DAILY ASSOCIATIONS BETWEEN CANNABIS USE AND ALCOHOL USE AMONG PEOPLE WHO USE CANNABIS FOR BOTH MEDICINAL AND NONMEDICINAL REASONS: SUBSTITUTION OR COMPLEMENTARITY?

SOPHIE COELHO

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Abstract

People who use cannabis for medicinal reasons tend to report elevated cannabis use and reduced alcohol use, which may reflect a cannabis–alcohol substitution effect. However, it is currently unclear whether cannabis is used as a substitute for or complement to alcohol at the day level among individuals who use cannabis for *both* medicinal and nonmedicinal reasons. This study used ecological momentary assessment (EMA) to examine day-level cannabis-alcohol associations linked to day-level variation in medicinal (versus nonmedicinal) reasons for cannabis use. People reporting cannabis use for both medicinal and nonmedicinal reasons (N=66) completed daily surveys assessing previous-day reasons for cannabis use, cannabis consumption, and alcohol consumption. Multilevel models revealed that days during which cannabis was used for medicinal (versus exclusively nonmedicinal) reasons were associated with reduced consumption of *both* cannabis and alcohol, and alcohol use was increased on days involving greater cannabis consumption. Further, the day-level association between medicinal (versus exclusively nonmedicinal) reasons for cannabis use and lower alcohol consumption was mediated by fewer grams of cannabis used on those days. Results suggest that day-level cannabis-alcohol associations may be complementary rather than substitutive among people who use cannabis for both medicinal and nonmedicinal reasons, and reduced (rather than increased) cannabis use may explain the link between medicinal reasons for cannabis use and reduced alcohol use. These individuals may still be at risk for cannabis-alcohol co-use-related harms, especially on days when they use cannabis for nonmedicinal reasons.

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

Table of Contents

List of Tables

List of Figures

1. Introduction

Amid a dynamic legal landscape, the prevalence of cannabis use continues to climb (Hasin & Walsh, 2021; Johnston et al., 2021; Reece & Hulse, 2021; Rottermann, 2021). In Canada, past-year cannabis use prevalence among individuals ages 15 and above reached 21% (6.4 million) in 2019 compared to 15% (4.4 million) in 2017, prior to the 2018 legalization of cannabis (Government of Canada, 2021b). Growth in cannabis use was especially pronounced among young adults, for whom past-year cannabis use prevalence increased from 33% (9.7 million) to 45% (13.7 million) from pre- to post-legalization (Government of Canada, 2021b). In addition to young adults, heightened cannabis use prevalence is also notable among certain subpopulations. For example, an estimated 35–46% of people living with HIV (PLWH) report using cannabis (Harris et al., 2014; Pacek et al., 2018; Tyurina et al., 2013) compared to 17–29% in the general population (Hammond et al., 2021). The increasingly widespread use of cannabis is of concern given the potential harms associated with frequent use. Indeed, frequent cannabis use is associated with increased risk of cannabis use disorder, adverse mental health outcomes (e.g., anxiety, depression, psychoses), cardiovascular problems, reduced functional connectivity in select brain networks, impaired academic and social functioning, and motor vehicle accidents (Feeney & Kampman, 2016; Subramaniam et al., 2019; Volkow et al., 2014).

Importantly, the harms associated with cannabis use may be compounded by the concurrent use of other substances. In particular, cannabis use frequently co-occurs with alcohol use (Subbaraman & Kerr, 2015). Co-use of cannabis and alcohol encompasses both *simultaneous use*, wherein cannabis and alcohol are used during the same occasion (with overlapping effects); and *concurrent use*, wherein an individual uses both cannabis and alcohol within a specified time period (e.g., past month or year), but does not use both substances on the same occasion (Bravo

et al., 2021; Subbaraman & Kerr, 2015). Importantly, the co-use of cannabis and alcohol is 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 social and behavioural consequences such as impaired driving (Yurasek et al., 2017). Consequently, there is interest in refining our understanding of the cannabis–alcohol relation. However, whether cannabis use may serve to increase or reduce alcohol use at the individual and population levels remains equivocal (Risso et al., 2020; Subbaraman, 2016).

1.1. Substitution and complementarity of cannabis and alcohol

Informed by behavioural economic theory, emerging research on the combined use of cannabis and alcohol has engendered two competing models of the cannabis–alcohol relation: *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, negative associations between cannabis use and alcohol use would be expected, whereas complementarity would invoke positive associations. Both substitutive and complementary patterns of alcohol and cannabis co-use have been observed in the extant literature (Risso et al., 2020; Subbaraman, 2016). Although some trends have emerged, such as the substitution of alcohol with cannabis under more lenient cannabis policies (Subbaraman, 2016), patterns of substitution versus complementarity have varied even across studies conducted within similar populations and legal contexts, obfuscating a clear tendency for either pattern (Risso et al., 2020; Subbaraman, 2016). This research is briefly reviewed below.

1.1.1. Between-person studies. Substitution and complementarity of alcohol and cannabis have been studied at both the aggregate population level (i.e., examining trends within the population rather than within individuals) and individual levels. At the aggregate level, policy studies have examined associations of cannabis- or alcohol-related policy with consumption (i.e., self-reported use, sales) or consequences (e.g., hospital admissions, fatalities) of the other substance. These studies have yielded mixed results (Risso et al., 2020), though with a slight tendency to support substitution (e.g., Baggio et al., 2020; Clements & Daryal, 2005; Kelly & Rasul, 2014; Mason et al., 2016). Similarly, economic relation studies have assessed whether increasing the price of one substance increases (substitution) or decreases (complementarity) demand for the other. Findings of this research have been mixed, (Risso et al., 2020), with some studies supporting substitution-only, others supporting complementarity-only, and still others supporting a combination of the two (Risso et al., 2020; Subbaraman, 2016).

Although policy and economic relation studies constitute the majority of the extant literature on substitution and complementarity, select studies have assessed cannabis use and alcohol use associations at the individual level (Risso et al., 2020). Specifically, these studies have examined correlations of individual differences in levels of cannabis use with individual differences in levels of alcohol use. Most of these studies have found evidence for complementarity (Risso et al., 2020), observing increased likelihood of alcohol use and related problems among those reporting cannabis use (e.g., Choi et al., 2018; Hammer & Vaglum, 1992). Others, similarly, have found increased likelihood of cannabis use among those reporting greater alcohol use (Pape et al., 2009).

1.1.2. Within-person studies. A major limitation of the extant literature on the direction of the association between cannabis and alcohol consumption is a relative dearth of research

examining substitution and complementarity at the within-person level. This is important, as despite often being generalized to encompass individual- and population-level associations between cannabis use and alcohol use (e.g., Risso et al., 2020), the very concepts of substitution and complementarity invoke a within-person process as the mechanism of these relations. Put simply, an individual is presumed to reduce (substitution) or increase (complementarity) their use of one substance during times when their use of the other substance is elevated (e.g., day-level associations). For instance, if an individual displayed a day-level pattern of use such that days during which they consume more cannabis correspond to days during which they consume less alcohol, a substitution effect at the day level would be supported. These types of within-person associations are not always evident through between-person studies (Curran & Bauer, 2011). For example, there may be a between-person association between cannabis use and alcohol use such that individuals who use cannabis more frequently overall tend to use alcohol more heavily overall, ostensibly supporting complementarity. However, an individual who uses large amounts of both cannabis and alcohol could still show a pattern of drinking relatively less heavily on days when their cannabis use is increased and vice versa, demonstrating a within-person substitution effect. In this example, generalizing the between-person complementarity effect to the individual would be an error of inference (Curran & Bauer, 2011), especially problematic given that substitution and complementarity fundamentally occur at the within-person level. Consequently, as between- and within-person associations may be discordant (Curran & Bauer, 2011), within-person analyses are especially critical when examining substitution and complementarity.

Despite the ubiquity of between-person analyses in examining cannabis and alcohol substitution and complementarity, 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 days relative to non-cannabis days among college students (Gunn et al., 2018; Ito et al., 2021), military veterans (Metrik, Gunn, et al., 2018), and community adults (Roche et al., 2019), supporting complementarity at the day level. Waddell et al. (2021), conversely, observed reduced drinking on cannabis days among veterans (indicative of substitution), though only for those low on specific domains of impulsivity.

Although informative, the day-level data for the aforementioned studies were obtained from retrospective interviews (e.g., Timeline Follow Back method), which may be prone to recall biases when assessing day-level co-use. 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). These studies have tended to observe a complementary relation or no relation between cannabis use on a given day and greater same-day alcohol consumption. However, these studies are limited in that they dichotomize cannabis use as present versus absent on a given day, and thus whether the quantities of cannabis and alcohol used 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 more 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 less alcohol relative to days when smaller quantities of cannabis are used (i.e., substitution). A recent study by Daros and colleagues (2022) examined the daily relation between the quantity of cannabis used (in grams) and the amount of alcohol consumed (in standard drinks), finding

support for complementarity in the amount of each substance used. However, this study also relied on retrospective reports of cannabis and alcohol use from Timeline Follow Back interviews, and thus there remains a need to apply daily diary and EMA methods to further investigate the daily associations between the quantities of cannabis and alcohol consumed to improve our understanding of the within-person processes involved in complementarity and substitution effects.

1.2. Medicinal and nonmedicinal reasons for cannabis use

Individual-level studies of cannabis and alcohol associations have predominantly focused on people who use cannabis nonmedicinally. Yet, a significant portion of individuals who use cannabis report medicinal motivations for use, including patient populations (such as people living HIV; Fogarty et al., 2007; Furler et al., 2004; Wardell et al., 2018), as well as those reporting cannabis use in the general population. For example, recent estimates suggest that 27.9% of young adults (ages 20 to 24 years) in Canada who use cannabis report medicinal reasons for use (Government of Canada, 2021a). Understanding the cannabis–alcohol relation among people who use cannabis for medicinal reasons is important given unique associations of medicinal reasons for cannabis use with both cannabis use and alcohol use patterns. With respect to cannabis use, data from the 2013 U.S. National Survey on Drug Use and Health demonstrated that adults reporting any past-year medicinal cannabis use used cannabis more frequently relative to those reporting exclusively nonmedicinal reasons for use (Lin et al., 2016). This finding has been replicated across several distinct populations, including adolescents (Wardell et al., 2021), people living with HIV (PLWH; Furler et al., 2004; Wardell et al., 2018), and veterans (Loflin et al., 2017). Moreover, studies have found that people who use cannabis for medicinal reasons, relative to people who use cannabis for exclusively nonmedicinal reasons, are more likely to

report using multiple routes of cannabis administration, in addition to smoking cannabis flower, such as eating and vaping cannabis (Mannes et al., 2018; Wardell et al., 2021).

In contrast to cannabis use, alcohol use is generally lower among adults reporting any medicinal reasons for cannabis use compared to those reporting exclusively nonmedicinal reasons for use (Lin et al., 2016; Loflin et al., 2017; Metrik, Bassett, et al., 2018; Wardell et al., 2018). These findings have been interpreted to suggest that the substitution of alcohol with cannabis is common among people using cannabis for medicinal reasons. Providing preliminary support for this interpretation, medical cannabis patients (i.e., people with medical authorization to purchase and use cannabis) across several studies have retrospectively reported using medical cannabis as a substitute for alcohol (Lucas et al., 2013, 2016; Lucas & Walsh, 2017; Piper et al., 2017). Alternatively, however, people who use cannabis medicinally may simply be more likely to exhibit cannabis–alcohol substitution given that the use of cannabis for medicinal reasons represents a different context (i.e., use for symptom management) than those in which alcohol use and nonmedicinal cannabis use typically co-occur (e.g., social settings, parties; Looby et al., 2021).

Most research on the cannabis–alcohol substitution effect among people using cannabis for medicinal reasons has only examined this effect at the between-person level. Yet, at the between-person level, designating medicinal and nonmedicinal cannabis use reasons as user characteristics imposes a false dichotomy (Gunn et al., 2022), wherein medicinal and nonmedicinal cannabis use reasons are presumed to be discrete constructs. Conversely, medicinal and nonmedicinal reasons for cannabis use are not mutually exclusive and may be endorsed concurrently. Indeed, most adults reporting medicinal cannabis use reasons also report nonmedicinal use (Turna et al., 2020; Wardell et al., 2018), rendering between-person

comparisons problematic. Thus, microlevel data are needed to establish whether among people reporting medicinal cannabis use motives, cannabis use and alcohol use each vary as a function of medicinal versus nonmedicinal cannabis use reasons across different occasions, according to a within-person pattern indicative of substitution (i.e., greater cannabis use and less alcohol use on medicinal use days relative to nonmedicinal use days).

Some preliminary work has begun to characterize patterns of cannabis and alcohol co-use among people reporting medicinal cannabis use at the within-person level. Namely, Gunn and colleagues (2019) found that veterans reporting medicinal cannabis use reasons consumed less alcohol on cannabis use days relative to those reporting exclusively nonmedicinal use reasons. Again, this study relied on retrospective reports of cannabis and alcohol use and did not measure cannabis use quantities, underscoring the need for examination of within-person patterns of co-use using daily diary and momentary assessments that incorporate quantities of cannabis used. The Gunn et al. study was also limited in that medicinal versus nonmedicinal reasons for cannabis use were specified only at the between-person level; consequently, the role of within-person variation in medicinal versus nonmedicinal reasons for cannabis use across different use occasions could not be ascertained.

If medicinal reasons for cannabis use invoke a substitution effect, which fundamentally is a within-person process, then three premises should be observed at the day level. First, more cannabis should be used on days when cannabis is used for medicinal versus nonmedicinal reasons, consistent with between-person findings of greater cannabis use among people who report medicinal (versus nonmedicinal) cannabis use (e.g., Lin et al., 2016; Wardell et al., 2021). 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 used on days when cannabis is used for medicinal versus nonmedicinal reasons, consistent with the between-person relation between medicinal use status and lower alcohol consumption (e.g., Lin et al., 2016; Loflin et al., 2017; Wardell et al., 2018). Third, increased cannabis consumption on medicinal use days should account for the day-level relation between medicinal reasons for cannabis use and reduced alcohol use, consistent with the substitution hypothesis. These premises, forming a mediation model wherein daily cannabis use quantities mediate the day-level association between medicinal cannabis use reasons and alcohol use, must be tested using daily diary or momentary assessments that capture daily variation in cannabis use and alcohol use, as well as in reasons for cannabis use. Support for this mediation model would suggest that medicinally-motivated cannabis use may confer lower risk for cannabis-alcohol co-use-related harms relative to cannabis use motivated by nonmedicinal reasons, which could inform medicinal cannabis policy.

1.3. The present study

The present study aimed to examine whether there is evidence for a within-person process underlying the cannabis-alcohol substitution effect among individuals using cannabis for medicinal reasons. We conducted a secondary analysis on day-level data from participants who reported both medicinal and nonmedicinal reasons for cannabis use. We examined day-level relations among medicinal versus nonmedicinal reasons for cannabis use and amounts of both cannabis and alcohol used. Consistent with the substitution hypothesis, we expected that relative to days during which participants reported using cannabis for exclusively nonmedicinal reasons, days during which they reported using cannabis for medicinal reasons would be associated with greater cannabis use, and in turn, lower alcohol use.

2. Method

2.1. 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 = 29) were recruited from across Canada using social media ads and fliers distributed to community agencies that serve PLWH. All 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) diagnosis of HIV received at least one year ago; (iv) current antiretroviral treatment; and (v) access to a compatible smartphone (Android or iOS). Exclusion criteria were: (i) heavy 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 (N = 155). Participants were recruited from across Ontario, Canada using online ads, social media posts, and fliers posted in the community and on university campuses. Although this study did not specifically recruit for medicinal cannabis use, n = 37 (23.87%) 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.[1]

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 27.79% and 31.81%, respectively. Characteristics of participants in both samples are provided in Table 1.

2.2. Procedure and measures

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.

2.2.1. 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 showed participants how to install the EMA

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

app (MetricWire, Inc., Waterloo, ON) on their mobile phone and provided participants with an orientation 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 drink units). At the end of the visit, participants were emailed a link to complete an online questionnaire, including cannabis- and alcohol-related measures used to characterize the sample of the current study. In both studies, participants were compensated with $40 CAD (cash or electronic gift card) for the baseline assessment.

2.2.2. Baseline measures

2.2.2.1. Demographic characteristics. Participants reported on age, assigned sex at birth, gender, race/ethnicity, highest level of education, and household income.

2.2.2.2. Cannabis use. Participants completed the Cannabis Use Disorder Identification Test–Revised (CUDIT-R; Adamson et al., 2010), 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 frequency of cannabis use (ranging from not at all to multiple times per day) and typical number of grams of cannabis flower used (per session, per day, and per week) were assessed. Participants also reported on the symptoms that they used cannabis to manage in the past six months (e.g., anxiety, pain, depression, headaches) and whether they had current and lifetime valid medical authorization for cannabis use.

2.2.2.3. 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.

2.2.3. 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. However, 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 2-5-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)[2]. 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?"*

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

(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 to allow for modelling as a count outcome in subsequent analyses. 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 compensated between $40 CAD and $115 CAD in cash or electronic gift cards for completion of the EMA (depending on the study), with increasing compensation provided for better compliance with the prompted surveys.

2.3. Data analysis

In the combined dataset, a total of 1065 daily morning surveys were fully completed across the 66 participants (n = 29 from Study 1, n = 37 from Study 2). The overall completion rate for daily morning surveys was 90.51% (93.35% Study 1, 88.29% Study 2). Given that this study aimed to examine within-person differences in cannabis use and alcohol use as a function of medicinal versus nonmedicinal reasons cannabis use, only daily surveys on which previous day cannabis use was reported were included (751 observations).

To examine the direct and indirect day-level associations among reasons for cannabis use (independent variable), amount of cannabis used (mediator), and amount of alcohol consumed (dependent variable), multilevel mediation models were specified using Mplus version 8 (Muthén & Muthén, 2021), wherein days (level 1) were nested within participants (level 2). Models were specified using syntax from Preacher et al. (2010) for unconflated 1-1-1 mediation, describing a mediation model wherein within- and between-person variance in variables are disaggregated. Number of standard drinks consumed each day was specified as the dependent variable and was regressed on both the mediator (amount of cannabis used) and independent

(reasons for cannabis use) variables to allow for partial mediation. As there were many non-drinking days (477, 63.52%) in our data, the standard drinks variable was specified as a count outcome using a zero-inflated Poisson model. This approach yields two sets of parameter estimates for predictors of standard drinks: (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 medicinal-only days were combined due to few medicinal-only days (74, 9.85%). The mediator, daily amount of cannabis used, was operationalized in two ways: (1) the number of different types of cannabis (e.g., cannabis flower, concentrates, edibles) used in a given day (including all 751 cannabis days), with 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[3]). 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 (some of which may be more commonly used for medicinal reasons such as oils); that is, additional types of cannabis products may be used in combination with one another or with cannabis flower 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

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

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.

Level 1 (i.e., day-level) covariates included weekend (Friday–Sunday, coded 1) versus weekday (Monday–Thursday, coded 0) in both models (predicting both cannabis use and alcohol use), and the use of any non-flower forms of cannabis (1 = yes, 0 = no) in the model with grams of cannabis used as the mediator (predicting alcohol use). Level 2 (i.e., person-level) covariates included age, sex, and sample (1 = Study 2, 0 = Study 1) in both models, and we also controlled for proportion of non-flower cannabis use days in the model with grams of cannabis used as the mediator. Standard drinks were regressed on all between-person covariates, and amount of cannabis used was regressed on all between-person covariates except for proportion of non-flower cannabis use days. To disaggregate within-person and between-person variance, all level 1 predictors and covariates were person-mean centered, and person-level means were grand-mean centered and included at level 2. The level 2 variable for medicinal versus nonmedicinal reason for cannabis use reflected the proportion of medicinal cannabis use days for a given participant. Person-mean centering level 1 categorical predictor variables and grand-mean centering person means of level 1 variables at level 2 is necessary to yield unconflated parameter estimates that disaggregate within- and between-person effects (Enders & Tofighi, 2007; Yaremych et al., 2021).

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 each random slope on a sample indicator (Study 1 versus Study 2), one by one, to determine whether sample moderated any path in the model.

Models were fit using maximum likelihood estimation with robust standard errors 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). Code for all analyses is publicly available at https://osf.io/mrn35/.

3. Results

3.1. 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 at least one other form 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 descriptive statistics of day-level data are provided in Table 1. 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 reasons for use are provided in Table 2.

3.2. Multilevel mediation models

3.2.1. 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 (ΔAIC, ΔBIC, and ΔSSA-BIC $\geq$ -0.62).

Figure 1A displays the main results of the multilevel mediation model, and Table 3 provides all parameter estimates in 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 that participants used more types of cannabis they were more likely to initiate drinking. In addition, using cannabis for medicinal (versus nonmedicinal-only) 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]). At the between-person level, no direct effects or indirect effects (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]) were statistically significant.

3.2.2. Grams of cannabis flower used

Sample was also not significantly associated with any of the random slopes, suggesting that within-person associations did not differ between samples (i.e., sample did not moderate any paths in the model), 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 (ΔAIC, ΔBIC, and ΔSSA-BIC ≥ -2.68) relative to a model with fixed slopes only. Thus, the random slopes were removed for parsimony.

Figure 1B displays the main results of the multilevel mediation model and Table 4 provides all parameter estimates in 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 nonmedicinal-only) 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 statistically significant (*B* = -0.031, *SE* = 0.014, 95% CI [-0.060, -0.001]), such that using cannabis for medicinal (versus nonmedicinal-only) reasons was associated with using fewer grams of cannabis flower, and in turn, consuming fewer standard drinks, at the day level. At the between-person level, no direct effects or indirect effects (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]) were supported.

4. Discussion

Given the established harms associated with the 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 relation 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 for both medicinal and nonmedicinal reasons. This study extends previous retrospective and EMA studies, which have modelled only the presence versus absence of cannabis use at the day level (e.g., Mallett et al., 2019; O'Hara et al., 2016), by modelling the amount of cannabis used (i.e., number of different types of cannabis used and grams of cannabis flower used). This approach allowed for a more comprehensive examination of substitution and complementarity with respect to associations between amounts of cannabis and alcohol consumed. This study is also the first to examine the role of within-person variation in medicinal versus nonmedicinal reasons for cannabis use in day-level patterns of both cannabis use and alcohol use. Overall, analyses revealed reduced cannabis use and reduced alcohol use on days when cannabis was used for medicinal (versus nonmedicinal) reasons. As analyses controlled for weekend versus weekday, this finding is more than just an artefact of recreational reasons for substance use being more likely on weekends, during which both cannabis and alcohol may be used in greater quantities. Alcohol use was also increased on days involving greater amounts of cannabis use, regardless of reason for cannabis use, suggesting a complementary cannabis-alcohol relation. Moreover, in models operationalizing cannabis use amount as grams of cannabis flower used, the day-level association of medicinal (versus nonmedicinal) reasons for cannabis use with lower alcohol consumption was mediated by using fewer grams of cannabis. Together, findings provide new insight into within-person processes involved in the cannabis-alcohol link among people who use cannabis for medicinal reasons.

It was hypothesized that medicinal reasons for cannabis use would invoke a cannabis–alcohol substitution effect at the day level, which would involve the following: (1) increased cannabis use on days when cannabis is used for medicinal versus nonmedicinal reasons; (2)

reduced alcohol use on days when cannabis is used for medicinal versus nonmedicinal reasons; (3) increased cannabis use on medicinal use days accounting for the day-level association between medicinal reasons for cannabis use and reduced alcohol use. Contrary to hypotheses, there was a negative day-level association between medicinal reasons for cannabis use and amount of cannabis used. Specifically, participants used fewer grams of cannabis flower on days during which they reported medicinal reasons for cannabis use, compared to days during which they reported exclusively nonmedicinal reasons for use. This is in contrast to between-person analyses in the extant literature that have found associations of medicinal reasons for cannabis use with *greater* amounts of cannabis use (Lin et al., 2016; Loflin et al., 2017; Wardell et al., 2018, 2021). This illustrates the potential for discordance between within-person and between-person associations (Curran & Bauer, 2011); that is, although people who use cannabis for medicinal reasons may use more cannabis overall than people who use cannabis for nonmedicinal reasons, they may still use relatively less cannabis on days during which they are using specifically for medicinal reasons compared to days during which they are using exclusively for nonmedicinal reasons. It is possible that the greater cannabis use observed among people reporting medicinal reasons for cannabis use is instead attributable to using cannabis more frequently relative to people reporting exclusively nonmedicinal reasons for use. Indeed, previous research has observed greater frequency of cannabis use among people reporting medicinal reasons for cannabis use (Woodruff & Shillington, 2016). Alternatively, it may be that for a large proportion of people who use cannabis for medicinal reasons, medicinal cannabis use is an adjunct to baseline levels of nonmedicinal cannabis use that mirror the levels of cannabis use observed among people who use for nonmedicinal reasons. This interpretation, though speculative, further illustrates the substantial overlap of medicinal and nonmedicinal cannabis

use at the individual level, underscoring the need for additional empirical research characterizing medicinal versus nonmedicinal reasons for cannabis use at the day or event level.

Interestingly, although medicinal (versus nonmedicinal) reasons for cannabis use were significantly associated with using fewer grams of cannabis flower at the day level, there was no significant day-level association of reason for cannabis use with number of different types of cannabis used, suggesting that reduced use of cannabis flower on medicinal use days is not offset by increased consumption of other forms of cannabis. Indeed, medicinal and exclusively nonmedicinal cannabis use days involved an average of 1.17 and 1.15 different types of cannabis used, respectively. This contrasts with previous between-person analyses which have found that people who use cannabis for medicinal reasons use a wider range of cannabis products relative to those who use for nonmedicinal reasons (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 although people who use cannabis for medicinal reasons may use a wider range of cannabis products overall, additional cannabis products may not be used specifically for medicinal reasons but may rather be a function of heavier cannabis use overall. Thus, further work examining specific types of cannabis used in relation to medicinal versus nonmedicinal reasons for cannabis use at the day level is needed.

Although the hypothesized increase in cannabis use on medicinal use days was not observed, there was some support for the hypothesized day-level association between medicinal reasons for cannabis use and reduced alcohol use. Specifically, in our model that included all cannabis use days, medicinal reasons for cannabis use (compared to exclusively nonmedicinal

reasons for use) were directly associated with reduced likelihood of initiating drinking at the day level. This 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, Bassett, et al., 2018; Roy-Byrne et al., 2015; Wardell et al., 2018). Taken together, findings indicate that that people who use cannabis for medicinal reasons may not only be lighter drinkers overall relative to those who use cannabis for exclusively nonmedicinal reasons, but also that this phenomenon may be explained by abstaining from using alcohol on medicinal cannabis use days, specifically. This may be because the use of cannabis for medicinal reasons represents a context in which alcohol use would not be harmful. For example, when reporting medicinal reasons for cannabis use, individuals may be using cannabis to alleviate symptoms such as nausea or appetite loss (Wardell et al., 2022), which may be exacerbated by alcohol use. In contrast, cannabis may be used nonmedicinally in contexts where alcohol use is common (e.g., social settings, parties). This explanation, however, remains speculative, as specific contexts in which medicinal and nonmedicinal cannabis use events occurred were not assessed in our daily surveys. Studies that include event-level assessments of cannabis use reasons and context are needed.

Importantly, among our sample of people reporting medicinal reasons for cannabis use, alcohol and cannabis were complements at the day level across different operationalizations of cannabis consumption. Specifically, using a greater number of different types of cannabis was associated with an increased likelihood of initiating alcohol use, and using more grams of cannabis flower 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 relation, which have largely supported day-level complementarity of cannabis and alcohol (Lee

et al., 2020; O'Hara et al., 2016). The present study extends the results of these studies by demonstrating that greater cannabis use quantities, and not just cannabis use initiation, are associated with increased alcohol use at the day level. On the other hand, our findings of cannabis–alcohol complementarity among people reporting medicinal reasons for cannabis use contradict the notion that people who use cannabis medicinally may use cannabis as a substitute for alcohol (e.g., Lucas et al., 2013; Lucas & Walsh, 2017). Rather, our results suggest that although people reporting medicinal reasons for cannabis use may use more cannabis and less alcohol overall relative to people reporting exclusively nonmedicinal reasons for use, they may still increase their alcohol use on days during which cannabis use is elevated (and vice versa). Initiating or increasing cannabis use, whether for medicinal or nonmedicinal reasons, may thereby serve to increase alcohol use, in contrast to the common notion that cannabis is a harm-reducing alternative to alcohol (e.g., Lau et al., 2015; Mikuriya, 2004; Reiman, 2009; Siklos-Whillans et al., 2021).

Moreover, day-level alcohol-cannabis complementarity may confer an increased likelihood of same-day alcohol-cannabis co-use, which is associated with greater harms relative to cannabis use or alcohol use alone. Indeed, in between-person studies, cannabis-alcohol co-use is associated with using more of each substance and with greater risk for cannabis and alcohol use disorders, mental health problems (e.g., depression, anxiety), and social and behavioural consequences (Yurasek et al., 2017). Similarly, daily diary and EMA studies have found cannabis–alcohol co-use to be associated with increased negative consequences in both social (e.g., acting rude or obnoxious, sexual risk-taking) and physical (e.g., hangovers, nausea, fainting or passing out) domains (Lee et al., 2020; Linden-Carmichael et al., 2020; Mallett et al., 2019). Our findings of cannabis-alcohol complementarity suggest that people who use cannabis

medicinally could still be at risk of harms associated with co-use should complementarity invoke increased simultaneous or concurrent cannabis and alcohol use.

Further contradicting the notion that cannabis–alcohol substitution underlies the reduced alcohol use observed among people reporting medicinal reasons for cannabis use, results provided evidence for a complementarity process in this association at the day level. In other words, it was the tendency to consume *fewer* grams of cannabis flower on days when cannabis was used for medicinal reasons that accounted for the within-person relation between medicinal reasons for cannabis use and reduced amount of alcohol used. The pattern of complementarity observed in relation to medicinal reasons for cannabis use may suggest a protective effect of using cannabis for medicinal reasons. That is, medicinal reasons for use were associated with reduced use of *both* cannabis and alcohol at the day level, and in turn, may involve lower cannabis- and alcohol-related risk. That said, using cannabis for medicinal reasons, exclusively, is rare. Our sample of people who use cannabis medicinally still reported many *non*medicinal cannabis use days. In contrast to medicinal cannabis use days, participants used more grams of cannabis flower on days when cannabis was used for exclusively nonmedicinal reasons, and in turn, increased their alcohol consumption. Nonmedicinal use days may thereby confer harms associated with cannabis–alcohol co-use among people who use cannabis medicinally. Our findings suggest that for people who use cannabis medicinally who are aiming to reduce their cannabis use or alcohol use, reducing their number of nonmedicinal cannabis use days may be effective, circumventing the need to reduce or eliminate cannabis used to manage physical or psychological symptoms. Moreover, interventions for cannabis and alcohol use should include tailored content for medicinal and nonmedicinal cannabis use occasions, as these reasons for use may be associated with different levels of risk for the same person across different contexts.

4.1. Limitations

The results of this study should be interpreted in the context of its limitations. First, although our sample of $N = 66$ provided ample daily observations for within-person analyses (i.e., 751 cannabis use days), there was limited power to examine associations at the between-person level. Given that within-person analyses are rarer in studies of substitution and complementarity of cannabis and alcohol, our focus was on within-person rather than between-person associations. Still, analyses were underpowered to examine person-level moderators of associations such as demographic and health-related variables, which should be examined in future larger studies. In particular, given sex differences in both cannabis use and alcohol use (Calakos et al., 2017; Salvatore et al., 2017), future larger studies should examine whether associations observed in the current study may be moderated by sex.

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 relation, future EMA studies are needed in which measurement of cannabis quantity is standardized across different forms of cannabis, for example using the recently introduced "standard THC units" (Freeman & Lorenzetti, 2020, 2021). Third, 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. Fourth, this study did not examine the sequence of cannabis use 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 of each substance (Gunn et al., 2021). Fifth, no participants in the present study reported heavy episodic drinking on three or more days per week. Consequently, findings of the

present study may not generalize across the full spectrum of alcohol use, and future studies should examine daily cannabis-alcohol associations among individuals engaging in heavier alcohol use.

An additional limitation is that although day-level data meaningfully improve the ability to disentangle medicinal versus nonmedicinal reasons for cannabis use relative to designating these reasons as between-person characteristics, a large proportion of cannabis use days involved both medicinal and nonmedicinal reasons for use. Thus, there is a need for future studies measuring medicinal versus nonmedicinal reasons for cannabis use in relation to cannabis use and alcohol use quantities at the event level (i.e., individual cannabis use events). Worth noting, however, is that a previous analysis of event-level data from Study 1 found that even within a single event, participants regularly reported both medicinal and nonmedicinal reasons for use (Wardell et al., 2022). It may thus be the case that medicinal and nonmedicinal reasons for cannabis use cannot be fully disentangled, even at the event level. Future research may assess reasons for cannabis use dimensionally (i.e., the degree to which cannabis use events are perceived as medicinal versus nonmedicinal), rather than as discrete categories.

4.2. Conclusions

In conclusion, this study demonstrated that among people who use cannabis for both medicinal and nonmedicinal reasons, alcohol and cannabis act as complements at the day level in that the amount of cannabis used on a given day is positively associated with the amount of alcohol used on the same day. In addition, medicinal reasons for cannabis use were associated with reduced cannabis use, and in turn, reduced alcohol use at the day level. Findings suggest that although medicinal cannabis use days may involve lower alcohol use relative to exclusively nonmedicinal cannabis use days, this is due to an underlying complementary relation between

cannabis and alcohol, rather than a substitutive relation. Consequently, people who use cannabis for medicinal reasons versus exclusively nonmedicinal reasons may still be at risk of experiencing harms associated with cannabis–alcohol co-use during days when they use cannabis for nonmedicinal reasons. Future work is needed to determine the utility of interventions selectively targeting nonmedicinal cannabis use events among the large proportion of people who use cannabis medicinally who engage in concurrent nonmedicinal use, which may be more likely to involve cannabis-alcohol co-use.

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Table 1. Person-level descriptive statistics

	Study 1 (*N* = 29)	Study 2 (*N* = 37)	Combined (*N* = 66)
	M (SD) or *n* (%)	M (SD) or *n* (%)	M (SD) or *n* (%)
Age	46.69 (10.77)	22.27 (2.17)	33.00 (14.20)
Sex			
Male	23 (34.84)	12 (18.18)	35 (53.03)
Female	6 (9.09)	25 (37.88)	31 (47.00)
Gender			
Man	22 (75.86)	13 (35.14)	35 (53.03)
Woman	6 (20.69)	23 (62.16)	29 (43.94)
Non-binary	0 (0)	1 (2.70)	1 (1.52)
Two-Spirited	1 (3.45)	0 (0)	1 (1.52)
Race/ethnicity			
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[b]			
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[b]	9.86 (5.03)	11.81 (5.92)	10.97 (5.60)
Met CUDIT-R threshold for hazardous use (yes)[b]	17 (60.71)	26 (70.27)	43 (65.15)
AUDIT score	12.14 (8.39)	8.76 (5.24)	10.24 (6.95)
Met AUDT threshold for hazardous use (yes)	20 (68.97)	20 (54.05)	40 (60.61)
DFAQ-CU current cannabis use frequency[c]			
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)
DFAQ-CU grams rams of cannabis flower used in a typical day	1.24 (1.16)	0.54 (0.52)	0.85 (0.92)
DFAQ-CU grams rams of cannabis flower used in a typical week	9.29 (11.59)	3.04 (3.04)	5.79 (8.53)

Proportion of EMA days on which medicinal[d] reasons for use were reported (%)	75.90 (31.16)	42.82 (31.74)	58.72 (35.53)
Person-level mean grams of cannabis flower used during EMA period	1.01 (1.14)	0.50 (0.46)	0.74 (0.89)
Person-level mean number of standard drinks consumed during EMA period	1.20 (1.63)	1.23 (1.08)	1.22 (1.37)
Person-level mean number of different cannabis types used during EMA period	1.19 (0.27)	1.14 (0.19)	1.17 (0.23)
Current valid medical authorization for cannabis use (yes)	17 (58.62)	2 (5.41)	19 (28.79)
Lifetime valid medical authorization for cannabis use (yes)	19 (65.52)	2 (5.41)	21 (31.81)
Symptoms treated using cannabis			
Anxiety	20 (68.97)	23 (62.16)	43 (65.15)
Pain	17 (58.62)	13 (35.14)	30 (45.45)
Stress	19 (65.52)	22 (59.46)	41 (62.12)
Insomnia	20 (68.97)	21 (56.76)	41 (62.12)
Depression	11 (27.93)	16 (43.24)	27 (40.91)
Appetite	17 (58.62)	12 (32.43)	29 (43.94)
Headaches	5 (17.24)	9 (24.32)	14 (21.21)
Nausea	9 (31.03)	4 (10.81)	13 (19.70)
Muscle spasms	5 (17.24)	3 (8.11)	8 (12.12)
HIV/AIDS	19 (65.52)	0 (0)	19 (28.79)
Other	2 (6.90)	1 (2.70)	3 (4.54)

Note: Study 1 = people living with HIV, Study 2 = young adults; AUDIT = Alcohol Use Disorder Identification Test; CUDIT-R = Cannabis Use Disorder Identification Test; DFAQ-CU = Daily Sessions, Frequency, Age of Onset, and Quantity of Cannabis Use Inventory; EMA = ecological momentary assessment.

[a]Four young adults declined to respond.

[b]One person living with HIV 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.

[d]Medicinal cannabis use days included days on which both medicinal and nonmedicinal reasons for use were reported.

Table 2. Day-level descriptive statistics for medicinal use and nonmedicinal use days

	Medicinal Use Day (441)	Nonmedicinal Use Day (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 3. Parameter estimates for multilevel mediation model examining number of cannabis types used as a mediator in the association between cannabis use reason (medicinal vs. nonmedicinal-only) and alcohol use

Level		Estimate	OR	SE	*p*
Within					
	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. nonmedicinal-only)	**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. nonmedicinal-only)	-0.254		0.133	.057
	Weekend (vs. weekday)	**0.376**		**0.104**	**.000**
Between					
	DV: Number of cannabis types used				
	Cannabis use reason (medicinal vs. nonmedicinal-only)	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. nonmedicinal-only)	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. nonmedicinal-only)	-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. nonmedicinal-only) 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.

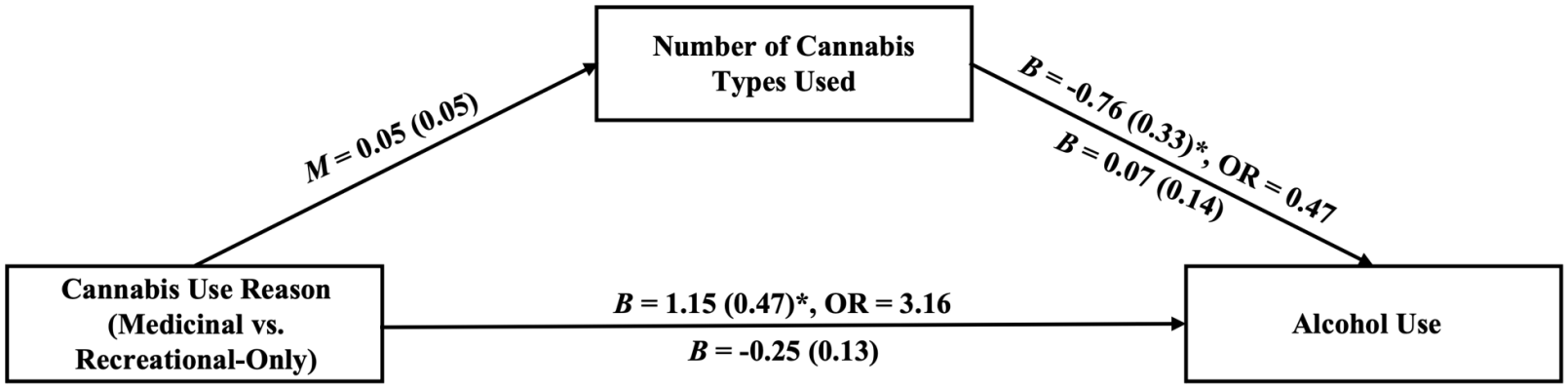
Table 4. Parameter estimates for multilevel mediation model examining grams of cannabis flower used as a mediator in the association between cannabis use reason (medicinal vs. nonmedicinal-only) and alcohol use

Level		Estimate	OR	SE	*p*
Within					
	DV: Grams of cannabis flower used				
	Cannabis use reason (medicinal vs. nonmedicinal-only)	**-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. nonmedicinal-only)	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. nonmedicinal-only)	-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					
	DV: Grams of cannabis flower used				
	Cannabis use reason (medicinal vs. nonmedicinal-only)	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. nonmedicinal-only)	-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-cannabis-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. nonmedicinal-only)	-0.215		0.239	.368
	Age	-0.168		0.177	.343
	Sex	0.140		0.182	.444
	Use of non-cannabis-flower forms of cannabis	0.214		0.219	.329
	Sample	-0.157		0.508	.758

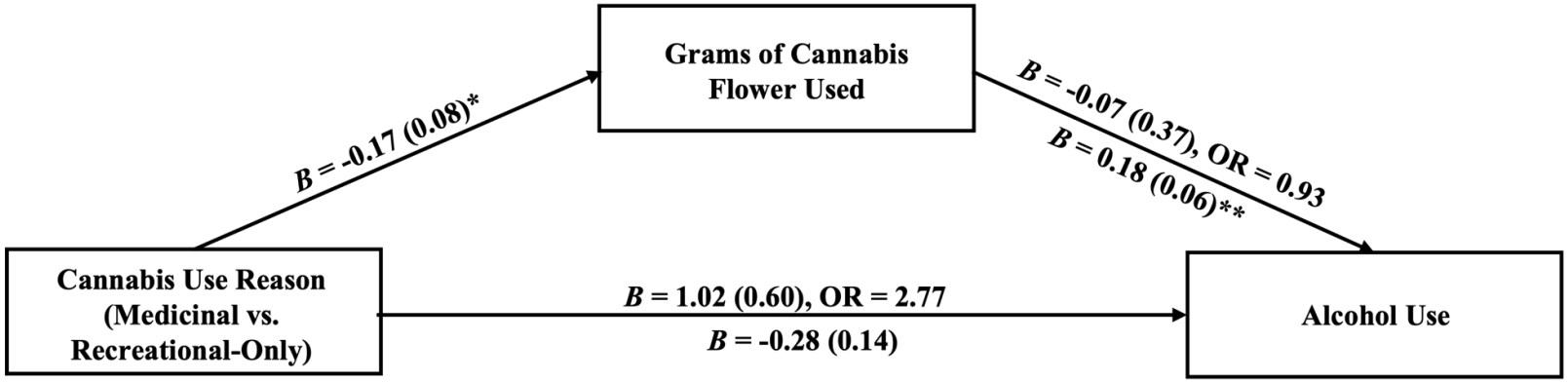
Note: All variables at the within-person level are person-mean centered, and all variables at the between-person level are grand-mean centered person means. OR = odds ratio; DV = dependent variable.

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 day 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. nonmedicinal-only) 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 in model B.
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$