is an important step towards standardized measurement of cannabis consumption in both clinical and research settings. However, there are still significant challenges caused by regional differences in cannabis potency and cultural differences in methods of administration that will need to be addressed.

Lorenzetti *et al.* [1] proposed the International Cannabis (iCann) Toolkit as a framework for international minimum standards for the measurement of cannabis use across multiple contexts based on agreement from international cannabis researchers. This is a crucial step forward to standardized measurements of cannabis consumption and has the potential to vastly improve comparability of evidence for the effects of cannabis consumption across contexts. As Lorenzetti *et al.* [1] point out, differences in legislation, cultural customs, cannabis products and patterns of consumption make the measurement of cannabis use particularly challenging. In a cannabis research setting, the proposed mid- and top layer measures are the most appropriate for quantifying cannabis use. However, challenges still lie ahead in how to integrate measurements across testing sites that often have distinct cannabis cultures.

The proposed top layer biological measures include quantifying cannabis consumption or abstinence through analysis of tetrahydrocannabinol (THC) and metabolites in urine and blood plasma. Although this will constitute a gold standard for cannabis use quantification, the related cost, practical and even legislative issues limit the feasibility of using these measures, highlighting the importance of harmonizing mid-layer assessments such as the Timeline Followback (TLFB). However, as Lorenzetti *et al.* [1] acknowledge, cross-cultural differences in potency, unit of measurement and method of administration result in extra challenges to consider when using the TLFB method.

The cannabinoid content of cannabis products is known to differ across regions [2] and can diverge substantially from the labelled amounts even in countries with legal dispensation [3]. Hence, patients and research participants may often not have an accurate perception of the potency of the cannabis products they typically use. This poses

significant challenges since the effects of cannabis consumption are known to be dependent on levels of THC (psychoactive), cannabidiol (CBD) (non-psychoactive) and their interaction (e.g. [4]). Although the TLFB is a relatively accurate and reliable self-report measure of cannabis exposure [5], it faces significant challenges in terms of detailed assessment of exposure to the main compounds in cannabis. This is particularly the case in cross-cultural cannabis research, in which regional differences in the typical THC:CBD ratio of cannabis products are common [2,6]. Moving towards a standard unit of THC can help in the effort to improve comparability of measurements and findings across studies from different regions. The proposed calculation of standard THC units in the mid-layer of the iCann Toolkit recommends the usage of visual aids to help participants estimate the type and quantity of product they use to calculate a proxy of potency. It is a priority to test whether these standard units will accurately reflect THC and metabolite exposure as measured via biological quantification, and furthermore, whether regional differences in the validity and reliability of standard THC units will emerge. Studies that calibrate top- and mid-level assessments of potency across regions should be of high priority since they can inform researchers with limited or no access to top-level measures.

Methods of administration differ substantially between individuals [7] as well as across countries and regions (e.g. [8]). These differences affect intoxication duration and sub-acute effects due to differences in bioavailability [9]. Thereby, it can differentially affect major research outcomes such as cognitive performance [10] and even affect cue-reactivity, a proposed mechanisms of heavy and dependent use [11]. As Lorenzetti *et al.* [1] point out a specific example of this is the combination of cannabis and tobacco. Extending the iCann toolkit, we strongly recommend the standard administration of the TLFB for tobacco to measure tobacco and cannabis co-use (e.g. blunts) as well as separate tobacco use (i.e. vaping, cigarettes).

The iCann Toolkit constitutes a valuable step forward. When possible, top-layer biological quantification should be used to provide insight into regional differences in cannabis content, as well as untangle the effects of potency on the effects of cannabis. Researchers that have the means to use biological quantification should collectively invest in validating and calibrating biological quantification relative to self-reports. Furthermore, cultural differences in methods of

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administration, including co-use of tobacco, should be systematically considered herein. Eventually, this will hopefully lead to high-quality accessible measures for the wider scientific community.

DECLARATION OF INTERESTS

None.

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AUTHOR CONTRIBUTIONS

Lauren Kuhns: Conceptualization; writing - original draft; writing - review & editing. **Emese Kroon:** Conceptualization; writing - original draft; writing - review & editing.

KEYWORDS

Cannabis research, cultural differences, measurement, method of administration, potency, standardization

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