Daily associations between cannabis use and alcohol use among people who use cannabis for both medicinal and nonmedicinal reasons: Substitution or complementarity?

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Abstract

Objective: People who use cannabis for medicinal (versus nonmedicinal) reasons report greater cannabis use and lower alcohol use, which may reflect a cannabis–alcohol substitution effect in this population. However, it is unclear whether cannabis is used as a substitute or complement to alcohol at the day level among people who use cannabis for *both* medicinal and nonmedicinal reasons. This study used ecological momentary assessment (EMA) to examine this question. **Method:** Participants (N = 66; 53.1% men; mean age 33 years) completed daily surveys assessing previous-day reasons for cannabis use (medicinal versus nonmedicinal), cannabis consumption (both number of different types of cannabis used and grams of cannabis flower used), and number of standard drinks consumed. **Results:** Multilevel models revealed that, in general, greater cannabis consumption on a given day was associated with greater same-day alcohol use. Further, days during which cannabis was used for medicinal (versus exclusively nonmedicinal) reasons were associated with reduced consumption of *both* cannabis and alcohol. Finally, the day-level association between medicinal reasons for cannabis use and lower alcohol consumption was mediated by using fewer grams of cannabis on medicinal cannabis use days. **Conclusions:** Day-level cannabis-alcohol associations may be complementary rather than substitutive among people who use cannabis for both medicinal and nonmedicinal reasons, and lower (rather than greater) cannabis consumption on medicinal use days may explain the link between medicinal reasons for cannabis use and reduced alcohol use. Still, these individuals may use greater amounts of both cannabis and alcohol when using cannabis for exclusively nonmedicinal reasons.

Keywords: Alcohol; medical marijuana; co-use; substitution; ecological momentary assessment

Public Health Significance Statement

This study found that among people who use cannabis for both medicinal and nonmedicinal reasons, greater cannabis consumption was associated with greater alcohol consumption at the day level. Further, both cannabis consumption and alcohol consumption were lower on days when cannabis was used (at least in part) for medicinal reasons, and higher on days when cannabis was used for exclusively nonmedicinal reasons. Results suggest that the likelihood of engaging in cannabis-alcohol co-use may be elevated during times when cannabis is used for nonmedicinal reasons among individuals who engage in both medicinal and nonmedicinal cannabis use.

Introduction

Amid a dynamic legal landscape, the prevalence of cannabis use in North America continues to climb (Hasin & Walsh, 2021; Johnston et al., 2021; Reece & Hulse, 2021; Rottermann, 2021). The increasingly widespread use of cannabis is of concern given the potential harms associated with frequent use, such as cannabis use disorder, adverse mental health outcomes, cognitive impairments, reduced academic and social functioning, and impaired driving (Feeney & Kampman, 2016; Subramaniam et al., 2019; Volkow et al., 2014). Further, cannabis harms may be compounded by the concurrent use of other substances, such as alcohol, with which cannabis use frequently co-occurs (Subbaraman & Kerr, 2015). There is evidence that in some contexts, co-use of cannabis and alcohol may be associated with heightened negative outcomes relative to the use of either substance alone, including greater consumption of each substance, increased risk of concurrent mental health problems, and greater likelihood of experiencing negative social and behavioural consequences such as impaired driving (Lee et al., 2020; Mallett et al., 2019; Sokolovsky et al., 2020; Yurasek et al., 2017). There is thus interest in refining our understanding of the cannabis–alcohol relationship.

Substitution and Complementarity of Cannabis and Alcohol

Emerging research on the combined use of cannabis and alcohol has engendered two competing models of the cannabis–alcohol relationship: substitution, describing the use of one substance to replace the effects of the other, and complementarity, describing the use of one substance to enhance the effects of the other (Subbaraman, 2016). Should cannabis act as a substitute for alcohol, increased cannabis use should be associated with reduced alcohol use, whereas complementarity would suggest that increased cannabis use should be associated with increased alcohol use. Both substitution and complementarity in alcohol and cannabis

relationships have been observed in the extant literature (Risso et al., 2020; Subbaraman, 2016). Although policy and economic relationship studies constitute the majority of existing research on substitution and complementarity, select studies have examined correlations of individual differences in cannabis consumption (e.g., frequency of use) with individual differences in levels of alcohol use (Risso et al., 2020). Most of these studies have found support for complementarity (Risso et al., 2020), observing increased alcohol use among those reporting greater cannabis use (e.g., Choi et al., 2018; Hammer & Vaglum, 1992) and vice versa (Pape et al., 2009).

A major limitation of existing research on the cannabis–alcohol association is that most studies examine substitution and complementarity in terms of between-person associations. However, the very concepts of substitution and complementarity invoke a within-person process wherein an individual is presumed to reduce (substitution) or increase (complementarity) their consumption of one substance during times (e.g., days) when their consumption of the other substance is elevated. Importantly, studies of between-person associations often cannot adequately capture such within-person processes, and within-person associations may be inconsistent with between-person associations (Curran & Bauer, 2011). For example, it may simultaneously be true that individuals who use cannabis more frequently may use alcohol more heavily overall (supporting a between-person complementarity effect), and that these same individuals may engage in their heaviest drinking on days when cannabis use is reduced or absent (supporting a within-person substitution effect). Thus, within-person analyses are needed to elucidate substitution and complementarity at the day level.

Select studies provide preliminary insight into within-person associations between cannabis use and alcohol use. For instance, studies have observed increased likelihood of same-day drinking or heavy drinking on cannabis use days relative to non-cannabis-use days (Daros et

al., 2022; Gunn et al., 2018; Ito et al., 2021; Metrik, Bassett, et al., 2018; Roche et al., 2019), supporting complementarity at the day level. Many of these studies, however, are limited by the use of retrospective assessments of substance use (e.g., Timeline Followback), which may be prone to recall biases when assessing day-level co-use patterns. Some studies have addressed this limitation using prospective daily diary or ecological momentary assessment (EMA) methods (e.g., Lee et al., 2020; Linden-Carmichael et al., 2020; O'Hara et al., 2016), and have generally observed day-level complementarity or no significant cannabis–alcohol association. However, these studies have dichotomized cannabis use as present versus absent on a given day, and thus whether the quantities of cannabis and alcohol consumed on a given day are positively or negatively associated remains unclear. This precludes a more nuanced understanding of within-person patterns of substitution and complementarity. For example, although some individuals may drink greater amounts of alcohol on days when they use cannabis relative to days when they do not (i.e., complementarity), it is also possible that on cannabis use days, using a greater quantity of cannabis is associated with drinking lower amounts of alcohol relative to days when smaller quantities of cannabis are used (i.e., substitution). Thus, there is a need for daily diary and EMA studies of co-use that model quantities of both cannabis and alcohol used.

Medicinal and Nonmedicinal Reasons for Cannabis Use

Studies of cannabis and alcohol complementarity and substitution have predominantly focused on people who use cannabis nonmedicinally. Yet, a significant portion of individuals who use cannabis report medicinal reasons for use, which can be defined as the use of cannabis to prevent or alleviate physical or mental health symptoms. Although it is not surprising that

medicinal cannabis use[1] is especially prevalent in patient populations (such as people living HIV; (Fogarty et al., 2007; Furler et al., 2004; Wardell et al., 2018), cannabis use for medicinal reasons also appears to be common in the general population; indeed, an estimated 27.9% of young adults in Canada who use cannabis report medicinal reasons for use (Government of Canada, 2021). Understanding the cannabis–alcohol relationship among people who use cannabis for medicinal reasons is important given unique associations of medicinal reasons for cannabis use with both cannabis and alcohol use patterns. Compared to people who use cannabis for exclusively nonmedicinal reasons, those who use cannabis for medicinal reasons tend to use more cannabis (Furler et al., 2004; Lin et al., 2016; Loflin et al., 2017; Wardell et al., 2018, 2021) and report using multiple forms of cannabis concurrently (Mannes et al., 2018; Wardell et al., 2021). In contrast, some studies have found that people who use cannabis for medicinal reasons consume less alcohol than people who use cannabis for exclusively nonmedicinal reasons (Lin et al., 2016; Loflin et al., 2017; Metrik et al., 2018; Wardell et al., 2018), which has been interpreted as support for a substitution effect among those using medicinally (see Lucas et al., 2013, 2016; Lucas & Walsh, 2017; Piper et al., 2017).

Most studies of the cannabis–alcohol association in relation to medicinal versus nonmedicinal reasons for cannabis use involve only between-person analyses. In one exception, Gunn and colleagues (2019) found that veterans who reported medicinal cannabis use reasons consumed less alcohol on cannabis use days relative to those reporting exclusively nonmedicinal use reasons. However, this study relied on retrospective reports of cannabis and alcohol use and did not assess quantities of cannabis used. Moreover, this study specified medicinal versus

[1] We use the term *medicinal cannabis use* broadly to refer to cannabis use that is motivated by medicinal reasons (i.e., symptom prevention or alleviation), irrespective of the source of cannabis or whether medical cannabis authorization is obtained from a healthcare provider.

nonmedicinal reasons for cannabis use only at the between-person level. Many individuals reporting medicinal reasons for cannabis use also report nonmedicinal reasons for use (Turna et al., 2020; Wardell et al., 2018), rendering between-person comparisons problematic. Thus, it is necessary to establish whether cannabis use and alcohol use each vary as a function of medicinal versus nonmedicinal cannabis use reasons across different occasions to understand whether there is a within-person pattern indicative of substitution linked specifically with medicinal cannabis use reasons (i.e., greater cannabis use and lower alcohol use on medicinal use days).

If medicinal reasons for cannabis use invoke a cannabis-alcohol substitution effect, then three patterns should be observed at the day level. First, cannabis consumption should be elevated on days when cannabis is used for medicinal (relative to nonmedicinal) reasons, consistent with between-person findings of greater cannabis use among people who use cannabis for medicinal (versus exclusively nonmedicinal) reasons. This effect may be driven by a tendency to use greater quantities of cannabis or to combine multiple cannabis products to achieve symptom relief on days when cannabis use is medicinally motivated. Second, less alcohol should be consumed on days when cannabis is used for medicinal (relative to nonmedicinal) reasons, consistent with the between-person relationship between medicinal use status and lower alcohol consumption. Third, increased cannabis consumption on medicinal use days should account for the day-level relationship between medicinal reasons for cannabis use and reduced alcohol use, consistent with the substitution hypothesis. However, these within-person associations have yet to be examined using EMA data.

The Present Study

The present study examined whether there is evidence for a within-person process underlying the cannabis-alcohol substitution effect among individuals reporting cannabis use for

medicinal reasons. We conducted a secondary analysis of day-level data from participants who reported both medicinal and nonmedicinal reasons for cannabis use. We examined day-level relationships among medicinal versus nonmedicinal reasons for cannabis use and both cannabis and alcohol consumption. Consistent with the substitution hypothesis, we expected that consuming more cannabis would generally be associated with consuming less alcohol at the day level. Moreover, we expected that relative to days on which participants reported using cannabis for exclusively nonmedicinal reasons, days on which they reported using cannabis for medicinal reasons would be associated with greater cannabis consumption, and in turn, lower alcohol consumption. In other words, we expected greater cannabis consumption on medicinal use days to explain the day-level relationship between medicinal reasons for cannabis use and reduced alcohol consumption.

Method

Participants and Recruitment

Participants (N = 66) were adults reporting both medicinal and nonmedicinal reasons for cannabis use. The current study represents a secondary analysis of data drawn from two separate EMA studies that each focused on a population commonly reporting medicinal reasons for cannabis use: people living with HIV (Study 1) and young adults (Study 2). Study 1 was an EMA study examining medicinal and nonmedicinal cannabis use among people living with HIV (PLWH; Wardell et al., 2022). Participants (N = 30) were recruited from across Canada using social media ads and fliers distributed to community agencies that serve PLWH; one participant chose to withdraw from the study, leaving a final sample of N = 29. All 29 participants from Study 1 were included in the current analysis. Inclusion criteria were: (i) ages 19 years or older; (ii) daily or near daily cannabis use; (iii) cannabis use for both medicinal and nonmedicinal

reasons; (iii) diagnosed with HIV at least one year ago; (iv) current antiretroviral treatment; and (v) access to compatible smartphone (Android or iOS). Exclusion criteria were: (i) heavy episodic drinking three or more times per week; (ii) using drugs other than cannabis, alcohol, or nicotine two or more times per week; (iii) history of treatment for substance use disorders; (iv) current attempts to reduce cannabis use; (v) diagnosis of a severe mental illness; (vi) physical illness that would interfere with participation; or (vii) current pregnancy or nursing.

Study 2 was an EMA study examining co-use of cannabis and alcohol among young adults. Participants were recruited from across Ontario, Canada using online ads, social media posts, and fliers posted in the community and on university campuses. A total of $N = 176$ were initially enrolled in the study. Of these, 17 participants were deemed ineligible following the baseline assessment and were withdrawn from the study, and an additional nine participants were withdrawn from the study due to extremely low compliance with the EMA (completing less than 10% of the prompted EMA surveys), resulting in a final sample of $N = 150$. Although this study did not specifically recruit for medicinal cannabis use, 37 (24.67%) participants reported using cannabis for both medicinal and nonmedicinal reasons during the EMA period and were included in the current analyses. Inclusion criteria for the larger study were: (i) ages 19–25 years; (ii) using both alcohol and cannabis at least once per week on average during the past month; (iii) using cannabis and alcohol at the same time at least twice during the past month; and (iv) access to a compatible smartphone (Android or iOS). Exclusion criteria were: (i) regular (monthly) use of substances other than cannabis, alcohol, or nicotine; (ii) exclusive use of cannabis for medical reasons; (iii) current treatment for or efforts to reduce cannabis or alcohol use; or (iv) severe

mental illness (e.g., psychosis, mania) or neurodevelopmental disorder.[2]

Across the full analytic sample for the current study, the mean age was 33.00 years old (*SD* = 14.20). 60.61% of participants identified as White, and 53.05% of participants identified as men. Current and lifetime medical authorization for cannabis use was reported by 27.27% and 30.30% of participants, respectively (see Table 1 for participant characteristics in each sample).

Procedure and Measures

All study procedures were approved by the Centre for Addiction and Mental Health and York University Research Ethics Boards. Detailed procedures for Study 1 are described elsewhere (Wardell et al., 2022) and many procedures and measures for Study 2 are beyond the scope of the present analyses and thus are not detailed here. Below, the procedures and measures that are pertinent to the aims of the current secondary analysis are described.

Baseline Assessment

Interested individuals were first screened for eligibility via telephone (Study 1) or online survey (Study 2). In both studies, eligible participants attended a one-on-one baseline visit with a research assistant, either in-person or via a secure videoconferencing platform, during which informed consent was obtained. A research assistant instructed participants in installing the EMA application (MetricWire, Inc., Waterloo, ON) on their mobile phone and oriented participants to the EMA protocol. The orientation included the use of visual examples to train participants to accurately report quantities of cannabis flower consumed in grams and quantities of alcohol consumed in standard drinks. At the end of the visit, participants were emailed a link to complete an online questionnaire, including cannabis- and alcohol-related measures used for descriptive

[2] Unlike in Study 1, participants in Study 2 were not excluded if they endorsed heavy episodic drinking three or more times per week; however, no participants from Study 2 included in the current analysis met this threshold for heavy drinking, and thus the analytic sample would not have changed had this exclusion criterion been applied.

purposes in the current study. In both studies, participants were compensated $40 CAD (cash or electronic gift card) for the baseline assessment.

Baseline Measures

Demographic characteristics. Participants reported age, sex, gender identity, race/ethnicity, and household income.

Cannabis use. Participants completed the Cannabis Use Disorder Identification Test–Revised (CUDIT-R; Adamson et al., 2010), which is an eight-item questionnaire assessing problematic cannabis use. Scores of eight or higher on the CUDIT-R indicate hazardous use. Participants also completed the Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory (DFAQ-CU; Cuttler & Spradlin, 2017), from which we drew typical frequency of cannabis use (ranging from not at all to multiple times per day) and typical number of grams of cannabis flower used per day. In addition, participants reported the symptoms that they used cannabis to treat in the past six months (e.g., anxiety, pain, depression, headaches) and whether they had current and lifetime valid medical authorization for cannabis use.

Alcohol use. Participants in both studies completed the Alcohol Use Disorder Identification Test (AUDIT; Saunders et al., 1993), which is a 10-item questionnaire assessing problematic alcohol use. Scores of eight or higher on the AUDIT indicate hazardous use.

EMA Protocol

Participants began completing EMA surveys the day after the baseline assessment. The EMA protocols for Studies 1 and 2 differed, as they were designed to address different research questions. Study 1 involved a 14-day EMA period, whereas Study 2 involved a 21-day EMA period. Both studies involved daily surveys completed each morning, randomly timed surveys

throughout the day, and event-contingent surveys completed during cannabis use events. In Study 2, medicinal reasons for cannabis use were only assessed on the daily morning surveys, and there were also differences across studies in the timing and number of event-contingent and randomly timed surveys that were administered. Thus, for the aims of the current study, only the daily morning surveys are included in analyses.

Participants were instructed to complete a 2- to 5-minute daily morning survey immediately upon waking up each day. The survey became available at 6:00 AM (Study 1) or 7:00 AM (Study 2) each day, and participants had until 1 PM (Study 1) or 2 PM (Study 2) to complete the survey before it was counted as missing. Several reminder notifications were sent leading up to the survey expiry time each day. The surveys asked participants to report whether they had used cannabis the previous day, and if so, their route(s) of cannabis administration (smoking, vaping, eating/drinking, other) and form(s) of cannabis used (cannabis flower, concentrates, edibles, other)[3]. Participants reporting cannabis flower use were asked to provide the total number of grams of cannabis flower used the previous day. Participants were then asked about the reasons for their previous-day cannabis use: *"Would you say you used cannabis yesterday for medicinal reasons, nonmedicinal or recreational reasons, or both reasons?"* (Study 1) or *"Yesterday, did you use cannabis for medicinal reasons only, recreational reasons only, or both reasons?"* (Study 2). In addition, participants were asked to report whether they had used alcohol in the previous day, and if so, the number of standard drinks they consumed. All standard drink responses with decimal values were rounded up to the next whole number. Participants could click on a link to view a standard drink conversion chart or image depicting various quantities of cannabis flower when completing the relevant questions. Participants were

[3] Forms of cannabis assessed were more specific in Study 1 but were combined into these three broader categories to be consistent with Study 2.

compensated between $40 CAD and $115 CAD in cash or electronic gift cards for completion of the EMA protocol (depending on the study), with increasing compensation provided for better compliance with the prompted surveys.

Data Analysis

In the combined dataset, a total of 1065 daily surveys were fully completed across the 66 participants (*n* = 29 from Study 1, *n* = 37 from Study 2). The overall compliance rate for daily morning surveys was 90.51% (93.35% Study 1, 88.29% Study 2). Only daily surveys that involved previous day cannabis use (751 observations) were included in the current analysis as medicinal versus nonmedicinal reason for use was only assessed on cannabis use days.

To examine the direct and indirect day-level associations among reasons for cannabis use (independent variable), cannabis consumption (mediator), and alcohol consumption (dependent variable), we specified multilevel mediation models using Mplus version 8 (Muthén & Muthén, 2021), wherein days (level 1) were nested within participants (level 2). Unconflated 1-1-1 mediation models were specified using syntax from (Preacher et al., 2010). Number of standard drinks consumed on each day was specified as the dependent variable and was regressed on both the mediator (cannabis consumption) and independent variable (reasons for cannabis use) to allow for partial mediation. We observed a large number of non-drinking days (477, 63.52%), and thus the standard drinks variable was specified as a count outcome using a zero-inflated Poisson model. This approach yields two sets of parameter estimates: (1) a logistic portion, predicting the absence (versus presence) of alcohol use on a given day; and (2) a count portion, predicting the number of standard drinks consumed on a given day.

The independent variable, daily reason for cannabis use, was coded as 1 = any medicinal cannabis use and 0 = exclusively nonmedicinal cannabis use. Mixed-reason days (i.e., when

participants reported using cannabis for both medicinal and nonmedicinal reasons; 367 observations) and exclusively medicinal days were combined due to few exclusively medicinal days (74, 9.85%). The mediator, daily cannabis consumption, was operationalized in two ways: (1) the number of different types of cannabis (cannabis flower, concentrates, edibles, other) used in a given day (including all 751 cannabis days), with the use of multiple different forms of cannabis in a given day providing an index of greater cannabis consumption; and (2) the grams of cannabis flower used on days involving cannabis flower use (541 observations[4]). This was done to account for the fact that the hypothesized increase in cannabis consumption on medicinal use days may be reflected not only in increased flower consumption, but also (or perhaps instead) in using additional types of cannabis products in combination with one another to achieve greater symptom relief. Separate models were run with each cannabis use variable as the mediator. In the model including grams of cannabis flower use, we excluded 11 participants who did not report medicinal reasons for cannabis use on any day during which cannabis flower was used given our focus on within-person variation in reasons for use.

We included weekend (Friday–Sunday, coded 1) versus weekday (Monday–Thursday, coded 0) as a level 1 covariate (predicting both cannabis and alcohol consumption) in both models, given that substance use among young adults is generally elevated on weekends relative to weekdays (Goldman et al., 2011). In the model with grams of cannabis flower used as the mediator, the use of any non-flower forms of cannabis (1 = yes, 0 = no) was additionally included at both level 1 (day level) and level 2 (proportion of days involving non-flower use) as a covariate predicting alcohol consumption, in order to account for additional forms of cannabis used on cannabis flower days that would not be captured within grams of cannabis flower. In

[4] One observation was excluded due to missing data on grams of cannabis flower used.

addition, given that amounts and motives of both cannabis and alcohol use differ by age (Grant et al., 2012; Mauro et al., 2018; Nicolai et al., 2012) and sex (Calakos et al., 2017; Hawke et al., 2018; Salvatore et al., 2017), we included age and sex as level 2 covariates (predicting both cannabis and alcohol consumption) in both models. At level 2, we also controlled for sample (1 = Study 2, 0 = Study 1) in both models to account for potential third variable differences between our patient and young adult samples. All level 1 predictors and covariates were person-mean centered, and person-level means were grand-mean centered and included at level 2. This follows recent guidance provided by Yaremych, Preacher, & Hedeker (2021), which recommends centering categorical predictors in multilevel models following the same approach that is typically applied to continuous predictors to disaggregate within- and between-person variance. As medicinal versus nonmedicinal reason for cannabis use was a dichotomous variable, the person-level mean (at level 2) can be interpreted as the proportion of days on which medicinal use was reported for a given participant.

All models were specified with random intercepts for the prediction of standard drinks (separate random intercepts for the logistic and count portion of the model). As the mediator variables (cannabis consumption) were person-mean centered at level 1, intercepts were fixed at zero for these variables (Preacher et al., 2010, 2011). A model building approach was used to examine whether random slopes should be included in the model. Specifically, random slopes were added one by one to the model for all paths included in the mediation effect. To achieve parsimonious models, only random slopes that resulted in improved model fit based on the Akaike Information Criterion (AIC), Bayes Information Criterion (BIC), and sample-size-adjusted BIC (SSA-BIC) were retained. Further, given that our data combined two distinct samples, we ran a separate series of models in which we regressed a sample indicator (Study 1

versus Study 2) on each random slope, one by one, to determine whether sample moderated any path in the model. Models were fit using maximum likelihood robust estimation to accommodate non-normally distributed variables. Monte Carlo confidence intervals were obtained for all indirect associations using code provided by Selig and Preacher (2008) for R and RStudio (R Core Team, 2022; RStudio Team, 2020).

Transparency and Openness

We report how we determined our sample size, all data exclusions, all manipulations, and all measures in the study, and we follow the Journal Article Reporting Standards (JARS; Kazak, 2018). Analysis code is available at https://osf.io/mrn35/. De-identified data will be made available (as allowable according to institutional IRB standards) by emailing the corresponding author. Materials used to conduct the study are not publicly available. Data were analyzed using Mplus version 8 (Muthén & Muthén, 2021) and R version 4.2.0 (R Core Team, 2022; RStudio Team, 2020). This study's design and its analysis were not pre-registered.

Results

Descriptive Statistics

On average, participants reported 11.38 cannabis use days (*SD* = 3.93) throughout the EMA period. Across the cannabis use days included in the analysis (total of 751), there were 275 days of alcohol use (36.62%). Number of different types of cannabis used in a given day ranged from 1 (632 days) to 3 (5 days), with a mean of 1.17 (*SD* = 0.39) different types of cannabis used each day. 562 (74.83%) cannabis days involved the use of cannabis flower, 182 (24.23%) involved the use of concentrates, 129 (17.18%) involved the use of edibles, and 2 (0.27%) involved the use of other unspecified forms of cannabis. An average of 1.00 grams (*SD* = 1.06) of cannabis flower was used on cannabis flower days, and 112 (19.93%) cannabis flower days

also involved the use of other forms of cannabis. Number of standard drinks ranged from 0 (477 days) to 13 (1 day), with a mean of 1.22 drinks (*SD* = 2.13) per day. Person-level means of day-level data are provided in Table 1, which are broken down by medical cannabis authorization status in Table S1. Of the 751 cannabis days, 74 (9.85%) involved only medicinal reasons for use, 310 (41.28%) involved only nonmedicinal reasons for use, and 367 (48.87%) involved both medicinal and nonmedicinal reasons for use. Day-level descriptive statistics for medicinal and nonmedicinal cannabis use days are provided in Table S2, and for weekday (Monday–Thursday) versus weekend (Friday–Sunday) days are provided in Table S3.

Multilevel Mediation Models

Number of different types of cannabis used. In the multilevel mediation model examining number of different types of cannabis used as a mediator, sample (Study 1 versus Study 2) was not significantly associated with variance in any of the random slopes, suggesting that within-person associations did not differ between the Study 1 and Study 2 samples (i.e., sample did not moderate any paths in the model). Thus, sample was included only as a between-person covariate in the model. The final model included only a random slope for the within-person path from cannabis use reason to number of cannabis types used, as the addition of the other random slopes did not improve model fit (all ΔAIC, ΔBIC, and ΔSSA-BIC $\geq$ -0.62).

Figure 1A displays the main results of the multilevel mediation model, and Table 2 provides all parameter estimates for the model. At the within-person level, after adjusting for weekend versus weekday, the mean of the random slope for the association between cannabis use reason and number of different types of cannabis used was not statistically significant, suggesting that on average, within-person variation in medicinal versus nonmedicinal reasons for cannabis use was not significantly associated with within-person variation in the number of

different types of cannabis used. In the logistic portion of the model, using a greater number of cannabis types was significantly associated with reduced likelihood of abstaining from drinking at the day level; in other words, on days during which participants used more types of cannabis, they were more likely to initiate drinking. In addition, using cannabis for medicinal (versus exclusively nonmedicinal) reasons was directly associated with increased likelihood of abstaining from drinking at the day level (i.e., reduced likelihood of initiating drinking). The indirect effect of cannabis use reason on the likelihood of abstaining from drinking through number of cannabis types used was not statistically significant (*B* = -0.037, *SE* = 0.038, 95% CI [-0.132, 0.033]). In the count portion of the model, neither cannabis use reason nor number of different cannabis types used were significantly associated with number of standard drinks, and the indirect effect of cannabis use reason on number of standard drinks through number of different types of cannabis used was not statistically significant (*B* = -0.003, *SE* = 0.007, 95% CI [-0.015, 0.025]). No between-person direct or indirect effects were supported (logistic: *B*= 0.000, *SE* = 0.022, 95% CI [-0.339, 0.263]; count: *B* = 0.000, *SE* = 0.006, 95% CI [-0.057, 0.082]).

Grams of Cannabis Flower Used. Sample was also not significantly associated with any of the random slopes in this model, suggesting that within-person associations did not differ between samples, and so sample was included as a covariate in the between-person part of the model only. The addition of random slopes did not improve model fit (all ΔAIC, ΔBIC, and ΔSSA-BIC ≥ -2.68) and thus the random slopes were removed for parsimony.

Figure 1B displays the main results of the multilevel mediation model and Table 3 provides all parameter estimates for the model. At the within-person level, after adjusting for covariates (including weekend versus weekday and use of non-flower forms of cannabis), cannabis use reason was significantly associated with grams of cannabis flower used, such that

participants tended to report using fewer grams of cannabis flower on days when they reported using cannabis for medicinal (versus exclusively nonmedicinal) reasons. Neither reason for cannabis use nor grams of cannabis flower used were significantly associated with the likelihood of abstaining from alcohol at the day level, and the indirect effect of cannabis use reason on the likelihood of abstaining from alcohol through grams of cannabis flower used was not statistically significant (*B* = 0.012, *SE* = 0.060, 95% CI [-0.160, 0.126]). However, in the count portion of the model, using more grams of cannabis flower was significantly associated with consuming more standard drinks, such that participants tended to drink more alcohol on days when they used a greater amount of cannabis flower (relative to their usual amount of cannabis flower). In addition, the indirect effect of cannabis use reason on number of standard drinks through grams of cannabis flower used was significant (*B* = -0.031, *SE* = 0.014, 95% CI [-0.060, -0.001]), such that at the day level, using cannabis for medicinal (versus exclusively nonmedicinal) reasons was associated with using fewer grams of cannabis flower, and in turn, consuming fewer drinks. At the between-person level, no direct or indirect effects were supported (logistic: *B* = 0.032, *SE* = 0.286, 95% CI [-0.512, 0.975]; count: *B* = 0.003, *SE* = 0.023, 95% CI [-0.086, 0.099]).

Discussion

Given the potential harms associated with co-use of alcohol and cannabis (Yurasek et al., 2017) and the higher levels of cannabis use observed among people who use cannabis for medicinal reasons (Lin et al., 2016; Loflin et al., 2017; Wardell et al., 2021), an understanding of the relationship between cannabis use and alcohol use in this population is needed to inform harm reduction efforts. Accordingly, the present study used EMA to examine day-level associations between cannabis use and alcohol use among people using cannabis, in part, for medicinal reasons. Overall, we observed lower consumption of both cannabis and alcohol on

days when cannabis was used for medicinal reasons, and greater consumption of both cannabis and alcohol on days when cannabis was used for exclusively nonmedicinal reasons. As we controlled for weekend versus weekday in our models, this finding is more than just an artifact of nonmedicinal reasons for substance use being more likely on weekends when cannabis and alcohol are typically used in greater quantities. As we observed positive associations between cannabis and alcohol consumption at the day level, regardless of reason for cannabis use, results suggest a complementary within-person cannabis-alcohol relationship overall. Moreover, the day-level association of medicinal (versus nonmedicinal) reasons for cannabis use with lower alcohol consumption was mediated by using fewer grams of cannabis flower on medicinal cannabis use days. Together, findings provide new insight into within-person processes involved in the cannabis-alcohol link among people who use cannabis in part for medicinal reasons.

We hypothesized that medicinal reasons for cannabis use would invoke a cannabis–alcohol substitution effect at the day level, which would involve: (1) greater cannabis consumption on days when cannabis is used for medicinal (relative to nonmedicinal) reasons; (2) reduced alcohol consumption on days when cannabis is used for medicinal (relative to nonmedicinal) reasons; and (3) increased cannabis consumption on medicinal use days accounting for reduced alcohol consumption on medicinal use days. Contrary to hypotheses, we observed a negative day-level association between medicinal reasons for cannabis use and cannabis consumption, such that participants used fewer grams of cannabis flower on days when they reported medicinal (versus exclusively nonmedicinal) reasons for cannabis use. This finding contrasts with prior between-person analyses that have found associations of medicinal reasons for cannabis use with greater cannabis use (Lin et al., 2016; Loflin et al., 2017; Wardell et al., 2018, 2021), illustrating the potential for discordance between within-person and between-person

associations (Curran & Bauer, 2011); although people who use cannabis for medicinal reasons may use more cannabis overall (perhaps driven primarily by greater frequency of use; Woodruff & Shillington, 2016), they may also use relatively less cannabis when using for medicinal reasons compared to when they are using for exclusively nonmedicinal reasons. This study extends prior research by examining the role of within-person variation in medicinal versus nonmedicinal reasons for cannabis use in day-level patterns of both cannabis and alcohol use.

Interestingly, although medicinal (versus nonmedicinal) reasons for cannabis use were associated with using fewer grams of cannabis flower at the day level, there was no significant day-level association between reason for cannabis use and number of different types of cannabis used. This suggests that reduced use of cannabis flower on medicinal use days is not offset by increased consumption of other forms of cannabis, despite previous between-person analyses showing that people who use cannabis for medicinal reasons use a wider range of cannabis products (Mannes et al., 2018; Wardell et al., 2021). Our findings may in part be due to limited variability in number of different types of cannabis used each day, or due to our broadly defined cannabis product categories, which combined various subtypes (e.g., all concentrates counted as one "type" of cannabis). Another interpretation is that the use of multiple cannabis products among people using for medicinal reasons may reflect heavier cannabis use overall rather than use of additional products specifically for medicinal reasons. Future work should examine specific types of cannabis used in relation to medicinal reasons for cannabis use at the day level.

Although we did not observe the hypothesized increase in cannabis use on medicinal use days, we did observe some support for the hypothesized decrease in alcohol use on medicinal cannabis use days. Specifically, in our model that included all cannabis use days (i.e., the model that included number of different cannabis types used as the mediator), we found that

participants were less likely to initiate alcohol use on medicinal (relative to nonmedical) cannabis use days. Further, in our model that included only cannabis flower days, we found that medicinal (versus nonmedicinal) reasons for cannabis use were indirectly associated with consuming fewer standard drinks (mediated through grams of cannabis flower used). The finding that medicinal cannabis use was associated with reduced alcohol consumption is consistent with previous between-person findings that people who use cannabis for medicinal reasons generally use less alcohol and have lower rates of alcohol use disorders (Lin et al., 2016; Loflin et al., 2017; Metrik et al., 2018; Roy-Byrne et al., 2015; Wardell et al., 2018). Our results indicate that this phenomenon may be explained by a tendency to drink less or abstain from alcohol use on medicinal cannabis use days, specifically. This may be due to alcohol use being less common in contexts in which cannabis is typically used medicinally (e.g., at home to cope with symptoms; Wardell et al., 2021) relative to those in which cannabis is typically used nonmedicinally (e.g., social settings, parties). This explanation remains speculative, as specific contexts in which medicinal and nonmedicinal cannabis use events occurred were not assessed in our daily surveys. Studies involving event-level assessments of cannabis use reasons and context are needed.

Importantly, we found that among our sample of people reporting both medicinal and nonmedicinal reasons for cannabis use, alcohol and cannabis were complements at the day level across different operationalizations of cannabis consumption. Specifically, using more types of cannabis on a given day was associated with increased likelihood of initiating alcohol use, and using more grams of cannabis flower on a given day was associated with consuming more standard drinks. On one hand, these findings are consistent with previous daily diary and EMA studies of the cannabis–alcohol relationship, which have largely observed day-level complementarity of cannabis and alcohol (Lee et al., 2020; O'Hara et al., 2016). On the other

hand, our findings contradict the notion that medicinal cannabis users may use cannabis as a harm-reducing substitute for alcohol (e.g., Lucas et al., 2013; Lucas & Walsh, 2017), since greater cannabis consumption was associated with greater (rather than lower) alcohol consumption at the day level. Further contradicting the notion that cannabis–alcohol substitution underlies the reduced alcohol use observed among people reporting medicinal reasons for cannabis use, we found that the tendency to consume *fewer* grams of cannabis flower on days when cannabis was used for medicinal reasons accounted for the within-person relationship between medicinal reasons for use and reduced alcohol consumption. This pattern of results suggests that using cannabis for medicinal (relative to nonmedicinal) reasons may protect against heavier consumption of *both* cannabis and alcohol, and thus there may be lower risk of cannabis- and alcohol-related harms when using cannabis for medicinal reasons. That said, using cannabis exclusively for medicinal reasons is rare (Government of Canada, 2021; Wardell et al., 2021). Indeed, our sample of medicinal cannabis users still reported many nonmedicinal cannabis use days, on which they tended to consume more cannabis, and in turn, consumed more alcohol. Consequently, supplementary cannabis use for nonmedicinal reasons among individuals who use cannabis for medicinal reasons may confer increased risk of co-using alcohol and cannabis and consuming larger amounts of each substance. Thus, harm reduction efforts in this population may benefit from tailored content targeting nonmedicinal cannabis use events, specifically.

The results of this study should be interpreted in the context of several limitations. First, although our sample of $N = 66$ provided ample day-level observations for within-person analyses (which were the main focus of our study), we had limited power to examine person-level moderators of associations, such as demographic and health-related variables. In particular, given sex differences in both cannabis and alcohol use (Calakos et al., 2017; Salvatore et al., 2017),

future larger studies should examine whether associations observed in the current study are invariant across sexes. Second, although our examination of cannabis consumption in terms of both number of different types of cannabis used and grams of cannabis flower used extends EMA studies of the cannabis–alcohol relationship that have tended to dichotomize cannabis use as present versus absent (e.g., Mallett et al., 2019; O'Hara et al., 2016), cannabis quantity in the current study could not be standardized across different forms of cannabis. Thus, quantities of non-flower cannabis use could not be captured in our models, which is a limitation. Future EMA studies would benefit from measuring cannabis consumption in terms of standard THC units (Freeman & Lorenzetti, 2020, 2021) to permit aggregation of consumption across various forms of cannabis. Third, we did not ask participants to report types and quantities of cannabis used separately for medicinal and nonmedicinal reasons, and thus our day-level cannabis consumption variables were aggregated across all reasons for cannabis use on a given day. Similarly, although day-level data improve the ability to disentangle medicinal versus nonmedicinal reasons for cannabis use, we observed a large proportion of days during which both medicinal and nonmedicinal reasons for use were endorsed. More nuanced assessments that link medicinal and recreational motives with specific types and quantities of cannabis used should be attempted in future research. Fourth, our daily surveys did not assess event-level contextual variables surrounding cannabis use, such as social setting or physical and mental health symptoms, which may have contributed to the associations observed. Fifth, we did not examine the sequence of cannabis and alcohol use (i.e., using cannabis before using alcohol or vice versa), which may have influenced complementarity versus substitution at the within-person level given the role of cannabis-alcohol ordering in consumption (Gunn et al., 2021). Sixth, the sample included participants with relatively moderate drinking levels, so our findings may not generalize to

individuals who drink more heavily or those who have an alcohol use disorder.

In conclusion, this study demonstrated that although medicinal cannabis use days may involve lower alcohol use relative to exclusively nonmedicinal cannabis use days, this appears to be due to an underlying complementary relationship between cannabis and alcohol at the day level (i.e., day-level reductions in the use of both substances), rather than a substitution effect. Consequently, cannabis use that is motivated exclusively by nonmedicinal reasons may result not only in increased overall cannabis use, but also increased alcohol use in this population. Future work is needed to characterize cannabis- and alcohol-related harms associated with exclusively nonmedicinal cannabis use among people who use cannabis for both medicinal and nonmedicinal reasons to inform prevention and harm reduction strategies.

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Table 1. Person-Level Descriptive Statistics

	M (*SD*) or *n* (%)			Study 1 vs. Study 2	*p*	Effect size
	Study 1 (*N* = 29)	Study 2 (*N* = 37)	Combined (*N* = 66)			
Age	**46.69 (10.77)**	**22.27 (2.17)**	33.00 (14.20)	**t(29.78) = -12.02**	**<0.001**	***d* = 3.14**
Sex				**X^2(1) = 12.52**	**<0.001**	***v* = 0.47**
Male	**23 (34.84)**	**12 (18.18)**	35 (53.03)			
Female	**6 (9.09)**	**25 (37.88)**	31 (47.00)			
Gender				***X*²(2) = 11.04**	**0.004**	***v* = 0.41**
Man	**22 (75.86)**	**13 (35.14)**	35 (53.03)			
Woman	**6 (20.69)**	**23 (62.16)**	29 (43.94)			
Non-binary or two-spirited	1 (3.45)	1 (2.70)	1 (3.03)			
Race/ethnicity				$X^2(6) = 3.29$	0.772	$v = 0.22$
White	19 (65.52)	21 (56.76)	40 (60.61)			
Black	2 (6.90)	3 (8.11)	5 (7.58)			
Asian	1 (3.45)	3 (8.11)	4 (6.06)			
Hispanic/Latinx	1 (3.45)	1 (2.70)	2 (3.03)			
East Indian	1 (3.45)	4 (10.81)	5 (7.58)			
Middle Eastern	1 (3.45)	0 (0)	1 (1.52)			
Mixed Race/Ethnicity	4 (13.79)	5 (13.51)	9 (13.64)			
Household income[a]				$X^2(3) = 1.42$	0.700	$v = 0.15$
Below $20,000	6 (21.43)	5 (13.51)	11 (16.92)			
$20,000-$49,999	9 (32.14)	12 (32.43)	21 (32.31)			
$50,000-$99,999	9 (32.14)	11 (29.73)	20 (30.77)			
$100,000 or more	4 (14.29)	9 (24.32)	13 (20.00)			
CUDIT-R score[a]	9.86 (5.03)	11.81 (5.92)	10.97 (5.60)	t(63) = 1.40	0.165	$d = 0.35$
Met CUDIT-R threshold for hazardous use[a]	17 (60.71)	26 (70.27)	43 (65.15)	$X^2(1) = 0.29$	0.588	$v = 0.10$
AUDIT score	12.14 (8.39)	8.76 (5.24)	10.24 (6.95)	t(44.49) = -1.90	0.064	$d = 0.48$
Met AUDIT threshold for hazardous use	20 (68.97)	20 (54.05)	40 (60.61)	$X^2(1) = 0.95$	0.329	$v = 0.15$
DFAQ-CU current cannabis use frequency[b]				***X*²(6) = 16.78**	**0.010**	***v* = 0.50**
2–3 times a month	1 (3.45)	1 (2.70)	2 (3.03)			
Once a week	0 (0)	2 (5.41)	2 (3.03)			
Twice a week	0 (0)	4 (10.81)	4 (6.06)			
3–4 times a week	2 (6.90)	7 (18.92)	9 (13.64)			
5–6 times a week	1 (3.45)	5 (13.51)	6 (9.09)			
Once a day	8 (27.59)	12 (32.43)	20 (30.30)			
More than once a day	**17 (58.62)**	**6 (16.22)**	23 (34.85)			
DFAQ-CU grams of cannabis flower used in a typical session	**0.66 (0.70)**	**0.36 (0.29)**	0.49 (0.63)	**t(35.60) = -2.21**	**0.033**	***d* = 0.57**

DFAQ-CU grams of cannabis flower used in a typical day	**1.24 (1.16)**	**0.54 (0.52)**	0.85 (0.92)	**t(36.94) = -3.00**	**0.005**	***d* = 0.77**
DFAQ-CU grams of cannabis flower used in a typical week	**9.29 (11.59)**	**3.04 (3.04)**	5.79 (8.53)	**t(31.03) = -2.83**	**0.008**	***d* = 0.74**
Percentage of EMA days on which medicinal[c] reasons for use were reported	**75.90 (31.16)**	**42.82 (31.74)**	58.72 (35.53)	**t(64) = -4.18**	**<0.001**	***d* = 1.04**
Person-mean grams of cannabis flower used per day during EMA period	1.01 (1.14)	0.50 (0.46)	0.74 (0.89)	t(35.13) = -2.33	0.026	*d* = 0.60
Person-mean number of standard drinks consumed per day during EMA period	1.20 (1.63)	1.23 (1.08)	1.22 (1.37)	t(64) = 0.20	0.838	*d* = 0.05
Person-mean number of different cannabis types used per day during EMA period	1.19 (0.27)	1.14 (0.19)	1.17 (0.23)	t(64) = -1.08	0.285	*d* = 0.26
Current valid medical authorization for cannabis use	**16 (55.17)**	**2 (5.41)**	18 (27.27)	**X^2(1) = 17.87**	**<0.001**	***v* = 0.55**
Lifetime valid medical authorization for cannabis use	**18 (65.52)**	**2 (5.41)**	20 (30.30)	**X^2(1) = 22.11**	**<0.001**	***v* = 0.61**
Symptoms treated using cannabis						
Anxiety	20 (68.97)	23 (62.16)	43 (65.15)	X^2(1) = 0.0005	0.981	*v* = 0.03
Pain	17 (58.62)	13 (35.14)	30 (45.45)	X^2(1) = 1.47	0.226	*v* = 0.18
Stress	19 (65.52)	22 (59.46)	41 (62.12)	X^2(1) = 0.16	0.687	*v* = 0.08
Insomnia	20 (68.97)	21 (56.76)	41 (62.12)	X^2(1) = 0.22	0.639	*v* = 0.09
Depression	11 (27.93)	16 (43.24)	27 (40.91)	X^2(1) = 0.47	0.492	*v* = 0.12
Appetite	17 (58.62)	12 (32.43)	29 (43.94)	X^2(1) = 3.36	0.066	*v* = 0.26
Headaches	5 (17.24)	9 (24.32)	14 (21.21)	X^2(1) = 2.84	0.092	*v* = 0.24
Nausea	9 (31.03)	4 (10.81)	13 (19.70)	X^2(1) = 2.05	0.152	*v* = 0.22
Muscle spasms	5 (17.24)	3 (8.11)	8 (12.12)	X^2(1) = 0.56	0.454	*v* = 0.14
HIV/AIDS	**19 (65.52)**	**0 (0)**	19 (28.79)	**X^2(1) = 28.53**	**<0.001**	***v* = 0.69**
Other	2 (6.90)	1 (2.70)	3 (4.54)	X^2(1) = 0.05	0.829	*v* = 0.10

Note: Study 1 = people living with HIV, Study 2 = young adults; *SD* = standard deviation; CUDIT-R = Cannabis Use Disorder Identification Test; AUDIT = Alcohol Use Disorder Identification Test; DFAQ-CU = Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory; EMA = ecological momentary assessment. Bolded values indicate significant differences between the Study 1 and Study 2 samples. For multicategorical variables, specific categories in which the samples differed significantly are bolded. Welch's correction for unequal variances was used for all t-tests.

[a]One person living with HIV declined to respond; [b]No participants reported using cannabis less than 2–3 times a month, and thus lower frequency categories are not included in the table; [c]Medicinal cannabis use days included days on which medicinal reasons for use were reported, either with or without concurrent nonmedicinal reasons for use.

Table 2. Parameter Estimates for Multilevel Mediation Model Examining Number of Cannabis Types Used as a Mediator in the Association Between Cannabis Use Reason (Medicinal vs. Exclusively Nonmedicinal) and Alcohol Use

Level		Estimate	OR	SE	*p*
Within-person					
	DV: Number of cannabis types used[a]				
	Weekend (vs. weekday)	0.028		0.025	.271
	DV: Absence (vs. presence) of drinking				
	Number of cannabis types used	**-0.764**	**0.466**	**0.325**	**.019**
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	**1.150**	**3.158**	**0.472**	**.015**
	Weekend (vs. weekday)	**-0.949**	**0.387**	**0.320**	**.003**
	DV: Number of standard drinks				
	Number of cannabis types used	0.069		0.135	.608
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	-0.254		0.133	.057
	Weekend (vs. weekday)	**0.376**		**0.104**	**.000**
Between-person					
	DV: Number of cannabis types used				
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	0.002		0.089	.983
	Age	0.026		0.037	.479
	Sex	-0.151		0.079	.054
	Sample	-0.066		0.114	.563
	DV: Absence (vs. presence) of drinking				
	Number of cannabis types used	0.250	1.284	1.539	.871
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	0.909	2.482	1.232	.461
	Age	**-1.421**	**0.241**	**0.692**	**.040**
	Sex	-0.437	0.646	0.885	.621
	Sample	-3.245	0.035	1.733	.061
	DV: Number of standard drinks				
	Number of cannabis types used	-0.063		0.345	.854
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	-0.066		0.304	.829
	Age	-0.084		0.158	.595
	Sex	-0.003		0.225	.990
	Sample	0.003		0.479	.995
	Random slope[a]				
	Mean	0.048		0.046	.298
	Variance	0.051		0.037	.169

Note: All variables at the within-person level are person-mean centered, and all variables at the between-person level are grand-mean centered person means. OR = odds ratio; DV = dependent variable. [a]A random slope is estimated for the within-person association between cannabis use reason (medicinal vs. exclusively nonmedicinal) and number of cannabis types used. Thus, the mean (average within-person association) and variance of the random slope are estimated at the between-person level of the model.

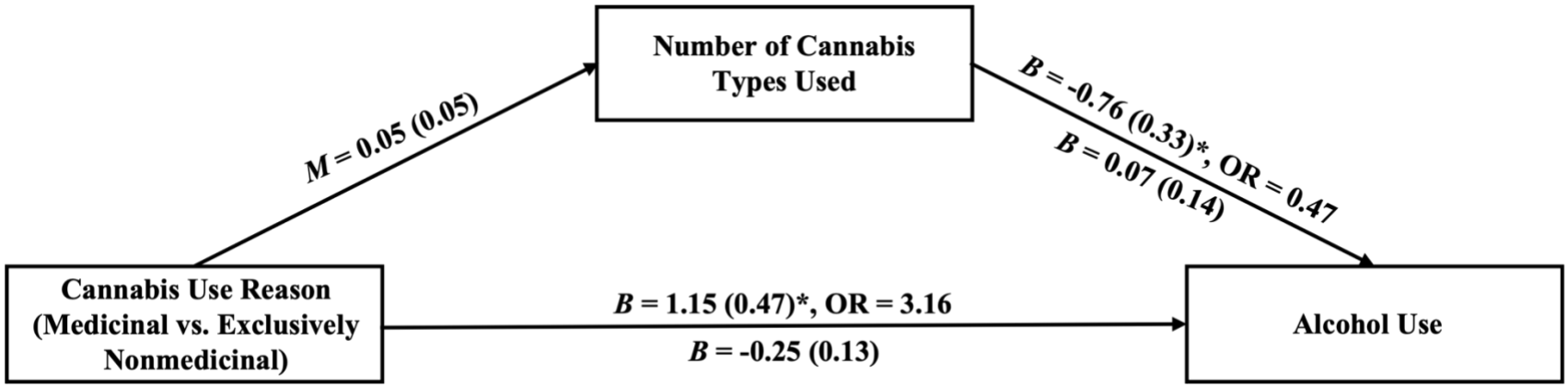
Table 3. Parameter Estimates for Multilevel Mediation Model Examining Grams of Cannabis Flower Used as a Mediator in the Association Between Cannabis Use Reason and Alcohol Use

Level		Estimate	OR	SE	*p*
Within-person					
	DV: Grams of cannabis flower used				
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	**-0.167**		**0.079**	**.036**
	Weekend (vs. weekday)	0.090		0.069	.194
	DV: Absence (vs. presence) of drinking				
	Grams of cannabis flower used	-0.070	0.932	0.373	.852
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	1.017	2.765	0.596	.088
	Weekend (vs. weekday)	**-0.928**	**0.395**	**0.348**	**.008**
	Use of non-cannabis-flower forms of cannabis	-0.857	0.424	0.462	.064
	DV: Number of standard drinks				
	Grams of cannabis flower used	**0.183**		**0.064**	**.004**
	Cannabis use reason (medicinal vs exclusively nonmedicinal)	-0.277		0.142	.052
	Weekend (vs. weekday)	**0.317**		**0.088**	**.000**
	Use of non-cannabis-flower forms of cannabis	0.160		0.210	.447
Between-person					
	DV: Grams of cannabis flower used				
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	0.033		0.289	.909
	Age	0.276		0.211	.190
	Sex	-0.154		0.272	.570
	Sample	0.126		0.421	.765
	DV: Absence (vs. presence) of drinking				
	Grams of cannabis flower used	0.960	2.612	0.695	.167
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	-0.205	0.815	1.200	.864
	Age	-1.207	0.299	0.747	.106
	Sex	-0.870	0.419	0.829	.294
	Use of non-flower forms of cannabis	-1.082	0.339	1.195	.365
	Sample	-3.389	0.034	1.777	.056
	DV: Number of standard drinks				
	Grams of cannabis flower used	0.077		0.123	.531
	Cannabis use reason (medicinal vs. exclusively nonmedicinal)	-0.215		0.239	.368
	Age	-0.168		0.177	.343
	Sex	0.140		0.182	.444
	Use of non-flower forms of cannabis	0.214		0.219	.329
	Sample	-0.157		0.508	.758

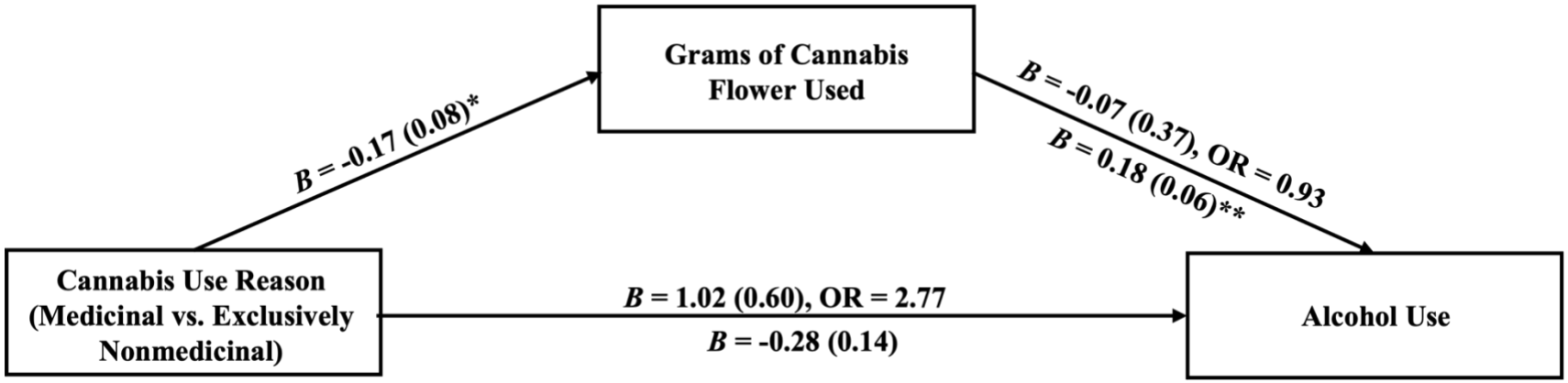
Note: All variables at the within-person level are person-mean centered, and all variables at the between-person level are grand-mean centered person means. OR = odds ratio; DV = dependent variable.

Figure 1. Multilevel Mediation Model Examining (A) Number of Cannabis Types Used and (B) Grams of Cannabis Flower Used as a Mediator of the Association Between Cannabis Use Reason and Alcohol Use at the Within-Person Level

A.



B.



Note: Standard errors are in parentheses. Parameters estimates for the logistic portion of the model are above the lines and parameter estimates for the count portion of the model are below the lines. The logistic portion of the model reflects the likelihood of abstaining from (versus initiating) alcohol use on a given day, and the count portion of the model reflects the number of standard drinks consumed on a given day.
In Figure 1A, as a random slope was specified for the path from cannabis use reason (medicinal vs. exclusively nonmedicinal) to number of cannabis types used, the mean of the random slope is presented in the figure. Weekend vs. weekday (both models) and the use of any non-flower form of cannabis (model B) were included as covariates; both number of grams of cannabis flower used and alcohol use were regressed on weekend vs. weekday, and alcohol use was regressed on the use of any non-flower form of cannabis.
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table S1. Comparison of participants with and without current medical authorization for cannabis

	M (SD) or *n* (%)		Test Statistic	*p*
	Participants with medical authorization for cannabis (*N* = 18)	Participants without medical authorization for cannabis (*N* = 48)		
CUDIT-R score[a]	9.78 (5.42)	11.43 (5.66)	t(63) = 1.06	0.292
Met CUDIT-R threshold for hazardous use[a]	11 (61.11)	32 (66.67)	$\chi^2(1) = 0.06$	0.811
AUDIT score	10.28 (7.93)	10.23 (6.64)	t(64) = -0.03	0.980
Met AUDIT threshold for hazardous use	11 (61.11)	29 (60.42)	$\chi^2(1) < 0.001$	> 0.999
DFAQ-CU current cannabis use frequency[b]			$\chi^2(6) = 10.06$	0.122
2–3 times a month	1 (5.56)	1 (2.08)		
Once a week	0 (0)	2 (4.17)		
Twice a week	1 (5.56)	3 (6.25)		
3–4 times a week	2 (11.11)	7 (14.58)		
5–6 times a week	0 (0)	6 (12.50)		
Once a day	3 (16.67)	17 (35.42)		
More than once a day	11 (61.11)	12 (25.00)		
DFAQ-CU grams of cannabis flower used in a typical session	0.67 (0.79)	0.43 (0.39)	t(20.09) = -1.23[d]	0.233
DFAQ-CU grams of cannabis flower used in a typical day	**1.27 (1.25)**	**0.69 (0.72)**	**t(64) = -2.33**	**0.023**
DFAQ-CU grams of cannabis flower used in a typical week	7.14 (9.44)	5.28 (8.21)	t(64) = -0.79	0.435
Proportion of EMA days on which medicinal[c] reasons for use were reported	**0.75 (0.32)**	**0.49 (0.34)**	**t(64) = -2.79**	**0.007**
Person mean grams of cannabis flower used per day during EMA period	0.96 (1.31)	0.55 (0.58)	t(19.52) = -1.27[d]	0.220
Person mean number of standard drinks consumed per day during EMA period	1.05 (1.72)	1.35 (1.34)	t(64) = 0.75	0.458
Person mean number of different cannabis types used per day during EMA period	1.17 (0.25)	1.14 (0.22)	t(64) = -0.49	0.627

Note: CUDIT-R = Cannabis Use Disorder Identification Test; AUDIT = Alcohol Use Disorder Identification Test; DFAQ-CU = Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory; EMA = ecological momentary assessment. Bolded values indicate significant differences between participants with and without medical authorization for cannabis.

[a]One participant declined to respond; [b]No participants reported using cannabis less than 2–3 times a month, and thus lower frequency categories are not included in the table; [c]Medicinal cannabis use days included days on which both medicinal and nonmedicinal reasons for use were reported; [d]Welch's t-test used due to unequal variances.

Table S2. Daily-Level Descriptive Statistics for Medicinal and Nonmedicinal Cannabis Use Days

	Medicinal Use Days (*n*=441)	Nonmedicinal Use Days (*n*=310)
	M (SD) or *n* (%)	M (SD) or *n* (%)
Grams of cannabis flower used	0.84 (1.05)	0.60 (0.93)
Number of different cannabis types used	1.17 (0.40)	1.15 (0.37)
Days involving cannabis flower use	343 (77.78)	219 (70.65)
Days involving concentrate use	103 (23.36)	79 (25.48)
Days involving edible use	70 (15.87)	59 (19.03)
Days involving other (unspecified) cannabis use	1 (0.23)	1 (0.32)
Number of standard drinks consumed	0.98 (1.75)	1.56 (2.53)

Table S3. Daily-Level Descriptive Statistics for Weekends and Weekdays

	Weekend Days (*n*=328)	Weekdays (*n*=423)
	M (SD) or *n* (%)	M (SD) or *n* (%)
Grams of cannabis flower used	0.76 (1.08)	0.73 (0.96)
Number of different cannabis types used	1.18 (0.40)	1.16 (0.38)
Days involving cannabis flower use	244 (74.39)	318 (75.18)
Days involving concentrate use	47 (14.33)	73 (17.26)
Days involving edible use	57 (17.38)	53 (12.53)
Days involving other (unspecified) cannabis use	1 (0.30)	1 (0.24)
Number of standard drinks consumed	1.75 (2.55)	0.80 (1.61)