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RISK OF INJURY FROM ALCOHOL AND DRUG USE IN THE EMERGENCY DEPARTMENT: A CASE-CROSSOVER STUDY

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Abstract

Introduction and Aims—A substantial literature exists demonstrating the risk of injury from alcohol, but less is known about the association of alcohol in combination with other drugs and injury. This study examined the risk of injury associated with alcohol and drug use prior to the event.

Design and Methods—Case-crossover analysis was used to estimate the relative risk (RR) of injury due to alcohol use alone, compared to alcohol in combination with other drug use in a sample of emergency department (ED) injured patients from two sites in Vancouver, BC (n=443). Alcohol and drug use in the six hours prior to injury was compared with the patient's use of these substances during the same six-hour period the day prior and the week prior to injury.

Results—Using multiple matching for the two control time periods, RR of injury was significantly related to both alcohol use (RR = 3.3) and to alcohol combined with drug use (RR=3.0), but not to drug use alone. Effect modification was found only for age for alcohol combined with drug use, with a significant increase in injury risk (p=.087) for those over 30.

Discussion—While a similar elevated risk of injury was found for alcohol use alone and alcohol used with other drugs, the literature suggests that alcohol in combination with some drugs may be potentially more risky for injury occurrence.

Conclusion—Findings suggest the need for future research on risk of injury for specific alcohol and drug combinations.

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Keywords

Alcohol; Drug use; Injury risk; Emergency department; Case-crossover

INTRODUCTION

While a substantial literature exists demonstrating a strong association of alcohol and injury in studies of emergency department (ED) patients (1), less is known about the risk of injury associated with alcohol in combination with other (recreational) drug use, although previous studies have suggested that many of those who have use alcohol have also used other drugs prior to the ED admission.

Much of the research on the association of psychoactive drugs and injury have focused on motor vehicular crashes (2), and these studies have shown that many drugs, in addition to alcohol, impair psychomotor skills and other critical dimensions of performance and may therefore place users at increased risk of injury.

Epidemiological studies of alcohol in combination with recreational drug use in probability samples of ED patients have found prevalence rates ranging from 16% to 22% (3, 4). Positive screens have been found to vary across substances, with highest rates for cocaine and marijuana (4–7), and the presence of either alcohol or other drugs is associated with a 40% higher rate of positivity for the other substance (8, 9), with rates for drug use in combination with alcohol higher than for drug use alone, across all classes of drugs (7).

While a number of case-crossover studies have demonstrated an elevated risk of injury due to alcohol in ED samples (10–16), we do not know whether the same patients who had been drinking prior to injury may also have been using other drugs, and if so, how much of this elevated risk in injury is due to the other drug(s), possibly in a synergistic interaction with alcohol. One study reported from a Swiss ED found an elevated risk for injury, using case-crossover analysis based on substance use the last week, for alcohol use alone, but not for marijuana use or for alcohol in combination with marijuana (17).

Studies have shown that the association of both alcohol and other drugs may be stronger for intentional injuries than for other types of injury (18). One study found intentional injuries more likely to be positive for alcohol in combination with other drugs, and for drug use alone, compared to unintentional injuries (3).

Drug use is becoming increasingly more prevalent in the U.S. and elsewhere and is especially common in heavy drinkers (19). The 2008 National Survey on Drug Use and Health (20) found among heavy drinkers, 29% reported current illicit drug use (compared to only 3% of those not reporting current alcohol use), while data from the National Epidemiology Survey on Alcohol and Related Conditions (NESARC) found a drug use disorder was more prevalent among those with a past year alcohol use disorder than among those without (21).

Despite the prevalence of drug use among heavy drinkers, little research has examined the risk at which alcohol, alone, places the individual for accidental injury, compared to the risk for alcohol in combination with other drugs. This is especially important considering the ongoing work in Comparative Risk Assessment in the Global Burden of Disease and Injury, Injuries and Risk Factors Study, presently underway (22) to establish the global burden of disease due to alcohol-related injury morbidity.

To fill this gap in the literature, the risk of injury due to alcohol use alone compared to alcohol in combination with other drug use (illicit drug use or other recreational drug use without a prescription) is reported in a sample of patients seeking treatment in two emergency departments in Vancouver, British Columbia (BC). The two hospitals were selected because of the clientele they serve living in the downtown Vancouver catchment area which includes the entertainment districts as well as drug using venues. Both are large academic and research hospitals and cover a large representative sample of the central city of Vancouver. We hypothesize that alcohol in combination with other drugs will significantly elevate risk of injury beyond that found for alcohol use alone.

METHODS

Samples

Data were collected over an 18-week period (April to August 2009) on probability samples of injured patients 18 years and older seeking emergency services at each Vancouver ED, drawn from computerized admission logs that reflected consecutive arrival to the hospital. Sampling over three weeks of days, three weeks of evenings and three weeks of nights at each ED provided equal representation of each shift for each day of the week, and yielded a total sample of 443 patients, reflecting a response rate of 69% among those who were contacted. Of those contacted, 27% refused to participate in the study and 4% were unable to provide inform consent due to medical reasons. The non-interviewed were no different on gender than those interviewed, but were older (greater than 65).

Data Collection

A cadre of interviewers were trained by the authors and supervised by survey research staff from the Centre for Addictions Research, BC. Patients were approached with written informed consent to participate in the study and were interviewed as soon as possible after registering for treatment. Interviews were conducted in a private area of the waiting room or in an adjacent space to ensure confidentiality of responses, and carried out prior to the patient's examination, if time permitted; otherwise the interview was completed after the examination. Patients who were too severely injured to be interviewed at that time, but who were hospitalized, were interviewed after their condition had stabilized.

Instruments

Data were collected using a 25-minute interviewer-administered questionnaire (23), adapted from the WHO Collaborative Study on Alcohol and Injury (http://www.who.int/substance_abuse/activities/injuries/en/injuriesinstrument), with additional questions on drug use. The questionnaire obtained data, among other items, on the type and cause of injury that brought the patient to treatment, whether violence was involved (an intentional injury), drinking and drug use within six hours prior to the injury and during the same six-hour period the previous day and the previous week, and the amount of alcohol consumed at each time period. Additionally, data were obtained on the frequency of consuming 5 or more drinks on an occasion (5+) and alcohol dependence in the last year, and demographic characteristics, as potential effect modifiers.

5+ drinking was determined from two questions, one regarding the frequency of 12 or more drinks on an occasion and the other the frequency of 5 to 11 drinks during the last year, as asked in previous U.S. National Alcohol Surveys (24), as well as ED studies conducted in the U.S., Canada and elsewhere (23). Alcohol dependence was measured by the four-item Rapid Alcohol Problems Screen (RAPS4) (25) which was developed in the ED setting based on an optimal set of screening items from several instruments and, with a cut point of one,

has been found to perform better than other instruments both in the ED and in the general population (26).

Drug use was obtained from a series of questions regarding use in the following categories: 1) methamphetamines, 2) other amphetamines, 3) cocaine, 4) sedatives including barbiturates, 5) methadone, 6) heroin, 7) other opiates including codeine, 8) psychedelics, 9) cannabis, 10) other drugs not including medication taken by prescription or over the counter.

Data Analysis

Case-crossover analysis was used to estimate the risk of injury associated with drinking and drug use within the six hours prior to the event (27, 28). Using this analytic strategy individuals serve as their own controls in studying the effect of a transient factor (alcohol consumption or drug use) on the risk of an acute event (injury), theoretically reducing confounding of the substance use-injury relationship from stable risk factors such as gender and age, and allows for an estimate of risk over and above that associated with usual alcohol or drug use. Using the pair-matched approach, alcohol and drug use, classified into 4 categories: no substance, alcohol only, drug only and both alcohol and drug use, during the six-hour period prior to the injury event was compared to use during the same six-hour period the day prior to the injury and, separately, the week prior, providing two separate estimates of the risk of injury due to alcohol and drug use. Similar case-crossover analysis was performed for levels of alcohol consumption (no alcohol, 1–2 drinks, 3–4 drinks and 5+ drinks) prior to injury compared to the two control time periods, to examine a dose-response relationship.

In the case-crossover design, each individual acts as his or her own control. The case-crossover method is thus considered one type of matched case-control design. For all matched case-control designs, selection bias is introduced through the matching process, thus the standard technique used in case-control studies generates biased estimates. For the matched case-control design, which includes the case-crossover design, unbiased estimates are derived from stratified analysis (29). One common approach for implementing a stratified analysis for the matched case-control design is the Mantel-Haenszel estimator for dichotomous exposures. For case-crossover analysis, the Mantel-Haenszel estimator is essentially the ratio of two exposure-discordant pairs; however, it cannot be used for multiple exposures as examined in this study. Therefore, a conditional maximum-likelihood estimator (which is also a type of stratified analysis), as implemented in conditional logistic regression, is used. Conditional logistic regression generates identical estimates as the Mantel-Haenszel estimator when the exposure is dichotomous (29).

In the present analysis, conditional logistic regression was used to calculate the relative risk (RR), and 95% confidence intervals (CIs) for matched pairs, i.e. injury time versus the same time last week, and separately, injury time versus the same time yesterday (both 1:1 matching) (27). The two control time periods were then combined for multiple (2:1) matching to balance biases due to the likelihood of drinking on a given day (the day of injury) when the previous day (a different day of week from the injury day) was used as the control period. For example, the likelihood of drinking on a Friday evening, regardless of injury, may be greater than drinking on the previous evening – a Thursday. Multiple matching also addresses recall bias when the previous week was used as the control period. It has been showed that recall of drinking diminishes the further removed the recall period (30).

Variations in the magnitude of the RR across levels of fixed characteristics -- gender, age (18–29, 30+), intentionality of injury, and in the last year, heavy drinking (5+ on an occasion) and alcohol dependence (positive on the RAPS4) -- were examined as possible

effect modifiers based on the multiple-matched control period for the effect of alcohol and drug use on risk of injury. Conditional logistic regressions were estimated for each level of potential modifier, e.g. separately for men and women (7). Strata-specific effect coefficients are presented and the χ^2 test of homogeneity is performed to examine whether the effects differ across levels of potential modifiers (29). Since conditional logistic regression is, by itself, a type of stratified analysis, i.e. stratified by individuals, tests for differences across strata of potential modifiers can only be conducted in separate analysis as described above, rather than by building interaction terms in the regression models as normally implemented in the standard case-control design.

RESULTS

Of the sample of 433 patients, 64% were male, 32% were under age 30, 8% reported an intentional injury, 57% reported 5 or more drinks on an occasion (5+) during the last year and 33% were positive on the RAPS4 (not shown). Table 1 shows drinking and drug use for the six-hour period prior to injury and the same time period the day before and the week before. Prevalence of drugs primarily reported in the six hours prior to injury were cannabis (45%), cocaine (20%), heroin (7%), methamphetamines (5%), and other drugs not including medications taken by prescription or over the counter medications (11%). Of all those reporting drug use, 37% reported using more than one substance, and no difference was found for multiple drug use between those who reported only using drugs, and those reporting drugs used in combination with alcohol.

Table 2 shows the RR for injury from alcohol use alone, drug use alone and alcohol in combination with drug use (vs. neither substance), based on the two control periods of yesterday and last week in comparison to the time of the injury event. Risk of injury did not differ substantially between the two control periods for any of the three substance-use groups. Using multiple matching, RR of injury was significantly elevated for alcohol use alone (RR = 3.3; 95% CI 2.2 to 5.2), and for alcohol in combination with drug use (RR=3.0; 95% CI 1.2 to 7.2), but not for drug use alone. The number of drinks consumed among those reporting alcohol in combination with drug use was significantly larger (mean of 15.8) than for those reporting alcohol use alone (mean of 5.4) (not shown).

As also seen in Table 2, the risk of injury shows a dose-response relationship with alcohol. Based on multiple matching, RR increased from 1.77 for 1 or 2 drinks, to 5.84 for 3 or 4 drinks and to13.8 for 5 or more drinks in the six hours preceding injury.

Table 3 shows RR of injury by potential effect modifiers (gender, age, intentionality of injury, heavy drinking and alcohol dependence) for alcohol use alone and alcohol in combination with other drugs, using the multiple-matched control period. Although drug use alone was included in the model as a level of exposure, its effects are not presented given the non-significant results shown in Table 2. Risk of injury was significantly elevated regardless of gender, age, intentionality of injury or heavy and dependent drinking for alcohol only. For both alcohol and drug use, risk was significant for only males, those 30 and older, unintentional injuries, 5+ drinking in the last year, and those positive on the RAPS4. The test of homogeneity showed a marginally significant effect modification, only for alcohol in combination with other drugs, with risk greater (p<0.08) for those 30 and older compared to those younger (RR = 7.1 vs. 1.42).

For alcohol use alone, effect variation was found for intentional compared to unintentional injuries (RR=7.0 vs. 3.1), but the test of homogeneity was not significant. It should be noted that the test for homogeneity is very sensitive to standard errors of effect estimates, which in turn are influenced by sample size.

DISCUSSION

A substantial literature exists demonstrating a strong association of alcohol and injury, and findings here support this. The RR of injury from alcohol was 3.3 based on multiple matching of drinking the day before and the week before. Prior case-crossover studies, based on drinking the day before, have found RR for injury ranging from 1.7 to 11.0, depending on the number of drinks consumed (15), and a 4-fold increase was found in a separate study (16). A similar study from an ED in Mexico City found RR for injury was 3.4 based on drinking the day before, but 7.6 based on drinking the week before (11), while a RR of 5.7 was found across EDs in 10 countries, based on drinking the week before (12).

A clear dose-response relationship for alcohol was evident, similar to other ED studies. Based on multiple matching, a RR of 1.77 was found for 1 or 2 drinks and 5.84 for 3 to 4 drinks, which increased to 13.8 for more than 5 drinks in the six hours prior to injury. While the Mexico City ED study found no risk at only one drink, injury risk increased to 7.98 for more than 5 drinks, while the 10-country ED study found a risk of 3.3 for one drink which reached 10.1 for more than 5 drinks. Similar dose-response relationships have also been reported in other case-crossover studies of ED patients (15, 16).

Alcohol in combination with drug use (RR=3.0) did not appear to significantly elevate risk of injury above that found for alcohol alone (RR=3.3), suggesting no synergistic effect, as hypothesized, and this was despite the fact that the number of drinks consumed was significantly greater among those reporting alcohol in combination with drug use than among those reporting alcohol use alone, as well as a dose-response relationship of alcohol with injury. Findings here may have been affected by the most frequently reported drug used in this study (cannabis in the six hours prior to injury), possibly biasing the risk of injury due to alcohol in combination downward, since cannabis use has not been found to elevate risk of injury, either alone or in combination with alcohol (17). However, data were not collected on the type of drug used in either of the two control time periods, so this could not be tested.

No increase in risk was found for drug use alone prior to injury, based on either control time period. The only other similar study reported, using case-crossover analysis (based on the last week) in an ED sample, found alcohol use alone, but neither marijuana use nor combined use with alcohol (as noted above), elevated risk of injury (17). While marijuana was the drug most often used in the study reported here, with 61% of patients reporting marijuana use (either alone or in combination with alcohol or other drugs prior to injury), the number of those reporting drug use alone (n=17), or drugs in combination with alcohol (n=24), was not large enough to analyze risk of injury for specific drugs or for specific alcohol-drug combinations.

This is especially important since not all drugs would be expected to act in a similar manner across all types and causes of injury. For example, alcohol is considered a central nervous system depressant, slowing reaction time and memory, and inducing sleep (31). By contrast, cocaine is a central nervous system stimulant which increases alertness and energy, inhibits appetite and sleepiness, and produces intense euphoria (32), and when used with alcohol, forms a new metabolite, cocaethylene, that has different pharmacological properties with greater and longer lasting behavioral effects than those from either substance used alone (33–36). Although the literature is mixed regarding marijuana use and injuries (17, 19), it has been found to impair behavioral and cognitive skills (6), and when used in combination with alcohol, appears to increase cognitive impairment additively`, and to especially impair driving performance (37, 38). Additionally, other illegal drugs (amphetamines, heroin, barbiturates, benzodiazepines) negatively influence psychomotor function, and when combined with alcohol, may result in additive impairment leading to accidental injury (39).

Given these differing pharmacological effects across classes of drugs, as well as their varying effects when combined with alcohol, one might expect an elevated risk of injury due to alcohol in combination with certain drugs (possibly a synergistic effect) but not with others.

While risk of injury was significantly elevated for alcohol use across gender, age, intentionality, heavy drinking and dependence status, injury risk was significantly elevated for alcohol in combination with drug use only for males, those 30 and older, unintentional injuries, 5+ drinking, and those positive on the RAPS4, and an effect modification suggested ($p=0.087$) only for gender, with males at higher risk than females. While a larger effect was found for males compared to females (RR=3.7 vs. 1.28) and for those positive on the RAPS4 compared to those negative (RR=4.2 vs. 0.71), differences were not significant, most likely because the test for homogeneity is sensitive to standard errors of effect estimates, which are affected by sample sizes.

Alcohol in combination with drugs was found to increase risk only for unintentional injury. Previous case-crossover studies of ED patients have found alcohol to increase risk for intentional injury (11, 12, 14), but no studies have examined the risk for intentional injuries from alcohol in combination with drug use. Again, given the diverse pharmacological effects across drugs, it would be important to analyze risk of intentional injury for specific alcohol-drug combinations.

Injury risk due to alcohol in combination with drugs was also found to be significantly elevated for those positive on the RAPS4 as an indicator of alcohol dependence. The case-crossover design is well suited to disentangle the effects of acute drinking (in the event) from chronic (usual drinking) patterns (28, 40). Data from a Swiss ED found at the same level of last-24-hour drinking prior to injury, usual high volume drinkers were at a lower risk of injury than usual low volume, suggesting that while all groups of drinkers were at increased risk for injury, those who usually drink little but on occasion drank heavily were at greater risk (41). ED studies using the case-crossover design have reported conflicting findings regarding the risk of injury from alcohol for those who are alcohol dependent, however, with some studies showing no elevated risk (11), others showing a greater risk (16), and still others showing a reverse relationship (10, 12). Given these conflicting findings, this is an area requiring more research.

Interestingly, risk of injury did not differ substantially between the two control periods as found elsewhere. The ED study reported from Mexico City found a RR of 3.4 for drinking the day prior to injury, but 7.6 based on reporting drinking the week prior to injury. Recall of alcohol consumption was found to decrease with the length of the recall period in an ED study, using a 7-day follow-back measure, and was most pronounced for sporadic drinkers (30). While one would expect an underestimation of both any drinking and the amount consumed, the further removed, temporally, from the recalled period (with a resulting increase in RR of injury), findings here did not support this.

While the case-crossover design eliminates potential between-person confounders, within-person confounding may still exist, such as contextual factors like activities undertaken at the time of injury, which may be independently correlated with both injury and substance use, and may result in either an underestimate or overestimate of the substance use-injury risk relationship, depending on the type of injury. For example, a motor-vehicular injury as a driver necessitates driving a motor vehicle, and a control period matched to the pre-injury period would ideally require the patient to have been driving at the time, but such confounding has been virtually ignored with two notable exceptions (16, 42).

Findings here are based on injuries for which treatment was sought in the ED, and prior research has found those who reported an injury treated in the ED were more likely to be younger, heavier drinkers and to report experiences of alcohol dependence compared to those who reported injuries that were not treated in ED (43). Consequently, these data are not representative of all injuries, nor are they necessarily representative of those treated at other ED facilities.

Other potential sources of biases may be related to the type of injury incurred, in which a patient may tend to underreport substance use in situations involving possible legal ramifications such as motor vehicular crashes, or overreport substance use in situations, such as intentional injuries, in which the substance may be used as an excuse for otherwise socially unacceptable behavior (44), suggesting the need for additional research on eliciting valid self-reports across a variety of situations.

Additionally, individuals using illegal substances prior to injury may be less inclined to present to an ED for treatment, or may be less likely to report use of drugs prior to injury or during control periods. However, use of marijuana is legal for medical reasons in British Columbia, and BC is unique in relation to drug use; cocaine is more normalized than in other parts of Canada or the U.S., and harm reduction is the predominant policy in BC (for example, safe crack pipes are distributed in Vancouver). This more permissive attitude suggests that denial of cocaine or other drug use may not be as likely as in other places outside of BC.

Finally, it should be noted that findings here only address acute use of alcohol and/or drugs prior to the injury event. Usual drinking patterns have also been found to be predictive of injury in other ED samples (45, 46), as well as a critical risk factor for numerous health and social consequences (47–49), including other chronic conditions affecting the global burden of disease (22, 50).

While drug use is becoming increasingly more prevalent in the U.S., especially among heavy drinkers, little research has been reported which examines the risk at which alcohol in combination with drug use places the individual for accidental injury. This is especially important to consider in light of ongoing work to establish the global burden of disease due to alcohol for non-fatal injury (22). The literature suggests that alcohol in combination with certain drugs (for example, cocaine) may be important to consider in injury risk, but numbers did not permit analysis by specific alcohol-drug combinations. While a similar elevated risk of injury was found for alcohol use alone and alcohol used with other drugs, the literature suggests that alcohol in combination with some drugs may be potentially more risky for injury occurrence, and findings suggest the need for future research on risk of injury for specific alcohol and drug combinations.

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Table 1

Substance Use Prior to Injury and During Two Control Periods (n in parentheses)

	6 hours prior to injury	Same time yesterday	Same time last week
Alcohol use only	19.3% (85)	8.6% (37)	9.3% (39)
Drug use only	3.9% (17)	6.8% (29)	5.7% (24)
Both alcohol & drug use	5.4% (24)	3.5% (15)	3.1% (13)
1–2 drinks	6.8% (30)	6.3% (27)	5.0% (21)
3–4 drinks	5.9% (26)	2.3% (10)	1.9% (8)
5+ drinks	11.6% (51)	3.0% (13)	4.5% (19)

Table 2

Relative Risks (RRs) of Injury Related to Alcohol and Drug Use from Case-crossover Analysis Based on Substance Use Yesterday and Last Week

Substance Use	**Yesterday**	**Last week**	**Multiple match**
Alcohol only	3.3 (2.0, 5.6) ***	3.6 (2.0, 6.6) ***	3.3 (2.2, 5.2) ***
Drug only	0.53 (0.23, 1.23)	0.83 (0.33, 2.09)	0.63 (0.30, 1.35)
Alcohol and Drug	4.6 (1.3, 15.8) *	3.5 (1.2, 10.1) *	3.0 (1.2, 7.2) *
Categorical volume (ref no)	Yesterday	Last Week	Multiple match
1–2 drinks	1.57 (0.83, 2.96)	2.39 (1.14, 5.00) *	1.77 (1.02, 3.07) *
3–4 drinks	8.13 (2.40, 27.6) **	5.39 (2.07, 14.0) **	5.84 (2.68, 12.7) ***
5+ drinks	N.A.[1]	6.53 (2.73, 15.) ***	13.8 (5.76, 32.9) ***

* $p<0.05$,

** $p<0.01$,

*** $p<0.001$

[1] Not available as all 5+ drinkers yesterday also had 5 or more drinks before injury, so the effect is not estimable given the empty cell.

Table 3

Relative Risks (RRs) of Injury Related to Alcohol and Drug use from Case-crossover Analysis by Demographic, Injury and Drinking Characteristics and Test of HomogeneityBased on Multiple Matching of Substance Use Yesterday and Last Week

	Alcohol only	Both alcohol and drugs
Gender	(p=0.583) [1]	(p=0.333)
Men	3.6 (2.1, 6.2)***	3.7 (1.4, 10.0)*
Women	2.8 (1.3, 6.1)*	1.28 (0.19, 8.58)
Age	(p=0.583)	(p=0.087)
18–29	3.0 (1.6, 5.5)***	1.42 (0.43, 4.71)
30+	3.8 (2.0, 7.3)***	7.1 (1.7, 29.5)**
Injury type	(p=0.283)	(p=0.732)
Intentional	7.0 (1.7, 29.9)**	4.0 (0.7, 23.3)
Unintentional	3.1 (1.9, 4.9)***	3.1 (1.03, 9.3)*
Heavy drinking	(p=0.893)	(N.A.) [2]
5+ at least once	3.2 (2.0, 5.2)***	2.6 (1.05, 6.4)*
No 5+ last year	3.4 (1.1, 10.1)*	N.A. [2]
Alcohol dependence	(p=0.829)	(p=0.108)
Positive Raps4	3.1 (1.6, 5.9)**	4.2 (1.4, 12.8)*
Negative Raps4	3.4 (1.8, 6.4)***	0.71 (0.10, 5.03)

*p<0.05,

**p<0.01,

***p<0.001

[1] χ^2 test of homogeneity

[2] Because all drug and alcohol users, either before the injury event or in the control periods, had 5+ at least once last year; the effect cannot be estimated