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Knowledge of Cannabinoid Content Among People Living With HIV Who Use Cannabis: A Daily Diary Study

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Abstract

Background: Many people living with HIV (PLWH) use cannabis for medicinal reasons. Patients' knowledge of the tetrahydrocannabinol (THC) and cannabidiol (CBD) concentrations of the cannabis products they use may be important in helping patients achieve symptom relief while guarding against potential risks of cannabis use. However, no studies have examined cannabinoid concentration knowledge among PLWH. **Methods:** PLWH (*N*=29; 76% men, mean age 47 years) reporting cannabis use for both medicinal and nonmedicinal reasons completed daily surveys over 14 days assessing cannabis products used, knowledge of cannabinoid concentrations of cannabis products used, cannabis use motives (medicinal, nonmedicinal, both), and positive and negative cannabis-related consequences. Across the 361 cannabis use days captured on the daily surveys, at least some knowledge of cannabinoid concentrations was reported on an average of 43.1% (for THC) and 26.6% (for CBD) of the days. **Results:** Generalized linear mixed models revealed that participants were more likely to report knowing THC and CBD concentrations on days when they used non-flower forms of cannabis relative to days when they used cannabis flower only. Participants who used cannabis for medicinal reasons on a greater proportion of days had greater knowledge of cannabinoid concentration overall across days. Further, greater overall knowledge of cannabinoid concentrations was associated with fewer reported negative cannabis-related consequences. **Conclusions:** Findings suggest that PLWH's knowledge of cannabinoid concentrations may be higher when using non-flower cannabis products and higher among those reporting primarily medicinal cannabis use. Moreover, knowledge of cannabinoid concentration may protect against negative cannabis-related consequences in this population.

Keywords: Marijuana; medical cannabis; delta-9 tetrahydrocannabinol; cannabidiol; AIDS; ecological momentary assessment

Introduction

Cannabis is widely used among people living with HIV (PLWH), with an estimated 34–39% reporting current cannabis use [1–3]. Many PLWH who use cannabis do so for medicinal reasons [2,4–7], describing the use of cannabis to prevent or alleviate physical or mental health symptoms. Observational studies examining the relative benefits and risks of cannabis use among PLWH and the perceived effectiveness of cannabis in managing HIV-related symptoms have yielded mixed results [8–10]. These mixed results may be in part attributable to the heterogeneity in the cannabis products used by PLWH for symptom management. That is, as many individuals who use cannabis for medicinal reasons obtain their cannabis from non-medical sources [11], a wide range of cannabis products of varying potencies may be used medicinally, especially in jurisdictions where cannabis is legal for nonmedical use and these products are thus readily available to those who can afford them. Indeed, concentrations of delta-9-tetrahydrocannibinol (THC) and cannabidiol (CBD)—two principal active cannabinoids in most cannabis products—vary widely both within and between cannabis product categories [12–14]. As products with high THC concentrations or high ratios of THC to CBD concentrations may be riskier if used in large quantities [15], PLWH's knowledge of cannabinoid concentrations of the products they use may be important in helping them to achieve the desired effects while also guarding against risks of cannabis use. For example, this knowledge may facilitate the selection of products and titration of doses to optimize symptom relief and avoidance of negative physical or psychological consequences [16].

Few studies to date have examined consumer knowledge of cannabinoid concentrations across various cannabis products, and none have focused on PLWH. Studies of people who use cannabis from the general adult population have found that only 6–33% of participants report

knowledge of cannabinoid concentrations for the cannabis they use, with even fewer participants providing plausible estimates of these concentrations [13,17]. Similarly, many people use guesswork or rely exclusively on knowledge of THC (but not CBD) concentrations when titrating cannabis dosages [18,19], and the majority do not know effective and safe THC and CBD dosages [20]. These studies suggest concerningly low knowledge of cannabinoid concentrations of cannabis products used by adults from the general population; however, whether this generalizes to PLWH remains unknown. PLWH may represent a unique subset of people who use cannabis given that they often endorse medicinal motives for use, which in at least one study were associated with greater likelihood of reporting valid cannabinoid concentrations [17]. PLWH who use cannabis for medicinal reasons also more frequently use smokeless cannabis products such as oils, sprays, and capsules [6,7], which, given variability in labelling practices across different cannabis products [16], may contribute to different levels of cannabinoid concentration knowledge.

An important limitation in the extant literature on consumer cannabinoid content knowledge is the exclusive use of cross-sectional surveys. Such surveys require participants to recall cannabinoid concentrations of cannabis products used retrospectively, which may engender biased estimates. Consequently, whether consumer knowledge of cannabinoid concentrations is truly low or is rather an artifact of recall biases remains unknown. Daily diary methods, which are often used to track symptoms or medication adherence among patients [21], may be useful for ascertaining consumer knowledge of cannabinoid concentrations by assessing cannabis use at frequent (e.g., daily) intervals, reducing retrospection periods and associated biases. Similarly, daily diary methods may allow for the examination of proximal predictors of cannabinoid concentration knowledge, such as day-level variation in cannabis products used and

motives for cannabis use (i.e., medicinal versus nonmedicinal).

Daily diary studies are also uniquely positioned to capture acute (e.g., day-level) consequences of cannabis use, facilitating examination of whether knowledge of cannabinoid concentrations is linked to lower likelihood of experiencing negative cannabis-related consequences—a notion that, though assumed, has yet to be empirically tested. Cannabis use has been linked to a range of acute negative consequences, such as social and interpersonal problems (e.g., interpersonal conflict), academic/occupational problems (e.g., neglecting obligations to work or school), impaired control (e.g., difficulty limiting cannabis consumption), negative self-perception (e.g., feeling bad about oneself because of cannabis use), risk-taking (e.g., driving a vehicle while high), and adverse physical and psychological symptoms (e.g., nausea, impaired concentration) [22]. Among PLWH, cannabis use may also be associated with antiretroviral therapy non-adherence [23]. It conceivable that when PLWH know the cannabinoid concentrations of their cannabis, they may be better equipped to select lower-risk (i.e., lower-THC [15]) cannabis products and to avoid levels of intoxication that may increase risk for these acute negative consequences. Thus, an examination of day-level associations of cannabinoid concentration knowledge with negative cannabis-related consequences is needed.

The current study used daily diary data to characterize knowledge of the cannabinoid concentrations of various cannabis products used among PLWH. We hypothesized that knowledge of cannabinoid concentrations would be greater for cannabis that is being used for medicinal (versus nonmedicinal) reasons, and that greater knowledge of cannabinoid concentrations would be associated with reduced likelihood of experiencing negative cannabis-related consequences.

Method

Participants and recruitment

The current study is a secondary analysis of data drawn from an electronic diary study of within-person differences between medicinal and nonmedicinal cannabis use motives among PLWH [24]. Participants ($N = 29$) were PLWH reporting both medicinal and nonmedicinal reasons for cannabis use, recruited from across Canada using social media (Facebook, Instagram) ads and flyers distributed to community agencies that serve PLWH. Inclusion criteria for the parent study were: (i) ages 19 years or older; (ii) diagnosed with HIV at least one year ago; (iii) on antiretroviral treatment; (iv) daily or near-daily cannabis use; (v) cannabis use for both medicinal and nonmedicinal reasons; and (vi) access to a compatible smartphone (Android or iOS). Exclusion criteria were: (i) heavy episodic drinking three or more times per week; (ii) current attempts to reduce cannabis use; (iii) use of substances other than cannabis, alcohol, or nicotine two or more times per week; (iv) history of substance use disorder treatment; (v) diagnosis of a severe mental illness; (vi) physical illness that would interfere with participation; or (vii) current pregnancy or nursing. Sample characteristics are provided in Table 1. See [citation removed for masking] for further details about the study sample.

Procedure and measures

Detailed study procedures are described elsewhere [citation removed for masking]. All study procedures took place between December of 2020 and July of 2021. Briefly, eligible participants were invited to attend a one-on-one baseline visit (via secure videoconferencing platform), during which participants provided informed consent and received an orientation to the electronic diary mobile application (MetricWire, Inc., Waterloo, ON) and study protocol. At the end of the baseline visit, participants completed an online questionnaire, which included

demographic items; the *Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory* (DFAQ-CU) [25], used to characterize cannabis use patterns (frequency of use, grams of cannabis flower used per day); and the *Cannabis Use Disorder Identification Test – Revised* (CUDIT-R) [26], used to assess hazardous cannabis use. Participants also reported whether they had current or lifetime medical cannabis authorization from a health care provider, the typical sources from which they obtained cannabis (regardless of whether it was medicinal or nonmedicinal) in the past 6 months, and the symptoms they used cannabis to treat in the past six months (e.g., anxiety, pain, appetite loss).

Participants then completed a 14-day electronic diary protocol to track their cannabis use, involving event-contingent, randomly-timed, and daily surveys. Knowledge of THC and CBD concentrations of cannabis used was assessed only in daily surveys, and thus only these surveys are included in analyses and subsequently described. Participants were asked to complete a two-to-five-minute daily survey immediately upon waking, which was available in the mobile app from 6:00 AM until 1:00 PM each day, with several reminder notifications sent leading up to the survey expiry time. In each survey, participants reported whether they had used cannabis during the previous day and, if so, the products they used (cannabis flower, concentrates, vape cartridges, edibles, oils/sprays, beverages, capsules/tablets) and reasons for use (medicinal, nonmedicinal, or both). Participants reporting previous-day cannabis use were also asked whether they knew all, some, or none of the THC and CBD concentrations for each cannabis product used and, if so, the maximum THC and CBD concentrations of each product (in % for cannabis flower, concentrates, and vape cartridges; and mg per unit for edibles, oils/sprays, beverages, and capsules/tablets). Participants were trained in how to report THC and CBD concentrations during their orientation, including instructions to report only the amount being

consumed. They were also asked to report only on cannabis products obtained from regulated sources; unregulated products, by definition, were assumed to be of unknown cannabinoid concentrations. Finally, participants were asked if they experienced any negative consequences (e.g., neglected obligations, took foolish risks, found it difficult to concentrate, felt sick to stomach) or positive consequences (e.g., had a creative experience, had a positive social connection, slept better than normal, experienced a sense of wellness) since the time they began using cannabis during the previous day, using selected items adapted from the Marijuana Consequences Questionnaire [22] as well as items generated for the current study in consultation with our community member co-authors (SM, EM). Participants were compensated with a $40 CAD gift card for the baseline interview and received between $40 CAD and $70 CAD in gift cards for completion of the diary protocol, depending on the proportion of prompted surveys completed. Informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Data analysis

To characterize cannabinoid concentration knowledge, we first calculated the weighted proportions of days during which THC and CBD concentrations were fully or partially known, both aggregated across all cannabis products used in a given day and stratified by cannabis product. Next, we calculated weighted means, standard deviations, and ranges for maximum THC and CBD concentrations reported, stratified by cannabis product, and the proportion of THC and CBD concentrations reported that were implausible. Plausible concentrations were those within the range of cannabinoid concentrations of cannabis products available for purchase

through the Ontario Cannabis Store by the end of the first quarter of 2022 (when data collection for the current study finished), as profiled in Tassone et al., 2023 [14]. We also obtained unweighted descriptive statistics (means, standard deviations, intraclass correlation coefficients) for the person-level proportions of days during which THC and CBD concentrations were each known, aggregated across all cannabis products used in a given day due to infrequent endorsement of several product categories.

To examine associations of cannabis products used and cannabis use motives with cannabinoid concentration knowledge, generalized linear mixed models were specified with days (level 1) nested within participants (level 2). Knowing cannabinoid concentrations for any cannabis used in a given day (1 = yes, 0 = no) was specified as the dependent variable and modelled using a binomial distribution, with separate models for knowledge of THC and CBD. In one set of models, cannabis product(s) used in a given day (1 = any non-flower cannabis products, 0 = exclusively cannabis flower products)[1] was specified as an independent variable at the day level (level 1), and the percentage of days during which non-flower cannabis products were used was specified as an independent variable at the person level (level 2) to examine between-person differences in propensity to use non-flower products across days [27,28]. In another set of models, cannabis use motives (1 = medicinal, 0 = exclusively nonmedicinal)[2] were specified as an independent variable at level 1, and the percentage of days during which medicinal motives for cannabis use were endorsed was specified as an independent variable at level 2 (to examine between-person differences). We also included sex assigned at birth (1 = male, 0 = female) and age as level 2 covariates in all models.

[1] Vape cartridges, edibles/beverages, concentrates, oils, capsules/tablets, and other unspecified cannabis products were merged into a single non-flower cannabis product category due to low frequencies in original product categories.
[2] Medicinal and mixed (i.e., both medicinal and nonmedicinal) cannabis use motives were combined due to few exclusively medicinal days (39, 10.80%).

Generalized linear mixed models were also used to examine associations of cannabinoid concentration knowledge with cannabis-related consequences reported the next day. Given low frequency of endorsement of most cannabis consequences at the daily level, models were specified to predict the likelihood of reporting at least one cannabis-related consequence on a given day (level 1), with separate models for positive and negative consequences. Knowing cannabinoid concentrations for any cannabis used (1 = yes, 0 = no) was specified as an independent variable at level 1, and the percentage of days during which any cannabinoid concentrations were known was specified as an independent variable at level 2. Separate models were estimated for knowledge of THC and CBD concentrations. We also included cannabis use motive (1 = medicinal, 0 = exclusively nonmedicinal) and use of non-flower cannabis (1 = yes, 0 = no) as covariates at both levels 1 and 2 of the models, and sex and age as level 2 covariates.

In each model, all level 1 independent variables and covariates were person-mean centered and all level 2 independent variables and covariates were grand-mean centered; this was done to fully disaggregate within- and between-person variance [27,28]. Models were specified with random intercepts and fixed slopes and were fit using maximum likelihood estimation. Analyses were conducted in R and RStudio using the lme4 package [29]. Analysis code is publicly available at https://osf.io/nmvzq/.

Results

Across all participants and all days, a total of 380 daily surveys were completed (93.60% completion rate), of which 361[3] (95.00%) involved reports of previous-day cannabis use and were included in analyses. On average, each participant contributed 12.45 (SD = 2.34) daily surveys involving previous-day cannabis use. The use of non-flower cannabis products was

[3] One daily survey in which previous-day cannabis use was reported was excluded as data were missing for all cannabis-related variables.

reported on 149 (41.27%) cannabis use days, and motives for cannabis use were reported as medicinal-only on 39 days (10.80%), nonmedicinal-only on 87 days (24.10%), and mixed medicinal and nonmedicinal on 235 days (65.10%).

Cannabinoid concentration knowledge

Across all cannabis use days, participants reported knowing all THC concentrations of cannabis used on 113 (31.30%) cannabis use days, some THC concentrations on 49 (13.57%) cannabis use days, and no THC concentrations on 199 (55.12%) cannabis use days. Participants reported knowing all CBD concentrations of cannabis used on 86 (23.82%) cannabis use days, some CBD concentrations on 13 (3.60%) cannabis use days, and no CBD concentrations on 262 (72.58%) cannabis use days. Knowledge of THC and CBD concentrations across different cannabis products is summarized in Table 2. At least some knowledge of THC was reported in more than 80% of observations for oils/sprays, beverages, and capsules/tablets; in 48.72% of observations for edibles; in 33.96% of observations for cannabis flower; and in less than 20% of observations for concentrates and vape cartridges. At least some knowledge of CBD was reported in more than 80% of observations for oils/sprays, beverages, and capsules/tablets, and in less than 20% of observations for cannabis flower, concentrates, vape cartridges, and edibles. Maximum self-reported THC and CBD concentrations and proportions of reported concentrations deemed implausible are also provided in Table 2. Implausible self-reported THC concentrations were observed only for cannabis flower (5.49% of reported concentrations), edibles (89.47% of reported concentrations), oils/sprays (73.33% of reported concentrations), and capsules/tablets (12.50% of reported concentrations), and implausible self-reported CBD concentrations were observed only for cannabis flower (33.33% of reported concentrations), vape cartridges (25.00% of reported concentrations), and oils/sprays (4.44% of reported

concentrations).

With respect to overall knowledge at the person level, the average participant reported knowing any THC and CBD concentrations during a respective 43.08% (*SD* = 43.97) and 26.63% (*SD* = 39.86) of their cannabis use days, and reported knowing all THC and CBD concentrations during a respective 30.46% (*SD* = 42.55) and 23.06% (*SD* = 38.59) of their cannabis use days. The intraclass correlation coefficients for knowing THC concentrations were 0.75 (for any cannabis used) and 0.82 (for all cannabis used), and for knowing CBD concentrations were 0.79 (for any cannabis used) and 0.81 (for all cannabis used), indicating that 75–82% of the variance in cannabinoid concentration knowledge was attributable to between-person differences rather than within-person differences across days.

Motive, product, and consequence associations with cannabinoid concentration knowledge

Table 3 provides results of generalized linear mixed models examining associations of cannabis products used with cannabinoid concentration knowledge. At the within-person level, participants were more likely to report knowing the THC and CBD concentrations of their cannabis on days when they used any non-flower cannabis product relative to days when they used cannabis flower only. At the between-person level, participants with a greater percentage of days involving non-flower cannabis use reported greater knowledge of THC and CBD concentrations overall across days.

Table 4 provides results of generalized linear mixed models examining associations of cannabis use motives with cannabinoid concentration knowledge. Although there were no differences in cannabis knowledge as a function of within-person differences in medicinal versus nonmedicinal motives across different days, participants who used cannabis for medicinal (versus nonmedicinal) reasons on a greater percentage of days reported knowledge of THC and

CBD concentrations more often overall (aggregated across days).

Table 5 provides results of generalized linear mixed models examining associations of cannabinoid concentration knowledge with cannabis-related consequences. Participants who knew the THC and CBD concentrations of their cannabis on a greater percentage of days were less likely to experience negative cannabis-related consequences overall across days. The within-person (i.e., day-level) associations of cannabinoid concentration knowledge with negative cannabis-related consequences and both the within- and between-person associations of cannabinoid concentration knowledge with positive cannabis-related consequences were not statistically significant in any model.

Discussion

With increasing diversity in the cannabis products available on the legal market for both medicinal and nonmedicinal use, it is important to understand PLWH's knowledge of the cannabinoid concentrations of the cannabis they are using to inform clinical guidance. The current study is the first to use daily diary methods to characterize knowledge of cannabinoid concentrations of cannabis used among PLWH—a population with high rates of both medicinal and nonmedicinal cannabis use [6,7]. On average, PLWH in our study reported knowing the THC and CBD concentrations of at least some of the cannabis they used on 43% and 27% of cannabis use days, respectively. Between 11% and 100% of reported THC and CBD concentrations were within plausible ranges, depending on specific cannabis products used. The rates of knowledge we observed are slightly higher than those observed in previous cross-sectional studies of non-patient samples from both legal and non-legal jurisdictions (approximately 6–33%) [13,17], perhaps because PLWH may be more attuned to the health effects of cannabis (and thus attend more to cannabinoid concentrations) relative to individuals

without chronic diseases. Still, results indicate that PLWH may not know the cannabinoid concentrations of the cannabis they are using a majority of the time. Our use of a prospective daily diary design suggests that these low rates of cannabinoid concentration knowledge are likely not merely an artifact of recall biases engendered by retrospective survey designs used in prior studies.

Importantly, our daily diary design extends previous research by permitting an examination of *within-person* differences in knowledge of cannabinoid concentrations across different cannabis products. This is important, as PLWH tend to use multiple forms of cannabis [4,6]. We found that cannabinoid concentration knowledge was greater on days involving the use of non-flower cannabis products (e.g., concentrates, edibles, vape cartridges, oils) relative to days when only cannabis flower was used. Further, participants reporting use of non-flower cannabis products on a greater percentage of days reported greater knowledge of cannabinoid concentrations overall across days. The association of non-flower cannabis use with increased cannabinoid concentration knowledge may reflect greater attention to THC and CBD content when using non-flower cannabis products. With respect to THC, certain non-flower cannabis products such as concentrates and vape cartridges are generally more potent than cannabis flower [30], and thus it is possible that PLWH may attend more carefully to potency and dosing information when using these products to avoid undesired levels of intoxication or to maximize strength of symptom relief. Conversely, products such as cannabis oils, capsules, and tablets are often higher in CBD and lower in THC relative to cannabis flower [30]. As CBD is generally perceived to have greater medicinal properties [31–33], individuals may attend more closely to CBD concentrations of these products to inform use for symptom prevention or reduction. These explanations, however, remain speculative, and future research is needed to better understand the

observed differences in cannabinoid concentration knowledge across cannabis products.

Knowledge of cannabinoid concentrations was also overall more likely among PLWH reporting a greater percentage of medicinal (relative to exclusively nonmedicinal) cannabis use days. This finding is consistent with prior research showing that people who use cannabis for medicinal reasons are better able to report valid cannabinoid concentrations of their cannabis [17,20]. We extend results of previous studies through the dimensional examination of medicinal cannabis use motives (i.e., percentage of days involving medicinal motives) rather than comparing medicinal to nonmedicinal users; the latter imposes a false dichotomy given that the majority of PLWH who use cannabis for medicinal reasons also use for nonmedicinal reasons [6,7,23]. Importantly, we found that among our sample of PLWH reporting both medicinal and nonmedicinal reasons for cannabis use, there was an exposure-response relationship wherein greater overall endorsement of medicinal motives was associated with increased likelihood of knowing cannabinoid concentrations. Interestingly, this association was observed only at the between-person level, suggesting that patient characteristics, rather than cannabis use event-level characteristics, link medicinal cannabis use motives to cannabinoid concentration knowledge. It is possible that PLWH who use cannabis primarily for medicinal reasons may attend more to the cannabinoid content of their cannabis products overall (even when using cannabis for nonmedicinal reasons) because they are generally more conscious of cannabis-related health benefits and risks and are motivated to avoid levels of consumption that may exacerbate existing health conditions or symptoms. Future research is needed to clarify the mechanisms by which medicinal cannabis use motives are linked with increased knowledge of cannabinoid concentrations.

Importantly, the current study found that, after controlling for cannabis products used (non-

flower cannabis products versus cannabis flower products), participants who reported knowing the cannabinoid concentrations of their cannabis products on a greater percentage of days were overall less likely to report negative cannabis-related consequences. These findings provide important new empirical support for the protective role of cannabinoid concentration knowledge among PLWH. One potential explanation for this protective effect is that greater knowledge of cannabinoid concentration may assist in titrating cannabinoid doses to maximize symptom relief while still minimizing adverse effects [16]. As cannabis consumption, alone, explains only some of the variance in negative cannabis-related consequences [34], it is also possible that PLWH who seek information about the cannabinoid content of their cannabis products may employ more protective behavioural strategies, overall, contributing to experiencing fewer negative consequences. Given the range of potential negative consequences associated with cannabis use [22] and widespread use of cannabis among PLWH [1–3], there is a need for public health interventions aimed at reducing cannabis-related harms in this population. In highlighting cannabinoid concentration knowledge as potentially protective in guarding against adverse consequences of cannabis use, our findings suggest that future research should evaluate interventions aimed at increasing patient awareness of the cannabinoid concentrations of the cannabis products they are using. These may include improved cannabis product labelling practices and patient and public education initiatives [16].

The results of this study should be considered in the context of several limitations. First, as the goal of the parent study from which data were drawn was to examine within-person differences in medicinal and nonmedicinal cannabis use motives, between-person analyses may have been underpowered. Future replication of findings in larger samples is therefore needed, and the non-significance of associations at the between-person level should not be interpreted as

evidence for an absence of between-person effects. Despite our small sample, however, participants generated more than 300 day-level surveys, providing ample power for within-person analyses. Second, participants were asked only to report their knowledge of cannabinoid concentrations for cannabis products obtained from regulated sources. Although it is reasonable to assume that cannabis products from unregulated sources were of unknown cannabinoid concentrations, this approach may have biased estimates of cannabinoid concentration knowledge in our sample to the extent that some participants had knowledge of cannabinoid concentrations of unregulated cannabis. Third, we did not assess current medical guidance participants were receiving about their cannabis use, which may have contributed to differences in knowledge of cannabinoid concentrations. Fourth, repeated assessment of cannabinoid concentration knowledge may have encouraged participants to seek out this information for subsequent surveys, potentially overestimating participants' knowledge. Fifth, our observational study was not able to establish causal associations with respect to predictors and outcomes of cannabinoid concentration knowledge. An additional limitation is that our sample may not be fully representative of the broader population of PLWH who use cannabis due to eligibility criteria that were specific to the parent study, such as daily or near-daily cannabis use for both medicinal and nonmedicinal reasons. The generalizability of our findings may also be reduced by the limited demographic diversity in our sample (i.e., most participants identified as men, White, and gay). Further, results may have limited generalizability to PLWH outside of Canada, especially to those in jurisdictions in which non-medical cannabis is not fully legal.

In summary, this study found that PLWH reported greater knowledge of cannabinoid concentration on days when they used non-flower cannabis products relative to flower products only, and a greater propensity for medicinally-motivated cannabis use was associated with more

frequently reporting knowledge of THC and CBD concentration overall. Moreover, knowing cannabinoid concentrations of cannabis products appears to protect against negative cannabis-related consequences among PLWH. Findings suggest a need to increase cannabinoid concentration knowledge among PLWH who use cannabis and support the role of cannabis education in improving help outcomes, which may help PLWH who use cannabis for symptom relief to avoid potential risk for cannabis harms.

Statements Page

Informed consent: Informed consent was obtained from all individual participants included in the study.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research ethics committee and with the relevant tenants of the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

References

1. Harris GE, Dupuis L, Mugford GJ, et al. Patterns and correlates of cannabis use among individuals with HIV/AIDS in Maritime Canada. *Can J Infect Dis Med Microbiol*. 2014;25(1):e1-e7.
2. Pacek LR, Towe SL, Hobkirk AL, Nash D, Goodwin RD. Frequency of cannabis use and medical cannabis use among persons living with HIV in the United States: Findings from a nationally representative sample. *AIDS Educ Prev*. 2018;30(2):169-181. doi:10.1521/aeap.2018.30.2.169
3. Shiau S, Arpadi SM, Yin MT, Martins SS. Patterns of drug use and HIV infection among adults in a nationally representative sample. *Addict Behav*. 2017;68:39-44. doi:10.1016/j.addbeh.2017.01.015
4. Costiniuk CT, Saneei Z, Salahuddin S, et al. Cannabis consumption in people living with HIV: Reasons for use, secondary effects, and opportunities for health education. *Cannabis and Cannabinoid Research*. 2019;4(3):204-213. doi:10.1089/can.2018.0068
5. Fogarty A, Rawstorne P, Prestage G, Crawford J, Grierson J, Kippax S. Marijuana as therapy for people living with HIV/AIDS: social and health aspects. *AIDS Care*. 2007;19(2):295-301. doi:10.1080/09540120600841930
6. Furler MD, Einarson TR, Millson M, Walmsley S, Bendayan R. Medicinal and recreational marijuana use by patients infected with HIV. *AIDS Patient Care STDS*. 2004;18(4):215-228. doi:10.1089/108729104323038892
7. Wardell JD, Shuper PA, Hendershot CS. A longitudinal investigation of the association between cannabis use and alcohol use among people living with HIV. *Drug and Alcohol Dependence*. 2018;193:7-13. doi:10.1016/j.drugalcdep.2018.08.026

8. Adams JW, Bryant KJ, Edelman EJ, et al. Association of cannabis, stimulant, and alcohol use with mortality prognosis among HIV-infected men. *AIDS Behav*. 2018;22(4):1341-1351. doi:10.1007/s10461-017-1905-4
9. Lake S, Kerr T, Capler R, Shoveller J, Montaner J, Milloy MJ. High-intensity cannabis use and HIV clinical outcomes among HIV-positive people who use illicit drugs in Vancouver, Canada. *Int J Drug Policy*. 2017;42:63-70. doi:10.1016/j.drugpo.2017.02.009
10. Montgomery L, Bagot K, Brown JL, Haeny AM. The Association between marijuana use and HIV continuum of care outcomes: A systematic review. *Curr HIV/AIDS Rep*. 2019;16(1):17-28. doi:10.1007/s11904-019-00422-z
11. Health Canada. Canadian Cannabis Survey 2021: Summary. Published December 23, 2021. Accessed November 11, 2022. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/canadian-cannabis-survey-2021-summary.html
12. Freeman TP, Lorenzetti V. "Standard THC units": a proposal to standardize dose across all cannabis products and methods of administration. *Addiction*. 2020;115(7):1207-1216. doi:10.1111/add.14842
13. Hammond D, Goodman S. Knowledge of tetrahydrocannabinol and cannabidiol levels among cannabis consumers in the United States and Canada. *Cannabis and Cannabinoid Research*. 2022;7(3):345-354. doi:10.1089/can.2020.0092
14. Tassone F, Di Ciano P, Liu Y, Rueda S. On offer to Ontario consumers three years after legalization: A profile of cannabis products, cannabinoid content, plant type, and prices. *Front Psychiatry.* 2023;14:1111330. doi:10.3389/fpsyc.2023.1111330

15. Fischer B, Russell C, Sabioni P, et al. Lower-risk cannabis use guidelines: A comprehensive update of evidence and recommendations. *Am J Public Health*. 2017;107(8):e1-e12. doi:10.2105/AJPH.2017.303818
16. Hammond D. Communicating THC levels and 'dose' to consumers: Implications for product labelling and packaging of cannabis products in regulated markets. *International Journal of Drug Policy*. 2021;91:102509. doi:10.1016/j.drugpo.2019.07.004
17. Sikorski C, Leos-Toro C, Hammond D. Cannabis consumption, purchasing and sources among young Canadians: The Cannabis Purchase and Consumption Tool (CPCT). *Substance Use & Misuse*. 2021;56(4):449-457. doi:10.1080/10826084.2021.1879142
18. Freeman TP, Morgan CJA, Hindocha C, Schafer G, Das RK, Curran HV. Just say 'know': how do cannabinoid concentrations influence users' estimates of cannabis potency and the amount they roll in joints? *Addiction*. 2014;109(10):1686-1694. doi:10.1111/add.12634
19. Wheeler M, Merten JW, Gordon BT, Hamadi H. CBD (Cannabidiol) Product attitudes, knowledge, and use among young adults. *Substance Use & Misuse*. 2020;55(7):1138-1145. doi:10.1080/10826084.2020.1729201
20. Kruger DJ, Kruger JS, Collins RL. Frequent cannabis users demonstrate low knowledge of cannabinoid content and dosages. *Drugs: Education, Prevention and Policy*. 2021;28(1):97-103. doi:10.1080/09687637.2020.1752150
21. Riekert KA, Rand CS. Electronic monitoring of medication adherence: When is high-tech best? *Journal of Clinical Psychology in Medical Settings*. 2002;9(1):25-34. doi:10.1023/A:1014131928789

22. Simons JS, Dvorak RD, Merrill JE, Read JP. Dimensions and severity of marijuana consequences: development and validation of the Marijuana Consequences Questionnaire (MACQ). *Addict Behav*. 2012;37(5):613-621. doi:10.1016/j.addbeh.2012.01.008

23. Mannes ZL, Burrell LE, Ferguson EG, et al. The association of therapeutic versus recreational marijuana use and antiretroviral adherence among adults living with HIV in Florida. *Patient Prefer Adherence*. 2018;12:1363-1372. doi:10.2147/PPA.S167826

24. Wardell JD, Rueda S, Fox N, et al. Disentangling medicinal and recreational cannabis use among people living with HIV: An ecological momentary assessment study. *AIDS Behav*. 2023;27(4):1350-1363. doi:10.1007/s10461-022-03871-7

25. Cuttler C, Spradlin A. Measuring cannabis consumption: Psychometric properties of the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU). *PLoS One*. 2017;12(5):e0178194. doi:10.1371/journal.pone.0178194

26. Adamson SJ, Kay-Lambkin FJ, Baker AL, et al. An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R). *Drug Alcohol Depend*. 2010;110(1-2):137-143. doi:10.1016/j.drugalcdep.2010.02.017

27. Yaremych HE, Preacher KJ, Hedeker D. Centering categorical predictors in multilevel models: Best practices and interpretation. *Psychological Methods*. Advance online publication. doi:10.1037/met0000434

28. Enders CK, Tofighi D. Centering predictor variables in cross-sectional multilevel models: a new look at an old issue. Psychological methods. 2007;12(2):121. doi:10.1037/1082-989X.12.2.121

29. Bates D, Mächler M, Bolker B, Walker S. Fitting linear mixed-effects models using lme4. *Journal of Statistical Software*. 2015;67(1):1-48. doi:10.18637/jss.v067.i01

30. Government of Canada. About cannabis. Health Canada. Published 2022. Accessed February 10, 2023. https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/about.html
31. Spanagel R, Bilbao A. Approved cannabinoids for medical purposes – Comparative systematic review and meta-analysis for sleep and appetite. *Neuropharmacology*. 2021;196:108680. doi:10.1016/j.neuropharm.2021.108680
32. Tran T, Kavuluru R. Social media surveillance for perceived therapeutic effects of cannabidiol (CBD) products. *International Journal of Drug Policy*. 2020;77:102688. doi:10.1016/j.drugpo.2020.102688
33. Hurd YL. Leading the next CBD wave—safety and efficacy. *JAMA Psychiatry*. 2020;77(4):341-342. doi:10.1001/jamapsychiatry.2019.4157
34. Pearson MR. A meta-analytic investigation of the associations between cannabis use and cannabis-related negative consequences. Psychology of Addictive Behaviors. 2019;33(3):190. doi:10.1037/adb0000452

Table 1. Sample characteristics

	M (SD) or *n* (%)
Age	46.69 (10.77)
Sex	
Male	23 (79.31)
Female	6 (20.69)
Gender	
Man	22 (75.86)
Woman	6 (20.69)
Two-spirit	1 (3.45)
Sexual orientation	
Gay	21 (72.41)
Lesbian	1 (3.45)
Bisexual	2 (6.90)
Heterosexual/straight	4 (13.79)
Other	1 (3.45)
Race/ethnicity[a]	
White	19 (65.52)
Black	2 (6.90)
Asian	1 (3.45)
Hispanic/Latinx	1 (3.45)
East Indian	1 (3.45)
Middle Eastern	1 (3.45)
Mixed Race/Ethnicity	4 (13.79)
Household income[b]	
Below $20,000	6 (21.43)
$20,000-$49,999	9 (32.14)
$50,000-$99,999	9 (32.14)
$100,000 or more	4 (14.29)
Highest level of education[b]	
Less than high school	2 (7.14)
High school diploma or GED	2 (7.14)
Some college	6 (21.43)
Associates degree or technical certificate	6 (21.43)
Bachelors degree	10 (35.71)
Masters degree or higher	2 (7.14)
DFAQ-CU current cannabis use frequency[c]	
2–3 times a month	1 (3.45)
Once a week	0 (0.00)
Twice a week	0 (0.00)
3–4 times a week	2 (6.90)
5–6 times a week	1 (3.45)
Once a day	8 (27.59)
More than once a day	17 (58.62)
DFAQ-CU grams of cannabis flower used in a typical session	0.66 (0.70)
DFAQ-CU grams of cannabis flower used in a typical day	1.24 (1.16)
DFAQ-CU grams of cannabis flower used in a typical week	9.29 (11.59)
Current valid medical authorization for cannabis use (yes)	16 (55.17)
Lifetime valid medical authorization for cannabis use (yes)	18 (65.52)
Obtained cannabis from regulated sources in the past six months	26 (89.55)

Obtained cannabis from unregulated sources in the past six months	28 (96.55)
Symptoms treated using cannabis in the past six months[a]	
Anxiety	20 (68.97)
Pain	17 (58.62)
Stress	19 (65.52)
Insomnia	20 (68.97)
Depression	11 (27.93)
Appetite	17 (58.62)
Headaches	5 (17.24)
Nausea	9 (31.03)
Muscle spasms	5 (17.24)
HIV/AIDS	19 (65.52)
Other	2 (6.90)

[a]Participants could select multiple options and thus may be counted in more than one category; [b]One participant declined to respond; [c]No participants reported using cannabis less than 2–3 times a month, and thus lower frequency categories are not included in the table.

Table 2. Cannabinoid concentration knowledge stratified by product

	Number of observations	Knowledge of cannabinoid concentrations for all cannabis used	Knowledge of cannabinoid concentrations for some cannabis used	Knowledge of cannabinoid concentrations for no cannabis used	Maximum cannabinoid concentration	Reported implausible maximum cannabinoid concentration
		n (%)	*n* (%)	*n* (%)	M (SD), range	*n* (%)
THC						
Cannabis flower[a]	275	51 (19.03)	40 (14.93)	177 (66.04)	23.08% (16.35), 2–89	5 (5.49)
Concentrates	35	1 (2.86)	0 (0.00)	34 (97.14)	25%	0 (0.00)
Vape cartridges	31	5 (16.13)	0 (0.00)	26 (83.87)	54.20% (30.65), 27–88	0 (0.00)
Edibles[b]	40	19 (48.72)	0 (0.00)	20 (51.28)	28.95 mg/unit (13.18), 10–50	17 (89.47)
Oils/Sprays[b]	45	40 (90.01)	2 (4.55)	2 (4.55)	19.95 mg/unit (10.86), 0–30	33 (73.33)
Beverages	1	1 (100.00)	0 (0.00)	0 (0.00)	0.1 mg/unit	0 (0.00)
Capsules/Tablets	16	14 (87.50)	0 (0.00)	2 (12.50)	8.75 mg/unit (3.89), 0–12.5	2 (12.50)
CBD						
Cannabis flower[c]	275	34 (12.78)	8 (3.01)	224 (84.21)	12.16% (15.90), 0–86	14 (33.33)
Concentrates	35	0 (0.00)	1 (2.86)	34 (97.14)	0%	0 (0.00)
Vape cartridges	31	4 (12.90)	0 (0.00)	27 (87.10)	23.55% (46.30), 0.4–93	1 (25.00)
Edibles[d]	40	2 (5.13)	0 (0.00)	37 (94.87)	0 mg/unit (0), 0–0	0 (0.00)
Oils/Sprays[d]	45	40 (90.91)	1 (2.27)	3 (6.82)	5.33 mg/unit (6.28), 0.5–30	2 (4.44)
Beverages	1	1 (100.00)	0 (0.00)	0 (0.00)	0.90 mg/unit	0 (0.00)
Capsules/Tablets	16	14 (87.50)	0 (0.00)	2 (12.50)	15.00 mg/unit (4.39), 5–20	0 (0.00)

Note: SD = standard deviation. SD and range are not reported when only one observation was available. [a]7 observations missing data on knowledge of THC concentrations; [b]1 observation missing data on knowledge of THC concentrations; [c]9 observations missing data on knowledge of CBD concentrations; [d]1 observation missing data on knowledge of CBD concentrations.

Table 3. Associations of non-flower cannabis use with cannabinoid concentration knowledge

	OR	Estimate	SE	*p*
THC				
Used non-flower cannabis	**8.47**	**2.14**	**0.79**	**0.007**
Used non-flower cannabis percentage of days	**1.08**	**0.07**	**0.04**	**0.037**
Sex	**97882.20**	**11.49**	**3.86**	**0.003**
Age	0.86	-0.15	0.12	0.190
CBD				
Used non-flower cannabis	**12.54**	**2.53**	**0.95**	**0.008**
Used non-flower cannabis percentage of days	**1.10**	**0.10**	**0.05**	**0.033**
Sex	**21974.54**	**10.00**	**4.71**	**0.034**
Age	0.83	-0.19	0.14	0.168

Note: OR = odds ratio, SE = standard error, THC = delta-9-tetrahydrocannabinol, CBD = cannabidiol. Bolding indicates statistical significance at al alpha level of 0.05.

Table 4. Associations of cannabis use motives with cannabinoid concentration knowledge

	OR	Estimate	SE	*p*
THC				
Medicinal (vs. exclusively nonmedicinal) cannabis use motives	2.75	1.01	0.65	0.123
Medicinal (vs. exclusively nonmedicinal) cannabis use motives percentage of days	**1.08**	**0.08**	**0.03**	**0.025**
Sex	**14096.62**	**9.55**	**2.96**	**0.001**
Age	0.88	-0.13	0.10	0.197
CBD				
Medicinal (vs. exclusively nonmedicinal) cannabis use motives	1.11	0.10	0.81	0.899
Medicinal (vs. exclusively nonmedicinal) cannabis use motives percentage of days	**1.10**	**0.09**	**0.04**	**0.033**
Sex	**1519.44**	**7.33**	**3.26**	**0.025**
Age	0.85	-0.16	0.13	0.241

Note: OR = odds ratio, SE = standard error, THC = delta-9-tetrahydrocannabinol, CBD = cannabidiol. Bolding indicates statistical significance at al alpha level of 0.05.

Table 5. Associations of cannabinoid concentration knowledge with positive and negative cannabis-related consequences

	Positive consequences				Negative consequences			
	OR	Estimate	SE	*p*	OR	Estimate	SE	*p*
THC								
Knowledge of THC concentrations for any cannabis used	2.28	0.82	0.65	0.205	2.19	0.78	0.72	0.279
Medicinal (vs. exclusively nonmedicinal) cannabis use motives	1.07	0.07	0.57	0.910	1.44	0.36	0.50	0.463
Use of non-flower cannabis	0.32	-1.13	0.59	0.057	0.81	-0.21	0.55	0.701
Knowledge of THC concentrations for any cannabis used percentage of days	0.98	-0.02	0.01	0.081	**0.97**	**-0.03**	**0.01**	**<0.001**
Medicinal (vs. exclusively nonmedicinal) cannabis use motives percentage of days	1.00	<0.01	0.01	0.746	1.00	<0.01	0.01	0.937
Use of non-flower cannabis percentage of days	**0.98**	**-0.02**	**0.01**	**0.011**	0.99	-0.01	0.01	0.092
Sex	2.64	0.97	1.16	0.401	0.37	-0.99	0.85	0.245
Age	1.04	0.04	0.04	0.300	1.01	0.01	0.03	0.606
CBD								
Knowledge of CBD concentrations for any cannabis used	1.72	0.54	0.80	0.496	1.05	0.05	0.92	0.955
Medicinal (vs. exclusively nonmedicinal) cannabis use motives	1.12	0.11	0.58	0.847	1.52	0.42	0.48	0.388
Use of non-flower cannabis	0.35	-1.04	0.58	0.072	0.92	-0.08	0.54	0.879
Knowledge of CBD concentrations for any cannabis used percentage of days	0.98	-0.02	0.01	0.146	**0.97**	**-0.03**	**0.01**	**0.019**
Medicinal (vs. exclusively nonmedicinal) cannabis use motives percentage of days	0.99	-0.01	0.01	0.559	0.99	-0.01	0.01	0.62
Use of non-flower cannabis percentage of days	**0.98**	**-0.02**	**0.01**	**0.016**	0.98	-0.02	0.01	0.133
Sex	1.47	0.39	1.01	0.702	**0.16**	**-1.84**	**0.88**	**0.038**
Age	1.04	0.04	0.04	0.249	1.02	0.02	0.03	0.456

Note: OR = odds ratio, SE = standard error, THC = delta-9-tetrahydrocannabinol, CBD = cannabidiol. Bolding indicates statistical significance at al alpha level of 0.05. As the model examining THC concentration knowledge as a predictor of positive consequences did not converge using the default optimizer, the bobyqa optimizer was used which resolved the convergence error; model results were the same across the two optimizers.