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Ordering in alcohol and cannabis co-use: Impact on daily consumption and consequences

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ABSTRACT

Background: Co-use of alcohol and cannabis is highly prevalent among young adults and college students. Between-person reports suggest that co-use is associated with the experience of more frequent consumption and related consequences, compared to single substance use. However, recent studies have found conflicting evidence regarding the impact of co-use use on consumption and consequences in daily or event-level investigations. Conflicting evidence may be due to understudied factors, such as the order in which alcohol and cannabis are used. The current study aimed to examine the effect of substance use order on a) alcohol consumption; b) cannabis consumption; and c) negative alcohol and cannabis consequences.

Methods: Data were collected from U.S. undergraduate college student alcohol and cannabis users (N = 258) who completed two 28-day longitudinal online assessment bursts examining alcohol and cannabis co-use patterns. Data were collected five times per day during both bursts (three months apart).

Results: Controlling for between-person alcohol and cannabis use, within-person mixed-effects models indicated that using cannabis first within a co-use day was associated with lower daily alcohol consumption, but greater daily cannabis consumption. Substance use ordering was not linked to consequences, whereas between-person levels of alcohol consumption and within-person number of drinks in a day were positive predictors of consequences.

Conclusions: Overall, results highlighted that order of substance use is a robust predictor of consumption on co-use days. Therefore, future research on co-use use should consider patterns of use in addition to level of use.

1. Introduction

Alcohol and cannabis are among the most commonly used substances among college students and young adults in the U.S. (Center for Behavioral Health Statistics and Quality, 2016; Midanik et al., 2007; Schulenberg et al., 2018). Concomitant increases in legalization of recreational cannabis and rates of cannabis use among young adults and college students (Schulenberg et al., 2018; Substance Abuse and Mental Health Services Administration, 2019) highlight the importance of examining the impact of alcohol and cannabis co-use on consumption and consequences. The need for this research is reflected by recent national and multi-campus surveys suggesting one quarter of college students report past-year simultaneous use of alcohol and cannabis (i.e., use of both substances together, so that the effects overlap) (Terry-McElrath and Patrick, 2018) and three-quarters of alcohol- and cannabis-using college students report past-year simultaneous use (White et al., 2019). College students who use alcohol and cannabis report a number of academic and social consequences from their use (Arria et al., 2008; Caldeira et al., 2008; Merrill and Read, 2010; Schulenberg and Patrick, 2012). Moreover, regarding alcohol specifically, college students consistently show higher rates of use and associated consequences, compared to their age-matched non-college attending peers (Blanco et al., 2008; Linden-Carmichael and Lanza, 2018; Slutske, 2005; Slutske et al., 2004). In studies comparing co-users to single substance users, co-users (in some cases simultaneous users specifically) reported more frequent negative substance-related consequences (Brière et al., 2011; Midanik et al., 2007; Subbaraman and Kerr, 2015; Yurasek et al., 2017). Results from a study using timeline follow-back interviews found that

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using cannabis (versus no cannabis use) was associated with higher levels of alcohol use in the same day (Metrik et al., 2018). Another study of college students revealed that using cannabis and alcohol on the same day was associated with increased alcohol use, and heavier use of cannabis in a single week was associated with more alcohol-related consequences (Gunn et al., 2018).

Recent event-level studies provide conflicting evidence and suggest that cannabis use may not consistently increase alcohol consumption or negative consequences. For instance, a recent ecological momentary assessment (EMA) study of adolescents found that co-use occasions were associated with higher likelihood of consequences, but these consequences could be largely attributed to the number of drinks consumed within an occasion (Lipperman-Kreda et al., 2017). In another event-level study examining consequences occurring on alcohol, cannabis, and simultaneous use days among college students, results suggested that using cannabis on heavy drinking days did not carry increased risk of consequences compared to heavy alcohol-only days (Mallett et al., 2019). In addition, recent work from our group suggests that number of drinks on a co-use occasion was the strongest predictor of number of daily consequences experienced (Sokolovsky et al., 2020). Conflicting findings may be due to understudied factors, such as the order in which substances are consumed and how between-person differences in alcohol or cannabis use (e.g., individual patterns of use) as well as within-person deviations from that pattern or other event- or day-level factors may impact use-related outcomes. Although no studies thus far have examined the impact of the order in which alcohol and cannabis are used within a co-use day on consequences, there is often informal wisdom among users regarding the impact of order of use. For example, colloquially, co-users tend to associate worse outcomes (e.g., nausea, dizziness, vomiting) when using cannabis after alcohol, whereas they anticipate fewer consequences when cannabis is used first (e.g., "grass before beer, you're in the clear").

Controlled laboratory studies often examine combined effects of alcohol and cannabis using a specific order of administration, where fixed alcohol doses are administered prior to fixed doses of cannabis when participants are at peak breath alcohol concentration. Findings from these studies suggest that combined administration reduces peak plasma ethanol levels and delays time to peak, but increases blood Δ-9 tetrahydrocannabinol (THC) levels, positive subjective effects, and subjective impairment (Downey et al., 2013; Hartman et al., 2016, 2015; Lukas et al., 1992; Lukas and Orozco, 2001; Perez-Reyes et al., 1988). These multiplicative intoxicating effects are confirmed with self-report data from young adult co-users and may contribute to increased risk associated with co-use (Lee et al., 2017). In one study where a very low dose of oral THC was administered with alcohol such that peak THC levels would coincide with peak ethanol levels, ratings for "wanting" more alcohol were attenuated relative to THC alone (Ballard and De Wit, 2011), suggesting robust interaction effects from combined administration of alcohol and cannabis. One study found low to moderate doses of alcohol did not influence subsequent cannabis self-administration among regular cannabis users (Chait and Perry, 1992). Preliminary data from another placebo-controlled laboratory study suggested that cannabis acutely decreases subsequent alcohol consumption (Metrik et al., 2019). However, no other studies to our knowledge have examined the effects of order of administration of one substance on self-administration of the other substance. Further, no naturalistic studies have compared the order in which alcohol and cannabis are used and its impact on consumption or consequences within the same day.

1.1. Current study

Given the high rates of alcohol and cannabis co-use (and corresponding negative acute public health harms) in college students (Jackson et al., 2020; O'Hara et al., 2016), we targeted a robust sample of undergraduate students for the present study. Specifically, we used daily-level data collected from college students to examine the effect of order (i.e., alcohol or cannabis first) in a co-use day on: a) alcohol consumption, b) cannabis consumption, and c) negative alcohol- and cannabis-related consequences. Given preliminary laboratory work suggesting THC may attenuate alcohol craving (Ballard and De Wit, 2011), we hypothesized that using cannabis first would result in less same-day alcohol use, more cannabis use, and fewer consequences. However, given recent event-level data suggesting that amount of alcohol consumption predicts consequences over and above co-use (Lipperman-Kreda et al., 2017; Mallett et al., 2019; Sokolovsky et al., 2020), we did not anticipate that order would uniquely predict consequences when number of drinks per day was also accounted for.

2. Methods

2.1. Procedures

2.1.1. Screening

Undergraduate students were recruited to participate in a two-wave longitudinal study on alcohol and cannabis use. Recruitment targeted three state universities in states with different recreational cannabis-use laws; medical use of cannabis was legalized in all states. Recreational cannabis use was criminalized in School A's state; illegal but decriminalized at School B's state; and legal (for adults age 21+) at School C's state. We randomly selected 8000 undergraduate students age 18–24 from each university's registrar database (stratified by anticipated graduation year; total $N = 24{,}000$) to e-mail online screening survey invitations. The invitation explained that the study was about alcohol and cannabis use but that the student did not have to use alcohol or cannabis to participate in the screening survey. Eligibility criteria for the baseline survey included: (1) full-time enrollment at one of the universities; (2) age 18–24 years; (3) past-year alcohol and cannabis use, and (4) verified e-mail address (see White et al., 2019 for details on recruitment and representativeness). Of 7000 screening responses, 2874 (41.1 %) met eligibility criteria. Participants were incentivized with a lottery to win a $100 Amazon.com gift card (10 per campus).

2.1.2. Baseline survey

A sample of 2501 eligible students (approximately evenly divided by school to ensure equal representation) were e-mailed invitations to participate in the baseline survey (before the daily component of the study began). In selecting this 2501, we oversampled for past-month alcohol and cannabis use to ensure enough students would be eligible for the subsequent daily survey phase. Of invitees who provided consent and were enrolled into the study ($N = 1610$), we retained 1390 participants (86.3 %) in the baseline sample; participants who provided baseline data inconsistent with eligibility criteria (and thus inconsistent with their own screening information) and those with technical issues were excluded from the study. Inconsistencies included no longer reporting past-year alcohol and/or cannabis use, falling outside the eligible age-range of 18–24, and no longer attending one of the three universities full-time. Compensation for the baseline survey was a $25 Amazon gift card. (For greater detail on the baseline survey, see Stevens et al., 2020 Supplemental Material.) Demographic data (e.g., race/ethnicity, sex, age, and class status) were also collected in the baseline survey.

2.1.3. Daily surveys

Students who reported past-month use of alcohol and cannabis "at the same time so their effects overlapped" at baseline were eligible for the daily phase of the study. These potential participants were sampled by frequency of past-month co-use occasions (i.e., 1–2 times versus 3+ times representing infrequent and frequent co-use, respectively) and sex (assigned at birth) to ensure heterogeneity, with a generally equal number of students invited from each school. Of students given access to the daily application ($n = 379$), 343 accepted (90.5 %); two students discontinued data collection during the first two days and were excluded

from further analyses, resulting in a final sample of 341 who completed the daily surveys. A flowchart depicting screening into the daily surveys is available in Supplemental Materials (Fig. S2). For these daily surveys, participants completed a 26-day (the first two days were deleted due to technical issues) burst of intensive longitudinal experience sampling comprising five daily surveys delivered via a custom-developed smartphone application. Three months later, 316 students (92.7 % of the first burst) completed a second 28-day burst. Participants were compensated $1 for each completed survey (up to $5 per day/$35 per week) with potential bonuses of $10 each week if they completed 85% of surveys for that week, $20 at the end of 4 weeks if they completed 90% of surveys, totaling $200 maximum (Amazon gift cards) per burst.

Daily surveys were predictably scheduled (9:00am; 2:00pm; 5:00pm; 8:00pm; 11:00pm). Surveys remained active for two hours (five hours for 9:00am survey). Each survey asked about behavior from the exact time that the last survey was completed (including up to one missed survey) until the time that the current survey was completed (except in the case of two missed surveys in a row, in which case the current survey would use the scheduled time of the previous survey as the first time anchor). For full details on missed surveys, see supplemental material in Stevens et al. (2020). Survey completion took approximately 1−2 min with an additional 2−3 min for the morning survey (triggered at 9:00am) because this survey contained two parts: (1) a daily survey assessing prior-day substance use behavior between the time of the last completed survey and bedtime, and (2) a morning survey which included items that retrospectively assessed yesterday's behavior from wake time through bedtime, including consequences. Completion of at least one daily survey was high (85.8%). All procedures were approved by the Institutional Review Board of Brown University and a Certificate of Confidentiality was obtained from NIDA.

2.1.4. Co-Use

Recent work from our group with this sample suggests no difference in subjective intoxication or negative consequences when comparing different operationalizations of simultaneous use (i.e., co-use based on timing of use) ranging from 1−240 min within a day (Sokolovsky et al., 2020). Therefore, and given that consequences were aggregated at the day level and assessed the following morning, we examined co-use at the day level. Across the two measurement bursts, a subset of 284 participants (83.2 % of the full sample of 341) reported same-day co-use at least once (meaning reporting alcohol use on at least one survey and cannabis use on at least one survey on the same day). Across all participants and assessment waves, we observed 2024 total co-use days. Given the need to determine substance use ordering within a day, we removed 443 total days with any period of data missingness, resulting in a final total of 1581 days and 258 participants. There were no significant differences in demographic characteristics between those students completing all daily assessments and the final sample (Cohen's h = .01–.02).

2.2. Measures

2.2.1. Substance use quantity

Participants were asked at each survey if they used alcohol, cannabis, both, or neither for each time interval: "What did you use between [time X] and [time Y]?" The timeframe for this question was anchored between the time the previous survey was submitted and the time the current survey was triggered. If alcohol and/or cannabis were endorsed, participants were presented with a timeline overlaid on a grid with time anchors (in minutes) and were instructed to tap on the screen at points corresponding to times when they had a drink or used cannabis (see Supplemental material, Fig. S1). Instructions were: "Tap your finger in the blue box each time you had a drink/used marijuana at the corresponding time"). Day-level alcohol and cannabis use quantity were indexed as the sum of the number of drinks (taps) and cannabis uses (taps), respectively, across all surveys in a given day.

2.2.2. Ordering

After aggregating the data to the day level, "ordering" was defined as the substance (alcohol or cannabis in any form) that was used first during a given day (reference group [ref]: alcohol). Days on which the first use of alcohol and cannabis reportedly occurred during the same minute (9 days across all respondents; 0.57 % of observations) were omitted from analyses.

2.2.3. Consequences

On the morning survey following co-use days, participants indicated whether the following consequences occurred "because of yesterday's use of [alcohol, marijuana, or alcohol and marijuana together]": hangover, nausea/vomiting, hurt self, drove car drunk/high, blackout, rude/aggressive, and unwanted sex. Categories of consequences were adapted from Read and colleagues (2006) consequences subscales, the Brief Young Adult Alcohol Consequences Questionnaire (BYAACQ; Kahler et al., 2005), the Marijuana Consequence Scale (MACQ; Simons et al., 2012), the Rutgers Alcohol Problem Index (RAPI; White and LaBouvie, 1989), and the Rutgers Marijuana Problem Index (RMPI; Johnson and White, 1995), with a focus on selecting acute consequences that would be observed at the daily level. Total daily number of consequences experienced was indexed as the number endorsed each day (range: 0–7)[1]. As consequences were identical across substances, daily consequences were measured here as the sum of consequences endorsed, regardless of substance.

2.2.4. Covariates

All models controlled for baseline demographic characteristics, including: sex (assigned at birth, ref: female), age (dichotomized as below age 21 [ref] or 21+ years old, ref), school (ref: School A), race (White [ref] versus non-White), and ethnicity (non-Hispanic/Latinx [ref] versus Hispanic/Latinx). Models also controlled for weekday (dichotomized as weekday [ref] or weekend [Friday or Saturday], based on inspection of use patterns), any drug use other than cannabis (dichotomized at the daily level, ref: no), and, due to the delayed and extended intoxication effects of edibles compared to other forms of cannabis (Barrus et al., 2016; Grotenhermen, 2003), whether edible cannabis was used (dichotomized at the daily level, ref: no)[2]. In alcohol and cannabis use models (see Analysis Plan), we included measures of typical quantity collected at the baseline survey: "How many drinks containing alcohol do you have on a typical day when you are drinking?"; 0="1 or 2', 1="3 or 4", 2="5 or 6", 3="7, 8, or 9", 4="10 or more" and hours high "How many hours were you 'stoned' on a typical day when you had been using cannabis?"; 0="Less than 1", 1="1 or 2", 2="3 or 4", 3="5 or 6", 4="7 or more"; taken from the Alcohol Use Disorder Identification Test (AUDIT; Saunders et al., 1993) and the Cannabis Use Disorder Identification Test Revised (CUDIT-R; Adamson et al., 2010), respectively. These covariates were selected in order to control for between-person differences in typical quantity used within an occasion to further parse out between- and within-person effects in each model. We also controlled for between-person and within-person alcohol use (average number of drinks per co-use day across the study and daily deviation from that average, respectively) in models examining number of cannabis uses as the dependent variable and between-person and within-person cannabis use (average number of cannabis uses per co-use day across the study and daily deviation from

[1] **Preliminary analyses examining the three most commonly endorsed consequences were also examined as binary outcomes with the same set of covariates. Order was not associated with any individual consequence.**

[2] **Given that edible consumption is associated with delayed effects, we also conducted a set of analyses in which all days including edible use were removed from the model, and the patterns of results were consistent (i.e., all effects were in the same direction and at the same level of statistical significance).**

that average, respectively) in models examining number of alcohol drinks as the dependent variable.

2.3. Analysis plan

To evaluate the influence of day-level substance ordering on alcohol and cannabis consumption and consequences, we structured the data such that each row represented one day for one participant. We conducted a series of generalized linear mixed models (GLMMs; Hedeker, 2005) specifying a negative binomial distribution (Ferrari and Cribari-Neto, 2004) with variance increasing quadratically with the mean due to overdispersion (Hardin and Hilbe, 2007), except for the GLMM examining consequences where a poisson distribution was specified (data were not overdispersed; $\sigma = 1.03$, $p[\sigma > 1] = .181$). Models were fit using the glmmTMB (Brooks et al., 2017) package in R 3.6.1 (R Core Team, 2017), using maximum likelihood estimation. Due to clustering of repeated observations (i.e., days) within participants, which violates typical assumptions of statistical independence, we computed intraclass correlations (ICCs) for focal outcomes and used a mixed-modeling analytic approach as noted above. In separate models, we regressed number of daily drinks (model 1), number of cannabis uses (model 2), and total number of consequences (model 3) onto the focal predictor of ordering, between- and within-person alcohol use (models 2 and 3), between- and within-person cannabis use (models 1 and 3), AUDIT consumption item (model 1), CUDIT-R consumption item (model 2), and all other person-level (sex, age, school, race, ethnicity) and day-level (weekday, use of other drugs, use of edibles) covariates (all models)[3] . Random intercept terms for subject were included in all models. Estimated model coefficients and 95 % confidence intervals (CIs) were exponentiated to obtain incidence rate ratios (IRRs) which are presented for all model terms. This analysis was not pre-registered and thus results should be considered exploratory.

3. Results

The average day-level delay between a participant's first drink or first cannabis use and their first use of the other substance was $M = 243.73$ min ($SD = 210.26$). However, this delay was notably positively skewed, with 24.8 % of days involving first use of both substances within 1 h, 35.9 % within 2 h, and 47.7 % within 3 h (range 1−1,258 min). A narrow timeframe was often observed between any one drink and any one cannabis use on a given day (20.8 % within 1 min, 54.1 % within 10 min, 76.5 % within 1 h, 85.8 % within 2 h, 90.3 % within 3 h, and 93.3 % within 4 h). Across all participants and days, cannabis was slightly more commonly endorsed as the first substance used that day (54.1 % of days). Across all co-use days, the mean time for first alcohol use was 7:39 pm and first cannabis use was 6:32 pm. Descriptive statistics for the subset of participants utilized for the present analyses are presented in Table 1.

3.1. Alcohol quantity

Results from LMEMs predicting daily number of drinks from substance use order (i.e., cannabis first vs. alcohol first) and disaggregated between- and within-person daily cannabis use are presented in Table 2. Results indicate that using cannabis first was associated with a lower daily alcohol quantity after adjusting for all covariates. By contrast, between-person average levels of cannabis use and within-person escalations in daily cannabis use (deviation relative to each participant's average) were both linked to increased daily alcohol quantity after adjusting for covariates. Covariate effects are reported in Table 2.

Table 1
Sample characteristics.

Variable	*M* (SD) or %
Sex (female)	51.9 %
Age	19.9 (1.35)
Race/Ethnicity	
Non-Hispanic White	70.2 %
Non-Hispanic Black	2.7 %
Hispanic/Latinx	9.3%
Asian	12.0 %
Other	1.9 %
More than 1	8.1 %
School	
A (illegal)	29.5 %
B (decriminalized)	37.9% %
C (legal)	32.6 %
Class	
Freshmen	19.8 %
Sophomore	25.6 %
Junior	24.8 %
Senior	24.8 %
≥ 5-year senior	5.0 %
AUDIT	9.78 (5.27)
CUDIT-R	10.26 (6.11)
Drinks per co-use day	5.70 (3.46)
Cannabis uses per co-use day	4.54 (5.19)
Proportion of edible use days per co-use day	7.9 %
Proportion other drug use days per co-use day	6.8 %

Note. $n = 258$ Proportion of edible days and other drug use days presented in Table 1 were aggregated to the subject level (i.e., mean of between-person proportions of co-use use days). AUDIT = Alcohol Use Disorders Identification Test; CUDIT-R = Cannabis Use Disorder Identification Test Revised.

Table 2
Effect of daily ordering of alcohol and cannabis use on daily number of drinks.

Predictors	B (SE)	95 % CI Low	IRR	95 % CI High	*p*
Intercept	1.232 (0.090)	2.872	3.428	4.091	–
Ordering (C >A)	**−0.249 (0.038)**	**0.723**	**0.780**	**0.841**	**<.001**
Cannabis use (B)	**0.031 (0.007)**	**1.017**	**1.031**	**1.046**	**<.001**
Cannabis use (W)	**0.024 (0.003)**	**1.018**	**1.025**	**1.031**	**<.001**
School (A)	−0.026 (0.073)	0.844	0.974	1.125	0.723
School (B)	−0.017 (0.071)	0.854	0.981	1.128	0.793
Male	−0.007 (0.059)	0.890	0.993	1.114	0.904
Age 21	**−0.122 (0.059)**	**0.788**	**0.885**	**0.994**	**0.040**
Non-white	0.006 (0.072)	0.874	1.006	1.159	0.933
Hispanic/Latinx	0.180 (0.104)	0.977	1.197	1.467	0.083
Weekend	**0.295 (0.034)**	**1.257**	**1.344**	**1.437**	**<.001**
Other drug use	**0.247 (0.059)**	**1.141**	**1.280**	**1.436**	**<.001**
Edible cannabis use	−0.143 (0.088)	0.730	0.867	1.030	0.105
AUDIT Item 2	**0.160 (0.028)**	**1.111**	**1.174**	**1.241**	**<.001**

Note. $n = 258$. IRR = incidence rate ratio. Ordering = first substance cannabis (vs. first substance alcohol). B = between-person effect; W = within-person effect. AUDIT = Alcohol Use Disorders Identification Test; C >A = cannabis first. Statistically significant effects ($p < .05$) are in bold typeface. ICC for between-person clustering of number of drinks is .26.

3.2. Cannabis quantity

Results from LMEMs predicting daily cannabis use from substance

[3] **We also conducted an additional analysis for model 3 in which we tested the interaction between order of use and within-person use frequency (cannabis and alcohol) and found no significant effects of either interaction on consequences.**

use order (i.e., cannabis first vs. alcohol first) and disaggregated between- and within-person daily alcohol use are presented in Table 3. Results indicate that using cannabis first was associated with an increased number of daily cannabis uses after adjusting for covariates. Likewise, between-person average levels of alcohol use and within-person elevations in daily alcohol consumption (deviation relative to each participant's average) were both related to an increased cannabis consumption over and above covariates. Covariate effects are reported in Table 3.

3.3. Alcohol and Cannabis consequences

Results from LMEMs predicting daily consequences from substance use order (i.e., cannabis first vs. alcohol first), between- and within-person daily alcohol use, and between- and within-person daily cannabis use are presented in Table 4. Between- and within-person alcohol use was associated with an increased number of consequences after adjusting for covariates. However, neither substance use ordering nor between- and within-person cannabis use were linked to consequences. Covariate effects are reported in Table 4.

4. Discussion

This study took a detailed look at co-use days to examine the effect of order (i.e., alcohol or cannabis first) on daily alcohol consumption, cannabis consumption, and negative consequences, while controlling for between-and within-person levels of use. Descriptively, we found that, across all sample days and individuals, cannabis was only slightly more likely to be used first (54 % cannabis first) and cannabis use tended to start earlier in the day. This is not surprising given the frequency of morning use (colloquially known as "wake and bake") among daily cannabis users (Earleywine et al., 2016). Results suggested that using cannabis first predicted more cannabis use, but less alcohol use (fewer drinks), within a co-use day. Substance use order did not predict number of consequences experienced, after controlling for consumption, whereas number of drinks within a co-use day positively predicted more consequences.

This is the first naturalistic study to examine the effect of ordering of alcohol and cannabis use on consumption and provides an important context for understanding the conflicting literature in this area. Given recent findings suggesting use of alcohol and cannabis concurrently (compared to alcohol alone) predicts increased alcohol consumption at the between person-level in adults (Subbaraman and Kerr, 2015) and the daily level in veterans (Metrik et al., 2018) and college students (Gunn et al., 2018), it is important to examine understudied factors that may contribute to this increased use. Our findings indicate that order has an important role in consumption rates and that using alcohol first on co-use days significantly contributes to more drinking, even though alcohol use tends to start later in the day. Together with studies suggesting earlier cannabis use in the day (i.e., morning use) predicts more cannabis-related problems (Earleywine et al., 2016), our findings support the idea that cannabis users should consider delaying their use later in the day to reduce overall consumption levels.

To our knowledge, this is also the first study to examine ordering and consider both within- and between- person predictors of use in the context of co-use days. Results suggested that both being a heavier cannabis user and using more cannabis within the day (deviation from typical use) predicted more drinking within a co-use day. Additionally, being a heavier drinker and drinking more alcohol within the day (deviation from typical use) predicted more frequent cannabis uses within the day. Results are consistent with between-person examinations, suggesting that more cannabis use predicts heavier drinking (Gunn et al., 2018; Metrik et al., 2018; Midanik et al., 2007; Stinson et al., 2006) and that heavier alcohol use is associated with more frequent

Table 3
Effect of daily ordering of alcohol and cannabis use on daily cannabis use.

Predictors	B (SE)	95 % CI Low	IRR	95 % CI High	*p*
Intercept	0.305 (0.121)	1.068	1.357	1.723	–
Ordering (C > A)	**0.480 (0.032)**	**1.517**	**1.615**	**1.720**	**<.001**
Alcohol use (B)	**0.084 (0.013)**	**1.060**	**1.087**	**1.115**	**<.001**
Alcohol use (W)	**0.031 (0.003)**	**1.025**	**1.032**	**1.038**	**<.001**
School (A)	0.133 (0.084)	0.969	1.142	1.345	0.112
School (B)	**0.24 (0.080)**	**1.088**	**1.272**	**1.488**	**0.003**
Male	−0.029 (0.067)	0.853	0.972	1.106	0.695
Age 21	−0.094 (0.067)	0.800	0.910	1.104	0.605
Non-white	−0.078 (0.083)	0.786	0.924	1.087	0.160
Hispanic/Latinx	−0.017 (0.121)	0.775	0.983	1.247	0.596
Weekend	−0.015 (0.029)	0.931	0.985	1.042	0.942
Other drug use	0.067 (0.048)	0.972	1.069	1.175	0.215
Edible cannabis use	−0.042 (0.073)	0.831	0.959	1.106	0.483
CUDIT-R Item 2	**0.160 (0.041)**	**1.082**	**1.173**	**1.271**	**<.001**

Note. $n = 258$. IRR = incidence rate ratio. Ordering = first substance cannabis (vs. first substance alcohol). B = between-person effect; W = within-person effect. CUDIT = Cannabis Use Disorders Identification Test-Revised; C >A = marijuana first. Statistically significant effects ($p < .05$) are in bold typeface. ICC for between-person clustering of cannabis use is 0.44.

Table 4
Effect of daily ordering of alcohol and cannabis use on total consequences.

Predictors	B (SE)	95 % CI Low	IRR	95 % CIHigh	*p*
Intercept	−1.979 (0.235)	0.087	0.138	0.219	–
Ordering (C>A)	0.044 (0.106)	0.849	1.045	1.285	0.681
Alcohol use (B)	**0.083 (0.009)**	**1.027**	**1.086**	**1.149**	**0.004**
Alcohol use (W)	**0.080 (0.009)**	**1.064**	**1.084**	**1.104**	**<.001**
Cannabis use (B)	0.003 (0.016)	0.973	1.003	1.035	0.832
Cannabis use (W)	−0.012 (0.008)	0.973	0.988	1.004	0.145
School (A)	−0.252 (0.178)	0.548	0.778	1.103	0.159
School (B)	0.237 (0.163)	0.922	1.267	1.743	0.145
Male	−0.169 (0.133)	0.651	0.844	1.096	0.203
Age 21	0.115 (0.138)	0.856	1.122	1.469	0.405
Non-white	0.056 (0.172)	0.754	1.057	1.481	0.749
Hispanic/Latinx	−0.144 (0.258)	0.522	0.866	1.437	0.577
Weekend	**0.358 (0.095)**	**1.188**	**1.430**	**1.723**	**<.001**
Other drug use	0.190 (0.145)	0.911	1.210	1.610	0.188
Edible cannabis use	0.254 (0.213)	0.849	1.289	1.956	0.234

Note. $n = 258$. IRR = incidence rate ratio. Ordering = first substance cannabis (vs. first substance alcohol). B = between-person effect; W = within-person effect; C >A = cannabis first. Statistically significant effects ($p < .05$) are in bold typeface. ICC for between-person clustering of daily consequences is .17.

cannabis use (Jackson et al., 2008; Terry-McElrath et al., 2017). This distinction of between- and within-person use is essential to consider when examining the impact of co-use, particularly given recent within-person investigations showing cannabis use can lead to decreased drinking and related consequences both acutely, in the lab, and in the natural environment (Mallett et al., 2019; Metrik et al., 2019). These findings have important implications for prevention and intervention messages. In particular, results suggest that although using cannabis first is associated with less drinking within a day, heavier users of cannabis and more use of cannabis within the day is associated with increased drinking. In turn, heavier drinking (both within- and between-person) is also associated with greater consequences, suggesting that interventions for co-use should focus on both cannabis and alcohol use.

This is the first study to examine the impact of co-use ordering with between-person indicators of substance use and daily predictors of consequences. Between-person examinations (co-users versus single substance users) have found that co-use is associated with more consequences (Brière et al., 2011; Jackson et al., 2020; Patrick et al., 2016), even controlling for frequency of heavy drinking episodes (Shillington and Clapp, 2006, 2001). In contrast, more recent studies focusing on event-level associations have suggested that daily alcohol consumption may be the primary driver of consequences in co-use occasions (Lipperman-Kreda et al., 2017; Mallett et al., 2019, 2017; Metrik et al., 2016; Sokolovsky et al., 2020), and that using cannabis may not be a primary driver of increased risk. Rather, individual frequency of use of both substances and alcohol consumption (at the event or daily level) remain more proximal predictors of consequences experienced. Our findings contribute to this mounting evidence, suggesting that alcohol consumption, but not cannabis consumption, is a significant predictor of consequences within a co-use day, whereas order of substance use is not. However, our selection of some consequences may have been biased toward consequences that are more acutely experienced due to alcohol use (e.g. hangover, blackout), to the exclusion of consequences that are more pertinent to cannabis. Nonetheless, prior work from our group shows that college students are more likely to attribute most consequences to alcohol alone than either to cannabis or co-use (Jackson et al., 2020). More research examining specific cannabis-related consequences on co-use days is needed. Further, with the rapidly evolving legislation surrounding recreational cannabis use, the impact of co-use should be considered when regulating marketing and sales of alcohol and cannabis together. Finally, as cannabis is increasingly being considered for medicinal purposes, treatment providers and patients should make careful considerations regarding the use of cannabis among those in treatment for alcohol misuse.

5. Limitations

The current study should be understood in the context of its limitations. First, given the widely varying formulations and patterns of cannabis use, it was at the discretion of the participant to define a cannabis use event. Importantly, the potential impact of this limitation was mitigated somewhat by including edible use as a day-level covariate, as edible use differs most significantly from concentrate and flower product use (eating a substance once versus smoking or vaping in multiple "hits") and by conducting within-person analyses. Second, although we sampled a diverse set of college students from three states differing in recreational cannabis laws, these findings may not generalize to other populations. Third, as discussed above, the consequences included in the daily surveys were derived primarily from subscales of alcohol consequences (Read et al., 2006), and, therefore, may not reflect consequences that are specific to co-use. Future studies should examine consequences that may be specific to co-use occasions or consequences that may be predicted by ordering. For instance, using alcohol first may predict blackout via increased alcohol use, whereas using cannabis first may predict driving under the influence, which we have found is more common than driving under the influence of alcohol alone (Jackson et al., 2020). Finally, this study focused specifically on day-level outcomes of co-use order, and therefore does not generalize to long-term outcomes that may result from co-use. Related to this, we measured order within the day, rather than within a specific event, resulting in some large time gaps between use occasions.

6. Conclusions

In summary, results indicated that using cannabis before alcohol within a co-use day predicted fewer drinks consumed but more cannabis uses. Order of substance use did not predict consequences experienced when controlling for consumption. Results further suggested that heavier use of alcohol and cannabis, both at the between- and within-person level, predicted increased use of the other substance within a co-use day. Finally, results suggested that heavier alcohol consumption at the between-person and within-person level predicted increased consequences on co-use days, whereas heavier cannabis use did not. Overall, results highlighted that order of substance use is a robust predictor of consumption within co-use days.

Contributors

Drs. Jackson and White designed the project that collected the data for the current study. Dr. Gunn conducted literature searches and provided summaries of previous research studies under the guidance of Dr. Metrik. Dr. Gunn, Dr. Sokolovsky, and Dr. Stevens collaborated on the analyses under the guidance of Dr. Jackson. Dr. Gunn wrote the first draft of the manuscript with significant contribution from all authors. All authors contributed to and have approved the final manuscript.

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The authors have no conflicts of interest to declare.

Declaration of Competing Interest

All of the listed authors declare that they have no conflicts of interests.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2020.108339.

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