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Alcohol and Marijuana Co-Use: Consequences, Subjective Intoxication, and the Operationalization of Simultaneous Use

Alexander W. Sokolovsky[a], **Rachel L. Gunn**[a], **Lauren Micalizzi**[a,b], **Helene R. White**[c], **Kristina M. Jackson**[a]

[a]Center for Alcohol and Addiction Studies, Brown University, Box G-S121-4, Providence, RI 02912

[b]University of Saint Joseph, 1678 Asylum Avenue, West Hartford, CT 06117

[c]Rutgers Center of Alcohol Studies, 607 Allison Road, Piscataway, NJ 08854-8001

Abstract

Background—Alcohol and marijuana are frequently co-used with overlapping effects. However, the absence of consistent operational definitions delineating simultaneous alcohol and marijuana use (SAM) from concurrent use (CAM) challenges consistent inferences about these behaviors. This study first examined whether daily alcohol and marijuana co-use predicted substance-use related consequences and subjective intoxication; and then evaluated whether competing operationalizations of SAM and CAM were associated with differences in these outcomes on co-use days.

Methods—A sample of 341 young adult college students who reported past-month use of both alcohol and marijuana "at the same time so that their effect, overlapped" completed a two- wave survey with paired 28-day daily experience sampling bursts examining alcohol and marijuana co-use. Outcomes were (a) daily substance-use related consequences; and (b) daily subjective intoxication. Focal predictors were daily drinks and marijuana uses; daily co-use versus single-substance use (Aim 1) or CAM versus SAM (Aim 2); and their interaction.

Results—Participants reported more negative consequences on co-use days versus marijuana-only days and greater subjective intoxication relative to alcohol or marijuana-only days. Competing operationalizations of SAM, defined as daily co-use occurring within 1–240 minutes in

Corresponding author: Alexander W. Sokolovsky alexander_sokolovsky@brown.edu.

Contributors

A. W. Sokolovsky developed the study concept. All authors contributed to the study design. H. R. White and K. M. Jackson developed and designed the parent study from which data were obtained. A. W. Sokolovsky, H. R. White, and K. M. Jackson were responsible for data collection. A.W. Sokolovsky performed the data analysis and interpretation. A. W. Sokolovsky, R. L. Gunn, and L. Micalizzi drafted the manuscript and H. R. White and K. M. Jackson provided revisions. All authors approved the final manuscript for submission.

Conflict of Interest

There are no conflicts of interest to declare.

Declaration of interests: none

increments of 1 minute, found no difference in consequences or subjective intoxication regardless of operationalization.

Conclusion—Co-use days involve greater risk than alcohol-only or marijuana-only days. Although there was no evidence of additional daily risk from simultaneous use regardless of the timeframe used to operationalize it, investigating these effects remains challenging due to the generally small timeframe between substances on co-use days in this sample.

Keywords

alcohol; marijuana; concurrent; simultaneous; CAM; SAM; co-use

1. Introduction

Aside from co-use with tobacco, alcohol and marijuana are the most commonly co-used substances nationwide, among young adults and on college campuses (Collins et al., 1998; Earleywine and Newcomb, 1997; Martin et al., 1996b; Midanik et al., 2007; Schulenberg nd Patrick, 2012; Subbaraman and Kerr, 2015; USDHHS, 2011). Co-users report more alcohol and marijuana use (Brière et al., 2011; Midanik et al., 2007; Subbaraman and Kerr, 2015), use-related negative consequences (Brière et al., 2011), greater likelihood of alcohol dependence and depression (Martin et al., 1996b; Midanik et al., 2007), and more intoxicated driving (Terry-McElrath et al., 2013) compared to those who use only one substance. However, the mechanisms by which co-use confers these risks remain unclear.

Among users of both alcohol and marijuna, most have used simultaneously (Brière et al., 2011; Martin et al., 1992; Subbaraman and Kerr, 2015; White et al., 2019). Research has shown that simultaneous alcohol and marijuana use (SAM) can be particularly hazardous, even relative to concurrent alcohol and marijuana use (CAM; using both substances but not in the same occasion) (Brière et al., 2011; Earleywine and Newcomb, 1997; Patrick et al., 2018b; Subbaraman and Kerr, 2015). SAM (versus CAM) is associated with higher levels of consumption (Briere et al., 2011; Patrick et al., 2018b, 2017; Subbaraman and Kerr, 2015), greater alcohol-related consequences (Brière et al., 2011; Jackson et al., 2020; Lipperman-Kreda et al., 2017; Mallett et al., 2017; Subbaraman and Kerr, 2015; Yurasek et al., 2017), and increased incidence of motor vehicle accidents (Arterberry et al., 2017; Chihuri et al., 2017; Terry-McElrath et al., 2015, 2013). Further, laboratory studies suggest that SAM use is associated with increased subjective impairment, and increased blood Δ−9 tetrahydrocannabinol (THC) levels (Downey et al., 2013; Hartman et al., 2016, 2015; Lukas and Orozco, 2001; Perez- Reyes et al., 1988). One challenge to drawing conclusions about the risk of SAM versus CAM is that distinguishing between SAM and CAM is difficult given the lack of consistent operational definitions. Definitions of SAM vary widely, including using both substances "*at the same time* " (Brière et al., 2011; Earleywine and Newcomb, 1997; Midanik et al., 2007), *"on the same occasion/event"* (Collins et al., 1998; Pape et al., 2009), *"within three hours"* (Martin et al., 1996a, 1996b), *"in combination"* (Pakula et al., 2009), *"so that the effects overlap"* (Terry-McElrath et al., 2013), *"at the same time, that is, so their effects overlapped"* (Lee et al., 2017; Patrick et al., 2018a, 2018b), *"within a few hours"* (Lipperman-Kreda et al., 2017), *"[marijuana] at any time before, during or after the last time [using alcohol] "* (Lipperman-Kreda et al., 2018), or

"using[marijuana] while drinking]" (Agrawal et al., 2009). Given the evidence for adverse outcomes specific to SAM use, there is a need for an empirically-justified definition of SAM that can be delineated from CAM.

Naturalistic data examining alcohol and marijuana use in higher resolution could facilitate testing if co-use of alcohol and marijuana connotes the greatest risk when acute effects are overlapping. Although some weekly and daily data show that co-use of alcohol and marijuana (CAM or SAM) is associated with higher levels of alcohol use (Gunn et al., 2018; Lee et al., 2020; Metrik et al., 2018) and negative consequences (Gunn et al., 2018; Linden-Carmichael et al., 2020), Lee et al. (2020) found no relationship between SAM (versus alcohol only) days and negative consequences after accounting for number of drinks. In contrast, Linden Carmichael et al. (2020) did observe increased daily negative consequences from SAM even when controlling for number of drinks, although they did not observe differences in levels of subjective intoxication across these days. Another event-level study found that the addition of marijuana use to heavy alcohol use occasions does not increase risk for consequences (Mallett et al., 2019). Ecological momentary assessment was also used to examine how alcohol consumption predicted problems during SAM occasions in adolescents (Lipperman-Kreda et al., 2017). However, these studies did not examine timing of co-use and its relation to consumption, subjective intoxication, or consequences. Little extant research has compared these outcomes between CAM and SAM. One retrospective study found young adults reported the highest levels of subjective intoxication during SAM versus alcohol or marijuana use only, but did not examine non-overlapping co-use (Lee et al., 2017). Thus, it remains unresolved if SAM is associated with different levels of intoxication or consequences than CAM, and if different SAM operationalizations yield different findings thus informing the 'optimal' definition of SAM.

1.1 Current Study

We sought to operationalize SAM among college students who reported using both alcohol and marijuana on the same day at least once during two 28-day daily measurement waves. We harnessed rich daily data to examine whether daily co-use (SAM or CAM) versus using alcohol and marijuana alone predicted daily consequences and intoxication (Aim 1). We hypothesized that daily co-use would result in more negative consequences and greater subjective intoxication compared to using these substances in isolation. We also explored if co-use moderated the relationship between number of drinks or marijuana uses and these focal outcomes. To explore alternate operationalizations of SAM, we systematically varied the timeframe that delineated SAM from CAM and then examined day-level associations between SAM (versus CAM) and negative consequences and subjective intoxication (Aim 2). These exploratory analyses examined how different operationalizations may influence the predictive utility of SAM (versus CAM) on subjective intoxication and daily consequences.

2. Methods

2.1 Procedures

2.1.1 Screening procedures—Students at three state universities with different laws regarding recreational marijuana use were recruited to participate in a study on alcohol and marijuana use. Marijuana was legalized for medical use in all states. Recreational marijuana use was illegal and criminalized at School A; illegal but decriminalized at School B; and legal for adults (21+) at School C. We emailed screening survey invitations to 8,000 students age 18–24 years randomly selected from each university's registrar database stratified by anticipated graduation year (2,000 from each class; total N=24,000). Eligibility criteria included: (1) full-time enrollment at one of the universities; (2) age 18–24 years; (3) past-year alcohol and marijuana use; and (4) verified e-mail address. Demographic differences between students completing the screener and those invited were small (Cohen's h=0.07−0.26) suggesting adequate representativeness of the student populations at these three universities (for more on recruitment see White et al., 2019). Of the 7,000 screening responses, 2,874 (41.1%) were deemed eligible.

2.1.2 Online procedures—A stratified random sample of 2,501 eligible students was invited by email to take the baseline survey. Past-month alcohol and marijuana users were over-sampled to ensure a robust sample for the daily study. Of invitees, 1,610 provided consent and were enrolled. Participants were excluded from the final sample if they provided responses inconsistent with eligibility criteria; 1,390 participants (55.6%) were retained. A 3-month follow-up survey retained 86% of the sample; attrition analyses indicated no significant differences in baseline demographic characteristics and alcohol or marijuana use between those retained and lost to follow-up. Participants were compensated for the baseline and 3-month surveys with $25 and $35 Amazon gift cards, respectively.

2.1.3 Daily procedures—Daily data collection occurred directly after the baseline survey and comprised 28 days of data collection with 5 daily surveys via custom smartphone application. Inclusion criteria for this phase were completion of baseline assessment and a baseline report of any past-month use of alcohol and marijuana "at the same time so that their effects overlapped" (n=693). We stratified recruitment based on frequency of past-month use and sex to ensure heterogeneity. Overall, 379 students were given access to the application, of which 343 accepted. Two students discontinued data collection during the first 2 days and were excluded (see Supplemental Figure 1[1]). Within the daily sample (n=341), 31.5% of participants were from School A, 34.7% from School B, and 33.8% from School C. Daily participants were invited to complete a second 28-day measurement burst immediately after the follow-up survey. Participants received $1 for completed surveys with weekly and overall bonuses for compliance totaling $200 in potential compensation (Amazon gift cards).

Daily surveys assessed behavior up to 24 waking hours daily (the first 2 days of the first burst were dropped due to technical problems) with predictable survey scheduling (9:00am,

[1]Supplementary material can be found by accessing the online version of this paper.

2:00pm, 5:00pm, 8:00pm, 11:00pm). Participants could complete each survey within 2 hours of the scheduled time (up to 5 hours for the 9:00am survey). Surveys took approximately 1–2 minutes to complete (2–3 minutes for the 9:00am survey). Compliance with at least one daily survey (85.8%) and morning surveys (79.2%) was high. Overall compliance with all available prompts was 61.3%, resulting in a high rate of complete daily coverage[2] (75.4%). Procedures were approved by the Institutional Review Board of Brown University and a Certificate of Confidentiality was obtained from NIDA.

2.2 Measures

Subjective Intoxication—At each survey, participants were first asked whether. they used alcohol, marijuana, both, or neither for a given time interval (see Supplemental Figure 2[3]). Participants were then presented with an image of a single grid with time anchors (in minutes) on the X-axis and level of subjective effect on the Y-axis. As we did not expect participants to have enough insight to accurately attribute subjective effects to a specific substance, we presented a single graph for both substances, with anchors: Not at all high/drunk, A little high/drunk, Moderately high/drunk, Very high/drunk. Participants were instructed to use their finger to draw a continuous line indicating how they felt during a given time interval (see Supplemental Figure 2). The survey coverage interval was bound by the current time and the completion time of the prior survey, or waking time (first report)/bedtime (last report). We aggregated survey level data to the daily level and computed daily peaks (ranging from 0 [Not at all high/drunk] to 3 [Very high/drunk]) to obtain a measure of maximal subjective intoxication that day.

Substance Consumption—Participants endorsing any alcohol/marijuana use were presented with their drawn figure from the assessment of subjective intoxication and the same X-axis grid of time anchors. On two separate screens participants tapped to indicate the number and timing of drinks (“Tap your finger in the blue box each time you had a drink at the corresponding time”) and discrete marijuana uses (“Tap your finger in the blue box each time you used marijuana at the corresponding time”; see Supplemental Figure 2[4]). Number of drinks and marijuana uses were aggregated to the daily level and grand mean-centered.

Substance Use Consequences—The morning following alcohol/marijuana use days, participants indicated whether the following consequences occurred due to their use (yes/no): hangover, nausea/vomiting, hurt self, drove car drunk/high, blackout, rude/aggressive, unwanted sex. We considered acute consequences across several established scales, including the Brief Young Adult Alcohol Consequence Questionnaire (Kahler et al., 2005), Brief Marijuana Consequences Questionnaire (Simons et al., 2012), Young Adult Alcohol Consequences Questionnaire (Read et al., 2006), Rutgers Alcohol Problem Index (White and Labouvie, 1989), Rutgers Marijuana Problem Index (White et al., 2005) and items developed by Lee et al. (personal communication). Participants reported on all seven

[2]If the prior survey was not completed, the current survey would cover the missed period. This was limited to one missed survey period (i.e., if two adjacent surveys were missed, the period only for the immediately preceding survey was covered).
[3]Supplementary material can be found by accessing the online version of this paper.
[4]Supplementary material can be found by accessing the online version of this paper.

consequences, with the instruction tailored to the type of use on the previous day (use of alcohol only, use of marijuana only, or use of alcohol and marijuana together[5]). As consequences were identical across different substances, daily consequences were indexed as the sum of consequences endorsed during a day, regardless of item (range: 0–7).

Co-use—We defined *co-use* as use of both alcohol and marijuana on a given study day, regardless of the timeframe between their use.

CAM and SAM—We operationalized SAM (versus CAM) dynamically by examining different timeframes between alcohol and marijuana use. On days when participants reported co-use of alcohol and marijuana, we calculated the smallest time interval between any one time participants "had a drink" and any one time participants "used marijuana." SAM days were delineated from CAM days (i.e., all non-SAM co-use days) by varying the criterion timeframe defining "simultaneous" use. For example, when 37 was used as the criterion, all co-use days with a drink and marijuana use reported within 37 minutes were defined as "SAM" while the remaining co-use days (i.e., those days with co-use but not within 37 minutes) were defined as "CAM." We investigated all operational definitions between 1–240 minutes in increments of 1 minute. We used 240 minutes as the upper bound for operationalizations of SAM as this timeframe captured 94.1% of all co-use days (see Results: Aim 2 below).

Covariates—We controlled for baseline demographic characteristics, including sex, age, school (reference group: School A), race (White vs. non-White), and ethnicity (non-Hispanic/Latino vs. Hispanic/Latino); and problematic alcohol and marijuana use based on the 10-item Alcohol Use Disorders Identification Test (AUDIT; Saunders et al., 1993) and the 8-item Cannabis Use Disorders Identification Test–Revised (CUDIT-R; Adamson et al., 2010). AUDIT scores range from 0–40 with higher scores indicating greater likelihood for past-year alcohol dependence (Cronbach's α=.74). CUDIT-R scores range from 0–32 with higher scores indicating more problematic or harmful cannabis use in the past 6 months (Cronbach's α=.79). All models controlled for weekday versus weekend (defined as Friday or Saturday), any nicotine use dichotomized at the daily level (yes/no), any drug use other than marijuana dichotomized at the daily level (yes/no), and form of marijuana use (at each survey, participants indicated: dry leaf, concentrate, and/or edible; we dichotomized the variable into leaf- or "plant-only" versus all other forms/combinations).

2.3 Analysis Plan

To evaluate the influence of alcohol and marijuana co-use on day-level consequences and subjective intoxication relative to the independent influences of alcohol or marijuana use alone (Aim 1), we structured the data such that each row represented one day for one

[5]Participants who used alcohol and marijuana in the same day but only in separate surveys were queried whether they used these substances such that their effects 'overlapped.' Those who denied overlapping effects reported consequences separately for alcohol ("because of yesterday's use of alcohol") and marijuana ("because of yesterday's use of marijuana"). Those who endorsed overlapping effects reported on their consequences "because of yesterday's use of alcohol and marijuana together." Participants who reported using both alcohol and marijuana within any one survey the prior day were also queried about consequences "because of yesterday's use of alcohol and marijuana together." Participants who received this prompt were not asked to attribute their consequences to alcohol or marijuana. Regardless of the phrasing of item(s), participants were shown the same list of seven daily consequences. Consequences were indexed as the total number of consequences experienced, regardless of the source of the consequences. (see Limitations).

participant. We had two comparisons of interest: day level co-use versus: a) alcohol alone; and b) marijuana alone. We conducted a series of linear mixed effects models (LMEMs; Hedeker, 2005) with unstructured covariance matrices regressing focal outcome variables onto day-level predictors: co-use versus alcohol (or marijuana) alone, number of drinks (or number of marijuana uses), and the interaction between co-use and consumption variables; day-level covariates (nicotine use; form of marijuana use; other drug use; weekday/weekend); and subject-level covariates (sex; race; ethnicity; age; school; AUDIT; CUDIT-R). Thus, focal effects examined: (1) the relationship between number of drinks (or marijuana uses) and daily consequences or intoxication; (2) the additive effect of co-use over alcohol (or marijuana use) alone; and (3) the potential interaction of the relationship between the focal substance and the outcome by co-use. We included random intercepts to account for subject-level clustering[6].

To explore how competing operationalizations of SAM may predict daily consequences and subjective intoxication (Aim 2), we limited our analyses to only those days on which co-use occurred. We conducted LMEMs regressing the same outcome variables onto day-level focal predictors (i.e., number of drinks and marijuana uses; day-level SAM [versus CAM]; interactions between SAM and the two substance use variables), and the same day- and subject-level covariates as our initial analyses. We fit parallel models for each operationalization of SAM. We then extracted parameter estimates from each model to identify regions of significance (ROS) for focal effects (Aiken et al., 1991; Preacher et al., 2006). In other words, we systematically examined whether changing the operational definition of SAM affected the relationship between consequences or subjective intoxication (dependent variables) and SAM (versus CAM), number of drinks or marijuana uses, and their interaction. This analytic approach was chosen to avoid selecting arbitrary cutoffs when investigating the operationalization of SAM.

To reduce spurious findings, ROSs were defined as ranges of at least 10 continuous minutes in operationalizations of SAM where parameters were significant and in the same direction[7]. For example, if we observed the number of marijuana uses significantly predicting consequences, but only in models where the timeframe for SAM was operationalized as 2–4 minutes, we did not consider this to be a region of significance. Similarly, at least 10 continuous minutes of non-significant model parameters within a region of significance delineate the end of a region of significance. As it is possible for multiple ROSs to be observed for a predictor, we report on all ROSs meeting these criteria (for a visual example of identifying an ROS see Supplemental Figure 3[8]). All analyses were conducted in R 3.6.0 (R Core Team, 2017).

[6]Random slope effects were evaluated but not included in our final models due to difficulties with model convergence, low variance attributable to these effects, and no a-priori hypotheses about the covariance between random slopes and intercepts

[7]Ten minutes was chosen as the criterion for regions of significance as this timeframe categorized approximately half (52%) of co-use days as SAM days. Ten minutes was thus the maximum point for the reliability of the standard errors of the SAM effect. Furthermore, the distribution of daily minimum times between alcohol and marijuana use was positively skewed. Given this distribution, increasing the operationalization timeframe beyond 10 minutes would not be expected to change the SAM (versus CAM) effect as rapidly as it changed at lower operationalizations (i.e., 1–10 minutes). Ten minutes was thus seen as the most strict criterion needed to avoid spurious findings.

[8]Supplementary material can be found by accessing the online version of this paper.

3. Results

3.1 Participant Characteristics

Of the total daily sample (n=341), 290 (85.0%) reported at least one alcohol-only use day, and 287 (84.2%) reported a marijuana-only use day. Further, 284 participants (83.2%) reported at least one day of alcohol and marijuana co-use during daily data collection and were included in Aim 2 analyses. Descriptive statistics are presented in Table 1; χ^2 and two-sample t- tests found that relative to participants reporting any daily co-use (n=284) those in the final sample but without daily co-use (n=57) were significantly younger, had lower AUDIT and CUDIT-R scores, had fewer drinks per drinking day and fewer marijuana uses per marijuana use day, and had lower proportions of nicotine and other drug use days. A total of 15,749 person-days of data were collected across all participants, with 7750 (49.2%) non-use days; 2073 (13.2%) alcohol-only days; 3909 (24.8%) marijuana-only days; and 2017 (12.8%) co-use days. The mean minimum time between any one drink and any one marijuana use on co-use days was M=51.98 minutes (SD=104.56).

3.2 Aim 1. Alcohol and Marijuana Co-Use, Negative Consequences, and Subjective Intoxication

Participants reported M=0.36 (SD=0.71); M=0.11 (SD=0.33); and M=0.38 (SD=0.67) total consequences on alcohol-only, marijuana-only, and co-use days, respectively. Respective mean levels of subjective intoxication were M=1.33 (SD=0.98); M=1.90 (SD=0.78); and M=2.11 (SD=0.76).

3.2.1 Negative Consequences—Results from LMEMs predicting daily negative consequences from alcohol and marijuana use, day-level co-use, and their interaction are presented in Table 2. In the model examining co-use versus alcohol-only days, daily co-use did not significantly increase risk for experiencing consequences at mean daily number of drinks. This main effect was qualified by the presence of a significant interaction indicating that on co-use days, the relationship between number of drinks and consequences was weaker than on alcohol-only days (see Figure 1a). In the model examining co-use versus marijuana-only days, daily co-use predicted increased consequences at mean daily number of marijuana uses. Alcohol co-use did not significantly impact the positive relationship between marijuana uses and consequences (see Figure 1b).

3.2.2 Subjective Intoxication—Results from LMEMs predicting peak daily subjective intoxication from alcohol and marijuana use, co-use, and their interaction are presented in Table 3. In the model examining co-use versus alcohol-only days, daily co-use significantly increased subjective intoxication at mean daily number of daily drinks. These effects were qualified by a significant interaction such that, on co-use days, the relationship between number of drinks and subjective intoxication was weaker than on alcohol-only days (see Figure 1c). We observed similar effects for the models examining co-use versus marijuana-only use (see Figure 1d).

3.3 Aim 2. Operationalization of CAM versus SAM

On co-use days, the cumulative proportions of minimum time between any use of alcohol and any use of marijuana were: 19.6% (co-use within 1 minute), 52.0% (10 minutes), 69.5% (1 hour), 78.2% (2 hours), 86.4% (3 hours), and 94.1% (4 hours).

3.3.1 Negative Consequences—Results from ROS analyses examining competing operationalizations of SAM on the prediction of daily consequences are presented in Table 4[9]. Number of drinks predicted increased consequences across all operationalizations. Consequences were not significantly higher on SAM (versus CAM) days, regardless of operationalization. However, these effects were qualified by a significant interaction between number of drinks and SAM such that the relationship between number of drinks and consequences was weakened on SAM days relative to CAM days, but only when SAM was operationalized as co-use occurring within a 114-minute timeframe (i.e., within 2 hours). At values greater than 114 minutes, there was no difference between SAM and CAM. Neither marijuana uses nor the interaction between marijuana uses and SAM significantly predicted daily consequences.

3.3.2 Subjective Intoxication—Results from ROS analyses examining competing operationalizations of Sam on the prediction of peak daily subjective intoxication are presented in Table 5. Subjective intoxication was not significantly higher on SAM (versus CAM) days, regardless of operationalization. Number of drinks predicted increased subjective intoxication across all operationalizations. However, these effects were qualified by a significant interaction between number of drinks and SAM such that the relationship between number of drinks and subjective intoxication was weakened on SAM relative to CAM days, but only when SAM was operationalized as co-use occurring within a 183-minute timeframe (i.e., within 3 hours). Similarly, number of marijuana uses predicted increased subjective intoxication, but this relationship was weakened on SAM relative to CAM days (all operationalizations).

4. Discussion

The present study had two aims: (1) to examine the extent to which co-use predicts subjective intoxication and consequences relative to use of a single substance, and (2) to explore competing operationalizations for SAM use at the daily level. Consistent with prior laboratory studies (Hartman et al., 2016; Lukas and Orozco, 2001) and work using fine-grained data (Brière et al., 2011; Gunn et al., 2018; Metrik et al., 2018), within-subjects analyses indicated that co-use of alcohol and marijuana predicted greater intoxication than use of either substance alone, and more substance use-related consequences than marijuana use alone. Given our findings on subjective intoxication were consistent with some (Lee et al., 2017) but not all (Linden-Carmichael et al., 2020) investigations of co-use, further research is needed to identify the characteristics of a co-use events most strongly associated

[9]Results from ad-hoc sensitivity analyses using bootstrapping to resample equal numbers of observations above and below the operationalization timeframes supported these findings and highlighted the conservative nature of our ROS estimates (i.e., ROSs may be wider than those observed with raw data due to the small number of observations in the CAM group at higher operationalization timeframes).

with perceived acute effects. Separately, the combination of marijuana with alcohol versus alcohol alone did not increase the number of negative consequences experienced (consistent with Lee et al. 2020), whereas the combination of alcohol with marijuana versus marijuana alone did. This pattern of findings suggests that alcohol may be the more salient driver for experiencing negative consequences than marijuana, consistent with other recent event-level findings (Mallett et al., 2019).

Our findings suggested that negative consequences and subjective intoxication did not vary regardless of the operationalization of SAM versus CAM. Although these findings appear to diverge from prior survey research (Brière et al., 2011; Patrick et al., 2018b; Subbaraman and Kerr, 2015), given that these prior studies focused on between-person effects (i.e., SAM compared to CAM users) versus the within -person comparisons of CAM versus SAM days, novel incongruent findings are expected. Additionally, among co-use days more than 50% of days involved co-use (i.e., report of having a drink or using marijuana) within 10 minutes and approximately 70% involved co-use within one hour. Taken together, these findings suggest that on co-use days the intoxicating effects of alcohol and marijuana likely overlap. Importantly, as our measures did not precisely capture onset or offset, it is likely that the true chronological proximity of co-use is closer than observed herein. Overall, these findings suggest that there is potentially little meaningful distinction between SAM and CAM days. However, given the exploratory nature of these analyses and limitations in the measurement of alcohol and marijuana use timing, future research should elucidate these effects.

Of critical importance for understanding the inter-relations between alcohol and marijuana, findings indicated that co-using alcohol and marijuana altered the relationship between substance consumption and outcomes. Greater consumption was unsurprisingly associated with greater subjective effects. However, this association was attenuated, by co-use of the other substance; similarly, heavier alcohol consumption was associated with more consequences experienced but this association was mitigated by co-use of marijuana.

Notably, these findings do not suggest that co-using alcohol and marijuana will reduce negative outcomes. Using marijuana with alcohol on the same day versus using either substance alone resulted in increased subjective intoxication that was not offset by the attenuating effect of the number of times the other substance was consumed, except days with very high use. Similarly, using marijuana and alcohol greatly increased daily consequences relative to marijuana use alone without an offsetting effect. These findings suggest that while co-using alcohol and marijuana on the same day increases risk for negative outcomes, this risk does not merely correspond to the number of drinks or marijuana uses. There are multiple potential explanations: using alcohol or marijuana after using the other substance may alter the rate of consumption, thus altering the relationship between substance use and negative consequences or subjective intoxication. Similarly, co-use days may involve substance use over a longer duration, which could attenuate the relationship between substance use and focal outcomes. Given that our findings are consistent with prior examinations of co-use (Mallett et al., 2019), the mechanisms underlying these attenuating relationships deserve further investigation.

4.1 Strengths and Limitations

This study benefitted from the using a large sample of daily participants, frequent assessments, nuanced assessments of negative consequences and subjective intoxication, and multi-site data collection. However, findings should be interpreted in light of several limitations. First, the scope is limited to the two outcomes under study. Daily SAM may confer additional risk over CAM for other outcomes (e.g., mental health) not investigated here. Similarly, focal outcomes are short-term and may not generalize to long-term health. Second, given challenges to measuring marijuana quantity, we cannot know how much marijuana was ingested (although we did control for product type). Third, the item used to assess subjective intoxication jointly queried the degree of intoxication from alcohol and marijuana. Although this decision was informed by preliminary qualitative data on the difficulty of disambiguating the relative contributions of alcohol versus marijuana to a given state of intoxication, future work should investigate whether these attributions are discernable and validate future measures accordingly. Similarly, our measure of co-use consequences queried events that happened due to the "use of alcohol and marijuana together." Although the decision not to allow attribution of co-use consequences to specific substances was informed by the same preliminary qualitative data, future research may elucidate the differential influence of alcohol or marijuana use on daily consequences and their attributions. Relatedly, the consequences outcome may reflect alcohol consequences more than consequences of co-use. As examinations of co-use and event-level specific consequences are developed, researchers may want to investigate whether study findings generalize to these novel outcomes. Fourth, although this study benefitted from including students attending three colleges in states with varying marijuana laws, these findings may not generalize to different populations. SAM and CAM may differentially predict outcomes among non-college attending young adults or during different developmental periods (e.g. adolescence, Lipperman-Kreda et al., 2017). For example, during the critical period of early adolescent brain development, SAM, compared to CAM, may be associated with more adverse consequences and co-use may have multiplicative effects (Lisdahl et al., 2013; Medina et al., 2007). While such findings would not invalidate the current research, developmental questions are important for future investigations. Fifth, participants were recruited into the daily portion of this study because they were past-month SAM users and, thus, the sample excluded individuals who are relatively naïve to SAM use. It is possible that this pattern of findings may not extend to first time or extremely infrequent SAM users. Finally, although multiple daily assessments were administered to reduce retrospective recall bias, there were no user-initiated reports due to the overall burden of the data-collection protocol. Timing of use may thus be subject to some degree of recall bias and replication of the current findings is warranted.

4.2 Conclusions

Daily co-use of alcohol and marijuana predicted greater subjective intoxication than use of either substance alone and more daily substance use-related consequences than marijuana use alone. Co-using alcohol and marijuana also attenuated the relationship between use of the other substance and these outcomes. This attenuating effect was small and unlikely to offset the increase in consequences or subjective intoxication attributable to co-use. Exploratory findings suggested little additional risk from using alcohol and marijuana

simultaneously versus concurrently, regardless of the timeframe used to operationalize SAM. However, given the small timeframe between using alcohol and marijuana observed on most co-use days in this study, distinguishing between CAM and SAM may be difficult and future research is needed to identify additional day-level risks of co-use.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- Alcohol and marijuana are frequently used simultaneously
- There is no consistent operational definition for “simultaneous” use
- Competing time-based operationalizations of simultaneity were investigated
- Daily co-use of alcohol and marijuana increased risk versus single-substance use
- Risks of simultaneous use remains significant, regardless of operationalization

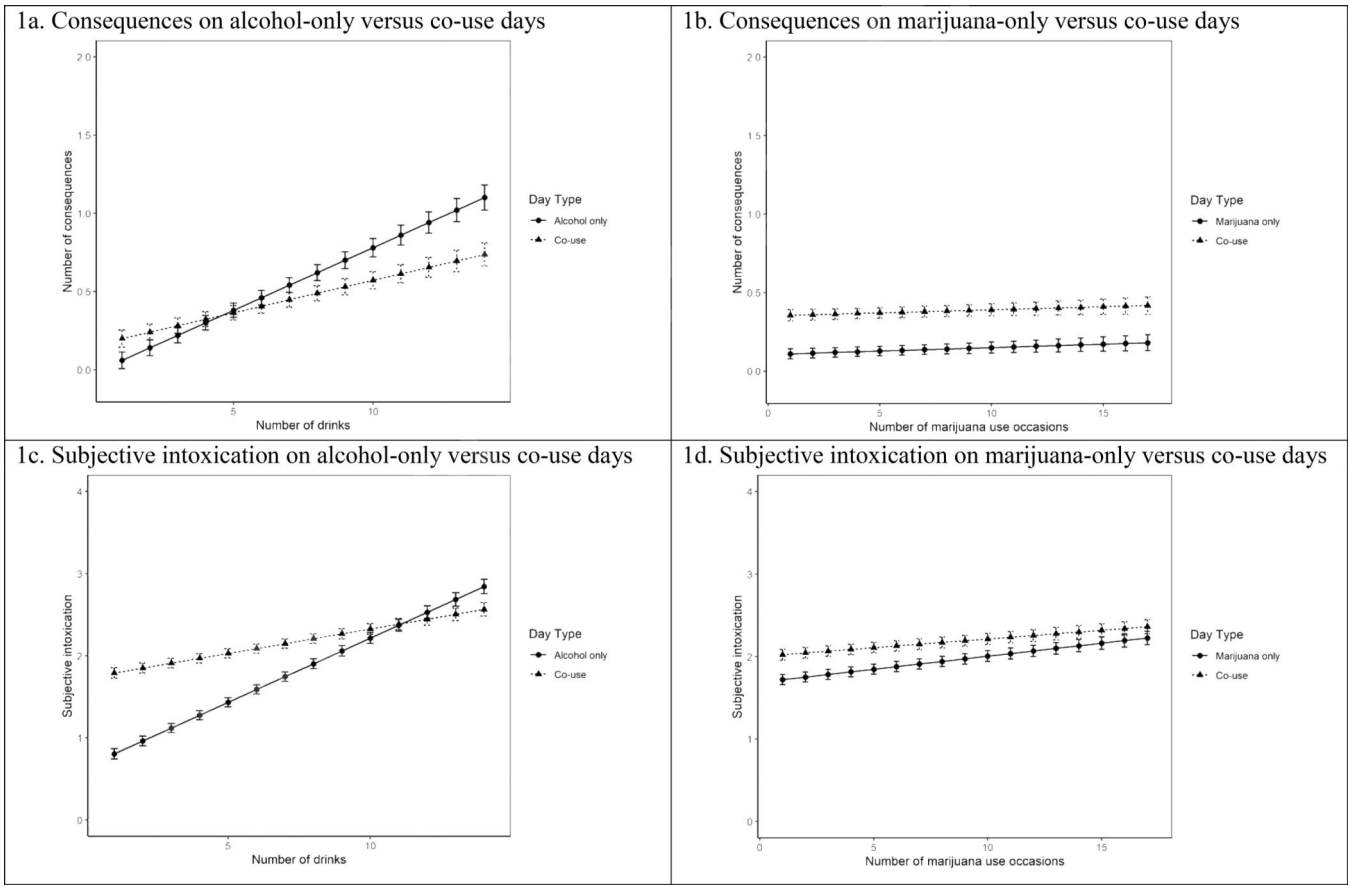

Figure 1. Consequences and subjective intoxication on alcohol only or marijuana only versus co-use days

X axes for number of drinks (or marijuana uses) range from 1 to mean daily number of drinks (or marijuana uses) plus two standard deviations rounded up, respectively (alcohol range = 1–15; marijuana range = 1–17).

Table 1.

Sample characteristics

Variable	*M* (SD) or %				
	Total sample (*n*=341)	Any daily co-use sample (*n*=284)	No daily co-use sample (*n*=57)	χ^2 or *t*	*p*
Sex (female)	51.3%	50.7%	54.4%	0.131	.717
White	74.8%	75.4%	71.9%	0.141	.707
Hispanic	10.0%	8.8%	15.8%	1.86	.172
Age	19.8 (1.32)	19.8 (1.35)	19.4 (1.10)	2.40	.018
AUDIT	9.71 (5.21)	9.92 (5.32)	8.72 (4.57)	1.75	.084
CUDIT-R	9.55 (6.10)	10.20 (6.05)	6.44 (5.39)	4.68	<.001
Drinks per drinking day	4.87 (2.67)	5.06 (2.50)	3.92 (3.21)	2.57	.012
Marijuana uses per use day	3.61 (3.32)	3.96 (3.40)	1.91 (2.22)	5.76	<.001
Proportion plant-only days	70.5%	70.2%	72.6%	0.385	.702
Proportion nicotine use days	23.0%	24.9%	13.9%	2.70	.008
Proportion other drug use days	3.4%	3.8%	1.9%	2.31	.023

Note: Proportion of plant-only use days, nicotine use days, and other drug use days were aggregated at the subject level (i.e., mean of subject-level proportions of use days) rather than the day level (i.e., proportion of days across all participants) for the sake of presentation in this Table but not in the analyses. Denominator for proportion of plant-only days is marijuana use days. Denominator for nicotine use days and other drug use days is total study days. AUDIT=Alcohol Use Disorders Identification Test; CUDIT-R=Cannabis use Disorder Identification Test Revised. χ^2 or *t difference tests reflect differences between the subset of participants with any daily co-use (n=284) and those in the final sample but no reports of daily co-use (n=57). Absolute vaue of t-tests is presented.*

Table 2.

Effect of daily co-use of alcohol and marijuana relative to single substance use on daily consequences

	Daily Consequences									
	Co-use versus Alcohol Only (*n*=328)					**Co-use versus Marijuana Only (*n*=314)**				
		95% CI					**95% CI**			
Predictors	**β**	**Low**	**High**	**SE**	***p***	**β**	**Low**	**High**	**SE**	***p***
Intercept	−0.074	−0.560	0.415	.253	–	0.023	−0.393	0.442	.217	-
Level 2 (Person)										
Male	**−0.102**	**−0.166**	**−0.038**	**.033**	**.002**	−0.051	−0.107	0.005	.029	.078
Non-white	0.039	−0.039	0.118	.041	.337	0.011	−0.058	0.080	.036	.756
Hispanic/Latino	0.001	−0.110	0.112	.058	.983	0.008	−0.088	0.103	.049	.869
Age	0.013	−0.011	0.036	.012	.303	−0.002	−0.023	0.019	.011	.851
School (A)	−0.046	−0.122	0.032	.040	.255	−0.020	−0.090	0.050	.036	.578
School (B)	0.058	−0.018	0.134	.040	.143	**0.089**	**0.020**	**0.157**	**.036**	**.013**
AUDIT	**0.012**	**0.006**	**0.019**	**.003**	**<.001**	**0.009**	**0.003**	**0.014**	**.003**	**.002**
CUDIT-R	0.004	−0.002	0.010	.003	.160	0.000	−0.005	0.005	.003	.982
Level 1 (Day)										
Any daily nicotine	0.028	−0.027	0.082	.028	.322	**0.040**	**0.002**	**0.077**	**.019**	**.037**
Any daily other drugs	**0.106**	**0.018**	**0.195**	**.045**	**.019**	**0.111**	**0.054**	**0.167**	**.029**	**<.001**
Non-plant	0.021	−0.045	0.087	.034	.541	0.020	−0.012	0.052	.017	.223
Weekend	**0.095**	**0.055**	**0.136**	**.021**	**<.001**	**0.088**	**0.061**	**0.114**	**.014**	**<.001**
# drinks	**0.080**	**0.073**	**0.087**	**.004**	**<.001**					
# marijuana uses						**0.004**	**0.001**	**0.008**	**.002**	**.009**
Daily co-use	−0.019	−0.085	0.048	.034	.584	**0.243**	**0.215**	**0.271**	**.014**	**<.001**
# drinks * daily co-use	**−0.039**	**−0.048**	**−0.029**	**.005**	**<.001**					
# marijuana * daily co-use						0.000	−0.005	0.004	.002	.815

Note. AUDIT= Alcohol Use Disorders Identification Test; CUDIT-R=Cannabis use Disorder Identification Test Revised. ICCs for subject-level clustering of consequences were .15 and .18, respectively, in data comparing co-use to alcohol only (left panel) and marijuana only (right panel).

Table 3.

Effect of daily co-use of alcohol and marijuana relative to single substance use on daily subjective intoxication

	Daily Subjective Intoxication									
	Co-use versus Alcohol Only (*n*=330)					**Co-use versus Marijuana Only (*n*=317)**				
		95% CI					**95% CI**			
Predictors	**β**	**Low**	**High**	**SE**	***p***	**β**	**Low**	**High**	**SE**	***p***
Intercept	2.351	1.690	3.014	.342	-	2.635	1.789	3.488	.437	-
Level 2 (Person)										
Male	0.004	−0.083	0.092	.045	.927	0.100	−0.013	0.214	.059	.089
Non-white	−0.034	−0.141	0.074	.056	.543	−0.039	−0.178	0.101	.072	.593
Hispanic/Latino	0.051	−0.099	0.200	.077	.510	**0.206**	**0.012**	**0.400**	**.100**	**.041**
Age	**−0.054**	**−0.087**	**−0.022**	**.017**	**.001**	**−0.058**	**−0.100**	**−0.016**	**.022**	**.009**
School (A)	−0.015	−0.121	0.091	.055	.787	0.039	−0.102	0.180	.073	.596
School (B)	0.084	−0.021	0.189	.054	.123	0.097	−0.043	0.237	.073	.183
AUDIT	−0.007	−0.015	0.002	.005	.146	0.005	−0.006	0.016	.006	.381
CUDIT-R	**0.014**	**0.006**	**0.021**	**.004**	**<.001**	0.010	−0.001	0.020	.005	.070
Level 1 (Day)										
Any daily nicotine	0.043	−0.017	0.101	.030	.151	**0.082**	**0.031**	**0.132**	**.026**	**.002**
Any daily other drugs	**0.123**	**0.034**	**0.212**	**.045**	**.007**	**0.130**	**0.058**	**0.202**	**.037**	**<.001**
Non-plant	0.000	−0.068	0.069	.035	.991	0.008	−0.035	0.050	.022	.720
Weekend	**0.161**	**0.120**	**0.201**	**.021**	**<.001**	**0.111**	**0.077**	**0.145**	**.017**	**<.001**
# drinks	**0.157**	**0.149**	**0.164**	**.004**	**<.001**					
# marijuana uses						**0.032**	**0.028**	**0.036**	**.002**	**< .001**
Daily co-use	**0.589**	**0.521**	**0.658**	**.035**	**<.001**	**0.262**	**0.226**	**0.298**	**.018**	**<.001**
# drinks * daily co-use	**−0.097**	**−0.107**	**−0.088**	**.005**	**<.001**					
# marijuana * daily co-use						**−0.010**	**−0.016**	**−0.005**	**.003**	**<.001**

Note. AUDIT= Alcohol Use Disorders Identification Test; CUDIT-R=Cannabis use Disorder Identification Test Revised. ICCs for subject-level clustering of subjective intoxication were .30 and .39, respectively, in data comparing co-use to alcohol only (left panel) and marijuana only (right panel).

Table 4.

Regions of significance in models predicting daily consequences from consumption and operationalizations of SAM

	Daily Consequences[a]							
	All βs		**ROS βs**[c, d]		**ROS Range**		***p*-value in ROS**[e]	
Variable	**Low**	**High**	**Low**	**High**	**Low**	**High**	**Low**	**High**
Intercept	−0.115	−0.035	-	-	-	-	-	-
Level 2 (Person)								
Male	−0.099	−0.091	−0.099 −0.095	−0.093 −0.094	1 62	10 151	.038 .046	.049 .049
Non-white	0.034	0.040	-	-	-	-	-	-
Hispanic/Latino	−0.085	−0.072	-	-	-	-	-	-
Age	0.010	0.015	-	-	-	-	-	-
School (A)	−0.060	−0.049	-	-	-	-	-	-
School (B)	0.122	0.135	0.122	0.135	1	240	.017	.030
AUDIT	0.014	0.015	0.014	0.015	1	240	.001	.003
CUDIT	0.004	0.004	-	-	-	-	-	-
Level 1 (Day)								
Any daily nicotine	0.029	0.038	-	-	-	-	-	-
Any daily other drugs	0.077	0.093	-	-	-	-	-	-
Non-plant	0.048	0.057	-	-	-	-	-	-
Weekend	0.088	0.094	0.088	0.094	1	240	.001	.003
SAM (versus CAM)	−0.094	0.016	-	-	-	-	-	-
# drinks	0.049	0.076	0.049	0.076	1	240	< .001	< .001
# drinks * SAM	−0.041	−0.012	−0.041	−0.018	3	114	< .001	.044
# marijuana uses	−0.031	0.001	-	-	-	-	-	-
# marijuana uses * SAM	−0.004	0.026	-	-	-	-	-	-

Note: AUDIT= Alcohol Use Disorders Identification Test; CUDIT-R=Cannabis use Disorder Identification Test Revised. ROS = region of significance. Low and high ROS range represents the range of SAM operationalizations (i.e., the duration between any one drink and one marijuana use on a given day that delineated SAM from CAM) during which a given variable was a significant predictor of daily

consequences. For example, ‘37’ falling within the ROS range (from 1 to 240) for a given variable implies that when 37 minutes is used to delineating SAM from CAM, the given variable is significant predictor of daily consequences.

a. Values for “ROS βs” and “ROS range” are not presented when the predictor is not significant for any operationalization.

b. Low and high values for “All βs” represent the lowest and highest estimate across all SAM operationalizations.

c. Low and high “ROS βs” represent the lowest and highest estimate within the ROS.

d. “All βs” are equivalent to “ROS βs” when “ROS range” is 1–240 (i.e., significant in all operationalizations).

e. *p*-values are given within the ROS where significant at $p < .05$.

Table 5.

Regions of significance in models predicting daily subjective intoxication from consumption and operationalizations of SAM

	Daily Subjective Intoxication[a]							
	All βs		ROS βs[c, d]		ROS Range		*p*-value in ROS[e]	
Variable	**Low**	**High**	**Low**	**Low**	**Low**	**High**	**Low**	**High**
Intercept	2.979	3.112	2.972	3.104	1	240	< .001	< .001
Level 2 (Person)								
Male	0.101	0.109	-	-	-	-	-	-
Non-white	−0.026	−0.014	-	-	-	-	-	-
Hispanic/Latino	0.162	0.190	-	-	-	-	-	-
Age	−0.063	−0.057	−0.063	−0.057	1	240	.005	.010
School (A)	0.067	0.091	-	-	-	-	-	-
School (B)	0.091	0.112	-	-	-	-	-	-
AUDIT	−0.005	−0.004	-	-	-	-	-	-
CUDIT	0.013	0.01	0.013	0.014	1	240	.007	.014
Level 1 (Day)								
Any daily nicotine	0.058	0.067	-	-	-	-	-	-
Any daily other drugs	0.050	0.078	-	-	-	-	-	-
Non-leaf	−0.041	−0.030	-	-	-	-	-	-
Weekend	0.112	0.129	0.112	0.129	1	240	< .001	< .001
SAM (versus CAM)	−0.091	0.095	-	-	-	-	-	-
# drinks	0.069	0.085	0.069	0.085	1	240	< .001	< .001
# drinks * SAM	−0.039	−0.017	−0.039	−0.020	1	183	< .001	.045
# marijuana uses	0.026	0.086	0.026	0.086	1	240	< .001	.001
# marijuana uses * SAM	−0.075	−0.016	−0.075	−0.016	1	240	< .001	.007

Note: AUDIT=Alcohol Use Disorders Identification Test; CUDIT-R=Cannabis use Disorder Identification Test Revised. ROS=region of significance. Low and high ROS range represents the range of SAM operationalizations (i.e., the duration between any one drink and one marijuana use on a given day that delineated SAM from CAM) during which a given variable was a significant predictor of daily subjective intoxication.

[a] Values for "ROS βs" and "ROS range" are not presented when the predictor is not significant for any operationalization.

[b] Low and high values for "All βs" represent the lowest and highest estimate across all SAM operationalizations.

[c] Low and high "ROS βs" represent the lowest and highest estimate within the ROS.

[d] "All βs" are equivalent to "ROS βs" when "ROS range" is 1–240 (i.e., significant in all operationalizations).

[e] p-values are given within the ROS where significant at $p < .05$.