THE IMPACT OF CANNABIS-ALCOHOL CO-USE ON DRINK CONSUMPTION: TIMING IS KEY

by

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B.A. (Spec. Hons.), University of British Columbia (Vancouver), 2017

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR

THE DEGREE OF MASTER OF ARTS

in

The College of Graduate Studies

(Psychology)

THE UNIVERSITY OF BRITISH COLUMBIA

(Okanagan)

July 2020

Examination Committee

The following individuals certify that they have read, and recommend to the College of Graduate Studies for acceptance, a thesis entitled:

THE IMPACT OF CANNABIS-ALCOHOL CO-USE ON DRINK CONSUMPTION:

TIMING IS KEY

Submitted by Joseph Marc Rootman in partial fulfilment of the requirements of the degree of Master of Arts.

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Abstract

Heavy episodic drinking (HED) of alcohol is a dangerous and highly prevalent behaviour among college students, and the risks associated with HED increase dramatically with each drink consumed. Past research has been inconsistent in determining if the co-use of cannabis and alcohol is more harmful than alcohol use (AU) on its own, or if co-use impacts drink consumption. Importantly, if co-use is not more harmful than AU on its own, and co-use is associated with reduced drink consumption, then it follows that co-use reduces the harm associated with HED by way of minimizing drink consumption. The present study used daily diary methods to explore the impact of co-use on drink consumption and built on past research through the consideration of 3 previously unexplored factors: 1) temporal precedence of cannabis use (CU) to AU, 2) intention to substitute CU for AU and 3) quantity of CU consumed in a given AU session. 146 college students completed 3 surveys daily and reported on characteristics of AU sessions. Multilevel models were used to assess within- and between-person variations in drink consumption. Results indicated that CU before or during an AU event was associated with lower levels of drink consumption relative to AU events where CU occurred only after an AU event. Additionally, although co-use was not associated with drink consumption levels, co-use before/during AU was associated with lower levels of drink consumption relative to drinking events wherein CU occurs only after AU or not at all. These findings extend past research by highlighting the importance of temporal precedence in the evaluation of the relationship between co-use and drink consumption, and suggest that CU before or during an AU event may reduce harm by way of its association to reduced drink consumption. Agencies that distribute harm reduction guidelines, as-well as government and private organizations, can incorporate these findings into practice by moving away from overarching prohibitions against co-use.

Lay Summary

Binge drinking is a dangerous and prevalent behaviour, and the risk associated with binge drinking increases with each drink. Cannabis use in the context of a binge drink event, known as co-use, is also common, yet past research has been inconclusive in determining if cannabis increases or decreases drink consumption. This study examined if, and what features of, co-use impact drink consumption in a binge session. Specifically, the association between drink consumption and the following co-use session characteristics were investigated: timing of cannabis use with respect to alcohol use, intention to replace cannabis with alcohol, and the amount of cannabis used in a co-use session. Co-use before and/or during a drinking event was associated with fewer drinks consumed relative to when cannabis was used only after alcohol use or not used at all. This suggests that co-use may increase the safety of binge drinking by reducing drink consumption.

Preface

The Behavioural Research Ethics Board of the University of British Columbia's Okanagan Campus granted ethics approval for this research. The certificate approval number for the project is H17-03523 and H17-03519. To date, the results of this study have not been published. Joseph Rootman was responsible for the conceptualization and design of the study, completing and overseeing data collection, as well as data analysis, and writing of the final thesis.

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Acknowledgements

This project could not have been possible without the support of several important people. First and foremost, I would like to express my deepest gratitude for the guidance provided by my research supervisor, Dr. Zach Walsh. I never dreamed that I would be so lucky to be able to spend my days reading, learning, talking and laughing about cannabis as I have in my time knowing him, and it speaks largely to his incredible supervision that my understanding of cannabis, psychedelics and the scientific process has expanded a hundredfold throughout my graduate education. I would also like to express my gratitude towards my committee members, Dr. Susan Holtzman and Dr. M-J Milloy, both of whom were integral to the success of this project through their critical eye towards my methods and conceptualization of my project, all of which was provided with a smile and plenty of kind words. Further, I would like to thank Dr. Brian O'Connor for his support and encouragement in the development of my statistical plan.

I would also be remiss if I didn't say thank you to my lab mates in the UBC-O Therapeutic, Recreational, and Problematic Substance Use Lab. Specifically, Michelle St. Pierre, Tatiana Sanchez, Sarah Daniels and Kim Crosby who have all consistently provided their ongoing support in my research and have made substantial contributions to the larger ongoing research project to which this thesis was built into which including: conception, design, distribution and quality control. In line with this, I would like to thank all my participants for doing their best to accurately recall the specifics of their last drinking event- I hope your nights were both fun and safe.

Finally, I especially would like to thank my close friends and family who have all been incredibly supportive of my research and work over the years. More critical to my success than

their support is the endless love and unbelievably fun times I continue to share with them as each day passes.

Dedication

This project is dedicated to the voice in my head that told me countless times that I couldn't do this. And, more importantly, the one person in the world who would never- ever- let me listen to that voice.

Chapter 1: Introduction

Alcohol is the most commonly used substance in Canada, with three quarters of Canadians reporting alcohol use (AU) in the past year (CCSA, 2017). Heavy episodic drinking (HED) is dangerous and highly prevalent among young adults in Canada (Canadian Centre on Substance Use and Addiction [CCSA], 2017). Cannabis is often co-used with alcohol (Subbaraman & Kerr, 2015; White et al., 2019) however, past research has been inconsistent in determining the impact of cannabis use (CU) during a HED session (Subaraman, 2016). The harms associated with HED increase with each drink consumed in a session (Taylor et al., 2010). As such, determining whether CU increases, decreases or has no effect on the number of drinks consumed in a HED session is critical to understanding the safety of cannabis-alcohol co-use. The present study builds on past research by investigating the impact of CU on HED session drink consumption while considering three previously unexplored factors. First, we examine the impact of whether CU occurs before/during or after AU. Second, we examine the influence of intention to use cannabis as a substitute for alcohol. Finally, we examine the impact of quantity of cannabis used in a HED session.

1.1 Heavy Episodic Drinking

Much of the health burden associated with AU is related to HED, which in females, is defined as three drinks consumed on a single occasion and four drinks in males (Butt, Beirness, Gliksman, Paradis, & Stockwell**,** 2011). In 2015, approximately 77,000 Canadians were hospitalized as a result of alcohol use (CCSA, 2017) and an estimated 232 deaths are reported in Canada annually as a result of alcohol poisoning (Statistics Canada, 2014). The harms associated with HED are not limited exclusively to drinkers. For instance, in 2015 more than 72,000 impaired driving incidents were reported, 96% of these cases were alcohol related (Kathryn, 2017). Moreover, alcohol related harms pose a financial burden, costing Canadian tax payers approximately $14.6 billion per year (Rehm et al., 2002). Taken together, HED represents a public health concern that impacts, not only those engaging in HED, but the safety and economic welfare of all Canadians.

There is a growing body of literature examining the negative physiological and psychological outcomes associated with HED. For instance, HED is associated with short-term consequences such as blacking out, alcohol poisoning, and injuries (Butt, Beirness, Gliksman, Paradis, & Stockwell, 2011; Caudwell, Mullan, & Hagger, 2016; Park & Grant, 2005; White & Hingson, 2014). HED has also been linked to harmful long-term outcomes including physical health problems, as well as cognitive, structural and functional brain changes (Briasoulis, Agarwal, & Messerli, 2012; Rehm et al., 2010; Stavro, Pelletier, & Potvin, 2013). Given this, identifying factors that might inhibit or exacerbate this often hazardous behaviour pattern, is essential.

Among college students, alcohol is reported as the most frequently used drug (Johnston, O'Malley, Bachman, & Schulenberg, 2013) and young adults (ages 18-25) are particularly at risk for adopting harmful drinking behaviour patterns. For example, nearly one third of college aged students report at least one HED episode per month in the past year (CCSA, 2017). The acute risks associated with alcohol intoxication increase exponentially with each drink consumed (Taylor et al., 2010). These risks disproportionately impact young adults such that they are at a significantly higher risk for injury when engaging in HED compared to older individuals (Stockwell & Greer, 2009). Outside of injury, research has shown that the consequences of HED can be considerably different than those of moderate alcohol use. For example, a study that compared college students who engaged in AU but not HED, to those that that engaged in HED three times over a two-week period, showed that the students who engaged in frequent HED were eight times more likely to report falling behind in their schoolwork, getting hurt or injured, or damaging property (Wechsler, Dowdall, Maenner, Gledhill-Hoyt, & Lee, 1998). These findings support an association between drinks consumed and negative outcomes, particularly in college aged students. Further understanding the contextual factors that may influence number of drinks consumed in AU sessions, may help to distinguish those most at risk and better inform development of harm reduction recommendations and policies.

1.2 Cannabis-Alcohol Co-Use

The use of cannabis and alcohol in a short time frame such that the effects overlap, hereafter referred to as cannabis-alcohol co-use, is common among college students who engage in substance use (Barrett, Darredeau, & Pihl, 2006; White et al., 2019). More than a quarter of college students report using both alcohol and cannabis (Shillington, & Clapp, 2006), of whom three quarters report co-use at least once in the past year, with an average co-use frequency of twice in the past month (White et al., 2019). Moreover, 95% of Canadian university students who use both cannabis and alcohol report lifetime co-use of these substances (Barrett et al., 2006). Additionally, co-use appears to be more common among university students in areas where recreational cannabis is legal, such as Canada, relative to regions where it is decriminalized or entirely prohibited (White et al., 2019). In sum, cannabis-alcohol co-use is highly prevalent among college students.

Despite the widespread co-use of cannabis and alcohol, research examining the associations between co-use and outcomes is limited. Co-users of cannabis and alcohol were more likely to experience negative social consequences, depressive symptoms (Midanik et al., 2007), use-related negative consequences (Briere et al., 2011), and more intoxicated driving

(Terry-McElrath et al., 2013) relative to those who do not report co-use. Perhaps in response to these findings which indicated negative outcomes associated with being a co-user, guidelines recommend that cannabis-alcohol co-use be avoided to prevent negative consequences such as injury and alcohol poisoning (Canadian Nurses Association, 2017; Delphi Behavioral Health Group, 2019; HealthLinkBc, 2019). While well intentioned, these recommendations may be generalizing between-person findings, which look at differences between individuals that do or not co-use, to a within-person situation: whether or not cannabis should be co-used in a given event.

Generalizing findings about co-users to the harms associated with co-use on a given night is problematic because associations between individual characteristics and outcomes may be due to shared risk factors rather than co-use increasing harm. The majority of research on co-users has focused on associations to externalizing behaviours such as intoxicated driving (Terry-McElrath et al, 2013) and other negative use-related and social consequences (Briere et al., 2011; Midanik et al., 2007). Further, research suggests that individuals exhibiting externalizing behaviours share a behavioural system characterized by behavioural undercontrol (Hicks et al., 2004). Given that substance use is an externalizing behaviour itself, it may be that much of the past literature linking co-users to harms is reflective of this shared behavioural system rather than a causal pathway whereby the acute effects of co-use increase harm. Thus, policies that limit, and guidelines that recommend against, should be developed largely under the consideration of within-person research.

In contrast to the between-person research which indicates negative outcomes associated with being a co-user, within-person findings have been mixed with respect to the association between co-use and negative consequences in a given event relative to AU alone. Three studies suggest that co-use is not associated with negative consequences over AU alone. First, one study found that university students did not experience more negative consequences from HED episodes with cannabis co-use compared to HED episodes without co-use. Additionally, this study found the number of negative consequences experienced did not differ between non-HED AU sessions, non-HED co-use sessions and CU only sessions, all of which were less risky than HED and HED co-use sessions (Mallett et al., 2019). In line with this, a study among a community sample of young adults found that the association between co-use and negative consequences is not significant after controlling for the extent of drinking in a given event (Lee et al., 2020), a finding which has been identified in adolescents as well (Lipperman-Kreda, 2017). While these studies suggest co-use does not impact negative consequences experienced over and above the effect of drink consumption, two studies suggest otherwise. In one study co-use was associated with increased consequences over and above drink consumption (Linden-Carmichael, 2020), but the results of another study suggest that, at high levels of drink consumption, co-use may actually reduce negative consequences experienced relative to AU (Sokolovsky et al., 2020). Taken together, the daily-level literature regarding the consequences associated with co-using cannabis and alcohol in a given event relative to AU alone is still developing, but it trends toward suggesting that co-use may not be increasing AU risk (Mallet et al., 2019; Lee et al., 2020; Lipperman-Lreda, 2017), with some research suggesting it may even minimize it (Sokolovsky et al., 2020). As such, firm recommendations against co-use may need to be reconsidered.

The impact of CU on the number of drinks consumed is pertinent to harm reduction recommendations. Research has not clearly identified the impact of co-use on negative consequences over the effect of drink consumption, with the majority of studies suggesting it reduces or has no effect (Mallet et al., 2019; Lee et al., 2020; Lipperman-Lreda, 2017; Sokolovsky et al., 2020), and the harms associated with HED are greater than light drinking (Taylor et al., 2010; Wechsler et al., 1998). In the context of a drinking event, these findings can be interpreted to suggest that 5 drinks without co-use may be more harmful than 4 drinks with co-use. Thus, if co-use decreases the number of drinks consumed in an AU session than it may be decreasing the risk associated with AU. Nonetheless, if co-use increases drink consumption than co-use may be increasing harm. In sum, it is not clear whether co-use increases or decreases drink consumption, but such information is critical to understanding if co-use is harmful or harm reducing.

1.3 CU and HED: Compliment or Substitute?

Behavioural economic theory (BET) provides one avenue for understanding how CU might impact AU. BET applies concepts from economics, such as supply and demand, to help understand how the availability of one good can either increase, decrease or have no effect on the use of another good. Within the context of substance use (SU), this framework helps to explain how substances interact with each other such that the use of one substance may exert a substitute effect that decreases other SU, compliment effect that increases other SU, or have no effect on the use of other substances (Hursh et al., 2005). Compliment and substitute effects can be explained in a number of ways. As an example, one drug may act as a substitute by fulfilling the primary purpose of using another drug. This is suggested to be one of the mechanisms of action of methadone replacement therapy. Specifically, methadone reduces opioid cravings and minimizes withdrawal symptoms over a longer period of time than other opioids such as heroin, and thus people that use primarily heroin as a means of overcoming withdrawal and cravings can fulfill this need with the safer and longer lasting drug methadone (Fareed, 2010). On the other hand, compliment effects may occur when subjective effects of co-use are more desirable than the use of either substance independently and are, therefore, often paired. For example, cocaine and alcohol are often used together because they tend to have stronger euphoric effects when used together than alone (Singh, 2019). If cannabis serves as a substitute for alcohol, co-use may decrease total amount of alcohol consumed thereby decreasing the likelihood that an AU session will escalate to HED. In contrast, if cannabis is a complement to alcohol, CU may increase the likelihood of HED.

Investigations into whether CU exerts substitutive or complimentary effects on AU dates back to the 1970's and have yet to be resolved. In a seminal early single subject study, a woman in recovery from an alcohol use disorder (Mikuriya, 1970) reported effectively substituting CU for AU, and finding CU to be a safer and more enjoyable alternative to AU. This finding has been echoed in a series of more recent studies; 25 - 45% of medical cannabis users report substituting cannabis with alcohol (Lucas, Baron, & Jikomes, 2019; Lucas & Walsh, 2017; Reiman, 2009). Despite the fact that many individuals use CU as a substitute for AU, the issue is far from closed as there is a competing body of literature suggesting that CU is best thought of as a compliment to AU.

A systematic review of cannabis and alcohol use (Subaraman, 2016) found that the literature is inconsistent, with evidence coming in support of the substitution effect, the compliment effect, or neither. Specifically, of the 39 studies reviewed, 16 reported evidence consistent with substitution effects, ten consistent with complementarity effects, 12 consistent with neither a substitution or compliment effect and one study consistent with both. The mixed findings were attributed to the use of heterogeneous populations, differences in the operationalization of dependent variables, such as the choice of any alcohol use vs. HED, and the reliance on a binary model of co-use wherein CU is either a compliment or substitute to AU. The inconsistency of these studies suggest that cannabis' substitutive effects on alcohol may be moderated by a number of variables, such as individual differences, motives, and contextual factors. First, age may moderate this relationship, as longitudinal studies of youth favor a complimentary effect (Anderson, Hansen, & Reese, 2012; Pacula, 1998), whereas studies of the general population indicated a substitution effect (Anderson & Rees, 2013). Additionally, gender, race, and individual SU patterns were identified as relevant factors in determining if substitution or complimentary effects were likely to occur. For example, one study suggested that European American males and African Americans may be more likely to compliment, whereas Native Americans and Hispanics may be more likely to substitute (Saffer & Chaloupka, 1998). Additionally, cannabis and alcohol were found to be economic compliments for all cannabis users but this relationship was particularly strong in those that report co-use of the substances (Williams & Mahmoud, 2004). Finally, it was noted that there seems to be a trend such that substitution is more likely to occur in regions with liberal cannabis regulations, such as decriminalization and legalization, in place (Anderson & Rees, 2011; Anderson, Hanson & Rees, 2013; Kelly & Rasul, 2014). Liberal cannabis regulations may support substitution effects by providing cannabis access to portions of the population that tends to consume only licit substances. These individuals may prefer cannabis to alcohol but choose alcohol due to the reduced legal risk, thus a liberal cannabis environment allows these individuals to consume their preferred substance thereby reducing their need for alcohol. In sum, cannabis and alcohol use may interact along a continuum with the substitution effect on one end and the compliment effect on the other. This review highlights that prior studies examining the relationship between AU and CU have been inconsistent, and that more research is needed to unpack this relationship.

One advancement to the methodology of prior studies is to move beyond macro-level economic, epidemiological, or broad cross-sectional data, all of which restrict analysis at the individual level. For example, DiNardo and Lemieux (2001) found that increasing the minimum legal drinking age from 18-21 increased rates of cannabis use among young adults while decreasing rates of AU. The results of this study indicate a substitution effect whereby alcohol availability decreases and is replaced with CU, but do not elucidate how this substitution occurs on an individual level. Specifically, it remains unclear whether 1) these young adults were supplementing AU with CU thereby reducing the number of drinks consumed in AU sessions, 2) CU reduced the occurrence of AU events but had no impact on the number of drinks consumed in AU sessions, or 3) CU both reduced the number of drinks consumed in an AU event and the frequency of these events. Daily-level data capture behaviour within the context of a single event, such as one session of drinking, and thus allow for a fine-grained look at how, and if, these substances interact to produce either a substitutive or complimentary effect.

1.4 Daily-Level Research

Daily-level data can be obtained in a number of ways. As an example, ecological momentary assessments (EMAs) are brief questionnaires that are sent directly to participants (on their mobile phones, e-mails or other devices) and are expected to be completed as soon as possible. EMAs have the benefit of obtaining participant responses close in time to the actual event of interest, making them less susceptible to recall bias compared to retrospective measures. This is particularly useful within SU research which often asks participants to report on highly specific details of a SU event. Moreover, EMAs can tap into other factors such as state levels of mood, motivation and other important, but transient, elements of a SU event (Shiffman, 2009). Other methods to evaluate SU at the daily level include daily diary and other retrospective methods (e.g., the *timeline follow back technique)* that ask participants to report SU details from particular events rather than general SU patterns. The following studies have used a myriad of daily-level techniques to approach the subject of cannabis-alcohol co-use.

1.4.1 Daily-Level Cannabis-Alcohol Co-Use Research. A review of the literature identified seven studies that have used daily-level data to examine the effect of CU on AU and HED (Gunn et al., 2018; Gunn et al., 2019; Lee et al., 2020; Linden-Carmichael, 2020; Mcketin et al., 2014; Metrik et al., 2018; Roche et al., 2019). First, a study of 688 young adult Australian cannabis users found that there were no significant differences in the rates of HED between cannabis users who had engaged in CU on the previous Saturday night to cannabis users who had not used cannabis (Mcketin et al., 2014). Specifically, 57% of individuals who had smoked cannabis on the previous Saturday night had engaged in HED compared to the 55% who had not smoked cannabis, and this effect remained non-significant after adjusting for demographic variables. This finding aligns with a 14 day daily dairy study of young adults which found that co-use of cannabis and alcohol was not associated with an increased drink consumption relative to AU only events (Linden-Carmichael, 2020). These results suggest that CU has no impact on the likelihood of engaging in HED

A study of US veterans ($N = 127$) examined differences in drinking patterns on days that cannabis was used compared to days where it was not (Metrik et al., 2018). Specifically, using the *timeline follow back technique* (Sobell and Sobell, 1992) participants were asked to report the amount of drinks they consumed, and whether cannabis was smoked, on each day in the 180 days prior to the assessment. Here, it was found that CU days were more likely to involve heavy, rather than moderate drinking, and more likely to involve moderate drinking compared to not at all, relative to days with no CU. This finding was moderated by substance-use disorders such that those with an Alcohol Use Disorder (AUD) or both an AUD and Cannabis Use Disorder (CUD) were significantly more likely to drink heavily on CU days. In contrast, those with only a CUD were significantly less likely to drink heavily on CU days. The same research group conducted a further analysis on this sample which suggested that recreational cannabis users consumed significantly more drinks on CU days relative to non-CU days, but that medicinal cannabis users drank significantly less on CU days (Gunn et al., 2019). Further, among these medical cannabis using veterans, individuals who reported a greater tendency to substitute CU for AU drank less on cannabis use days relative to those who did not report such a tendency to substitute. In sum, these study falls in line with the idea that CU may act as either a substitute or compliment to AU depending on individual characteristics.

Another study collected 36 bi-weekly assessments over the span of two years in a sample of 488 college students. These surveys asked participants to report if cannabis was used and the quantity of drinks consumed for each day in the previous week (Gunn et al., 2018). Alcohol consumption was greater on days of CU. In line with previous studies (Metrik et al., 2018), ratings of AUD moderated this relationship such more severe alcohol use problems were associated with heavier drinking on CU days.

One study from the state of Washington, where recreational CU is legal, looked at the impact of co-use on drink consumption in a community sample of 488 individuals using daily diaries completed over 28 days (Lee et al., 2020). Here it was found that, relative to AU only days, co-use days were significantly associated with greater drink consumption. Specifically, co-use was associated with drinking 14% more than AU only.

A study which used the timeline follow back technique dating back 30-days to assess daily cannabis and alcohol use found that cannabis use on a given day predicted any alcohol use on that same day while controlling for cigarette use, age and ethnicity (Roche et al., 2019). Further, a significant interaction effect indicated that the association between CU and an increased probability of AU was significantly stronger in men than it was for woman. Drink consumption quantity was not included in the analysis, thus, although CU on a given day is associated with increased likelihood of AU on that day, this study did not clarify if CU increased or decreased the intensity of AU. These researchers also found that engaging in AU increased the probability of participants engaging in any CU on a given day while controlling for the effects of cigarette use, age and ethnicity.

Two more studies have used daily-level data to evaluate if AU has either a substitutive or complimentary effect on CU (Hughes et al., 2014; O'Hara et al., 2016). A 2014 longitudinal study (Hughes et al., 2014) asked 144 participants to call an interactive voice messaging system daily over the span of three months to report SU behaviors. Both any AU, as well as HED engagement on any given day predicted the number of times that CU occurred on that day. Additionally, the effect of AU on increasing CU was evidenced at the bivariate level, as well as found to increase CU over and above other variables in the study. Examples of these other variables include environment context variables, such as being at a party, and mood variables, such as being angry. Despite the fact that these findings were significant, the magnitude of these effects were small. Specifically, although participants engaged in CU a median of 4 times per times per day on CU days, the difference was only 0.1 CU instances greater for HED days and .03 for AU days.

Finally, one 30-day daily diary study asked 876 participants to log the number of drinks consumed on the previous day and if any CU occurred (O'Hara, Armeli, & Tennen, 2016). Participants entered responses daily. Analysis at the daily-level indicated that evening AU levels predicted if any cannabis was used that evening for both weekday and weekend reports. Specifically, on weekdays, each drink was associated with a 1.07 odds of any CU, and on weekends each drink was associated with a 2.13 odds of any CU. Additionally, this study considered motivations for SU as a potential moderator of the relationship between AU and CU. Indeed, there was a significant interaction between evening AU and the motivation to cope via SU, such that a high motivation to cope was associated with substitutive use and a low motivation to cope with complimentary use. The magnitude of this moderated effect and the association between AU and odds of CU on weekdays were both small.

In conclusion, research suggests that AU's impact on CU and CU's impact on AU is either complimentary, or the two substances do not interact in either a complimentary or substitutive way. Importantly, five of these studies noted that the co-use effects of these substances are unstable across individual differences such as psychopathology, coping motives, gender, and CU motives (Gunn et al., 2018, 2019; Metrik et al., 2018, O'Hara et al., 2016; Roche et al., 2019). This is consistent with the mixed findings in previous macro-level studies. Specifically, previous literature has found that AU and CU either compliment or substitute for each other depending on factors such as age (Anderson, Hansen, & Reese, 2012; Pacula, 1998, Anderson & Rees, 2013), gender and ethnicity (Saffer & Chaloupka, 1999), or cannabis regulation (Anderson & Rees, 2011; Anderson, Hanson & Rees, 2013; Kelly & Rasul, 2014). This indicates that cannabis and alcohol are not absolute compliments or substitutes for each other, but rather may exert either substitutive or complimentary effects depending on specific factors.

These daily-level studies have added substantially to our appreciation of the interrelationships among CU, AU and HED However, a number of gaps remain. First, no daily-level study has examined temporal precedence of SU: it is unknown if CU occurred before, during or after AU initiation. The effects of co-use may vary depending on the order which the substances are used; CU prior to, or during, a HED session may have a different effect on AU than if CU occurred only after the HED session because the acute effects of CU can impact drink consumption throughout the duration of the drinking event. The acute effects of cannabis may reduce drink consumption via two mechanisms. For one, co-use may increase subjective intoxication (Gunn et al., 2018; Hartman et al., 2016; Lukas & Orozco, 2001; Metrik et al., 2018; Sokolovsky, 2020) and allow for individuals to achieve their desired level of intoxication more efficiently thus fulfilling the need for further drink consumption. Secondly, the sedating effects of cannabis (Green et al., 2003) may slow drink consumption or increase a desire for co-users to end a drinking event earlier in favour of sleep or relaxation. In contrast, a third type of co-use may occur following the resolution of AU wherein individuals engage in CU as a means of recovering from AU following the resolution of a heavy drinking event. Recovery use has been noted in other substance use literature, such as the case where benzodiazapenes are used following a night of stimulant use (Kurtz et al., 2006). In this case CU may be associated with heavy drink consumption because there is a greater need for a recovery aid in instances of HED (Morean & Corbin, 2010), yet the acute effects of CU could not have contributed to these higher levels of drink consumption because CU only occurred post-AU. Therefore, when temporal precedence is not considered, CU may appear to be associated with increased AU because instances of recovery use are incorrectly considered co-use events despite drink consumption occurring entirely in the absence of the acute effects of CU. As such, it may be more meaningful to consider CU following AU to be an AU only event. This grouping of CU post-AU events with CU before/during co-use events may help to explain compliment effects found in previous studies by artificially inflating mean drink consumption in the co-use group.

Another potentially important gap in the literature concerns the intentions of the individual using these substances. Does intention to use cannabis as a substitute for AU in a given co-use session reduce AU consumption in co-use sessions? A high proportion of medical cannabis users choose to use cannabis as a substitute for alcohol (Lucas & Walsh, 2017, Lucas et al., 2019, Reiman, 2009), which suggests that CU acts as a substitute. These medical cannabis users that report substitution may be motivated to reduce alcohol use in order to facilitate the management of, or recovery from, a medical condition which they have been prescribed cannabis for. For example, 10% of medical cannabis prescriptions in American medicalized cannabis states are written for the management of cancer (Boehnke et al., 2019), a condition wherein alcohol use is often contraindicated (American Cancer Society, 2017). Thus, individuals diagnosed with cancer, or other medical conditions where alcohol is contraindicated, may be intentionally substituting CU for AU which helps to explain why so many medical cannabis users report CU-AU substitution (Lucas & Walsh, 2017, Lucas et al., 2019, Reiman, 2009), Indeed, daily level investigations suggest that this tendency to use cannabis as a substitute for AU predicts reduced drink consumption in co-use sessions among medical cannabis users (Gunn et al., 2020). Moreover, previous research has identified that substitution occurs amongst individuals with a CUD (Metrik et al., 2018). Similar to medical cannabis users, people with a CUD may prefer CU more than AU and thus when both substances are available they engage in CU and their desire for AU drops. If cannabis is unavailable to these individuals, they may default to alcohol as a substitute. Conversely, individuals with an AUD or both an AUD and CUD may not have such a preference and therefore engage in CU only to compliment the experience of their preferred substance: alcohol. Thus, for both medical cannabis users and individuals with a CUD, intention to substitute may relate to reduced drink consumption in a given co-use session.

Importantly, these prior findings consider whether differences between people in their intention to substitute AU for CU *in general* predict reduced drink consumption in co-use sessions (Gunn et al., 2020), but it is still unknown whether variations in intention to substitute within-persons, predict drink consumption in a given co-use session. CU motives are known to vary across CU sessions (Shrier et al., 2013**)**. As such, the intention to substitute cannabis for alcohol may be high in some co-use sessions, but lower in others. An investigation into whether variations in this intention across sessions predicts changes in drink consumption would help to inform whether CU substitution effects could be activated by an individual should they hope to reduce alcohol consumption with CU.

Another important gap in previous daily-level studies is that none have measured the quantity of cannabis consumed in a given co-use session. Just as temporal precedence and intent may play a role in whether either a substitution or complimentary effect occurs, so might quantity of CU and AU. Indeed, one experimental study (Lukas & Orozco, 2001) noted that the combination of CU and AU increased the number of reported euphoric subjective effects in participants, but that this was maximized at a mild dose of both substances, and beyond these mild doses participants reported more euphoric effects when using one substance alone. Considering this finding, it follows that individuals may co-use the substances as compliments at low doses but substitute one for the other at higher doses of cannabis. Further, if an individual is engaging in co-use in order to increase the efficiency of AU, such that they can achieve their desired level of intoxication with fewer drinks, it follows that larger quantities of CU would substitute for larger quantities of AU relative to smaller quantities of CU. Nonetheless, it is currently unknown whether the potential substitution and complimentary effects of CU on AU are exhibited via a dose response relationship or if any CU, regardless of dose, can impact AU.

To summarize, three important within-person factors may help to explain inconstancies in the literature. First, the order in which CU occurs with relation to AU: either before/during or after AU. Second, the intention of the individual to substitute CU for AU in a given co-use session. Finally, the quantity of cannabis used in an AU session. All three of these gaps in the literature are important in delineating if, when, for whom, and how cannabis may act as a substitute for alcohol.

Chapter 2: The Current Study

The present study used detailed daily-level data which includes information of: the order in which AU and CU occurs in the context of a co-use event, motivation to substitute CU for AU in a given co-use event, and the quantity of alcohol and cannabis consumed in a particular co-use event. Broadly, the present study aimed to unravel the relationship between CU and AU in order to more adequately understand under what circumstances either substitution or complimentary effects may occur.

2.1 Research Aims & Hypotheses

This research sought to fill the gaps in the literature described above regarding temporal precedence, intention to substitute and quantity of cannabis consumed with the following four aims:

Replication Aim: Examined if the findings of previous daily-level CU substitution research, which suggest that CU exerts a compliment effect on AU, would be replicated in the data of the present study.

H.R.I. It was expected that AU sessions with CU would be associated with a greater number of drinks consumed compared to AU sessions when cannabis was not used.

H.R.II. It was expected that AU sessions with CU would be associated with a higher probability of HED compared to AU sessions when cannabis was not used.

Aim 1: Examined if the order in which CU occurred (before, during or after) in an AU session impacted the extent of drinking in that session.

H1.A.I. Co-use sessions where CU occurred before/during AU will be associated with fewer drinks consumed in the session relative to co-use sessions where CU occurred after AU.

H1.A.II. Co-use sessions where CU occurred before and/or during AU will be associated with a lower probability of HED relative to co-use sessions where CU occurred after an AU session.

Aim 2: Did intention to substitute CU for AU in a given co-use session impact the extent of an AU session?

H2.A.I. Intention to use to use cannabis as a substitute for alcohol in a given session will be negatively associated the number of drinks consumed in that session.

H.2.A.II. Intention to use cannabis as a substitute for alcohol in a given session will be associated with a higher probability of HED in that session.

Aim 3: Did the quantity of cannabis consumed in a co-use session impact the extent of drinking in that session?

H3.A.I. Large quantities of cannabis used in a co-use session will be negatively associated with the number of drinks consumed in that session relative to co-use sessions where small quantities of cannabis were used.

H3.A.II Large quantities of cannabis used in a co-use session will be associated with a lower probability of HED in that session relative to co-use sessions where small quantities of cannabis were used.

H3.B.I. The negative association between quantity of cannabis used in a co-use session and number of drinks consumed will be stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session.

H3.B.II. The association between quantity of cannabis used in a co-use session and a lower probability of HED will be stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session.

Chapter 3: Methods

The data used for the present study was collected as part of a larger ongoing study assessing CU, mental health and the impact of legalizing CU. This larger study contained three main components: an online survey, two in-person sessions, and up to 30 days of daily mobile phone surveys. In order to provide a succinct description of the experimental procedure, relevant components of the current study are discussed.

3.1 Procedure

Participants ($N = 146$) were recruited from undergraduate psychology courses through the SONA psychology subject pool. Data was collected from individuals who reported CU in the past six months. Individuals that were not between the ages of 18-25, that could not read and understand English, that did not completed the online survey, at least one in-person session and at least one entry in the EMA mobile phone surveys were excluded.

Eligible participants first completed an online self-report survey. The online survey began with a consent form that provided participants with information regarding the nature of the study. Course credit was offered as compensation for participation in the online survey.

Participants were invited immediately after completing the online survey to participate in two in-person sessions. The second session was conducted between 4 – 8 months from the first. Each in-person session took approximately 90 minutes to complete. Compensation was $20 and $30 for the first and second in-person sessions respectively. Participants that used cannabis in the six months prior to the in-person session were recruited to participate in a period of EMAs.

The EMAs began the day following each in-person session. Participants were asked to complete three short questionnaires on their mobile phone every day for a week. Each questionnaire took approximately 5 minutes to complete for a total time commitment of 15 minutes per day. These questionnaires were sent to the participant's mobile phone via the Metricwire mobile phone application at 11am, 4pm, and 9pm. The surveys assessed mood, SU and social functioning. Participants received $40 at the end of the first week of EMAs and $45 at the end of the second week of EMAs.

A change to the EMA procedure was implemented partway through the study in order to increase participation and sample size. First, an additional 10 day EMA period was added to the procedure. All participants that had completed at least one EMA period were invited to participate in this additional period. Next, all EMA periods were extended from one week to 10 days and the timing of the survey alerts were changed to 9am, 1pm and 9pm. The EMA period was changed from 7 to 10 days with the intent of extending the EMA period over two weekends for some participants. Drinking events among college students most commonly occur on weekends (Del Boca et al., 2004; Hoeppner et al., 2012; Maggs et al., 2011), thus we expected that extending the EMA period over two weekends would be an efficient way of capturing more drinking events in single EMA period. Finally, the compensation scheme was changed to compensate participants $1.66 per survey for a total possible amount of $50 for completing 30 surveys throughout the EMA period.

3.2 Measures

3.2.1 Baseline Measures

Demographic Questionnaire. A demographics questionnaire with gender, ethnicity, health, and location of residence was included in the baseline survey.

Between-person substitution practices. A individual's overall tendency to use cannabis as a substitute for alcohol was gathered through a single item included in the baseline survey. Specifically, participants were asked to indicate the extent to which they agree to the following statement: “I use cannabis purposefully to reduce the amount of alcohol I drink”. Responses to this question were rated on a Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree).

3.2.2 Ecological Momentary Assessment Measures

EMA. The EMAs used in the present study were sent to participant’s mobile phones via the Metricwire mobile phone application available for free on the Apple and Google Play stores. The EMA in the present study consisted of a total of 73 questions, but due to branching logic, no participant answered all questions and most participants did not answer more than 30. All questions call for either dichotomous yes/no, numeric, likert scale, open text or ranked responses. The EMAs assessed SU, mood and social functioning. Relevant to the present study are questions that tap into: the number of drinks consumed in the most recent AU session, the amount of cannabis used in a given AU-CU co-use session, intention to use cannabis as a substitute in a given co-use session, and temporal precedence of CU in a given co-use session. Appendix A includes all the EMA questions relevant to the present study, in the order which they appear with branching logic noted. The following measures were included in the EMA:

Temporal precedence of CU in a given co-use session. Participants that responded that they have used both alcohol and cannabis since the last assessment were asked to respond to the following question: “Which best describes your cannabis and alcohol use during this drinking occasion? Check all that apply.” The following options were presented: 1) I used cannabis before I started drinking (within two hours of initiation), 2) I used cannabis while drinking (i.e., during drinking occasion) and 3) I used cannabis after I finished drinking (i.e., no drinks consumed after cannabis use).[1]

Amount of cannabis used before and/or during a given alcohol-cannabis co-use session. Quantity of cannabis used in a co-use session was assessed with up to six questions. Participants that indicated that they had engaged with CU before or during a drinking event were asked "How much cannabis did you use before (within two hours) and/or during this drinking event (not including cannabis used after finishing drinking)?" This question was repeated three times so that participants could respond to the question with respect to: 1) smoked grams used, 2) edibles used in milligrams and 3) puffs from a distillate pen used. Participants that responded that they engaged in CU after finishing AU were asked: "How much cannabis did you use after this drinking event (within two hours of your last drink)?" This question was, again, asked 3 times with respect to smoked CU, edible CU and distillate pen CU.

Intention to use cannabis as a substitute. Intention to use cannabis as a substitute for alcohol was assessed with the following question: "Please sort the following motivations in rank order according to how they apply to your use of cannabis in this drinking occasion. Please rank them in order from 1 = most accurate to 8 = least accurate. "I used cannabis":" The following options were provided to respondents, in a randomized order, to be ranked: so I could drink less, for enjoyment/fun, because others were doing it, to experiment, to be social, to relax, because I was bored, other. CU motives used in this question have been identified as the most frequently endorsed motivations for engaging in CU in young adults (Lee, Neighbors, & Woods, 2007).

[1] Participants were also asked to indicate when they consumed their first and last drink, and when they first engaged in CU with respect to AU (within two hours before first drink) and when was the last time they engaged in CU with respect to AU (within two hours after the last drink). Despite a high level of consistency between the two variables (94.8%), this second variable included a number of responses that were missing (3%). Additionally, a number of responses were not within the timeframe described in the question (within two hours; 16.3%), which indicated that participants may not have correctly read this question before responding or responded accidentally. As such, this measure of temporal precedence was not used in the present study.

These rankings were reversed prior to analysis such that higher numbers indicate a stronger motivation.

Number of drinks consumed in the heaviest AU session since prior assessment. Drink consumption was measured with the following question. First, participants were asked if they have used alcohol since the last assessment. If a participant reported AU, they were asked to report the number of drinks that were consumed since the last assessment. This was followed by a question which asked if those drinks were consumed in one drinking occasion/7-hour period. If a participant responded that these drinks were not consumed in one drinking occasion, they were asked to report how many drinks were consumed in the heaviest (most drinks) drinking occasion.

HED. In line with the Canadian low-risk drinking guidelines (Butt et al., 2011), three or more drinks was considered HED among females, and four or more drinks was considered HED among males. Any AU session that met or exceeded these number of drinks was operationalized as HED, whereas anything below these thresholds was considered moderate AU.

3.3 Statistical Analysis

The lme4 package within the Rstudio statistical computing software version 1.2.5033 was used for all multilevel analyses in the present study. A summary of model specification, steps of model building and model estimates are reported in Appendix B. Correlations, descriptive analyses, within and between analyses and missing data imputation were completed within IBM SPSS version 23.

A preliminary analysis was conducted to describe elements of AU, CU, and co-use. Following this, multi-level modeling (MLM) was used to assess within- and between-person factors associated with the extent of drinking in a given AU session. MLM was selected primarily for two reasons. First, MLM is the appropriate procedure when investigating hierarchical data structures wherein individual observations are nested within an overarching grouping factor (e.g., Hox, 2010; Nezlek, 2008; Raudenbush & Bryk, 2002; Snijders & Bosker, 2012). In the present study, repeated measure EMA assessment data was nested within participants. As such, Level-1 and -2 data estimated within- and between-person variability, respectively. The nested nature of this data contributes to a dependency in Level-1 observations that is problematic for statistical methods such as independent ANOVA or multiple regression (Field et al., 2012; Nezlek, 2008). Additionally, MLM presents a secondary benefit over other methods of repeated measure analysis in that it does not assume a balanced research design wherein all participants contribute the same number of observations. In the present study, within-person data was limited to AU events and thus each participant's contribution to the dataset was dependent on their drinking patterns across the duration of the EMA period. As such, there was substantial variation in the number of observations provided by each participant. These benefits of MLM support its use in the present study to assess the influence of between- and within-person factors, such as co-use session characteristics, on alcohol consumption.

Four multi-level models were constructed in order to address research aims. The two models predicting number of drinks consumed, which is the outcome variable considered in hypotheses H.R.I., H1.A.I, H2.A.I., H3.A.I, and H3.B.I., were estimated using a count distribution with a log link. Hypotheses H.R.II., H1.A.II., H2.A.II., H3.A.II., and H3.B.II. considered the impact of predictor variables on the binary outcome variable drinking session type: moderate or HED drinking session. This variable will hereafter be referred to as *session type*. The two models related to this binary variable were estimated using a Bernoulli distribution with a logit link. Moderate drinking was coded as 0 and HED was coded as 1. Three or more drinks was considered a HED session among females, and four or more drinks was considered a

HED session among males, with any fewer drinks consumed considered moderate drinking. For all models, Level-1 assessed for within-person effects, whereas Level-2 assessed for between-person effects.

Three covariates were included in all models. First, day of the week has been identified as a within-person factor associated with AU consumption (O'Hara et al., 2016), and was thus included as a Level-1 covariate in all models with weekdays coded as 0 and weekends coded as 1. This variable will hereafter be referred to as *weekday*. Likewise, it is recommended that the impact of time on outcomes be considered in all longitudinal research designs even in cases where change over time is not a variable of interest (Bolger & Laurenceau, 2013). Participants were recruited in up to 3 non-consecutive EMA blocks. The first block was coded as 0, the second as 1 and the third as 2. This variable will hereafter be referred to as *EMA block*. Finally, due to the gender differences in both CU and AU that have been identified in past literature (Cuttler et al., 2016; Erol & Karpyak, 2015; O'Hara et al., 2016), gender was considered as a between-person covariate in all models with males coded as 0 and females as 1.

3.3.1 Within and Between Analysis

Within and Between Analyses (Dansereau Alutto, & Yammarino, 1984) were used in the present study to determine what level variables should be entered into multi-level models and what order they should be entered in. Within-and-Between Analysis (WABA) is broken into three components. WABA I indicates whether the predominant source of variability of a given variable is either within-persons, between-persons or equivocally within- and between-persons. This portion guided the level of entry for the variables in the present study. Specifically, E-tests of practical significance, which are not dependent on degrees of freedom and thus better suited for smaller sample sizes (O'Connor, 2004), indicated where the predominant source of variability lied within all variables. When variability was suggested to be: primarily within-persons, variables were entered at Level-1; primarily between-persons, aggregated and entered at Level-2; or equivocally within- and between-persons, entered at both levels of multi-level models. In WABA II the covariation between predictor variables and dependent variables is broken into within- and between-person components. This portion of the WABA analysis guided the order which Level-1 variables were entered into multi-level models: variables with stronger within-person covariation with the outcome variable of a given multi-level model were entered prior to those with weaker within-person covariation to those same outcome variables. Finally, WABA III integrates the findings of WABA I and WABA II to provide a summary comparison of the within- and between-person components of each variable with respect to outcome variables of interest.

3.3.2 Models 1 and 2: Any CU Predicting Drinking Outcomes

Hypothesis H.R.I. Examined if AU sessions with CU were associated with a greater number of drinks consumed compared to AU sessions when cannabis was not used. Number of drinks consumed in an AU session was used as the outcome measure. Three variables were considered as Level-1 predictors in Model-1 and -2: a dichotomous measure of CU, EMA block, and weekday. No CU was coded as 0 and any CU as 1. This measure of CU will hereafter be referred to as *any CU.* Gender and the person mean of any CU, which reflected a tendency to co-use cannabis and alcohol, were entered into Level-2 of this model to assess for between-person effects. This aggregated variable will be referred to as *CU BTW*.

Hypothesis H1.R.II. Examined if AU sessions with CU was associated with a higher probability of HED compared to AU sessions when cannabis was not used. Session type was used as the outcome measure. Any CU, EMA block and weekday were considered as Level-1 variables in this model. Gender and CU BTW were considered as Level-2 predictors.

3.3.3 Models 3 and 4: Differences in Co-Use Sessions Predicting Drinking Outcomes

In order to compare differences in co-use sessions, the sample used in the following models was restricted to AU sessions wherein cannabis was used during, or within 2 hours of, the AU session. This sample will be referred to as the *co-use only sample.* Two models were constructed, Model-3 used number of drinks consumed as the outcome measure, whereas Model-4 used session type as the outcome variable.

Hypothesis H1.A.I. Examined if co-use sessions where CU occurred before/during AU was associated with fewer drinks consumed in the session relative to co-use sessions where CU occurred only after an AU session. To test hypothesis H1.A.I. the binary variable of CU temporal precedence was considered as a Level-1 predictor in Model-3. In this model, CU before/during the AU session was coded as 0 and CU after the AU session was coded as 1. This variable will be referred to as *temporal precedence.*

Hypothesis H1.A.II. Examined if co-use sessions where CU occurs before/during AU was associated with a lower probability of HED relative to co-use sessions where CU occurred after an AU session. To test hypothesis H1.A.II temporal precedence was considered as a Level-1 predictor in Model-4.

Hypothesis H2.A.I. Examined if greater intention to use to use cannabis as a substitute for alcohol in a given session negatively predicted the number of drinks consumed in that session. To test hypothesis H2.A.I. intention to use cannabis as a substitute for AU was considered as a Level-1 predictor in Model-3. This variable will be referred to as *intention.*

Hypothesis H2.A.II. Examined if greater intention to use to use cannabis as a substitute for alcohol in a given session was associated with a lower probability of HED in that session. To test hypothesis H2.A.II Intention was considered as a Level-1 predictor in Model-4.

Hypothesis H3.A.I. Examined if large quantities of cannabis used in a co-use session was negatively associated with the number of drinks consumed in that session relative to co-use sessions where small quantities of cannabis were used. To test hypothesis H3.A.I. the binary variable of CU quantity used was considered as a Level-1 predictor in Model-3. Small quantities of CU in a session were coded as 0 and large quantities of CU were coded as 1. This variable will be referred to as *CU Quantity*. The lowest quartile was used as a cutoff point for cannabis quantity such that any value that exceeded the lowest quartile was considered a large amount. For participants that used more than one modality of cannabis, such as an individual who smoked cannabis and consumed an edible cannabis product, CU quantity in all modalities was converted to a percentage of the lowest quartile cut-off score and summated. If the summated percentage exceeded 100% than the quantity was considered to be large. For example, if the quartile cutoffs were .2 grams and 10mg for smoked CU and edible CU respectively, and an individual smoked .1 of a gram and consumed 7mg of oral cannabis then the following equation would apply:

$$([.1/.2]*100) + ([7/10]*100) = 120\% = \text{large/non-trivial quantity}$$

Hypothesis H3.A.II. Examined if large quantities of cannabis used in a co-use session were associated with a lower probability of HED in that session relative to co-use sessions where small quantities of cannabis were used. To test hypothesis H3.A.II. CU Quantity was considered as a Level-1 predictor in Model-4.

Hypothesis H3.B.I. Examined if the negative association between quantity of cannabis used in a co-use session and number of drinks consumed was stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session. To test hypothesis H3.B.I. the interaction between CU quantity and temporal precedence was entered as a Level-1 predictor in Model-3.

Hypothesis H3.B.II. Examined if the association between quantity of cannabis used in a co-use session and lower probability of HED was stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session. To test hypothesis H3.B.II. the interaction between CU Quantity and Temporal Precedence was entered as a Level-1 predictor in Model-4.

The two within-person covariates, EMA block and weekday, were considered as Level-1 predictors in Model-3 and -4. Gender was included as a between-person covariate in Level-2 of both Model-3 and -4. In cases were WABA I indicated that the predominant source of variation in a given variable was either between-person or equivocally within- and between-person, this variable was aggregated and entered into Level-2 of the model. Additionally, if a Level-2 variable was significantly associated with the outcome of interest, cross-level interaction terms were added in order to investigate if the relationships between significant Level-1 variables and outcome measures were dependent on significant Level-2 variables, such as gender.

In order to facilitate interpretation of model coefficients, all categorical variables in the present study were left un-centered such that scores at each time point can be compared to the mean of the group coded as 0 in the analysis (Nezlek, 2012). The variable of intention was the only continuous Level-1 variable used in the present study and was group-mean centered, in order to allow for the comparison of values at each time point to be compared to the mean level of intention to substitute across co-use sessions in each person. Continuous Level-2 variables were grand-mean centered, which allowed for individual scores at each time point to be compared to the overall mean of the sample on a given variable.

3.3.4 Multilevel Modeling

The two outcome variables of interest in the present study follow non-linear distributions. Specifically, the outcome variable in Model-1 and -3 is a count variable, whereas the outcome variable used in Model-2 and -4 is a binary variable. The assumption of normally distributed, homoscedastic errors is violated when non-normal outcome variables are used (Hox, 2010; O'Connell et al., 2008), as such, non-linear outcome variables in MLM require generalized linear mixed model (GLMM) methods rather than the traditional linear mixed model (LMM) method. In GLMM, outcome variables are transformed via the use of a non-linear canonical link function in order to create an analysis that parallels LMM and can be interpreted accordingly. In the present study, the log link transformation was used in Model-1 and -3 whereas the logit link function was used to transform the binary outcome of Model-2 and -4 (Heck et al., 2013; Hox 2010). Next, unlike LMMs which allow for model estimation via the maximum likelihood (ML) procedure, the use of ML in GLMMs is not appropriate. Instead, estimation techniques which approximate to ML are used. The Laplace approximation method (Tierney & Kadane, 1986), which is a numerical integration approach that has been shown to produce minimally biased estimates in the context of count and binary distributions (Plan et al., 2009), was selected for use in the present study. Full model construction steps, and associated parameters are reported in Appendix B. The following steps were taken in the construction of multilevel models according to the recommendations of Nezlek, 2012.

Prior to constructing multilevel models, the count variable used in Model-1 and -3, number of drinks consumed, was tested for the possibility of over-dispersion in order to guide the selection of an appropriate distribution. While the Poisson distribution is the most commonly used distribution for modeling count data (Puig & Valero, 2006), it makes strong assumptions about the underlying distribution of the data which are often violated in count models of alcohol consumption (Horton et al., 2007). Specifically, the Poisson distribution assumes that the variance of the count variable does not exceed the mean. When this does occur we encounter a phenomenon known as overdispersion. When data is found to be overdispersed, distributions robust to violations of this assumption, such as the negative binomial distribution, are more appropriate for use in estimations (Hox, 2010). The negative binomial distribution accounts for dispersion via the inclusion of an extra estimated parameter in the variance function (Hox, 2010; McCullagh & Nelder, 1989), and therefore is often the better fitting model with respect to overdispersed data. The one-sample Kolmogorov-Smirnov (KS) test was used in the present study in order to detect the presence of overdispersion in the data (Karlis & Xekalaki, 2000). In the case that overdispersion was detected through the KS test, unconditional, intercept only, multilevel-models were constructed and estimated under the Poisson and negative binomial distributions. Model fit statistics from the two models were then compared and the better fitting model was used to guide the selection of the appropriate distribution (Heck et al., 2013; Hox, 2010).

Next, an unconditional model was constructed in order to examine the variability in the dependent variable that existed when no predictors were included in the model. This unconditional model is useful for two reasons. For one, it can be used as a reference point to assess whether the inclusion of predictors of interest in further models serves to improve model fit. Secondly, the construction of this unconditional model is necessary in order to produce the statistics required for the calculation of the intraclass correlation (ICC). The ICC indicates the proportion of variance that exists in the dependent variable due to the grouping variable. For example, the ICC in the present study represents the variance in the dependent variable that is due to between-person differences. ICC values for Model-1 and -3, which predicted the number of drinks consumed in a given co-use session, were computed using the trigamma function which is suggested to estimate the observation level variance most accurately (Nakagawa et al., 2017).

Next, Level-1 predictors were added to the model as fixed. In other words, the relationship between the predictor and the outcome was considered to be consistent across individuals. Each predictor was added one at a time and predictors that did not improve model fit were dropped from the model before the following variable was added. This process ensures the construction of a maximally parsimonious model (Nezlek, 2012). Level-1 predictors were added to the models based on the strength of their within-person covariation to the outcome variables, as indicated by the WABA II analyses, in descending order such that the variable with the strongest covariation was entered first. In the case that a given predictor was found to be significantly related to the outcome variable, the model was then reconstructed with the predictor allowed to vary randomly and model improvement was assessed again. Significant improvement to model fit upon allowing a variable slope to vary randomly indicated that the relationship between the Level-1 variable and the outcome differs between people.

Finally, Level-2 predictors were added to the model as a means of examining the influence of between-person characteristics, such as gender, on the outcome variables. Level-2 predictors were entered, in order, based on the strength of their bivariate correlations to the outcome variable with the most strongly correlated variables entered first. Level-2 predictors that did not improve model fit were dropped.

Due to the fact that estimation procedures for multilevel models with categorical outcomes are approximate, test statistics which rely on deviance statistics, such as the -2LL, are biased (Hox, 2010). For this reason, model improvement was assessed via inspection of the

Akaike information criterion (AIC) and the Bayesian information criterion (BIC). Lower AIC and BIC values indicated a better model fit. As such, AIC and BIC values can be used by applying following equations:

$$\Delta_{AICi} = AIC_i - AIC_{min}$$

$$\Delta_{BICi} = BIC_i - BIC_{min}$$

wherein AIC_{min} and BIC_{min} are the AIC and BIC values corresponding to the best fitting model constructed thus far. As such, any model with a $\Delta_{AICi} < 0$ and $\Delta_{BICi} < 0$ is considered to be the new best fitting model and can be used as AIC_{min} and BIC_{min} in further model construction. In cases where AIC and BIC values contradict in selecting best model fit, the AIC value was followed. It has been suggested that AIC values are more appropriate for use in cases where samples are finite as seen in psychological research (Vrieze, 2012). In addition to AIC and BIC indices for the assessment of model fit, a R^2 value was calculated in order to estimate the proportion of variance accounted for by each model. The trigamma function was used in the derivation of R^2 values for all models in the present study according to the calculation proposed by Nakagawa et al., (2017).

Random effects models were estimated with the use of a unstructured covariance-correlation matrix. The use of a unstructured covariance-correlation matrix is appropriate when the covariance structure is not known as it assumes that covariance patterns are completely unpredictable (Field, 2012; Garson, 2013).

Chapter 4: Results

4.1 Sample Selection

One hundred and forty-six individuals participated in at least 1 EMA period throughout the study duration. The number of responses provided by each participant varied considerably across participants ranging from 1 - 80 (M = 40.7, SD = 21.16). A total of 5947 individual observations were collected. One participant was removed from analyses due to impossible responses which indicated random responding. Additionally, one participant responded as "other" when asked about their gender. Due to the fact that gender was included as a covariate in all primary analyses, and this participant was the only individual in the "other" group, this participant was removed from the sample in order to prevent inferences of non-binary gender identity based on one individual. As such, the complete sample consisted of 144 participants and a total of 5797 (M = 40.2, SD = 20.9) individual observations.

From this overall sample, two subsets were created for analysis: one sample consisting of participants that contributed at least one AU event, the *any AU sample*, used in Model-1 and -2, and one sample consisting of participants that contributed at least one co-use event, the *co-use only sample,* used in Model-3 and -4. The any AU sample consisted of 81 participants and a total of 449 individual observations which corresponds to each participant contributing a mean of 5.54 AU events (SD = 3.9). The co-use only sample consisted of 44 participants and a total of 141 observations which corresponds to a mean of 3.20 co-use events per person (SD = 1.76).

4.1.1 Outliers

Three observations within the any AU sample were identified as outliers, based on *z*-scores exceeding 3.29 (Tabachnick,& Fidell, 2007) on the outcome variable of number of drinks consumed. These 3 observations were removed from the dataset. The removal of these three observations brought the any AU sample to a total of 81 participants and 446 individual observations (*M* = 5.5*, SD* = 3.8). One of these observations were also part of the co-use only sample, bringing the co-use only sample to 43 participants and a total of 140 observations (*M* = 3*, SD = 1*.7) following removal. No further observations or participants were removed from the any AU sample.

4.1.2 Missing Data

9 observations out of a possible 140 in the co-use only sample were considered missing due to problematic or uninterpretable responses to the CU quantity items. This variable allowed for text to be input directly by the participant so that they may indicate how much cannabis they smoked, consumed orally or consumed via concentrate pen. The 9 observations contained responses such as "zero", which indicates that the participant had not co-used that night and should be removed from the co-use sample, or text responses not corresponding to any possible CU quantity such as "Jaish" which may be a consequence of a typing error. These 9 observations were removed from the dataset which brought the final co-use only sample to 43 participants and 131 individual observations (*M* = 3*, SD = 1.7*).

The intention variable was added subsequent to study initiation. The late addition of this variable contributed to missing data on this variable for 41 observations out of a total 131. The pattern of missing data is unrelated to any variables in the study, but rather a design issue, and as such can be classified as missing completely at random (Eekhout, 2014). In order to preserve these cases and maintain power in Model-3 and -4, mean imputation (MI) was used to replace missing values. All predictor variables expected to be included in Model-3 and -4 were used as predictors in the imputation process. Five iterations of MI were computed, which is considered to be an adequate number of iterations to produce unbiased results (Van Buuren, 2012). Mean imputation has been shown to produce more accurate estimates in datasets where more than 10% of data is missing on the variable of interest, relative to other methods of missing data replacement such as mean imputation or single stochastic regression (Eekhout, 2014).

Additionally, data was missing for one participant on the between-person variable of intention to substitute CU for AU. This variable will hereafter be referred to as *intention BTW*. This participant contributed four observations to the co-use only sample which required complete values on this variable for analysis in Model-3 and -4. The participant's responses to the Level-1 intention variable, wherein they indicated their intention to use CU as a substitute for AU in a given co-use session, was averaged, rescaled and aggregated to the between-person level in order to replace the missing data associated with this participant's 4 observations.

4.2 Sample Characteristics

4.2.1 Any AU Sample

The sample for Model-1 and -2, which included all individuals that reported at least one AU event, was comprised of 81 participants (32.1% Male, 67.9% female). The mean age was 19.6 (*SD* = 1.8). With respect to ethnicity, 69.1% of the sample identified as Caucasian, 8.6% identified as Asian, 7.4% identified as Hispanic, 6.2% identified as South Asian, 3.7% identified as Metis, 2.5% identified as Black, 1.2% identified as First Nations and 1.2% identified as "other". When asked to report their living situation, 32.1% reported living on campus, 21% reported living off campus with friends, 18.5% reported living off campus with parents, 8.6% reported living off campus with a romantic partner, 4.9% reported living off campus alone, and 14.8% did not have data for this variable because it was added prior to study initiation. The mean number of AU sessions, HED sessions, and co-use sessions reported by participants in this sample were 5.5 (*SD* = 3.8), 2.6 (*SD* = 2.4), and 1.9 (*SD* = 2) respectively. Comparisons of AU only events and co-use events in this sample on outcome variables of interest are presented in Table 1.

Table 1
Comparison of AU events and co-use events on outcome variables of interest

	AU only events (n = 306)	Co-use events (n = 140)
Mean drinks consumed across AU sessions (SD)	3.6 (3)	3.5 (3)
Mean % of AU sessions that were HED (SD)	48.4% (50.1)	45.7% (50)

Note. AU = Alcohol use. HED = Heavy episodic drinking.

4.2.2 Co-Use Only Sample

The sample for Model-3 and -4, which included individuals that reported at least one co-use event, consisted of 43 participants (30.2% male, 69.8%). The mean age was 19.7 (SD = 1.8). With respect to ethnicity 74.4% of the sample identified as Caucasian, 7% identified as Asian, 4.7% identified as Metis, 4.7% identified as South Asian, 2.3% identified as Hispanic, 2.3% identified as Black, and 2.3% identified as First Nations. With respect to living situation, 27.9% reported living on campus, 20.9% reported living off campus with their parents, 18.6% reported living off campus with friends, 9.3% reported living off campus with a romantic partner, 4.7% reported living off campus alone and 18.6% did not have data for this variable because it was added prior to study initiation. The mean number of co-use sessions and HED sessions reported by participants in this sample were 3 (SD = 1.7) and 1.4 (SD = 1) respectively. The mean number of drinks consumed across co-use sessions was 3.6 (SD = 3). Table 2 and 3 present further descriptive statistics for variables relevant to the co-use only sample analyses.

Table 2.
Descriptive statistics for the co-use only sample on key variables of interest.

Descriptive Statistics	
% of co-use sessions categorized as small CU quantity	19.8%
Median CU smoked in grams (*SD*) (zeros removed)	0.5 (1.3)
25th percentile CU smoked in grams (CU quantity cut off; zeros removed)	0.3
Median oral CU in milligrams (*SD*) (zeros removed)	7.5 (16.2)
25th percentile oral CU in milligrams (CU quantity cut off; zeros removed)	2
Median number of puffs from a concentrate pen (*SD*) (zeros removed)	2 (13.5)
25th percentile number of puffs from a concentrate pen (CU quantity cut off; zeros removed)	1
% of co-use sessions wherein CU occurred only after the AU session	24.4%
Mean level of intention to use CU as a substitute for alcohol across co-use sessions where 1=min intention and 8= max intention (*SD)*	5.7 (2)

Note. CU = Cannabis use. AU = Alcohol use.

Table 3.
Descriptive statistics of outcome variables within the co-use only sample at different levels of predictor variables

	Mean number of drinks (*SD*)	% HED (*SD*)
Temporal Precedence		
Before/During	3.1 (2.4)	41.4% (49.5)
After	4.9 (4.1)	59.4% (49.9)
CU Quantity		
Small	3.6 (4.1)	34.6% (48.5)
Large	3.5 (2.7)	48.6% (50.2)
Intention		
High (≥ 5)	3.3 (3.3)	39.02% (49.4)
Low (< 4)	3.7 (2.9)	48.9% (50.3)

Note. CU = Cannabis use. AU = Alcohol use.

4.3 WABA Results

Given the use of different samples to assess the aims of the present study, two WABA analyses were conducted. The WABA analysis is broken up into three portions. WABA I identified the predominant source of variability, either between- or within-persons, for the predictor variables of interest. The results of WABA I are included in Table 4. Predominant source of variability was determined using the E-test of practical significance, which is a measure of effect magnitude not dependent on degrees of freedom (O'Connor, 2004). The results of WABA I indicated that, with the exception of CU Quantity used, the predominant source of variability across all predictor variables was either equivalently between- and within-persons or within persons. Given this, all variables were entered into Level-1 of their respective models except for CU quantity which was aggregated and entered in at Level-2 of the model. This aggregated quantity variable is hereafter referred to as *CU quantity BTW.* Additionally, WABA I suggested the predominant source of variability was within-persons for the EMA block variable in the AU sample and the weekday variable in the co-use sample. As such, these variables were not aggregated and entered into Level-2 of their corresponding models.

Table 4
WABA I Results: Proportion of Variance Between and Within Persons, by variable

		Proportion of Variance		Predominant Source of Variability
		Between-Person	Within-Person	
	Cases	η^2	η^2	
Any AU Sample				
Number of Drinks	446	.37	.63	Within
Session Type	446	.24	.76	Within
Any co-use	446	.46	.54	Equivalent
Weekday	446	.42	.57	Equivalent
EMA Block	446	.16	.84	Within
Co-Use Only Sample				
Number of Drinks	131	.43	.43	Equivalent
Session type	131	.37	.63	Within
Intention	131	.52	.48	Equivalent
CU Quantity	131	.60	.40	Between
Temporal precedence	131	.50	.50	Equivalent
EMA block	131	.50	.50	Equivalent
Weekday	131	.32	.67	Within

Note. AU = alcohol use, CU = cannabis use.

Table 6
WABA II Results: Between, Within, and Total Correlations

	WABA II: Correlations			
	DV: Number of Drinks		DV: Moderate or HED	
	Between	Within	Between	Within
Any AU Sample				
Any co-use	-.03	.05	-.04	.04
Weekday	.02	.003	.02	-.01
EMA block	.10	.01	-.08	-.004
Co-Use Only Sample				
Intention	.18	-.07	.25	-.03
CU quantity	-.10	.01	.15	.09
Temporal precedence	.21	.30	.11	.19
Weekday	.17	-.09	.19	.001
EMA block	.21	.003	-.04	.003

Note. AU = alcohol use, CU = cannabis use.

Results of WABA II were used to provide a gauge of effect size with respect to the within- and between- covariation between Level-1 predictor variables and the two outcome variables of interest. The results of the WABA II, which are presented in Table 6, guided the order of entry into the four multilevel models. Specifically, predictor variables were entered into multilevel models in descending order based on the strength of their within-person covariation with the outcome variables of each model. The only statistically or practically significant finding across all predictor variables, in all models, was the within-person variable of temporal precedence to number of drinks consumed. Given the lack of significant findings here, only effect size, rather than significance, was used as a guide in the model building process.

Table 7
WABA III Results: WABA Components, between pairs of predictor and outcome variables

	WABA III: WABA Components					
	DV: Number of Drinks			DV: Moderate or HED		
	Raw/Total Correlation	Between	Within	Raw/Total Correlation	Between	Within
Any AU sample						
Any co-use	.02	-.01	.03	.01	-.01	.02
Weekend	.01	.01	.002	-.002	.01	-.01
EMA Block	.03	.02	.01	-.02	-.02	-.002
Co-use only sample						
Intention	.05	.08	-.04	.09	.11	-.01
CU quantity	-.05	-.05	.01	.11	.07	.04
Temporal precedence	.26	.10	.16	.15	.05	.11
Weekday	.006	.05	-.05	.08	.08	.00
EMA block	.08	.08	.002	-.01	-.01	.002

Note. AU = alcohol use, CU = cannabis use.

Finally, WABA III provides insight into wherein the effects lie in the data. Specifically, a large within-person WABA component relative to the between-person component indicates that the variation and covariation lies primarily within-persons for a given pair of variables. The results of the WABA III are presented in Table 7. The results of WABA II and III align in suggesting that the largest effect lies in the within-person component of the temporal precedence variable.

4.4 Model 1: Any AU Sample Predicting Number of Drinks Consumed

Prior to model construction, analysis was conducted in order to determine the appropriate distribution to be used in estimation of the number of drinks model. Comparison of the mean and the variance in the present study indicate that the data was overdispersed (M = 3.64, S^2 = 8.82). Further, a Kolmogorov-Smirnov test indicated that the number of drinks consumed variable did not follow a Poisson distribution, D(459) = .17, $p < .001$. Finally, intercept only, unconditional, models were constructed under the Poisson and negative binomial distributions and model fit statistics were compared. AIC and BIC values indicated that the negative binomial distribution was a better fit (Poisson: AIC = 2019.9, BIC = 2028.10; negative binomial: AIC = 1963.6, BIC = 1975.9). As such, a negative binomial distribution with a log link was used in the estimation of Model-1.

A model was constructed using the results of WABA I and II to guide the level in which the variables should be entered at and in which order. First a unconditional model was created which included only the intercept, but no predictor variables. This model was established to create a baseline for comparison of model fit against further models that include predictor variables. Level-1 of the unconditional model for the number of drinks consumed at time point i in individual j was defined by the following equation:

$$\text{Level 1: } \eta_{ij} = \log(\gamma_{ij}) = \beta_{0j}$$

where the number of drinks consumed at a given time point (η_{ij}) equates to the natural logarithm of the event rate λ_{ij}. There is no separate residual variance modeled at level 1 in negative binomial models. This is the within-person model. The between-person, Level-2 unconditional model is defined by the following equation:

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

Where γ_{00} represents the fixed effect of the between-person intercept and u_{0j} represents the random variance. This Level-2 model indicates that an individual's mean number of drinks consumed across all observations (β_{0j}) is equal to the grand mean drinks consumed summated with the remaining unexplained variance. Two parameters are estimated in the unconditional model. One fixed parameter (γ_{00}) and one random parameter (u_{0j}). The ICC value for this model was 0.1916, indicating that approximately 19.16% of the variance associated with this model can be attributed to between person effects. This ICC value is lower than the between person variance indicated by the WABA I analysis, which may be attributed to the fact that WABA analysis was designed and intended for continuous variables (O'Connor, 2004) whereas the ICC calculation used in the present study was designed specifically for negative binomial count models (Nakagawa, Johnson, & Schielzeth, 2017).

The any co-use variable was first entered into the model as fixed. This addition did not improve model fit, Δ_{AICi} = 1965.6-1963.7 = 1.9 = > 0, Δ_{BICi} = 1982-1975.9 = 6.1 = > 0, as such this variable was dropped from the model. Next, the EMA block variable was entered into the model as fixed. Again, this addition did not improve model fit and was thus dropped from the model, Δ_{AICi} = 1965.3-1963.7 = 1.6 = > 0, Δ_{BICi} = 1981.7-1975.9 = 5.8 = > 0. Finally, the weekday variable was entered into the model. Once again, this predictor did not improve model fit and was therefore dropped from the model, Δ_{AICi} = 1965.6-1963.7 = 1.9 = > 0, Δ_{BICi} = 1982-1975.9 = 6.1 = > 0. Given that there were no improvements to model fit with the addition of any of the three predictors, the final model at Level-1 remained as the intercept only.

Next, between-person covariates were added to the model. The results of WABA I indicated that the predominant source of variability in two Level-1 predictors, any co-use and weekday, was equivocally within- and between-person. As such, these two predictors were aggregated and entered into the model at Level-2 in order to assess if the overall tendency for an individual to co-use, or to drink alcohol on the weekend, impacts the number of drinks consumed in a given co-use session. The aggregated any co-use variable and weekday variables will hereafter be referred to as *co-use BTW* and *weekday BTW.* Variables were entered into Level-2 of the model one at a time based on the strength of their bivariate correlations to the outcome variable (see Table 8). The inclusion of gender at Level-2 improved model fit according to the AIC index but this contradicted the findings of the BIC index, $\Delta_{AICi} =$ 1961.9-1963.7 = -1.8 = < 0, $\Delta_{BICi} =$ 1978.2-1975.9 = 2.3 = > 0. The AIC value was used to guide model selection in the present study, so this model, which included gender as a predictor, was retained**.** Next, weekday BTW was added to the model. Adding this variable did not improve model fit, Δ_{AICi} = 1963.6-1961.9 = 1.7 = > 0, $\Delta_{BICi} =$ 1984.1-1975.9 = 8.2 = > 0, and was therefore was not retained in the final model. Finally, the co-use BTW variable was added to the model but did not improve fit, Δ_{AICi} = 1963.9-1961.9 = 2 = > 0, $\Delta_{BICi} =$ 1984.4-1975.9 = 8.5 = > 0, and was therefore dropped from the model. The best fitting model was therefore defined by the following equation:

$$\text{Level 1: } \eta_{ij} = \beta_{0j}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + \gamma_{01}(Gender_j) + u_{0j}$$

Table 8.
Bivariate Correlations between Level-2 Variables and outcome variables used in model-1 and -2

	1	2	3	4
1. Number of Drinks				
2. Session Type	.69**			
2. Co-Use BTW	-.03	.01		
3. Gender	-.163**	.03	.05	
4. Weekday BTW	.050	-.04	.09	.05

Note. Co-Use BTW = Co-use aggregated to the between person level, Weekday BTW = day of the week variable aggregated to the between person level.

Replication Aim 1

Hypothesis H.R.I. AU sessions with CU were expected to be associated with a greater number of drinks consumed compared to AU sessions when cannabis was not used.

The results of this model do not support hypothesis H.R.1. Specifically, cannabis alcohol co-use in a given AU session was not significantly associated with a greater number of drinks consumed. Although not related to the hypothesis, gender was significantly associated with number of drinks consumed (γ_{01} = -.23, SE = .11, p < .05), such that males tended to consume more drinks than females across AU sessions.

4.5 Model 2: Any AU Sample Predicting Moderate or HED AU Session

The model building approach to examine H.R.II. was identical to the one described above. The outcome variable relevant to this model was session type. First, an unconditional model was as defined by the following equation:

$$\text{Level 1: } \eta_{ij} = log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right) = \beta_{0j}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

The AIC and BIC values corresponding to this model are 614.4 and 622.6 respectively. The ICC value was 0.091 indicating that approximately 9.1% of the variance was due to between-person differences. Next, Level-1 predictors were added to the model one at a time. Neither the any co-use or weekday variables significantly improved the model fit, and thus were not retained in the model. The AIC and BIC values for the model including the any co-use variable were 616.1 and 628.44 respectively, whereas the AIC and BIC values for the model which included the weekday variable were 616.2 and 628.5 respectively. The EMA block variable was added to the model next, but did not improve model fit, AIC =616.3, BIC=628.6. Next, Level-2 variables were added to the model in descending order according to the strength of their bivariate relationship to the outcome variable. Bivariate correlations can be seen in Table 8. Again, no Level-2 predictors improved model fit. The AIC values for the models including the weekday BTW, gender, and co-use BTW variables were 615.8, 616, and 616.3 respectively. The BIC values for the models including the weekday BTW, gender, and co-use BTW variables were 628.1, 628.3, and 628.6 respectively.

Replication Aim 1

Hypothesis H.R.II. AU sessions with CU were predicted to be associated with a higher probability of HED compared to AU sessions when cannabis was not used. Given that none of the predictors, including any co-use, significantly improved model fit, the unconditional model was retained as the best fitting model. As such, hypothesis H.R.II. was not supported suggesting that co-use was not associated with a higher likelihood that HED would occur in a given co-use session.

4.6 Model 3: Co-Use Only Model Predicting Number of Drinks

This model was used to assess the following hypotheses: H1.B.I, H2.A.I., H3.A.I, and H3.B.I. Comparison of the mean and the variance of outcome variable indicated that the data was overdispersed (M = 3.56, S^2 = 9), which aligned with findings from a Kolmogorov-Smirnov test, D(131) = .18, $p < .001$, and comparisons of model fit (Poisson: AIC = 611.8, BIC= 617.6, Negative Binomial: AIC = 592.7, BIC = 601.3). As with prior models, the first step in building Model-3 was to form the unconditional model as defined by the same equations described above for Model-1:

$$\text{Level 1: } \eta_{ij} = \log(\gamma_{ij}) = \beta_{0j}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

The ICC value was 0.1602 indicating that approximately 16.02% of the variance was due to between-person differences.

Level-1 of Model-3 was built according to the following steps. The results from WABA I suggested that a there was equivalent between- and within person variability in the following variables: temporal precedence, intention, weekday and EMA block. As such, all these variables were entered as Level-1 predictors in Model-3 one at a time. In contrast, WABA I result's indicated that the variance within CU quantity was predominantly between-person. For this reason, CU quantity was not entered as a predictor in Level-1 of this model, but instead, aggregated and entered only at Level-2. Further, results of WABA II dictated the order in which these variables should be entered based on the magnitude of their within-person co-variation with the outcome variable (Table 6).

Adding temporal precedence improved model fit, Δ_{AICi} = 583.6-593.7 = -10.1 = < 0, Δ_{BICi} = 595.1-601.3 = -6.2 = > 0. The slope of this variable was then permitted to vary randomly, but model fit was not improved, Δ_{AICi} = 587.4-583.6= 3.8 = > 0, Δ_{BICi} = 604.6-595.1 = 9.4 = > 0. As such, the model which included temporal precedence as fixed was retained. Adding the remaining Level-1 predictors did not improve model fit any further. The AIC values corresponding to the models including the weekday, intention, EMA block and Temporal Precedence X CU Quantity interaction term were 584.9, 585.6, 585.6, and 587.1 respectively. The BIC values corresponding to the models including the weekday, intention, EMA block and Temporal Precedence X CU Quantity interaction term were 599.3, 600, 600, and 604.3 respectively.

Next Level-2 variables, as indicated by the results of WABA I, were added to the model, one at a time, based on the strength of their bivariate correlations to the outcome variable (see Table 9). The inclusion of gender improved model fit according to its AIC value, Δ_{AICi} = 582.2-

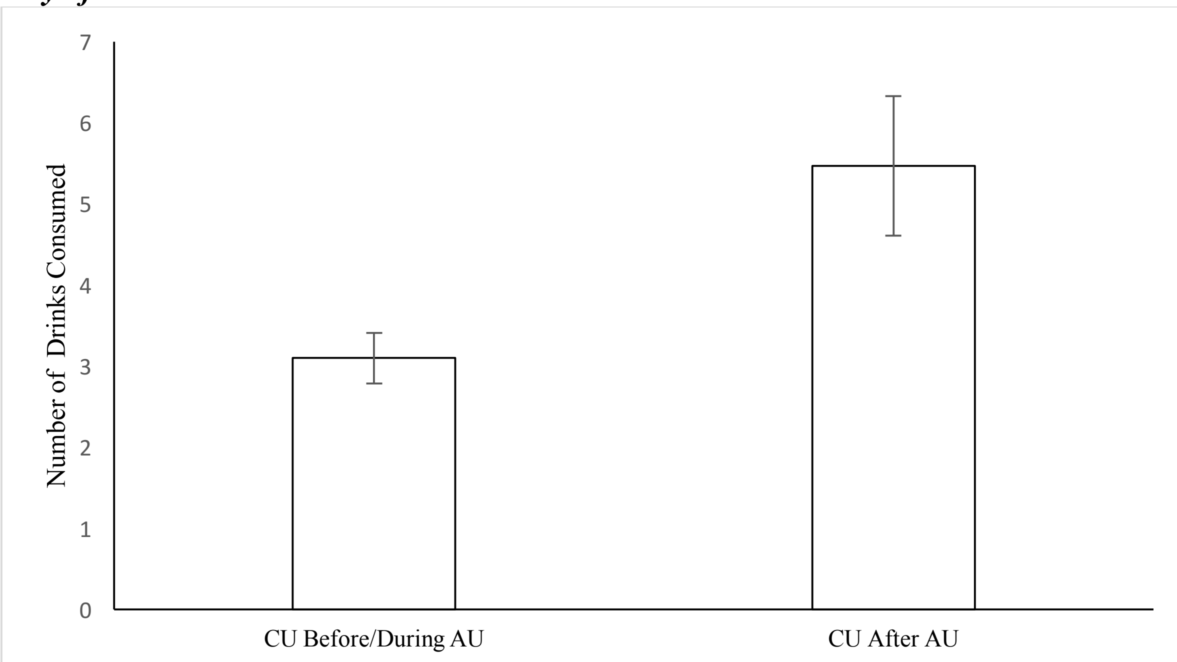
583.6= -1.4 = > 0, Δ_{BICi} = 596.6-595.1 = 1.5 = > 0. None of the remaining Level-2 variables improved model fit. The AIC values corresponding to models including CU quantity BTW, the aggregated temporal precedence variable (*temporal precedence BTW*), intention BTW, and the aggregated EMA block variable (*EMA BTW*) were 584.2, 583.3, 583.5, 582.6 respectively. The BIC values corresponding to the models that included the CU quantity BTW, temporal precedence BTW, intention BTW and EMA BTW variables were 601.5, 600.5, 600.7, 599.8 respectively. Finally, a cross level interaction between the two significant predictors included in the model, temporal precedence and gender, was included. This inclusion did not improve model fit. The AIC and BIC values corresponding to this model were 583.2 and 600.3 respectively. The final model was thus defined by the following equation:

$$\text{Level 1: } \eta_{ij} = \beta_{0j} + \beta_{1j}(Temporal\ Precedence_{ij})$$

$$\beta_{0j} = \gamma_{00} + \gamma_{01}(Gender_j) + \gamma_{02}(Temporal\ Precedence\ BTW_j) + u_{0j}$$

Figure 1.

Comparison of estimated mean number of drinks consumed in co-use sessions between co-use sessions wherein CU occurred before/during AU and co-use sessions wherein CU occurred only after AU.



Note. Estimated mean values represent the mean number of drinks consumed in a given co-use session across groups while controlling for the effect of gender and the between-person temporal precedence variable. CU = cannabis use, AU = alcohol use.

Table 9.
Bivariate Correlations between Level-2 Variables and outcome variables used in model-3 and -4.

	1	2	3	4	5	6
1. Number of drinks						
2. Session type	.71**					
2. Gender	-.22*	.05				
3. CU quantity BTW	-.08	-.08	.429**			
4. Temporal precedence BTW	.13	.10	-.10	.15		
5. Intention BTW	-.07	-.03	.00	.07	-.02	
6. EMA BTW	.08	.12	.21*	.12	.02	-.01

Note. Session type = moderate or HED drinking session, CU Quantity BTW = the aggregated cannabis quantity consumed variable, Temporal Precedence BTW = the aggregated temporal precedence variable, Intention BTW = the between person variable corresponding to the general intention an individual has to substitute cannabis to alcohol. EMA BTW = the aggregated variable corresponding to the EMA block which observations were sourced from.

Research Aim 1: Examine if the order in which CU occurs (before/during or after) in an AU session impacted the extent of an AU session.

Hypothesis H1.A.I. Results from Model-3 support the confirmation of Hypothesis H1.A.I.. Specifically, co-use sessions wherein CU occurred either directly before or during an AU session were associated with less drinks consumed relative to sessions wherein CU occurred only after AU had stopped (β_{1j} = .57, SE = .19, p = .002).

Research Aim 2: Examine if intention to substitute CU for AU impacted the extent of an AU session.

Hypothesis H2.A.I. Results from Model-3 do not support hypothesis H2.A.I.: intention to use to use cannabis as a substitute for alcohol in a given session did not predict the number of drinks consumed in that session. The inclusion of this variable in the model did not improve model fit and the slope of this variable was not significantly associated with the outcome.

Research Aim 3: Examine if the quantity of cannabis consumed in AU-CU co-use sessions impacts the extent of an AU session.

Hypothesis H3.A.I. Results from WABA I indicated that the predominant source of variability in the CU quantity variable was between people. This suggests a within-person analysis for this variable would not be meaningful (O'Connor, 2004). Therefore, hypothesis H3.A.I., which predicted that co-use sessions wherein large quantities of cannabis were used, could not be tested in the present study. Instead, the CU quantity variable was aggregated and entered at the between person level of Model-3.

Hypothesis H3.B.I. This hypothesis sought to examine if the negative association between quantity of cannabis used in a co-use session and number of drinks consumed was stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session. The interaction term between the two variables of interest, CU quantity and temporal Precedence, did not improve model fit and was not significantly associated with the number of drinks consumed in an AU session. These results do not support hypothesis H3.B.I.

In summary, the results of Model-3 suggest that co-use sessions wherein CU occurs before or during a co-use session are associated with fewer drinks consumed in that session relative to if CU only occurred after AU finished. On the other hand, intention to engage in CU as a means of substituting AU in a given co-use session did not significantly impact the number of drinks consumed in that session. Finally, research aim 3, pertaining to the impact of CU quantity in a given AU session, was not tested in the present study because the results of WABA I indicated that the predominant source of variability in CU quantity was between-persons and a within-person analysis would not be meaningful.

4.7 Model 4: Co-use Only Sample Predicting Moderate or HED AU Session

First, the unconditional model was built according to the following equation:

$$\text{Level 1: } \eta_{ij} = log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right) = \beta_{0j}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

The AIC and BIC values corresponding to this model were 184.4 and 190.2 respectively. The ICC value was .0417 indicating that approximately 4.17% of the variance was due to between-person differences. Next, level 1 variables were added to the model one at a time. The inclusion of the temporal precedence variable improved model fit according to its AIC value, Δ_{AICi} = 183.1-184.4= -1.3 = < 0, Δ_{BICi} = 191.7-190.2 = 1.5 = > 0. Because the fixed effect of the temporal precedence variable was not significantly related to the outcome, instead only trending towards significance (p = 0.8), the slope of the variable was not permitted to vary randomly in the next step of model construction. The remaining Level-1 predictor variables did not improve model fit. The AIC values corresponding to the models that included the intention, EMA block, weekday variables and the Temporal Precedence X CU Quantity interaction variables were 185.1, 184.1, 185.1, 185.1, and 185.5 respectively. The BIC values corresponding to the models which included the intention, EMA block, weekday, and the Temporal Precedence X CU quantity interaction term variables were 196.6, 195.5, 196.6, and 199.9 respectively.

Next, Level-2 variables were added to the model according to their bivariate correlations to the outcome variable (see Table 9). None of the included Level-2 predictors improved model fit. The AIC values corresponding to temporal precedence BTW included model, gender included model, intention BTW included model, and the CU quantity BTW model were 185.1, 184.6, 185 and 184.5 respectively, whereas the BIC values corresponding to these models were

196.6, 196.1, 196.5, and 196 respectively. The final model was therefore defined by the following equation:

$$\text{Level 1: } \eta_{ij} = log\left(\frac{\pi_{ij}}{1-\pi_{ij}}\right)\beta_{0j+}\beta_1(Temporal\ Precedence)_{ij}$$

$$\text{Level 2: } \beta_{0j} = \gamma_{00} + u_{0j}$$

Research Aim 1: Examine if the order in which CU occurs (before/during or after) in an AU session impacted the extent of an AU session.

Hypothesis H1.B.II. Results from Model-4 do not support Hypothesis H1.B.II.. Specifically, co-use sessions wherein CU occurred before/during an AU session were not associated with a lower probability of HED relative to sessions wherein CU occurred only after AU had stopped.

Research Aim 2: Examine if intention to substitute CU for AU impacted the extent of an AU session.

Hypothesis H2.A.II. Results from Model-4 do not support hypothesis H2.A.I.: intention to use to use cannabis as a substitute for alcohol in a given session was not associated with a lower probability of HED in that session.

Research Aim 3: Examine if the quantity of cannabis consumed in AU-CU co-use sessions impacts the extent of an AU session.

Hypothesis H3.A.II. This hypothesis predicted that large quantities of cannabis used in a co-use session would be associated with a lower probability of HED in that session relative to co-use sessions where small quantities of cannabis are used. WABA I result's suggested that the predominant source of variability for the CU quantity variable was between-persons. As such, this hypothesis was not tested in Model-4.

Hypothesis H3.B.II. Results of Model-4 do not support hypothesis H3.B.II. Specifically, the association between quantity of cannabis used in a co-use session and a lower probability of HED was not stronger in co-use sessions wherein CU occurred before/during an AU session relative to when CU occurred after an AU session.

Taken together, neither temporal precedence or intention were significantly related to an increased probability that HED would occur in a given co-use session. Additionally, hypothesis H3.A.II. which related to cannabis quantity used in a given co-use session as a predictor of session type was not assessed in the present study due to the fact that findings from WABA I indicated that this variable should not be used in group-level analyses.

4.8 Supplemental Analysis

4.8.1 Model 5: Any CU Predicting Drinking Outcomes adjusted for the findings of Model-3.

The findings of Model-3 suggested that CU consumption post AU session resolution was associated with more drinks consumed relative to when CU is consumed before/during an AU session. In light of this finding, a supplemental analysis was conducted to reassess Replication Aim 1 after adjusting for temporal precedence. CU following AU sessions are conceptually similar to AU only sessions in the sense that all drinks were consumed without the impact of cannabis' psychophysiological effects. As such, the time prior to CU in co-use sessions can be conceptualized as an AU only event, and therefore when CU only occurs after AU, drink consumption can be wholly attributed to AU. Thus, co-use sessions where CU only occurred after AU resolution were grouped with AU only sessions and Model-1 was reconstructed. This modified Replication Aim 1 to examine whether the psychophysiological effects of CU before/during an AU session were associated with deceased drink consumption relative to sessions where these psychophysiological effects could not have contributed to further drink consumption because CU was not used or only used after AU.

The unconditional model here is the same as the one constructed earlier for Model-1. Specifically, the ICC value for this model indicated that 19.2% of the variance in the outcome variable can be attributed to between person effects, and the AIC and BIC values for this model were 1963.6 and 1975.9 respectively. A new WABA analysis was conducted with the new co-use variable replacing the any co-use variable used in Model-1. The WABA results relevant to all other variables in Model-5 are unchanged from those described in tables 4, 5 and 6. WABA I indicated that the predominant source of variability for this new co-use variable was equivocally within and between-persons according to the E-test, between-person $\eta^2 = .37$, within-person $\eta^2 = .63$. According to WABA II, the between-groups and within-groups correlation to number of drinks was $r = -0.09$ and $r = -0.09$ respectively, both $p > .05$. Finally, WABA III results indicated that the raw correlation, the within-person WABA component and the between person WABA component to number of drinks was $r = -.09$, $r = -.05$, and $r = -.04$ respectively.

Adding the new, modified, co-use variable improved model fit, Δ_{AICi} = 1961.5-1963.6= -2.1 = < 0, Δ_{BICi} = 1977.8-1975.9 = 1.9 = > 0. The co-use variable was significantly associated with drink consumption, ($\beta_{1j} = -.19$, SE = .09, $p = .04$), so the slope associated with this coefficient was allowed to vary randomly in the next step of model construction. This adjustment did not improve model fit: AIC = 1962.6, BIC = 1987.2. Adding the remaining Level-1 variables did not improve model fit further. The AIC values corresponding to the models which included the weekend variable and the EMA block variables were 1963.4 and 1963.2 respectively. The BIC values corresponding to the models which included the weekend variable and the EMA block variables were 1983.9 and 1983.7 respectively.

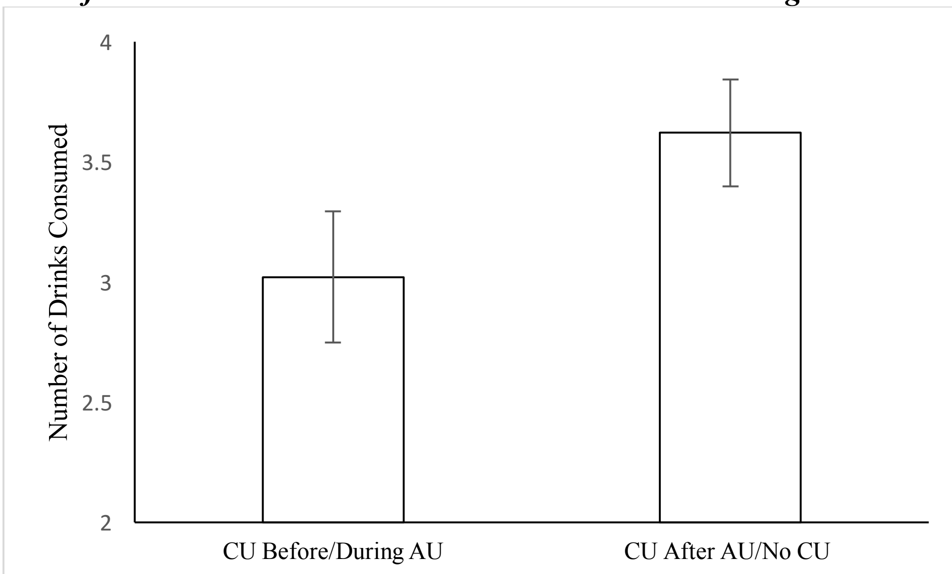
Next, Level-2 variables were entered into the model. The magnitude of the bivariate correlation between the new co-use variable aggregated to Level-2 to number of drinks consumed was $r = -.05$, $p = .249$. Gender was added to the model first which improved model fit, Δ_{AICi} = 1959.8-1961.5= -1.7 = < 0, Δ_{BICi} = 1980.3-1977.8= 2.5 = > 0. Gender was not significantly related to number of drinks, but was trending towards significance, p =.051 Adding the aggregated modified co-use variable and the EMA block BTW variable did not improve model fit. The AIC and BIC values corresponding to the model which included the modified co-use variable aggregated to Level-2 were 1961.5 and 1986.1. The AIC and BIC values for the model including the EMA block BTW variable were 1961.3 and 1985.9.

To summarize, co-use sessions wherein CU only occurred following AU were grouped with AU only sessions. This made the comparison groups: 1) AU sessions wherein CU occurred before/during AU and 2) AU sessions where CU only occurred after or not at all. After making this adjustment it was found that, while controlling for gender, using cannabis before/during an AU session was significantly associated with consuming 16.58% fewer drinks in a given AU session. The final model was therefore defined by the equation:

$$\text{Level 1: } \eta_{ij} = \beta_{0j} + \beta_{1j}(Modified\ Co - Use_{ij})$$

$$\beta_{0j} = \gamma_{00} + \gamma_{01}(Gender_j) + u_{0j}$$

Figure 2.
Comparison of estimated mean number of drinks consumed in drinking sessions between co-use sessions wherein CU occurred before/during AU and co-use sessions wherein CU occurred either after AU or cannabis was not consumed in the drinking session.



Note. Estimated mean values represent the mean number of drinks consumed in a given co-use session across groups while controlling for the effect of gender. CU = cannabis use, AU = alcohol use.

Chapter 5: Discussion

The present study examined how the co-use of cannabis and alcohol impacts the extent of drinking in a given AU event, and if characteristics of co-use events are associated with higher or lower levels of drink consumption. Two findings of the present study are particularly noteworthy. First, co-use events where CU occurs either before or during an AU event was associated with fewer drinks consumed relative to co-use events where CU only occurred after the last drink had been consumed. Second, cannabis-alcohol co-use before/during a drinking event was associated with lower levels of drink consumption in a given drinking event relative to AU events wherein CU occurred only after AU consumption or did not occur at all.

These findings suggest CU before/during an AU event may substitute for drink consumption in an AU event.

The present study first sought to replicate past daily level examinations of cannabis-alcohol co-use by evaluating the impact of co-use on drink consumption in an AU event. Contrary to expectations, co-use events were not associated with heavier drinking in a given event relative to AU only events. Likewise, the probability of a drinking event being characterized as HED rather than moderate drinking was not higher in co-use events relative to AU only events. These two findings contradict previous daily level studies which have suggested that CU is associated with heavier drinking events relative to when CU did not occur on the day of drinking (Metrik et al., 2018; Gunn et al., 2018; Lee et al., 2020; Gunn et al., 2019). Importantly, three of these studies (Metrik et al., 2018; Gunn et al., 2018; Gunn et al., 2019) examined co-use in a sample of veterans with substantially different sociodemographic characteristics than the sample examined in the present study which may explain the divergence in findings. The study conducted by Lee and colleagues (2020) aligns closest with the present study in sample and methodology making the divergence in our findings more difficult to reconcile, yet some key differences remain. For one, the study conducted by Lee and collegues took place in Washington state in the United States. Despite both studies being conducted in the context of legal recreational CU, key CU regulations, such as locations where legal CU is permitted, vary even across legal CU contexts. Moreover, Attitudes towards, and patterns of, substance use have been shown to vary by country along with other critical factors (Simons-Morton et al., 2010; Toumbourou et al., 2005; Beyers et al., 2004). For example, college students in the United States have lower rates of lifetime and past year AU, but tend to have higher rates of past year and lifetime HED (Kuo et al., 2002). Thus, geographic region may be an important factor to consider in future studies of cannabis-alcohol co-use.

Following this replication, three primary aims sought to examine if characteristics of co-use sessions impact the extent of drinking in a given co-use session. Each of these aims were assessed with two paralleling hypotheses that used different outcome measures: either number of drinks or a dichotomous measure of moderate vs. heavy drinking.

The first of these aims examined the role of temporal precedence in predicting the extent of drinking in a given co-use session. Hypothesis H1.A.I. which predicted that engaging in CU only after AU would be associated with more drinks consumed relative to when CU occurred before/during a drinking event was confirmed in the present study. A critical difference between co-use events where CU occurs before/during AU and co-use events where CU only occurs after AU is the impact that the acute effects of CU can have on further drink consumption. The time prior to CU in a co-use event is better conceptualized as an AU only event rather than a co-use event because the acute effects of CU have not yet overlapped with AU. It follows then, that if cannabis-alcohol co-use decreases the likelihood of further drink consumption then this effect should be most pronounced when co-use is extended throughout the duration of a drinking event rather than only at the end. Therefore, the finding that CU before/during AU is associated with fewer drinks consumed in a given co-use event relative to when CU only occurs after AU indicates that the acute effects of CU may substitute those of AU.

It may be that individuals augment AU with CU as a means of reaching their desired level of intoxication more efficiently, which helps to explain why there is less need for further AU after the onset of CU's acute effects. The synergistic effect on intoxication when these substances are used together has been demonstrated in both laboratory (Hartman et al., 2016; Lukas & Orozco, 2001) and daily diary studies (Gunn et al., 2018; Metrik et al., 2018; Sokolovsky, 2020). Therefore, individuals may be able to meet their desired level of intoxication by drinking 4 drinks and engaging in CU rather than drinking 5. Further, the sedating effects of cannabis (Green et al., 2003) may play a role in slowing drinking, such that individuals may be more likely to go home and relax after CU rather than continuing to drink in a party environment. In contrast, individuals that engage in CU post-AU may be doing so as a means of recovering from AU. As such, this need for recovery CU may be most salient following HED when the negative effects of AU are most pronounced (Morean & Corbin, 2010). In summary, CU before or during AU may evoke mechanisms that promote substitution, whereas CU after AU may be associated with higher levels of drinking because of the context it is likely to occur despite the acute effects of CU playing no role in this increased drink consumption.

Hypothesis H1.A.II. predicted that co-use sessions where CU occurred before/during AU would be associated with a lower probability of HED relative to co-use sessions where CU occurred after an AU session. The results of the present study did not confirm this hypothesis. Nonetheless, it should be noted that the association between temporal precedence and HED was trending towards significance in the predicted direction. This trend towards significance is an important consideration given that this model was underpowered to detect small or medium Level-1 effects. A number of rules of thumb for sample sizes in MLM have been proposed, all of which recommend a sample size of Level-1 units, in this case observations per person, greater than the average of 3 found in the present study (McNeish and Stapleton, 2014; Kreft, 1996; Snijders and Bosker, 2012; Hox 1998, 2010). Additionally, power is further reduced when variables are dichotomized (Altman & Royston, 2006; Cohen, 1983; MacCallum et al., 1983) which explains why a significant effect was found when the temporal precedence aim was assessed using a count outcome variable rather than the dichotomous variable used here. Considering this reduced power, it may be best to conceptualize the results of this dichotomous analysis as consistent with the count analysis although less pronounced.

Although not directly related to the hypotheses purposed in the present study, two findings related to gender are noteworthy. First, drink consumption was found to be associated with gender such that males tended to drink 37% more in a given drinking event. This result aligns with the well-established finding in previous AU literature that men tend to drink more than females in a given drinking event (Wilsnack et al., 2009; Wilsnack & Wilsnack et al., 2013) Secondly, a cross-level interaction between gender and temporal precedence was assessed in the present study in order to examine if the impact of temporal precedence on the number of drinks consumed in a given session varied across genders. This cross-level interaction failed to improve model fit, and was not significantly related to drink consumption which suggest that temporal precedence impacts drink consumption in co-use sessions consistently in both males and females. As such, the findings of the present study suggest that males drink more than females, but that CU post-AU is associated with increased drink consumption in both genders.

With respect to Aim 2, both hypotheses were not supported by the results: intention to use cannabis as a substitute for alcohol was not associated with fewer drinks consumed or a reduced probability of HED. One explanation for these null findings is that our models did not included any non-drinking events. Given this, any drinking event that was entirely substituted for by CU was not accounted for in our models. It may be the case that individuals who have a high intention to substitute CU for AU on a given night are choosing to often not drink at all. Indeed, one study, which accounted for non-drinking days in their analysis, found that an overall intention to substitute across drinking days (i.e., between persons) was associated with reduced drink consumption on CU days (Gunn et al., 2019). Beyond accounting for non-drinking days, participants in their analysis were medical cannabis using veterans, whereas participants in the present study were young adult college students. Veterans have higher rates of problematic drinking relative to the general population (Teeter et al., 2017) which may increase substitution motivations in the context of light drinking as a means of craving reduction. In contrast, motivations for substitution like cost and safety, which tend to be more pertinent on nights of heavy drinking, may be more relevant to a non-clinical sample of college students. Given this, it may be that substitution intention is associated with HED events relative to moderate drinking events, but also associated with reduced drink consumption in the context of these HED events. Finally, it is possible that the acute effects of AU reduce behavioural control such that drinkers do not behave consistently with their initial intentions in the context of HED. Indeed, in the context of sexual behaviour, drinkers report being less safe than they initially intended following drinking (Wells et al., 2010). To summarize, three factors may account for the non-significant relationship between intention and drink consumption: 1) non-drinking events not being accounted for in the present study, 2) substitution motivations being more relevant to our sample in the context of heavy drinking and 3) intention being wiped out following heavy drinking.

Aim 3 sought to investigate the role of CU quantity consumed on the extent of drinking in a given co-use event. Here, results of the preliminary WABA analysis suggested that there was not enough within-person variation in CU quantity consumed to conduct a meaningful Level-1 analysis on this variable. As such, hypotheses H3.A.I. and H3.A.II. could not be tested in the present study. The majority of the within-person variation in CU quantity consumption was likely minimized in the dichotomization of the variable due to the fact that even light CU sessions for frequent cannabis users are large relative to typical CU sessions of occasional users. Indeed, past research has suggested that there is a considerable range in CU consumption quantity across cannabis users such that daily cannabis users are estimated to consume between

2-3 times the amount of daily cannabis relative to occasional users on CU days (Caulkins et al., 2020; Zeisser et al., 2011). This lack of within-person variation may have also contributed to the non-significant interaction between CU quantity and temporal precedence proposed in hypotheses H3.B.I. and H3.B.II.. These hypotheses predicted that the negative association between quantity of cannabis used in a co-use session and the extent of drinking in a co-use session would be stronger in co-use sessions when CU occurred before/during an AU session relative to when CU occurred after an AU session. Future research should aim to maintain continuous measures of CU quantity when evaluating within-person effects.

Finally, an additional supplemental analysis revealed that cannabis alcohol co-use before/during AU was associated with fewer drinks consumed in a drinking session relative to when cannabis is not used or only used after AU is resolved. This finding suggests that CU can act as a substitute for AU when used before/during an AU session, and adds to the literature by highlighting the importance of temporal precedence in the consideration of substitution effects. The grouping of post-AU co-use events with AU only events is justified by the fact that all drink consumption in post-AU co-use events is done in the absence of CU's acute effects. As such, mechanisms by which CU may decrease drink consumption, for example efficiency and sedation, are most active when co-use occurs before/during an AU event. In contrast, mechanisms by which AU increases drink consumption, such as reduced inhibitory control (Sher et al., 2005), act independently in post-AU co-use events and AU only events. Finally, individuals may be motivated to consume CU-post AU as a means of recovering from heavy AU thereby further increasing mean drink consumption in post-AU co-use events relative to before/during co-use events. Past research which indicates complementary effects associated with co-use that did not account for temporal precedence should be considered in light of these critical conceptual differences between before/during co-use events and post-AU co-use events.

5.1 Strengths and Limitations

The present study should be considered in light of its limitations. First, responses were typically provided in the morning following a drinking event, or if the participant had missed some surveys, even later. Minimizing the time between event and recall was particularly important in the context of the present study. Individuals tend to lower their estimates of recalled drink consumption as time passes between drinking event and recall such that estimates of consumption are nearly 1 drink lower when participants are asked a week after drinking rather than the day following (Gmel, & Daeppen, 2007). Thus, although recall bias was minimized in the present study through the use of daily EMA questionnaires, it cannot be ignored as a limitation relative to in-situ measures of drink consumption such as asking participants to report drink consumption at regular intervals throughout a drinking event (Simons et al., 2014).

Secondly, Analyses in the present study lacked power. The average number of observations per participants was 5.5 and 3 for the any AU sample and co-use only samples respectively. These level-1 sample sizes are below traditional rules of thumbs which estimate the sample sizes required to adequately detect small to moderate Level-1 effects (McNeish and Stapleton, 2014; Kreft, 1996; Snijders and Bosker, 2012; Hox 1998, 2010). Nonetheless, the limited sample size in the present study is offset by the repeated measurement of drinking events which allowed for a fine grained analysis of which co-use characteristics are associated with varying levels of AU consumption.

Next, two issues arose with the variable corresponding to quantity of cannabis consumed in a given co-use session. For one, participants were required to input a text entry as a response to the questions intended to measure CU quantity. As a consequence of this response method, a number of observations were removed from analysis due to lack of interpretability of the response. Further, all analyses involving CU quantity consumed were dichotomized into small or large quantities which reduced within-person variation in this variable to the extent that it could not be included in its intended analyses. This dichotomization was necessary in order to obtain an objective measure of cannabis quantity consumption in cases where participants used more than one modality of consumption, such as when an individual smoked cannabis and consumed it orally in the same event. The ideal progression beyond this limitation is the development of a standard cannabis unit, similar to a standard drink unit which allows for measurement of AU across different drink types, yet no such standard cannabis unit has been established. Thus, the measurement issues with CU quantity in the present study are reflective of a grander limitation in the field of cannabis research rather than a methodological issue relevant exclusively to the present study.

Finally, the data for present study was collected in the years directly following the legalization of recreational cannabis in Canada. The rapidly evolving social, political and cultural context surrounding CU in Canada may pose problems for generalization to other countries or legal contexts. Indeed, CU policies and regulations were developing in Canada throughout the duration of the present study, with large scale changes, such as the legal sale of orally ingested cannabis products, being implemented midway. Further, Cannabis has been incredibly salient in the media since legalization which may have disrupted the findings of the present study in unforeseen ways. Nonetheless, the investigation of cannabis-alcohol co-use in the context of legal recreational CU is still rare, and thus represents a strength of the present study. Massive changes to cannabis regulation are constantly unfolding across the world, and it is critical that any newly developed CU policies are informed by empirical evidence that can be confidently generalized to legal environments.

5.2 Implications

Harm reduction guidelines from government and health agencies have, in the past, regularly advised against the co-use of cannabis and alcohol under the assumption that co-use of these substances is more harmful than the use of either substance alone (Canadian Nurses Association, 2017, Delphi Behavioral Health Group, 2019; HealthLinkBC, 2019)**.** The results of this study, however, suggest that CU before/during a drinking event may serve to substitute for an additional, non-negligible, amount of drinks. Specifically, co-use before/during an AU session was found to be associated with a 16.58% reduction in drink consumption in the present study. In the context of HED, this reduction is the difference between an individual consuming 10 or 8 drinks throughout an AU event. This reduction from 10 to 8 drinks has been suggested by meta-analytic reviews to translate into reducing the odds of a motor vehicle accident by more than half, and the odds of a non-motor vehicle accident by 40% (Taylor et al., 2010). Further, daily diary studies have found that the negative consequences of co-use are driven by alcohol (Mallet et al., 2019; Lee et al., 2020; Sokolovsky et al., 2020), which suggests that 10 drinks without co-use is more dangerous than 8 drinks with co-use. In conclusion, the findings of the present study suggest that the co-use of cannabis and alcohol before/during an AU session may reduce drink consumption in a given drinking session, which ultimately may serve to reduce overall HED related negative consequences. As such, harm reduction guidelines which caution against the co-use of cannabis and alcohol may be misplaced.

The notion of cannabis-alcohol co-use as a means of reducing harm associated with AU has far reaching implications. Perhaps the most salient of these implications is that the prohibition of recreational cannabis use, which is the status quo in the majority of world, may serve to increase the harms associated with AU. Alcohol presents a massive global burden: it is the leading cause of premature death and disability among individuals aged 15-49 and accounts for a quarter of total deaths among individuals aged 20-39 years old (World Health Organization, 2010). Considering this substantial harm associated with AU, any measure mitigating AU harm cannot be ignored, and the results of the present study suggest that cannabis legalization should be considered as one of these mitigating factors. Further, the findings of the present study apply to legal CU environments as well. For one, government regulatory bodies have, in the past, established cannabis policies under the running assumption that the co-use of cannabis and alcohol increases risk associated with substance use. For example, on September 19th, 2019 the British Columbia Government introduced a policy directive which restricted the advertisement of cannabis products at liquor licensed establishments and at events held under a special event permit (British Columbia Liquor and Cannabis Regulation Branch, 2019). Likewise, the British Columbia government has left it up to the discretion of liquor license holders to establish policies permitting or restricting the use of cannabis on open-air portions of their property (British Columbia Liquor and Cannabis Regulation Branch, 2019). While some licensees may be tempted to prohibit the use of cannabis in order to reduce the risk of their patrons and minimize liability, the results of the present study suggest that this restriction would be misplaced. In sum, the findings of the present study can help guide policy decisions of government and private organizations.

5.3 Future directions

Future research may wish to extend the findings of the present study in three ways. First, the present study found that intention to use cannabis as a substitute for alcohol was not associated with reduced alcohol consumption in co-use sessions. This null finding may be explained by the fact that this intention to substitute may be most relevant to college students in the context of HED. As such, it may be the case that intention to substitute is associated with reduced drinking in college students, but only during HED sessions. Given the importance of minimizing drink consumption in HED sessions, future research should aim to investigate this finding. Secondly, CU quantity consumed as a contributing factor to reduced AU in co-use sessions could not be evaluated due to a lack of within-person variation. This lack of variation may be due to the dichotomization of the variable to small or large amounts as a means of synthesizing responses across the three CU quantity items. Given the lack of consensus regarding the standard cannabis "unit" across CU modalities (Volkow & Weiss, 2020) and the vast range in tolerance across cannabis users (Colizzi & Bhattacharyya, 2018), an alternative means of measuring CU quantity consumed while retaining variation may be to ask users to report how much cannabis they used with respect to their typical dose. A Likert scale ranging from "much less than usual dose" to "much more than usual dose" would likely provide a more ecologically valid operationalization of CU quantity consumed. Finally, the findings of the present study considered along-side past research suggests that CU before/during AU may reduce negative alcohol related consequences by way of reduced drink consumption. Future research should aim to empirically test this possible mediation model.

5.4 Conclusions

Current harm reduction guidelines, including those put forward by the provincial government of British Columbia (HealthLinkBC, 2019), suggest that cannabis-alcohol co-use should be avoided because the risk associated with co-use is greater than the use of either substance on its own. Nonetheless, past research has suggested that co-use does not present any additional risk for negative consequences over AU alone (Mallet et al., 2019; Lee et al., 2020;

Sokolovsky et al., 2020). Further, the consequences associated with AU increase dramatically with each drink consumed (Taylor et al., 2010). Finally, the findings of the present study suggest that co-use may reduce drink consumption when CU occurs before/during AU. Given these findings, co-use may actually contribute to reduced harm associated with AU by means of reducing drink consumption. As such, the present study draws into question the merit of harm reduction guidelines, as-well as government and private organization policy, which recommend against or prohibit the co-use of cannabis and alcohol with the intention of reducing harm.

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Appendix A: EMA questions relevant to the present study

#	Branching logic	Question	Response options
1		"Have you used any substances other than cannabis since the last assessment?"	1. "Alcohol" 2. "Tobacco"
2	If "alcohol" selected in #1	"Were these drinks consumed in one drinking occasion/one 7 hour period?"	1. "Yes" 2. "No"
3	If "no" is selected in #2	"how many drinks were consumed in the heaviest (most drinks) drinking occasion?"	Open numeric response
4		"Have you used cannabis since the last assessment?"	1. "Yes" 2. "No"
5	If "yes" is selected in #2 and #5	"What best describes your cannabis and alcohol use since the last assessment? Check all that apply"	1. "I used cannabis before I started drinking (within two hours of initiation)" 2. "I used cannabis while drinking (i.e., during drinking occasion") 3. "I used cannabis after I finished drinking (i.e., no drinks consumed after cannabis use)"
6	If "yes" is selected in #2 and #5	"Please select what time you had your first drink of alcohol in this drinking occasion".	Drop down menu with time options at 30 minute intervals.
7	If "yes" is selected in #2 and #5	"Please select what time you had your last drink of alcohol in this drinking occasion."	Drop down menu with time options at 30 minute intervals. "Still drinking included as an option"
8	If "yes" is selected in #2 and #5	Please select the first time you used cannabis in this drinking occasion (within two hours of your first or last drink)."	Drop down menu with time options at 30 minute intervals.
9	If "yes" is selected in #2 and #5	"Please select the last time you used cannabis in this drinking	Drop down menu with time options at 30 minute intervals.

		occasion (within two hours of your first or last drink)."	"Still smoking" included as an option
10	If "I used cannabis before I started drinking (within two hours of initiation)" is selected or "I used cannabis while drinking (i.e., during drinking occasion") is selected in # 5	"How much cannabis did you use before (within two hours) and/or during this drinking event (not including cannabis used after finishing drinking)?" Grams [*avg. joint =.3-.5 grams,eighth = 3.5 grams, quarter = 7 grams, 1 oz. = 28 grams*]	Open text response
11	If "I used cannabis before I started drinking (within two hours of initiation)" is selected or "I used cannabis while drinking (i.e., during drinking occasion") is selected in # 5	"How much cannabis did you use before (within two hours) and/or during this drinking event (not including cannabis used after finishing drinking)?" Edibles (amount; estimated mg)	Open text response
12	If "I used cannabis before I started drinking (within two hours of initiation)" is selected or "I used cannabis while drinking (i.e., during drinking occasion") is selected in # 5	"How much cannabis did you use before (within two hours) and/or during this drinking event (not including cannabis used after finishing drinking)?" Puffs on a distillate pen	Open text response
13	If "I used cannabis after I finished drinking (i.e., no drinks consumed after cannabis use)" is	How much cannabis did you use after this drinking event (within two hours from your last drink)?	Open text response Open text response

	selected in #5	Grams [avg. joint =.3-.5 grams, eighth = 3.5 grams, quarter = 7 grams, 1 oz. = 28 grams]	
14	If "I used cannabis after I finished drinking (i.e., no drinks consumed after cannabis use)" is selected in #5	How much cannabis did you use after this drinking event (within two hours of your last drink)? Edibles (amount; estimated mg)	Open text response
15	If "I used cannabis after I finished drinking (i.e., no drinks consumed after cannabis use)" is selected in #5	How much cannabis did you use after this drinking event (within two hours of your last drink)? Puffs on a distillate pen	Open text response
16	If "yes" is selected in #2 and #5	Please sort the following motivations in rank order according to how they apply to your use of cannabis in this drinking occasion. Please rank them in order from 1 = most accurate to 8 = least accurate."I used cannabis:"	In random order: 1. So I could drink less 2. For enjoyment/fun 3. Because others were doing it 4. To experiment 5. To be social 6. To relax 7. Because I was bored 8. Other.
17		Please rate how well each of these statements describes your last use of cannabis: I used cannabis instead of using other drugs (i.e., alcohol, recreational drugs, prescription or non-prescription pharmaceuticals).	1. 1 = Disagree 2. 2 3. 3 4. 4 5. 5 = agree

Appendix B: Model Building Specifications

Table B1
Model testing specifications summarized

	Sample: All AU events			Sample: Co-use events only	
	Model-1	Model-2	Model-5	Model-3	Model-4
Dependent Variable	Number of Drinks	Moderate AU or HED	Number of Drinks	Number of Drinks	Moderate AU or HED
Level-1 (within-person)	Any Co-use	Any Co-use	**Co-use before/during AU**	**Temporal Precedence**	**Temporal Precedence**
	Weekday	Weekday	Co-use before/during AU (Random)	Temporal Precedence (Random)	Intention
	EMA Block	EMA Block	Weekday	Weekday	EMA Block
			EMA Block	Intention	Weekday
				EMA Block	Timing X CU quantity
				Timing X CU quantity	
Insufficient variation				CU-Quantity	CU-Quantity
Level-2 (between-person)	**Gender**	Weekday BTW	**Gender**	**Gender**	Timing BTW
	Weekday BTW	Gender	Co-use before/ during BTW	CU-Quantity BTW	Gender
	Co-use BTW	Co-use BTW	Weekday BTW	Temporal precedence BTW	EMA block BTW
				Intention BTW	Intention BTW
				EMA Block BTW	CU–Quantity BTW
				Timing X Gender	
Insufficient variation				Weekday btw	Weekday btw

Note. Shaded rows indicate that the variable was not included in models due to indication of insufficient variation to warrant meaningful analysis. Bolded variables were included in the final model. Variables are entered as fixed unless otherwise noted. CU = Cannabis use. AU = Alcohol use. HED = Heavy episodic drinking. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable.

Table B2.

Co-use predicting number of drinks consumed in a given AU session

	Level 1 predictors				Level 2 predictors		
	Null model	Co Use (fixed)	Weekday (Fixed)	EMA Block (fixed)	Gender	Weekday BTW	Co Use BTW
Fixed Components							
Intercept	1.19	**1.19**	**1.20**	**1.18**	**1.36**	**1.36**	**1.36**
Co-Use		0.01					
Weekday			0				
EMA Block				0.04			
Gender					**-0.23**	**-0.23**	**-0.23**
Weekday BTW						0.12	
Co-Use BTW							-0.01
Random components							
Intercept	0.13	0.13	0.13	0.13	0.12	0.11	0.12
Slope							
Intercept-Slope Covariance							
Model Fit information							
# Parameters	2	3	3	3	3	4	4
AIC	1963.6	1965.6	1965.7	1965.3	1961.9	`1963.6	1963.9
BIC	1975.9	1982	1982	1981.7	1978.38	1984.1	1984.4
ICC	19.16%						
% Variance Explained		19.19%	19.16%	19.20%	19	18.43%	18.52%

Note. Bolded values are significant at $p < .05$. † = $p < .1$. Shaded columns did not significantly improve the model. % Variance explained represents the total variance explained by the model including both fixed and random effects. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; ICC = Intraclass Correlation. X-Level interact = cross level interaction. Co-use was coded as 0 = co-use, 1 = no co-use. Weekday was coded as 0 = weekday, 1 = Weekend. EMA block was coded as: 0 = first EMA Block, 1 = second EMA block, 2 = third EMA block.. Gender was coded as 0 = male, 1 = female.

Table B3.

Co-use predicting session type, either moderate drinking or heavy episodic drinking

	Level 1 predictors				Level 2 predictors		
	Null model	Co Use (fixed)	Weekday (Fixed)	EMA Block (fixed)	Weekday BTW	Gender	Co Use BTW
Fixed Components							
Intercept	-0.12	-0.08	-0.09	-0.15	-0.12	-0.24	-0.12
Co Use		-0.11					
Weekday			-0.1				
EMA Block				0.06			
Weekday					-0.48		
Weekday BTW						0.18	
Co Use BTW							0.12
Random components							
Intercept	0.33	0.33	0.33	0.33	0.33	0.33	0.33
Slope							
Intercept-Slope Covariance							
Model Fit information							
# Parameters	2	3	3	3	3	3	3
AIC	614.4	616.1	616.2	616.3	615.8	616	616.3
BIC	622.6	628.4	628.5	628.6	628.1	628.3	628.6
ICC	9.12%						
% Variance Explained		7.6%	7.6%	7.6%	7.7%	7.8%	7.7%

Note. Bolded values are significant at $p < .05$. † = $p < .1$. Shaded columns did not significantly improve the model. % Variance explained represents the total variance explained by the model including both fixed and random effects. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; ICC = Intraclass Correlation. X-Level interact = cross level interaction. Weekday was coded as 0 = weekday, 1 = Weekend. EMA block was coded as: 0 = first EMA Block, 1 = second EMA block, 2 = third EMA block.. Gender was coded as 0 = male, 1 = female.

Table B4.

Characteristics of co-use predicting number of drinks consumed in a given co-use session

	Level 1 predictors							Level 2 predictors					X-Level Interact
	Null model	Temporal Precedence (fixed)	Temporal Precedence (Random)	Weekday (Fixed)	Intention (fixed)	EMA Block (fixed)	Timing X Amount	Gender	CU Quantity BTW	Temporal precedence BTW	Intention BTW	EMA Block BTW	Timing X Gender
Fixed Components													
Intercept	**1.23**	**1.07**	**1.08**	**1.03**	**1.07**	**1.09**	**1.04**	**1.31**	**1.31**	**1.29**	**1.33**	**1.35**	**1.23**
Temporal Precedence		**0.50**	**0.48**	**0.51**	**0.50**	**0.50**	**0.72**	**0.46**	**0.46**	**0.57**	**0.45**	**0.45**	**0.65**
Weekday				0.12									
Intention					0.00								
EMA Block						-0.03							
Temporal Precedence X CU Quantity							0.05						
Gender								-0.32†	-0.31†	**-0.34**	-0.32†	**-0.38**	-0.20
CU Quantity BTW									-0.01				
Temporal Precedence BTW										-0.30			
Intention BTW											-0.06		
EMA Block BTW												0.23	
Temporal Precedence X Gender													-0.33
Random components													
Intercept	0.12	0.12	0.10	0.12	0.11	0.12	0.11	0.09	0.10	0.09	0.09	0.09	0.08
Slope			0.02										
Intercept-Slope Covariance			0.44										
Model Fit information													
# Parameters	2	3	4	4	4	4	4	4	5	5	5	5	5
AIC	592.71	583.63	587.37	584.92	585.62	585.56	587.06	582.22	584.22	583.28	583.47	582.57	583.09
BIC	601.34	595.13	604.618	599.30	600	599.94	604.32	596.70	601.47	600.53	600.72	599.82	600.34
ICC	16.04%												
% Variance Explained		23.57%	24.43%	23.46%	23.56%	23.81%	22.94%	23.41%	23.41%	23.22%	23.63%	23.94%	21.53%

Note. Bolded values are significant at $p < .05$. $^{\dagger} = p < .1$. Shaded columns did not significantly improve the model. % Variance explained represents the total variance explained by the model including both fixed and random effects. CU = Cannabis use. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; ICC = Intraclass Correlation. X-Level interact = cross level interaction. Temporal precedence was coded as: 0 = before/during AU, 1 = After AU. Weekday was coded as 0 = weekday, 1 = Weekend. EMA block was coded as: 0 = first EMA Block, 1 = second EMA block, 2 = third EMA block. CU quantity was coded as: 0 = small amount, 1 = large amount. Gender was coded as 0 = male, 1 = female.

Table B5.

Characteristics of co-use predicting session type, either moderate or HED

	Level 1 predictors						Level 2 predictors			
	Null model	Temporal Precedence (fixed)	Intention (Fixed)	EMA Block (fixed)	Weekday (Fixed)	Temporal Precedence X CU Quantity	Timing BTW	Gender	Intention BTW	CU Quantity BTW
Fixed Components										
Intercept	-0.15	-0.35	-0.35	-0.51†	-0.35	-0.73	-0.38	-0.57	-0.33	-0.33
Temporal Precedence		0.80†	0.79†	0.81†	0.80†	0.35	0.87	0.82†	0.79†	0.77†
Intention			-0.00							
EMA Block				0.32						
Weekday					-0.02	0.47				
Temporal Precedence X CU Quantity						0.47				
Timing BTW							-0.17			
Gender								0.30		
Intention BTW									-0.05	
CU Quantity BTW										0.49
Random components										
Intercept	0.14		0.21	0.21	0.21	0.21	0.21	0.19	0.21	0.2
Slope										
Intercept-Slope Covariance										
Model Fit information										
# Parameters	2	3	4	4	4	4	4	4	4	4
AIC	184.4	183.1	185.1	184.1	185.1	185.5	185.1	184.6	185	184.5
BIC	190.2	191.7	196.6	195.6	196.6	199.8	196.6	196.1	196.5	196
ICC	4.17%									
% Variance Explained		7.5%	7.5%	8.2%	7.5%	8.8%	7.4%	7.5%	7.6%	8.0%

Note. Bolded values are significant at $p < .05$. † = $p < .1$. Shaded columns did not significantly improve the model. % Variance explained represents the total variance explained by the model including both fixed and random effects. CU = Cannabis use. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; ICC = Intraclass Correlation. X-Level interact = cross level interaction. Temporal precedence was coded as: 0 = before/during AU, 1 = After AU. Weekday was coded as 0 = weekday, 1 = Weekend. EMA block was coded as: 0 = first EMA Block, 1 = second EMA block, 2 = third EMA block. CU quantity was coded as: 0 = small amount, 1 = large amount. Gender was coded as 0 = male, 1 = female.

Table B6.

Co-use before/after AU predicting number of drinks consumed in a given AU session

	Level 1 predictors					Level 2 predictors		
	Null model	Co-Use before/during (fixed)	Co-Use before/during (random)	Weekday (Fixed)	EMA Block (fixed)	Gender	Co Use before/during BTW	Weekday BTW
Fixed Components								
Intercept	1.19	**1.24**	**1.23**	**1.20**	**1.22**	**1.4**	**1.41**	**1.41**
Co-Use before/during		**-0.19**	-0.16	**-0.19**	**-0.18**	**-0.18**	**-0.22**	**-0.21**
Weekday				0.01				
EMA Block					0.03			
Gender						-0.23†	**-0.23**	**-0.22**
Co-Use before/during BTW							0.1	
Weekday BTW								0.1
Random components								
Intercept	0.13	0.13	0.14	0.13	0.13	0.12	0.12	0.12
Slope			0.18					
Intercept-Slope Covariance			-.62					
Model Fit information								
# Parameters	2	3	4	4	4	4	5	5
AIC	1963.6	1961.5	1962.6	1963.4	1963.16	1959.8	1961.5	1961.5
BIC	1975.9	1977.9	1987.2	1983.9	1983.7	1980.3	1986.1	1986.1
ICC	19.16%							
% Variance Explained		20.06%	20.85%	20.05%	20.06%	19%	19.3%	19.3%

Note. Bolded values are significant at $p < .05$. † = $p < .1$. Shaded columns did not significantly improve the model. % Variance explained represents the total variance explained by the model including both fixed and random effects. EMA = Ecological Momentary Assessment. BTW = the variable is a between person variable. AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria; ICC = Intraclass Correlation. X-Level interact = cross level interaction. Co-use before/during was coded as 0 = co-use before/during, 1= co-use after or no co-use. Weekday was coded as 0 = weekday, 1 = Weekend. EMA block was coded as: 0 = first EMA Block, 1 = second EMA block, 2 = third EMA block.. Gender was coded as 0 = male, 1 = female.