Published in final edited form as:

Accid Anal Prev. 2015 February ; 75: 137–143. doi:10.1016/j.aap.2014.11.020.

The rate ratio of injury and aggressive incident for alcohol alone, cocaine alone and simultaneous use before the event: A case-crossover study

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Abstract

Objectives—(i) To estimate the Rate Ratio (RR) of use of alcohol alone, cocaine alone, and both substances simultaneously on acute injury or an aggressive incident, (ii) To compare the RRs for simultaneous use within 3 or 6 hours of the event; and (iii) To compare the RRs of two measures of exposure, “hours of feeling effects” versus estimates based on self-reported quantity and frequency of use.

Methods—The study employed a case-crossover design with the frequency approach. Clients (N=616) in substance abuse treatment for alcohol or cocaine issues from 2009 to 2012 completed a self-administered questionnaire on their substance use within 3 and 6 hours before a recent injury or physically aggressive incident. Clients also reported detailed quantity and frequency information in relation to their typical substance use, as well as information on “feeling effects”. The RR of acute harms due to substance use was estimated using the Mantel-Haenszel estimator.

Results—In the 6-hour window before the event, use of cocaine alone, alcohol alone and simultaneous alcohol and cocaine use were each significantly ($P < 0.05$) related to a recent injury and aggressive incident. Simultaneous use was not significantly greater than use of either drug alone. Estimates of RR based on simultaneous use for a 3-hour window before the event were consistently larger than those based on a 6-hour window, and comparisons were significant ($P < 0.05$) for an aggressive incident but not an injury. With reference to the two measures of

exposure, three of eight comparisons of RRs were significantly larger for feeling the effects of the substance in comparison to quantity and frequency of substance use.

Conclusion—These findings are consistent with increased likelihood of harms related to the acute effects of alcohol alone, cocaine alone or simultaneous use. The results are suggestive that the acute effects of these drugs may be better measured within a 3-hour time window than a 6-hour window. Finally, we found that “hours of feeling effects” yielded higher estimates of RR than the quantity-frequency approach; however both measures support the overall findings.

Keywords

alcohol; cocaine; case-crossover; injury; aggression

1. Introduction

Research on psychoactive substance use is largely focused on studies of a single substance. Several studies have found that alcohol consumption increased the risk of acute harms such as injury and violence (Borges, Cherpitel et al. 2004, Ye and Cherpitel 2009, Ye, Cherpitel et al. 2010, Borges, Cherpitel et al. 2013, Zerhouni, Begue et al. 2013). Other studies found that cocaine use also increased the risk of some acute conditions (Macdonald, Anglin-Bodrug et al. 2003, Macdonald, Erickson et al. 2008). However, little research has been conducted on simultaneous use of cocaine and alcohol on acute harms.

Combined use of some substances such as alcohol and cocaine might synergistically increase risks of acute harms such as injury or aggression. Among treatment populations, research has shown that clients frequently use alcohol and cocaine together (Martin et al, 1996; Wiseman and MacMillan, 1996; Pakula et al., 2009). Moreover, several studies have shown that the majority of treatment clients who abuse cocaine also consume alcohol, and a high proportion are dependent on both (Heil, Badger et al. 2001). One study found that the lifetime prevalence of alcohol problems among cocaine abusers was about 60% (McCance, Price et al. 1995) while another study showed that 88% of cocaine abusers in treatment also used alcohol (Wiseman and McMillan 1996). Compared to the general population, people with alcohol use disorders are more likely to use cocaine (Walsh, Hingson et al. 1991).

The little research that has been conducted on simultaneous use of cocaine and alcohol pertains to vehicle collisions specifically. Insights on possible effects of simultaneous use can be deduced from this research. A recent study asked cocaine users in treatment to describe how cocaine use affected their ability to drive a car. The most common responses were found to be that cocaine increased the likelihood of racing or driving recklessly and that cocaine reduced driving ability (Macdonald, Erickson et al. 2008). If these cocaine-related effects are combined with psychomotor decrements caused by alcohol, the results could synergistically increase the risk of a collision. Specifically, various health-related harms are likely associated with simultaneous use of cocaine and alcohol as compared to the use of each substance alone. If the high is more intense when the substances are combined, thereby impairing one's cognitive and psychomotor coordination, acute consequences such as violence or injury could be greater than the consequences associated with use of either drug alone.

Experimental and biological studies have also found that alcohol (a depressant) and cocaine (a stimulant), when mixed together, produce a new metabolite that can result in different pharmacological effects compared with either drug used alone (Pennings, Leccese et al. 2002). This might suggest that the alcohol and cocaine combination can increase the tendency towards violent thoughts, leading to an increase in violent behaviors (Pennings, Leccese et al. 2002). However, due to some challenges, few field studies have been conducted to investigate effects of simultaneous use of cocaine and alcohol on the risk of physical harms such as injury or physical aggression (Martin, Clifford et al. 1992, Adlaf and Ialomiteanu 2005). For example, assessing the rate ratio (RR) of the acute effects of cocaine in the event of an injury or aggressive incident has been challenging, as current drug tests for urine specimens detect prior exposure within a long detection period that exceeds the acute effects (Lum and Mushlin 2004) and potentially more accurate blood tests are intrusive. Furthermore, self-reports of general populations have limitations of under-reporting. To overcome these challenges, we propose a study that uses self-reports of clients in treatment for alcohol and cocaine, and given their admission of problematic use, honest responses are expected (Chatham, Turkiewicz et al. 1994).

The objectives of this study are: (i) To estimate the Rate Ratio (RR) of use of alcohol alone, cocaine alone, and both substances simultaneously on acute injury or aggressive incident, (ii) To compare the RRs for combined use within 3 or 6 hours of the event; and (iii) To compare the RRs of two measures of exposure, “hours of feeling effects” versus estimates based on self-reported quantity and frequency of use.

2. Methods

2.1. Study design

The study is cross-sectional with a retrospective component, where subjects provided data on their typical use of cocaine and alcohol before an injury or aggressive event in the prior year. The retrospective aspect is exemplified by subjects reporting key aspects of injury or aggression in the prior year. Clients in treatment for their use of cocaine alone, alcohol alone or simultaneous use of cocaine and alcohol were identified from five substance abuse treatment centres in British Columbia and Ontario from March 2009 to March 2012. Since we aimed to have roughly equal numbers of men and women in our sample and men are much more likely to be in treatment, we recruited 112 women from three treatment agencies for women only. Most clients resided in British Columbia (BC) and Ontario. The response rate was extremely high at 97.8% (Macdonald, Pakula et al. 2014), identifying 616 clients qualifying for the study.

Within the larger sample of cocaine, alcohol, or simultaneous substance users, those with injuries or aggressive incidents were identified. A case-crossover analysis with the usual frequency approach was conducted to investigate the RR of these acute harms which is an approximation of relative risk. This approach contrasts exposure in the hazard period with the expected exposure based on each individual's usual frequency of exposure over the year preceding his/her acute condition. In this type of study, each patient acts as his/her own control where particular substance use (e.g., alcohol only, cocaine only, or combined use) at the time of the injury or aggressive incident is compared to typical frequency of substance

use for each person (Maclure 1991, Mittleman, Maclure et al. 1993, Mittleman, Maclure et al. 1995). Substance use in the hazard period, the 3 hour and 6 hour period immediately preceding the acute event, was compared with its expected frequency based on control data obtained from the patients. Employing the usual frequency of substance use over the year prior to acute events estimated its expected frequency in an average 6 hour period in this patient population. The study was approved by the ethics review board at the University of Victoria and respective ethics boards of the treatment providers in situations where treatment was provided within a hospital context.

2.2. Measures of outcome

Injury and aggression were measured using client's self-reported most recent injury or aggressive incident in the 12 months prior to treatment (see Appendix I for the exact questions). Alcohol and/or cocaine use was conceptualized as an exposure that has a time-limited physical effect. Alcohol and/or cocaine produces short-term biological, psychological and behavioural changes until it is metabolized. Therefore, the case-crossover study is designed to investigate the acute alcohol and/or cocaine effect (Maclure 1991). Alcohol exposure has been defined as at least one drink within six hours prior to each event in several studies (Vinson, Maclure et al. 2003, Borges, Cherpitel et al. 2004, Borges, Cherpitel et al. 2006, Bond, Ye et al. 2014). Cocaine exposure was defined as at least one line, one rock or one injection of cocaine/crack within six hours prior to each event. Exposure to both substances simultaneously was defined as use of alcohol and cocaine within 3 or 6 hours prior to the injury or aggressive incident. Questions used to define outcomes; relevant exposures to alcohol or cocaine are presented in Appendix I and Appendix II.

2.3. Measures of exposure

2.3.1. Typical alcohol consumption—To investigate typical alcohol consumption, i.e., usual use, clients were asked questions relevant to quantity and frequency of consumption based on days per week drinking, as well as number of drinks consumed on those days. To be consistent with the definition of a “six-hour window” of drinking prior to the outcomes, this usual quantity-frequency approach assumes the effect period on a drinking day is 6 hours if the usual drinking quantity over the past year is one to six drinks, 12 hours if the quantity is seven to 12 drinks, 18 hours if the quantity is 13–18 drinks and 24 hours if the quantity is 19+ drinks (Borges, Cherpitel et al. 2006). The amount of expected person-time exposure to alcohol was estimated by multiplying the reported usual annual frequency (drinking days) by the effect duration (hours) in a drinking day, i.e., one hour per drink. Estimated alcohol exposure was also calculated from questions regarding the hours of feeling the effects of alcohol in comparison to the hours spent sleeping or being sober in a 24 hour day. We rationalized that “feeling effects” may be a better measure than quantity-frequency due to logistical problems in assessing typical use, which can be influenced by several variables, including body weight and duration of use.

2.3.2. Typical cocaine use—To investigate typical cocaine consumption, i.e. usual use, clients were asked questions relevant to quantity and frequency of consumption based on days per month snorting/smoking/injecting cocaine as well as grams of cocaine used in a

normal week (1 ounce=28 grams, about 10 lines=1 gram or 1 eight ball=3.5 grams). Employing the usual quantity-frequency approach, we assumed that the effect period on a day when cocaine was used is 6 hours if the quantity of usual cocaine use over the past year is 3 to 18 lines (the effect of 1 line lasts about 20 minutes), 12 hours if the quantity is 19 to 36 lines, 18 hours if the quantity is 37–54 lines and 24 hours if the quantity is 54+ lines (National Institute on Drug and Abuse 2010). The amount of expected person-time exposure to cocaine use was estimated by multiplying the reported usual annual frequency (days per month using cocaine) by the effect duration (hours) in a cocaine use day, i.e., one hour per gram of cocaine. Estimated cocaine exposure was also calculated from questions regarding the hours of feeling the effects of cocaine/crack in comparison to the hours spent sleeping or being sober in a 24 hour day.

2.3.3. Use of cocaine and alcohol within three hours of the event—To

investigate typical combined use of cocaine and alcohol, clients were asked questions for both drugs, using similar procedures described above.

2.4. Data collection

The data collection protocols were standardized, such that information was collected equivalently for all groups. Also, each measure included in the questionnaire package was a validated and well-structured instrument with very specific and detailed questions to aid in accurate recall. Furthermore, when answering questions, participants were given adequate time to think through each item of the questionnaire so as to allow for reflection of events, if necessary. Certain steps were taken to minimize biases including recall bias. We conducted 20 qualitative interviews in Ontario and BC to clarify issues with combined use of alcohol and cocaine and incorporated temporal ordering and possible differential consequences into the questionnaire. The questionnaire was refined to ensure that any ambiguities were removed and comprehension was enhanced. The methods used to refine the questionnaire included: asking probe questions and going through the questionnaire twice, first answering the questions in the usual manner and then having a discussion with the client about the response tasks (Fowler 1995). Additional techniques included paraphrasing clients' understanding of the question, defining terms, identifying areas of uncertainty or confusion and indicating the extent to which clients' answers were accurate (Fowler 1995). The self-administered questionnaire also included several validated scales. Eligible clients were asked to complete the self-administered questionnaire to reduce discomfort and social desirability issues as compared to a personal interview since many of the questions covered sensitive topics such as violence. The questionnaire was completed anonymously. If clients were not able to complete the questionnaire on time, appointments were made to complete it at a later date. Subjects were offered a \$20 gift certificate as compensation for completing the questionnaire.

2.5. Statistical analysis

Case-crossover analyses were conducted to calculate RR of acute exposure related to each outcome. Each patient serves as his/her own control where particular substance use (e.g., alcohol only, cocaine only, or simultaneous use) at the time of the injury or aggressive incident is compared to typical use for each person (Maclure 1991, Mittleman, Maclure et al.

1995). Case-crossover analyses with two different measures of typical use were conducted; one using the usual quantity and frequency of use as a control period, and the other using the average number of hours feeling the effects of use.

The analysis of case-crossover studies with the usual frequency approach follows standard methods for stratified analyses (Maclure 1991, Mittleman, Maclure et al. 1995). In the case-crossover design, the individual subject is the stratifying variable. In the usual frequency case-crossover analysis, the RR estimates were generated by comparing acute drinking of the injured or aggressive clients before the event to their usual frequency of drinking. The case-crossover analysis was considered as a stratified self-matched case-cohort analysis with the RR generated from Mantel-Haenszel estimator for dichotomous exposure (Greenland and Rothman 1998). The RR of an acute condition was calculated by comparing the observed odds to the expected odds estimated from a control period (Greenland and Rothman 1998). Due to the study time interval being quite short, the RR can be interpreted as the short-term risk of a sudden onset injury or aggressive incident. This estimate is unbiased for follow-up studies with sparse person-time data (Greenland and Robins 1985).

The χ^2_{Wald} test of homogeneity is used to evaluate differences in the estimates of RR of injury or aggressive incident for combined use of cocaine and alcohol versus use of cocaine or alcohol only (Greenland and Rothman 1998). The χ^2_{Wald} test of homogeneity is also used to examine whether the different measures of typical use of cocaine and alcohol have different effects. All statistical analyses were performed using SAS 9.3 (SAS Institute 2011).

3. Results

Table 1 presents the number and percentage of injured or aggressed patients among 616 treatment clients. Compared to the national survey in two provinces, more young and divorced or separated people with low education and income tended to be included in the study. Among 616 treatment clients, 193 (31.3%) reported an injury or accident in the past year (mean age=34.86, males=101 and females=92), and 224 (36.4%) reported a physically aggressive incident (mean age=34.86, males=107 and females=117). The prevalence of injury and aggression by subgroups varied.

For each group, the analyses of substance use on injury or aggressive incident included those who reported using the specific substance and those who reported using neither alcohol nor cocaine. Specifically, this resulted in 96 subjects (67 used alcohol only + 29 used neither alcohol nor cocaine) in the alcohol group, 54 subjects (25 used cocaine only + 29 used neither alcohol nor cocaine) in the cocaine group, 54 subjects (25 used both alcohol and cocaine + 29 used neither alcohol nor cocaine) in the simultaneous substances within 6 hours group, and 76 subjects (47 used both alcohol and cocaine + 29 used neither alcohol nor cocaine) in the simultaneous substances within 3 hours group (Table 2). The same procedures were used for estimating RRs for cocaine and simultaneous alcohol and cocaine in the events.

Table 2 presents the RR of injury and aggressive incident due to alcohol alone, cocaine alone, and simultaneous use prior to the injury or aggressive incident. The RR was

significantly higher for alcohol use with respect to injury and aggression: 2.41 times increased risk of injury (RR: 2.41 and 95% CI: 1.53–3.79); 2.92 times increased risk of aggression (RR: 2.92 and 95% CI: 1.74–4.91). Similar findings were observed for cocaine use: 1.94 times increased risk of injury (RR: 1.94 and 95% CI: 1.15–3.26); and 3.28 times increased risk of aggression (RR: 3.28 and 95% CI: 1.82–5.91).

Finally, use of both cocaine and alcohol, within either 6 or 3 hours before the incident, significantly increased the risk of each of the two outcomes, respectively: 3.35 and 5.12 times increased risk of injury (RR: 3.35 and 95% CI: 2.19–5.13, 5.12 and 2.96–8.86); 3.18 and 16.09 times increased risk of aggression (RR: 3.18 and 95% CI: 1.74–5.82, 16.09 and 9.43–27.46). Further analyses also indicated that the 3-hour window produced higher RR values in every instance, and were statistically significant ($P < 0.05$) for an aggressive incident but not an injury.

Similar results were found when using the number of hours of feeling effects to estimate typical exposure time. For every comparison, using feeling the effects to assess exposure produced higher estimates of RR than the traditional quantity and frequency approach.

4. Discussion

In this study we found that the acute effects of alcohol and cocaine, whether consumed alone or simultaneously, significantly increased the risk of injury and aggressive incidents. Although simultaneous use did not produce significantly greater RRs of injury than use of either substance alone, the RRs were higher, raising the possibility that our sample size did not have sufficient statistical power for these analyses. Our study found that drinking alcohol significantly increased the risk of injury (RR=2.41) and aggressive incidents (RR=2.92). These results are consistent with several previous studies which showed that alcohol use has been associated with increased risk of injury in a wide variety of settings (Vinson, Maclure et al. 2003, Borges, Cherpitel et al. 2004, Borges, Cherpitel et al. 2006) and alcohol use has been strongly associated with aggression (Graham and Wells 2001, Cherpitel, Ye et al. 2012). Our study found that cocaine not only increased the risk of injury (RR=1.94) but also increased the risk of aggressive incidents (RR=3.28) which is consistent with other studies (Budd 1989, Licata, Taylor et al. 1993, Zautcke, Morris et al. 1998, Peden, van der Spuy et al. 2000).

Previous studies suggested a synergistic effect of simultaneous use of cocaine and alcohol on corresponding outcomes (McCance, Price et al. 1995, Pennings, Leccese et al. 2002, Harris, Everhart et al. 2003). In our study, we found higher RRs but they were not statistically significant. Research has shown that use and harmful effects of alcohol are common among those receiving treatment for a primary problem with cocaine, regardless of whether a client reported an alcohol problem upon intake (Macdonald, Anglin-Bodrug et al. 2005). A review of the experimental literature on the simultaneous use of cocaine and alcohol showed the effects may be synergistic in terms of learning deficits, psychomotor deficits and increased cardiovascular effects (Pennings, Leccese et al. 2002). Other studies have also found that subjects experience more euphoria after the simultaneous use of cocaine and alcohol than after using either drug alone (McCance, Price et al. 1995, Harris,

Everhart et al. 2003). These findings on the pharmacological effects of simultaneous use suggest that the corresponding acute and chronic outcomes may be more severe than those associated with cocaine or alcohol alone. Our study also found that RRs increased significantly ($P < 0.05$) when simultaneous alcohol and cocaine use occurred within 3 hours of an aggressive event compared to 6 hours. These findings underscore the importance of temporal proximity of use in relation to this event. No previous studies were found to investigate this issue.

Two measures of typical use of alcohol and cocaine (i.e., number of drinks consumed/amount of cocaine used in a regular day, or duration of feeling the effects in a regular day) were used to estimate the RR of acute harms due to alcohol consumption, cocaine use and simultaneous use of alcohol and cocaine. Rate ratios based on “feeling the effects” of alcohol and cocaine for the control period were consistently greater than the quantity-frequency method. Some researchers have indicated that the quantity-frequency approach may produce upward biased estimates of risk (Ye et al., 2013). Since the “feeling effects” approach produces higher estimates than the quantity-frequency method, a reasonable argument can be made that it is biased as well. This potential bias may not exist for non-problematic users, as heavy users will have developed tolerance to the perceived effects of substances. While the present study cannot determine which measure is better, future research should examine the validity and reliability of these measures.

One major limitation of this research is that we did not have a precise measure for substance dose in the occasion preceding the injury. Specifically, exposure was defined as at least one drink of alcohol or one line/rock/injection of cocaine/crack within six hours prior to each event. Thus, subjects could have consumed a range in quantity prior to the injury. Moreover, the retrospective component of the research design requires that we rely on subjective recall for incidents of injury or aggression in the past year. Subjective recall is often prone to individual bias, as events can be forgotten. Patients were asked about their usual quantity and frequency of alcohol use during the prior 12 months, which was used to estimate the expected exposure to alcohol and/or cocaine. It is possible that subjects more accurately recalled substance use immediately prior to the event, but less accurately in relation to their usual use over a year. This difference in recall may lead to an overestimation of the association (Ye et al., 2013). As with any study using self-report methods, recall bias is always an issue. Although the case-crossover studies are well suited to control for time-invariant confounders, the possibility remains that time-varying confounders may still exist. Finally, the sample was composed of clients who were in treatment for substance use issues, and therefore results may not be generalizable to other populations. This sample had significantly more young, single persons, lower education and/or lower income than the general population. The rate ratio may be higher in the general population due to a lack of tolerance to drugs and alcohol.

In summary, alcohol use, cocaine use, and simultaneous use increased the risk of acute harms. Moreover, the feeling effect measure of substance use in a typical day can yield a higher risk estimate of acute harms due to alcohol or cocaine use than the quantity-frequency method. A 3-hour window for assessing the effects of substance use on injury may be more appropriate than a 6-hour window, since our RRs were consistently higher for

3 versus 6 hours. Additional research on the appropriate time frame for assessing the effects on substance use would be beneficial.

Acknowledgments

Funding for this research was provided by the Canadian Institutes for Health Research by a means of the operating grant #89906 "Patterns and consequences of cocaine and alcohol use for substance abuse treatment clients" (PI: Scott Macdonald). We are grateful to the people (Judy Brennan, Alissa Greer, Lisa Fielding, Nancy Lipsky and Marina Verdichevski) who coordinated data collection for this study and to Bellwood Health Services, Jean Tweed Centre, New Port Centre of the Niagara Health System, and Peardonville House for their co-operation.

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Appendix I. Questions on acute outcomes and use of alcohol and cocaine prior to the event

Outcome and exposure	Injury	Aggression
Definition of acute harms	Q: In the past 12 months before treatment, have you had an injury or accident? A: Yes or no.	Q: In the past 12 months before treatment, have you been personally involved in an incident where someone was pushing, grabbing, hitting, kicking, threatening with a weapon or being physically aggressive in any other way? A: Yes or no.
Alcohol use within 6 hours prior to outcome	Q: In the six hours before your most recent injury, how many drinks did you have? A: Number of drinks.	Q: In the six hours before your most recent incident of physical aggression, how many drinks did you have? A: Number of drinks.
Cocaine use within 6 hours prior to outcome	Q: In the six hours before your most recent injury, how much cocaine/crack did you use? A: Snorted number of lines; number of rocks smoked; number of injections.	Q: In the six hours before your most recent incident of physical aggression, how much cocaine/crack did you use? A: Snorted number of lines; number of rocks smoked; number of injections.
Simultaneous use of cocaine and alcohol within 6 hours prior to outcome	Q: In the six hours before your most recent injury, did you use cocaine/crack and alcohol within three hours of each other? A: Yes or no.	Q: In the six hours before your most recent incident of physical aggression, did you use cocaine/crack and alcohol within three hours of each other? A: Yes or no.

Appendix II. Questions on typical use of alcohol and cocaine

	Alcohol use only	Cocaine use only	Simultaneous use
Drinking frequency	Q: On average, how many days per week did you have a drink of alcohol? A: __days per week	Q: How many days per month would you normally snort cocaine, smoke crack and inject cocaine? A: __days per month	Q: On an average week, how many days per week would you normally use both cocaine and alcohol? A: __days per week
Number of drinks	Q: On those days when you drank alcohol, how many drinks did you usually have? A: Number of drinks__	Q: In a normal week how much cocaine/crack did you use? (There are about 28 grams in an ounce.) A: __ounces (1 ounce=28 grams) per week or __grams per week or __eight balls (=3.5 grams) per week	Q: On a typical day when you used both cocaine/crack and alcohol on the same occasion (cocaine and alcohol were either taken together or within three hours of each other)? A: __number of drinks and __number of grams
Hours of feeling effects of alcohol	Q: In a typical 24 hour day, how many hours	Q: On a typical 24 hour day, how many hours would you	Q: On a typical 24 hour day, how many hours would

Alcohol use only	Cocaine use only	Simultaneous use
would you normally feel effects of alcohol?	normally feel effects of cocaine/crack?	normally feel effects of both cocaine/crack and alcohol?
A: __hours	A: __hours per day	A: __hours per day

Table 1

Percentage of injured or aggressed patients to treatment clients of subgroups

Demographic variables		Population % in 2008 Survey [†]		Injured patients		Aggessed patients	
	Sample (%)	N	%	N	%	N	%
Age in years							
18–39	38.77	100	28.09	146	41.01		**
40–80	61.23	93	35.77	78	30.00		
Sex							
Male	48.54	101	33.67	107	35.67		
Female	51.46	92	29.07	116	37.06		
Ethnic							
White	80.50	158	31.66	176	35.27		
Other	19.50	35	29.91	48	41.03		*
Marriage							
Married/common-law	69.96	54	28.88	57	30.48		
Other	30.04	139	32.40	167	38.93		**
Education							
High school or lower	32.54	85	31.95	114	42.86		
Above high school	67.46	108	30.86	110	31.43		
Household income							
<\$50,000	21.88	72	30.00	77	32.08		
\$50,000+	78.12	121	32.18	147	39.10		
Total	3,621	616	31.33	224	36.36		

Note:

[†] Population aged 18-80 years old in Ontario and British Columbia in the 2008 Canadian Alcohol and Drug Use Monitoring Survey, χ^2 statistic:

* P<0.05

** P<0.01.

Table 2

Rate ratio of injury and aggression due to alcohol consumption, cocaine use, and simultaneous use within six and three hours prior to the injury and/or aggressive incident

Acute outcomes/substance use	N of users + not users) [†]	Exposed time estimated using drinks/grams		Exposed time using hours of feeling effects		Homogeneity test for quantity frequency vs feeling effects [‡]
		RR	95% CI	RR	95% CI	
Injury ^{II}						
Alcohol only within 6 hours	96 (67+29)	2.41	1.53 – 3.79	3.34	2.11 – 5.28	ns
Cocaine only within 6 hours	54 (25+29)	1.94	1.15 – 3.26	4.29	2.39 – 7.69	*
Cocaine and alcohol within 6 hours	54 (25+29)	3.35	2.19 – 5.13	5.45	3.58 – 8.30	ns
Cocaine and alcohol within 3 hours	76 (47+29)	5.12	2.96 – 8.86	8.39	4.55 – 15.48	ns
Test for homogeneity b/w alcohol & cocaine only 6 hrs		2.41 vs 1.94; ns		3.34 vs 4.29; ns		
Test for homogeneity b/w alcohol only & combined use 6 hrs		2.41 vs 3.35; ns		3.34 vs 5.45; ns		
Test for homogeneity b/w cocaine only & combined use 6hrs		1.94 vs 3.35; ns		4.29 vs 5.45; ns		
Test for homogeneity b/w 3 hrs & 6 hrs for combined use		3.35 vs 5.12; ns		5.45 vs 8.39; ns		
Aggressive incident ^{II}						
Alcohol only within 6 hours	73 (51+22)	2.92	1.74 – 4.91	5.91	3.20 – 10.91	*
Cocaine only within 6 hours	59 (37+22)	3.28	1.82 – 5.91	7.40	3.86 – 14.19	*
Cocaine and alcohol within 6 hours	38 (16+22)	3.18	1.74 – 5.82	3.54	1.93 – 6.49	ns
Cocaine and alcohol within 3 hours	120 (98+22)	16.09	9.43 – 27.46	18.45	10.52 – 32.37	ns
Test for homogeneity b/w alcohol & cocaine only 6 hrs		2.92 vs 3.28; ns		5.91 vs 7.40; ns		
Test for homogeneity b/w alcohol only & combined use 6 hrs		2.92 vs 3.18; ns		5.91 vs 3.54; ns		
Test for homogeneity b/w cocaine only & combined use 6 hrs		3.28 vs 3.18; ns		7.40 vs 3.54; ns		
Test for homogeneity b/w 3 hrs & 6 hrs for combined use		3.18 vs 16.09; ***		3.54 vs 18.45; ***		

Note:

[†] Each analysis included users and non users of substances.

Subjects who reported combined use of alcohol and cocaine within three hours before an incident also reported combined use of alcohol and cocaine within six hours prior to an incident.

^{II} Test for homogeneity hypothesis to test the difference in the impacts of alcohol use only, cocaine use only or combined use of cocaine and alcohol on acute harms.

[†] Test for homogeneity hypothesis to examine the difference in the estimate of RR of acute harms between the method of estimated exposed time using the number of drinks or grams consumed and the method of estimated exposed time using the number of hours of feeling effects. ns = not significant ($P > 0.05$).

* $P < 0.05$

*** $P < 0.001$.