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The Influence of the Combination of Alcohol and Benzodiazepines on Driving

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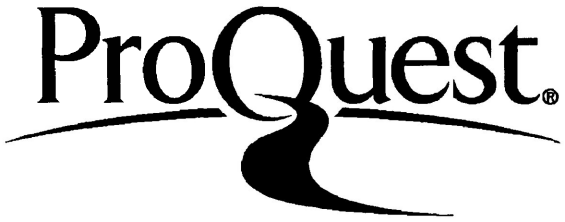
April 28, 2008



Abstract

Although the increased risk associated with driving under the influence of alcohol or benzodiazepines on their own has been recognized, several variables make their combined effects difficult to study. As a result, the small body of research on the subject is contradictory. The current study aimed to further explore the effects of the combination of alcohol and benzodiazepines on driving. Data from the years 1993 – 2006 were taken from the American Fatality Analysis Reporting System and examined using a case control design. All subjects were drivers, aged 20 years and older, had been tested for alcohol and drugs, and, if positive for benzodiazepines, were only positive for a single half-life class of benzodiazepine. Cases had at least one unsafe driver action (e.g., weaving) recorded in relation to the crash. Controls had no such record. Logistic regression was performed to determine the odds of performing an unsafe driver action (UDA) for drivers positive for benzodiazepines (stratified by short, intermediate and long half-life) with BACs ranging from 0.00 to 0.10 mg/100 ml. When compared to an alcohol- and benzodiazepine-free referent group, the alcohol plus benzodiazepine groups showed significantly higher odds of committing an UDA at nearly every BAC / half-life combination. When using the alcohol only and benzodiazepine only groups as referents, additive, possibly synergistic effects were observed for long benzodiazepines in combination with alcohol at BACs of 0.02 and 0.04 mg/100 ml. This study demonstrates the detrimental effects that the combination of alcohol and benzodiazepines can have on driving, and suggests that further research is necessary.

Acknowledgements

The author acknowledges the support of CanDRIVE, a New Emerging Team funded by the Canadian Institute of Health Research (CIHR).

The Influence of the Combination of Alcohol and Benzodiazepines on Driving

The combination of alcohol and driving is a serious public health issue. Although it is difficult to quantitatively describe the impact of drinking and driving on a global level (World Health Organization [WHO], 2004a; Zador, Krawchuk & Voas, 2000) the World Health Organization (2004b) has declared that traffic injuries represent a very serious public health issue, and cites drinking and driving as one major factor behind this predicament. Fatalities caused by drinking and driving vary widely around the world. Approximately 20% of fatally injured drivers in high-income countries and a range of 33% to 69% in low-income countries have blood alcohol levels above the legal limit (WHO, 2004a). However, as alluded to previously, it is difficult to make comparisons between countries, because factors such as health care, traffic and road conditions, laws, and a variety of other risk factors for crashes (age and sex of the average driver, socio-economic status, etc.) vary widely, affecting exposure to risk, crash severity, and injury outcomes. Even if these factors could be controlled for, the methodology used to collect data on drinking and driving also show considerable inconsistency around the world, as recently discovered by the United State's National Highway Traffic Safety Administration [NHTSA] when it failed to make any direct comparisons between countries (Stewart, 2001).

Although drinking and driving has been a well-known problem for some time, the issue of drugged driving (driving with licit and/or illicit drugs in the bloodstream) has more recently garnered the attention of researchers as well as policy makers. Many types of drugs (Kelly, Darke & Ross, 2004) have been shown to negatively impact driving

ability and the benzodiazepine family of medications has been brought into the spotlight. Benzodiazepines, most often used for anxiolytic and hypnotic purposes, include some of the most commonly prescribed medicines today (RxList, n.d.). Although the research is still emerging, it seems clear that certain benzodiazepines negatively affect performance on a number of tasks, such as driving, by inducing daytime drowsiness (Harrison, Subhan & Hindmarch, 1985; Mattmann et al., 1982; Van Laar, Volkerts & Verbaten, 2001; Vanakoski, Mattila & Seppala, 2000; Versteer, Vokerts & Verbaten, 2002), slowing reaction time (Harrison et al., 1985; Ingrum, Bjorkland, Bjorneboe, Christopherson, Dahlin & Mørland, 1992; Willumeit, Ott, Neubert, Hemmerling, et al., 1984), impairing both the anticipation of problems (Berthelon, Bocca, Denise & Pottier, 2003; de Gier, 't Hart, Nelemans & Bergman, 1981) and the ability to control lateral position (Brookhuis, Volkerts & O'Hanlon,1990; O'Hanlon, Vermeeren, Uiterwijk, van Veggel & Swijgman, 1995; O'Hanlon & Volkerts, 1986; Partinen, Hirvonen, Hublin, Halavaara & Hiltunen, 2003; Van Laar et al., 2001; Van Laar, Volkerts & Willigenburg, 1992). These detriments are especially clear for benzodiazepines that have a long half-life, or, in other terms, take a long time to be eliminated from the body.

Considering the widespread incidence of driving under the influence of alcohol and the extensive use of benzodiazepines, it is no surprise that alcohol and benzodiazepines are regularly found together in the bloodstreams of drivers around the world (Appenzeller, Schneider, Yegles, & Wennig, 2005; Augsberger & Rivier, 1997; Barbone et al., 1998; Seymour & Oliver, 1999; Skurtviet, Abotnes & Christopherson, 2002). However, the current research addressing the combined effects of alcohol and benzodiazepines on driving has led to contradictory results. According to several

researchers, the result is an additive response; in other words, resulting detriments are greater than those that could be explained by either agent alone (Burns & Moskowitz, 1977; Linnoila et al., 1990; Longo, Lokan & White, 2001; Willumeit, Ott & Neubert, 1984). But other researchers have failed to find such a response, citing that effects are no different than those found with alcohol alone (Longo, Hunter, Lokan & White, 2000a; Palva & Linnoila, 1978; Terhune et al., 1992; Willumeit et al., 1984).

Alcohol

In 1964, Borkenstein and colleagues completed what is now considered to be one of the most influential studies on drinking and driving. Often referred to as the Grand Rapids Study, this pioneering research looked at how blood alcohol concentration levels (BACs) affect the odds of being in a traffic crash (Traffic Safety Centre, 2003). By matching over 3,300 cases of drivers that had been in crashes with 17,000 controls, the researchers found odds as high as 25 to 1 (drivers with BACs of 0.15 mg/100 ml). They revealed an increased risk for crashes with any detectable level of alcohol in the bloodstream (Ogden & Moskowitz, 2004). As a result of this research, lawmakers had the information they needed to create justifiable legal cut-offs for driving under the influence of alcohol. This research also served to introduce Borkenstein's invention of the Breathalyzer, a tool widely used in law enforcement today.

Current Laws on Alcohol and Driving

Although most countries in the world do have laws concerning drinking and driving, they vary greatly. For example, some countries such as the Czech Republic and Hungary (International Centre for Alcohol Policies, n.d..), reportedly have legal BAC limits of 0 mg/100 ml. Limits range up to a legal BAC cut-off point of 0.08 mg/100 ml.

Although it has been shown that reducing the legal BAC limit for drinking and driving results in a decrease of both drinking and driving behaviour and alcohol-related traffic incidents, the United States (certain states), Canada, and the United Kingdom all currently have BAC limits of 0.08 mg/100 ml, as do several developing countries such as Botswana, Nicaragua, and Malaysia (Mothers Against Drunk Driving [MADD] Canada, 2007).

Prevalence and Demographics of Alcohol and Driving

In the early 1980s, the universally troublesome drinking and driving rates around the world began to significantly improve, as many developed countries began implementing successful programs aimed at reducing drinking and driving. Governments introduced new legislation, launched education campaigns, and ensured penalties were enforced (WHO, 2007). Non-governmental organizations like MADD (2005) also embarked on their efforts to instigate change. However, by the early 1990s, the momentum of the movement began to slow (Sweedler et al., 2004) as drinking and driving rates began to stabilize, with both minor improvements and set-backs since.

It is difficult to examine the rates of drinking and driving amongst general populations around the world. Most of the epidemiological studies on drinking and driving look at injury and fatality records. Such data allow researchers to compare the crash risk rates of drinking and non-drinking drivers. However, crash data are only a small part of the picture. In order to determine drinking and driving rates amongst the general population, one must look at all drivers, regardless of whether or not a crash resulted. Using random roadside tests, a few researchers from different countries have attempted to determine the percentage of drivers on the road who are under the effects of

alcohol. However a mismatch of methodologies makes it difficult to compare these findings. As an example, Mock and colleagues found that around 22% of drivers in Ghana (as cited in Global Road Safety Partnership, 2004) randomly stopped for roadside testing were positive for any level of alcohol. Another study from the UK showed that about 1% of randomly selected drivers had BACs at 0.08 mg/100 ml or greater (Everest, Davies & Banks as Global Road Safety Partnership, 2004). It would seem that countries define the problem of drinking and driving in different ways, making it unfeasible to describe the rates of this behaviour around the world.

One aspect of drinking and driving which does show some consistency around the world is the type of person who is likely to drink and drive. From a demographic standpoint, this person is most likely male, between the ages of 18 and 24, of low-economic standing, single, has a blue collar job, limited education and poor self esteem (WHO, 2007).

Pharmacology and Effects of Alcohol and Driving

It is not surprising that creating tougher drinking and driving laws brings about reductions in crashes, injuries and deaths. Since Borkenstein's research, advancements in technology have allowed studies to become far more sensitive in detecting impairments caused by alcohol, and there is "no evidence of a threshold below which impairment does not occur" (Ogden & Moskowitz, 2004, p. 185). In fact, detriments related to driving behaviour have been documented in subjects with BACs below 0.01 mg/100 ml (Moskowitz & Robinson, 1998). A review by Moskowitz and Fiorentino (2000), showed that around one third of the 112 studies they summarized found detriments in subjects

whose BAC was 0.039 mg/100 ml. At 0.079 mg/100 ml, 92% of the studies revealed impairment in subjects.

One of the reasons alcohol is believed to cause impairments at such low concentrations is that it is rapidly absorbed. Once absorbed through the gastrointestinal tract, alcohol is quickly distributed by the blood, reaching peak effects in about one hour, although this can vary depending on time of last meal, weight and body type (Becker, 1970). Age, extreme BACs and abuse of alcohol may also affect elimination; alcohol is generally metabolized at a rate of about one drink (15 ml) per hour, with the liver playing the largest role in excretion. When alcohol is ingested at a higher rate than it is eliminated, BAC increases.

Alcohol is a central nervous system depressant, and its impact on the CNS is approximately proportionate to the amount of alcohol in the blood (Moskowitz & Robinson, 1998). At very low levels, alcohol can cause decreased inhibitions. At moderate levels (beginning at 0.03 mg/100 ml) diminished attention and the weakening of some fine motor skills may result. Increased reaction time, reduced visual acuity and drowsiness generally become noticeable at 0.09 mg/100 ml, followed by confusion, disorientation and physical in-coordination at 0.25 mg/100 ml. Coma is a possibility at 0.35 mg/100 ml, and death at 0.45 mg/100 ml (Dubowski, 1989).

Alcohol's specific influences on driving ability have been very closely studied, and although a full exploration of this research is beyond the scope of this review, an overview of some of the basic findings is important. Moskowitz and Fiorentino (2000) addressed the results of 112 studies performed between 1991 and 1998 on the topic of drinking and driving-related-skills. As touched on above, the vast majority of these

studies reported impairments at some level of BAC. But some of the behavioural areas or tasks addressed by these studies showed greater sensitivity than others. Table 1 shows a breakdown of these behavioural areas and tasks into 12 categories, and displays the lowest sensitivity reported for each. Some tests (such as the hallmark experiments employing actual driving or simulators) showed very high sensitivity to alcohol's effects, while others did not, casting doubt on the usefulness of tests like finger tapping, simple reaction time and critical flicker fusion for this application. Driving is a complex task, simultaneously calling upon several cognitive, physiological and self-belief (such as comfort level and confidence) components (Michon, 1979). As such, the best experiments to assess driving ability are those multi-faceted tests which call upon all of these components.

Epidemiological Studies on Alcohol and Driving

In addition to the laboratory research discussed above, epidemiological studies are very important in showing the dangers of drinking and driving. By examining the vehicular crashes (or lack thereof) of individuals with various BACs, it is possible to compare and contrast the risks, culpability and outcomes related to drinking and driving.

Relative risk. In 2000, Zador and colleagues picked up where previous research had left off in an effort to examine alcohol-related fatal crash risk using recent data. Using American crash information from the Fatality Analysis Reporting System (FARS) and exposure data gleaned from the National Roadside Survey, the researchers were able to compare the BACs of crash-involved drivers with those who had not been involved in crashes, and once again showed a positive correlation between BAC and risk of a fatal crash. The researchers went further to compare the rates of single with multiple vehicle

crashes; it has been argued (Zador, 1991), that single vehicle crashes provide the best measure of the contribution of alcohol to crashes. A non-impaired driver may be able to avoid a multiple vehicle crash with an impaired driver (or in a sense compensate for the impaired driver), thereby affecting collision rates. Conversely, in single vehicle collisions, there is no fault to be shared. In Zador's recent study, at BACs between 0.08 and 0.10 mg/100 ml, relative risks as high as 51.9 (male drivers under the age of 21) were reported for single vehicle crashes. At the low end of the scale, drivers over the age of 35 were still 11.4 times at greater risk of being in a single vehicle crash when compared to those with a BAC of zero. Even when looking at all crashes (multiple and single vehicle), relative risks were still high, ranging from about a six fold increase for those over 35 years, to 24 times in the young male group. As BACs rose, so too did the relative risk, with a staggering 15,560 for young males with a BAC of 0.15 mg/100 ml or higher.

Culpability. When studying alcohol-related relative crash risk as described above, there is the possibility that the control sample is not representative of the population. There is also the possibility that those who drive after drinking may be somehow different from those who don't; they may have different driving habits which could contribute to their likelihood of being in a collision (Longo et al., 2000a) such as driving more regularly or in more dangerous locations. Because analyzing crash risk only involves measuring crash involvement and not responsibility, an over-representation of intoxicated drivers in crash data could result. Culpability analysis is an alternative method of investigating the issue. Using a variety of criteria (including police evaluations and environmental factors), it is possible to assign responsibility for a crash, and in turn compare the culpability rates of impaired and non-impaired drivers. Research

from Drummer, and colleagues (2004), Terhune (1982) and colleagues (1992), and Timby, Sjogren, Bjornstig and Eriksson, (1998), all support a recent culpability analysis by Longo and colleagues (2000a). This analysis showed that of the 2500 injured Australian drivers involved, 52.8% of those who were alcohol-free were deemed culpable. For alcohol-impaired drivers, culpability rates ranged from 68.6% for those with a BAC of 0.05 mg/100 ml or less, up to 96.3% for those with a BAC of 0.15 mg/100 ml or greater, showing a positive relationship between BAC and responsibility for a crash.

Outcomes. Besides the greater odds of being in a crash and being deemed responsible for that crash, another important public health concern surrounding drinking and driving is that a driver positive for alcohol also faces poorer outcomes than a non-impaired driver given the same crash (Committee on Trauma Research, 1985). In other words, given the same force, deaths are greater and injuries more serious amongst those who are impaired. Evans and Frick (1993) estimated that a BAC of 0.10 mg/100 ml resulted in a twofold risk of death compared to a non-impaired driver given the same crash; a threefold risk was estimated at BACs of 0.25 mg/100 ml. These findings are substantiated by findings from Waller and colleagues (1986) who showed that alcohol in the bloodstream increased the chance of a fatality in a crash by over 200%, and further reported an odds ratio for serious injury of 1.59 for both drivers and passengers positive for alcohol compared to those who were not. Sjörgen and colleagues (1997) also reported significantly higher rates of severe injuries in drivers positive for alcohol. Although different explanations for this phenomenon have been suggested, such as a temporary change in hormones (Woolf, Cox, Kelly, McDonald & Harnill,1990) and cell

membrane structure, and cellular swelling (Waller, Hill, Maio & Blow, 2003), the relationship between alcohol and injury severity and fatality is not clear.

In summary, alcohol is decidedly harmful to driving ability. Despite this knowledge and the resulting actions taken by lawmakers, drinking and driving remains a serious dilemma around the world. Now, additional alarms have been raised in response to reports of increased polydrug use by drivers, which includes mixing alcohol with other licit or illicit agents (Cusack, Harrington, Furney, Flynn & Leavy, 2002; Varga, Mágori, Hideg & Somogyi, 2006). The combination of alcohol with drugs in the benzodiazepine family falls into this concerning category.

Benzodiazepines

Compared to the 8,000 year history of alcohol, the introduction of benzodiazepines is relatively very recent, dating back to the early 1960s when chlordiazepoxide (Librium) was made available, shortly followed by diazepam (Valium). There are now approximately 30 types of benzodiazepines available on the North American and European markets (Ashton, 2005). As mentioned previously, there are many uses for these drugs, but about 75% of prescriptions for benzodiazepines in the United States are for anxiolytic purposes.

Although benzodiazepines gained excessive popularity in the 1990s, use of these drugs in a monotherapy setting has declined recently since concerns arose regarding their problematic side effects, tolerance and potential for abuse (Valenstein et al., 2004). That being said, the move away from benzodiazepines has been a gradual one, and the drugs remain a common prescription today, especially in older populations, where usage rates have been documented as high as 25% (Tu, Mamdami, Hux & Tu, 2001). They are also

still very popular in dealing with the initial treatment of anxiety and panic disorders in combination with selective serotonin re-uptake inhibitors (SSRIs), because, in comparison to SSRIs, benzodiazepines have a very rapid onset (Stevens & Pollack, 2005).

Current Laws on Benzodiazepines and Driving

Whereas laws concerning drinking and driving have been well established, there are several logistical problems on the path to defining and enforcing laws for licit drugged driving such as operating a vehicle under the influence of benzodiazepines. One of these difficulties is the lack of consistent research data to establish legal cut-off levels. There is also a call for an efficient and effective testing procedure to quantify impairment in the field, including evidentiary screening instruments combined with behavioural assessments. The behavioural aspect is important, considering drug plasma level alone may not be a sufficient indicator of impairment (Ellinwood & Heatherly, 1985). In addition, drug effects can differ dramatically from person to person, depending on a number of physical characteristics and whether a person's drug use is acute or chronic (Walsh, de Gier, Christopherson, & Verstraete, 2004). For this reason, many countries have no specific laws addressing driving under the influence of medicinal drugs, and those few that do vary in their approaches. Sweden, for example, has made it illegal to drive under the effects of certain licit drugs (including benzodiazepines) if these medications have not been prescribed, or if they are detected at excessive levels. Several countries abide by a European Union regulation that states that drivers' licenses cannot be renewed to individuals whose driving abilities are hampered by medication. Although there are different interpretations of this rule, some countries (such as Spain) require that

individuals who take these identified medications be tested for driver fitness before their license can be re-issued (del Rio & Alvarez, 2003).

Of those countries which don't specifically address the legalities of mixing driving with medications, many still have laws surrounding benzodiazepine use in general. Hong Kong classifies benzodiazepines as a dangerous drug under their Drug Ordinance Act (Chung, 1997), which requires detailed record keeping for all prescriptions. Around the world, extensive paper trails have also been enforced for many prescriptions (Weintraub, 1989), and medically used benzodiazepines are listed on Schedule IV in the United States and Canada, which, among other things, limits prescription refills due to the possibility of dependence (Department of Justice of Canada, 2007; U.S. Drug Enforcement Administration, n.d.). Australia usually does not allow for any repeat prescriptions of benzodiazepines. Because benzodiazepines have the potential for abuse, there is also global concern surrounding the trafficking of benzodiazepines (United Nations, 2001).

Prevalence and Demographics of Benzodiazepines and Driving

A good deal of research has investigated the drugged driving issue by looking at prevalence rates amongst drivers who have been in crashes or who were suspected of driving under the influence, and some of these studies will be discussed below. However, details on the prevalence of driving under the influence of a benzodiazepine(s) in the general population are sparse. Data on any sort of drugged driving within the general population is challenging to collect—testing methods can be expensive and unreliable, and sampling is difficult. Self-report surveys have been used in the United States (Substance Abuse and Mental Health Services Administration, 2002) and Australia

(Australian Institute of Health and Welfare, 2002), and show that around 4% of the population will drive after consuming some sort of drug (licit or illicit) over a 12-month period (Kelly et al., 2004). But questionnaires such as those used in these studies often result in an under-reporting of negative behaviour.

We know from actual prescription records in developed nations that around 5% of the population will be taking a prescribed benzodiazepine (Bramness, Skurtveit & Mørland, 2002) at any given time. But to the author's knowledge, population-wide driving behaviour has not been linked to such records. The German Roadside Study (Krűger, Schulz & Magerl, 1995) showed that 2.7% of the over 12,213 drivers randomly screened for drugs and alcohol was positive for benzodiazepines. A much smaller study in Denmark (Behrensdorff & Steentoft, 2003) found that 0.7% of the 1,000 randomly screened drivers was under the influence of benzodiazepines. But the results of these studies are limited. In both, drivers were allowed to decline from participation in the research; the Danish study had a very small sample; some of the German data are now outdated. Therefore generalization of these results to the general population of each geographic study area is highly doubtful, and more so globally.

As indicated above, a variety of studies from around the world have looked at the prevalence of benzodiazepine detections in drivers apprehended by police under the suspicion of some kind of impairment. A number of these studies are listed in Table 2. The benzodiazepine detections range broadly, from around 10% of apprehended drivers in some parts of Scandinavia, to a high of nearly 50% of drivers in Scotland. There are various limitations within these studies, including sampling concerns. Toxicology issues are also apparent, such as the questionable sensitivity of some of the testing equipment.

In certain countries law enforcers are very cognisant of the issues surrounding benzodiazepines and driving, and may be more likely to identify and/or screen drivers, resulting in higher detections rates (Christophersen, Ceder, Kristinsson, Lillsunde, & Steentoft, 1999; Walsh et al., 2004). This is just one of the variables that combine with use of a variety of different methodologies that make it difficult to compare rates between countries.

Nevertheless, these studies have been helpful in producing a better picture of the type of person likely to drive while under the effects of a benzodiazepine. Although men are apprehended more often for suspicion of impairment, the percentage of apprehended women who test positive for benzodiazepines is often higher than that of men. In a study by Skurtveit, Christopherson and Mørland (1995) around 12% of the nearly 3000 individuals apprehended for suspicion of impairment were female. Approximately 40% of these women were positive for one or more benzodiazepine, compared to just over 30% of the men. It has been suggested that this result is due to the fact that benzodiazepine prescription rates are higher for women (Kelly et al., 2004). Indeed, studies from the Netherlands (Zandstra et al., 2002), Great Britain (Dunbar, Perera & Jenner, 1989) and Canada (Cooperstock, 1982) have shown that twice as many women are prescribed benzodiazepines when compared to men. In addition to higher prescription rates amongst women as compared to men, benzodiazepine prescriptions are more common amongst middle-aged and older populations as compared to their younger counterparts. This explains why this group of drivers is most likely to test positive for a therapeutic level of benzodiazepine. However, at levels above therapeutic doses, drivers are likely to be younger (Appenzeller et al., 2005). It is this group that most likely

represents a large portion of those using benzodiazepines for recreational purposes, such as enhancing the effects of or reducing the impact of withdrawal symptoms from harder, illicit drugs (Drummer, 2002; O'Brien, 2005).

Pharmacology and Effects of Benzodiazepines on Driving

The information presented to this point suggests that there may be a relationship between benzodiazepines and driving ability. A closer look at how these drugs affect the body will further illuminate the complexities of the issue.

Benzodiazepines act on the gamma-aminobutyric acid (GABA) neurotransmitter system. In very simplified terms, GABA calms the brain by inhibiting many of the messages between neurons (Ashton, 2002). Benzodiazepines strengthen this calming effect by binding to the GABA receptor-site, thereby mimicking the effects of GABA, and further reducing any excitement in the brain. There are a variety of benzodiazepines available, and the effects of each depend on the specific site(s) it is able to bind to, and can be sedative (alpha 1 subtype), anxiolytic (alpha 2) or anticonvulsant (alphas 1, 2 and 5). As such, benzodiazepines are often prescribed for insomnia, anxiety and panic disorders, muscle disorders and epilepsy, and can also be used as a mild anaesthetic. Some of the most commonly prescribed benzodiazepines are listed in Table 3, along with corresponding information on each drug's market aim and half-life. Half-life refers to the amount of time it takes for half of one dose of the drug to be eliminated from the body. For benzodiazepines, half-life varies greatly, from around three hours for midazolam, to up to 250 for the active metabolites of flurazepam.

Because benzodiazepines have a tranquilizing effect on the brain, some of the side effects from use are not surprising. Psychomotor slowing, drowsiness, and memory

impairment (Ashton, 2002) are concerns. Paradoxically, a stimulated response has been reported in some patients, manifesting itself in behaviours such as decreased inhibition, aggression, and anxiety (Bramness et al., 2006). Depression has also been reported (Longo & Johnson, 2002). All of these side effects may be augmented in older patients, as they are more sensitive to central nervous system depressants in general, and they metabolize drugs less efficiently than their younger counterparts (Cusack, 2004).

In order to further explore the side effects of benzodiazepines and how they specifically impact driving ability, many researchers have performed simulator and on-the-road driving experiments. Results have shown that the administration of benzodiazepines results in increased reaction times (Palva & Linnoila, 1978; Vanakoski et al., 2000; Willumeit et al., 1984), decreased control over the vehicle's lateral position (Brookhuis et al., 1990; O'Hanlon & Volkerts, 1996; Partinen et al., 2003; van Laar et al., 2001), difficulty maintaining constant speed (O'Hanlon & Volkerts, 1986; Staner, Ertle, Boeijinga, Rinaudo, Arnal, Muzet, et al, 2005; van Laar et al., 1992), impaired visual attention (Berthelon et al., 2003) and increased effort (Verster et al., 2002). When certain studies examined results based on benzodiazepine half-life (Brookhuis et al., 1990; Ingrum et al. 1992; O'Hanlon & Volkerts, 1986), drugs that took a longer time to be eliminated from the body had a more detrimental effect on driving ability. In their study comparing the effects of short- and long-acting benzodiazepines on driving, Willumeit, and colleagues (1984) not only found that lormetazepam (short half-life) yielded far fewer problems than diazepam and flurazepam (long half-lives), but their results actually suggested that the drug may even improve driving ability over baseline performance in some respects, perhaps because subjects were well-rested after taking the hypnotic the

night before. In 2004, Verster, Veldhuijzen and Volkerts compiled evidence from several studies, corroborating earlier research on benzodiazepine half-life and driving ability. When looking at hypnotic benzodiazepines, they found that those with a long half-life showed the greatest change over placebo in the ability to control a vehicle's lateral position. For example, in one study a typical dose of flurazepam (long half-life) resulted in subjects deviating an average of 8 cm from the position observed with placebo. This is a significant difference, and comparable to a blood alcohol level of more than .10 mg/100 ml. Non-significant differences were reported between a typical dose of lormetazepam (short half-life) and placebo in other experiments.

Most of the simulator and on-the-road driving tests mentioned above employed healthy subjects to investigate the effects of benzodiazepines on driving ability. One must question whether these healthy subjects somehow differ from actual patients who have been prescribed benzodiazepines. In other words, do the driving skills of anxious or insomniac patients significantly differ from those of healthy subjects? An integration of three studies addressed this question as it pertains to anxious patients (O'Hanlon et al., 1995), and found that no significant differences existed between the baseline driving ability (as measured with standardized on-the-road driving tests) of un-medicated patients and healthy controls. Once under the effects of diazepam, lorazepam or placebo, both groups exhibited the same deficits (or lack thereof) in driving ability for the one week test period.

When it comes to insomniac patients, it has been argued that the good night's rest provided by benzodiazepine treatment may in fact improve driving ability. A study by Staner and colleagues (2005) looked for differences by comparing the effects of

lormetazepam versus a placebo in insomniac patients' driving abilities. Although this experiment was not able to directly compare insomniac patients with healthy controls or establish baseline driving performance for patients, it was able to show that even though subjects under the effects of a benzodiazepine reported improved sleep quality, driving performance was significantly impaired when compared to the placebo condition. These results are in-line with research on healthy subjects, suggesting that the findings from studies on insomniac patients could be generalized to the general population and vice versa.

Epidemiological Studies

Even though laboratory studies show that driving ability is negatively affected by benzodiazepines, it takes epidemiological evidence to demonstrate that these detriments translate into risk. Much like the previous section on alcohol, looking at benzodiazepine use amongst drivers who have been in a crash reveals that relative risk and culpability rates are higher for medicated individuals.

Relative Risk. In 1997, Hemmelgarn, Suissa, Huang, Boivin, and Pinard endeavoured to examine the crash risk resulting from the use of long- and short-half-life benzodiazepines. Their study population consisted of 224,734 men and women between the ages of 67 and 84 residing in Quebec, Canada. Using data obtained from driver's license files, police reports and health insurance records between 1990 and 1993, they were able to compare over 5000 cases who had been in a injurious crash over the period with controls who had not. Results showed that use of a long-half-life benzodiazepine yielded an increased risk of a crash, with an adjusted rate ratio of 1.45 within the first week of drug use. Risks decreased somewhat over time, with a ratio of 1.26 after one

year of usage, but remained statistically significant. Short-half-life benzodiazepines did not generate a statistically significant increased crash risk at any point. Even when half-life was not taken into consideration, Ray, Frought and Decker (1992), had previously confirmed a significantly increased crash risk (relative risk of 1.5) for elderly patients who had been prescribed benzodiazepines.

Compared to elderly drivers, risk may be more subtle when looking at younger age groups. When drivers of all age groups are included in analyses, half-life has not always been taken into account; this could explain the mix of research showing both significantly higher crash risk rates for benzodiazepine users (Movig, Mathijssen, Nagel, van Egmond, de Gier, & Leufkens, 2004; Neutel, 1995) and risk rates that are not significantly different from non-users (Smink, Ruiter, Lusthof, de Gier, Uges & Egberts, 2005).

Barbone and colleagues (1998) took half-life into consideration (short, intermediate and long) when they examined risk rates associated with benzodiazepine usage across all age groups. With a pool of over 400,000 individuals from the United Kingdom, the researchers looked at anyone who had experienced a first car crash between 1992 and 1995. Prescription records served as a measure of benzodiazepine exposure, with each subject's period prior to the crash serving as their own control in this case-crossover design. For long-half-life benzodiazepines, the risk of a crash was over twofold. Most of the risk was confined to anxiolytics, with an odds ratio of 2.22. Unfortunately, the risk associated with short-half-life benzodiazepines could not be accurately calculated due to exposure to other drugs in all cases. However intermediate half-life benzodiazepines showed no statistically increased risk. Examining the risks

further, researchers showed a dose-response effect, from an odds ratio of 1.27 for low doses, to 1.68 for an intermediate dose, to 2.67 for high doses.

In addition to half-life and dosage, some researchers have shown a relationship between tolerance to benzodiazepines and crash risk. Neutel (1995), revealed that crash risk was highest in the week following an initial benzodiazepine prescription (OR of 9.1 for hypnotics and 13.5 for anxiolytics). Odds ratios for anxiolytics were non-significant after week one, while hypnotics continued to be associated with a higher risk of crash (OR = 5.0) through the second week. Although no significant increase in risk was reported after these points, this could be due to the fact that the researcher was limited by a small sample size. Other researchers have confirmed that the initial period after filling a benzodiazepine prescription is associated with the highest risk of traffic crash (Hemmelgarn et al., 1997; Oster, Russel, Huse, Adams & Imbimbo, 1987), and, as shown by the Quebec study mentioned above (Hemmelgarn et al., 1997), significantly increased risks have been reported even after one year after the commencement of benzodiazepine treatment, suggesting that only a partial tolerance develops amongst users. A possible explanation is that many patients (especially those taking hypnotics for insomnia) only take their prescribed medication on an as-needed basis, which could impede or even prevent the development of tolerance (Verster et al., 2004).

Culpability. The preceding studies that used government driving and health database information to determine relative risk (Barbone et al., 1998; Hemmelgarn et al., 1997; Neutel, 1995; Oster et al., 1997; Ray et al., 1992) showed strength in their large study populations and their classification of cases, controls, and variables. However, there were several factors that limited these studies, including their inability to assess

their subjects' medication compliance, as they relied on prescription records (Thomas, 1998), and their use of crash involvement as a dependent variable rather that crash responsibility.

Some researchers have tried looking at the effects of benzodiazepines on driving by way of culpability analysis, just as outlined in the previous section on alcohol. Drummer and colleagues (2004) attempted such an investigation, and were not able to show any significantly increased risk for benzodiazepine users being deemed responsible for a crash as compared to non-impaired controls (OR=1.27). Similarly, The Benzodiazepine and Driving Collaborative Group (1993) reported no significant difference between the culpability of benzodiazepine users and non-users in their study (OR=0.97), but their analysis did not control for the use of other drugs by cases. Results from Terhune and colleagues (1992) were similar (66.7% benzodiazepine users were deemed culpable for a crash, compared to 67.7% of those who were drug- and alcohol-free), although again these findings were also not statistically significant. Thus, three attempts at conducting a culpability analysis yielded no significant findings.

In response to their inconclusive findings, Drummer and colleagues (2004) re-configured their data by differentiating between drug concentration levels, and revealed a significantly higher culpability rate amongst certain benzodiazepine users. When drivers whose benzodiazepine levels were at or above the therapeutic range were compared with drug-free drivers, their culpability rates were significantly higher. By excluding those drivers with very low benzodiazepine concentrations from the analysis and employing a relatively larger sample size, Drummer and colleagues were able to demonstrate what they and other researchers previously could not. However, when looking at

benzodiazepine users with levels above therapeutic levels, these researchers may have been looking at a unique type of user—perhaps one who abuses drugs. In this case, other factors (such as risk-taking behaviours) may be confounding the results.

There are still more facets of this culpability issue that need to be explored before any sort of conclusion can be drawn, including taking drug half-life and tolerance into account. Nevertheless, between such culpability analyses, relative risk studies, and information gleaned from actual experiments, the pieces to this complex puzzle allude to dangers resulting when benzodiazepines and driving mix.

Alcohol and Benzodiazepines in Combination

Compared with the number of investigations performed on alcohol or benzodiazepines, there is relatively little research on their combination. Of the limited number of studies on the interactions between alcohol and benzodiazepines, a number have simply led to further questions. It is clear from the previous sections that several variables need to be taken into consideration in order to get a clear picture of how either alcohol or benzodiazepines alone impairs drivers or lead to increased risk of crashes. It stands to reason that the study of their combined effects would involve an even greater complexity of variables.

Epidemiology

A handful of epidemiological studies have reported on the number of drivers discovered to be positive for both alcohol and benzodiazepines, however they looked at rates within driver populations that have been involved in a crash and/or apprehended under the suspicion of impaired driving. These individuals represent those most clearly unfit to drive, and by no means are representative of what is happening in the general

population, a situation which, to the author's knowledge, has not been explored. An Australian study looking at non-fatally injured crash-involved drivers (Longo et al., 2000a) found a relatively small percentage (1%) of their 2500 subjects were positive for both agents. Although this percentage may seem small, nearly one quarter of those drivers who tested positive for benzodiazepines were also positive for alcohol. This suggests that within this study's population of benzodiazepine users, combining the drug with alcohol and driving is a fairly common occurrence. Other research has yielded similar results to the Australian findings. A Swiss study (Augsberger et al., 1997) detected the combination in 4.1% of their sample of 641 drivers suspected of driving under the influence of alcohol or drugs. Again, the findings seem different knowing that nearly 30% of those who were positive for benzodiazepines were under the effects of alcohol. A Norwegian study (Skurtveiet et al., 2002) found the combination in around 8% of their 3343 apprehended subjects, representing a quarter of those positive for benzodiazepines. Still another study (Seymour et al., 1999) found that 7% of their 752 blood or urine tests were positive for both agents. Unlike the previous studies, this Scottish research had more detections of benzodiazepines than alcohol, and a total of 30% of those drivers found to be under the influence of alcohol were also positive for benzodiazepines. This reversal of findings is most likely due to the fact that apprehended Scottish drivers who fail a Breathalyzer are not required to undergo a urine or blood test. Thus the researchers were only looking at samples taken from those drivers who were suspected to be impaired even though their breath test was negative. The three previous studies looked at all drivers.

Although the findings of the above mentioned studies are interesting to note, it should be re-stated that these behaviours cannot be generalized to the general population, and provide only trivial insight into the demographics of the person likely to drive under the combined effects of alcohol and benzodiazepines. However, these are important details considering the noted differences between those likely to drive under the effects of these agents individually. The Scottish research discussed above indicated that drivers with both agents in their system had a much lower BAC than when alcohol was found alone; when the Australian study investigated the same relationship, BACs did not differ significantly between benzodiazepine users and non-users. These studies contradict other findings showing benzodiazepine use associated with higher BACs (Appenzeller et al., 2005). There is clearly nothing conclusive on this particular trait of combination users. Looking to other characteristics, the Norwegian study discussed above found that of the approximately 250 apprehended drivers who tested positive for both agents, just over one third tested positive for a single benzodiazepine, 60% of which presented at a therapeutic drug level. The remaining 40% of these single benzodiazepine users presented at above-therapeutic levels. Of the original 250 subjects, the remaining two thirds were either positive for more than one benzodiazepine, or had a combination of benzodiazepines with other licit or illicit drugs in their systems. This suggests that although several of these apprehended drivers were likely under the effects of a prescribed benzodiazepine, there were also a number of drivers abusing benzodiazepines, often in combination with other licit and/or illicit drugs. This could indicate that there are two distinct groups of individuals who fit into the category of being likely to combine alcohol and benzodiazepines with driving.

Effects

The effects associated with mixing alcohol and benzodiazepines have not been well studied. There are generally two conflicting theories on how these agents combine to affect driving ability. The first body of research suggests that the result is an additive or even a synergistic interaction (Burns & Moskowitz, 1977, Linnoila et al., 1990; Longo et al., 2001b; Willumeit et al., 1984). In simple terms, an additive interaction results when two agents combine to form an effect greater than that which could be explained by either agent alone; it is the summing of the effects of two agents. A synergistic interaction (also known as potentiation) is the result of one agent enhancing the effect of another; it could be defined as a multiplicative effect (Hanson, Venturelli & Fleckenstein, 2006). In contrast, the second body of research purports a non-interaction between alcohol and benzodiazepines. It claims that the effects are not greater than those found with alcohol alone (Longo et al., 2000a; Palva & Linnoila, 1978; Terhune et al., 1992; Willumeit et al., 1984).

It is noted that some researchers have encountered findings supporting both sides, exacerbating the confusion. However, most research is in line with the concept that there is an interaction that results when alcohol and benzodiazepines are administered close together and the alcohol is consumed in small doses (Hollister, 1990); it is when larger doses of alcohol are added to the mixture that contradictory results are reported. The reasoning behind this situation is unclear; it could be that alcohol is the stronger of the two agents. One finding by Linnoila and Mattila (1973) suggests that in some situations interactions between the agents may be short lived. They found that the combination of diazepam and alcohol produced the greatest additive response at 30 minutes, a point

before blood alcohol levels peak. By 90 minutes that interaction was no longer apparent. Thus, some research may be overlooking potential additive effects due to timing issues. There is also the possibility that studies haven't been sensitive enough, that the methods employed are not ideal for measuring the detriments resulting from the combination. For example, Linnoila and Mattila used choice reaction time and a coordination test similar to pursuit tracking as their measure of the interaction effects. As discussed above and summarized in Table 1, these are two of the tests which have since been shown to be inadequate measures of the effects of alcohol, with sensitivity at around 0.06 ml/100ml. Another important consideration overlooked is the role that drug half-life plays in the interaction. Also, and perhaps most importantly, the results from most laboratory experiments are difficult to generalize to real-life driving situations.

It is an understatement to say that the combination of alcohol, benzodiazepines and driving is a difficult subject to study, as evidenced by the lack of systematic research on this important issue. However, from the research that has been performed, it does appear that a dangerous interaction between alcohol and benzodiazepines may occur given certain conditions. As a result of this speculation, physicians are advised to caution benzodiazepine users about the potential dangers of combining their medication with alcohol, especially when driving. Yet, epidemiological evidence has demonstrated that a significant number of patients either haven't been adequately warned, or are not adhering to these recommendations (del Rio & Alvarez, 2003). It is clear from research to date that further research needs to be performed to uncover the specific conditions under which this additive alcohol-benzodiazepine interaction occurs.

The current study aimed to clarify the effect that the combination of alcohol and benzodiazepines have on driving. By utilizing a significant sample size, employing epidemiological data, stratifying benzodiazepines by half-life and alcohol by BAC, this study takes into consideration what many of its predecessors did not.

Method

Data

Data were obtained from FARS (the Fatality Analysis Reporting System). Based on information compiled by the National Highway Traffic Safety Association and the National Center for Statistics and Analysis, FARS includes information on every fatal traffic incident on public roads in the United States since 1975. This rich data set consists of details from a number of sources, including police and medical reports, drivers' license files and vital statistics. These variables are coded into the database, and work together to describe the crash via the physical events of the incident, contributing factors and characteristics of the people involved.

Data files for the years 1993 to 2006 (inclusive) were downloaded from the FARS ftp website. Prior to 1993, detailed drug information was not included in the database. Each SEQL (2002 and earlier) and SAS formatted file (2003 and later) was then imported into SPSS Version 15.0. In order to maintain consistency, the splitting, merging, or redefinition of variables was reconciled by adapting all files to match the original 1975 format. However, in some cases, earlier files required the addition of dummy variables to accommodate new variables added in later years. Once tested for uniformity, all files were stacked to create a single dataset. To validate this dataset, frequencies for various

variables were computed by year, and then compared externally to statistical tables available on the FARS website.

From this stacked dataset, subjects were selected to meet criteria specific to the current study. First, only drivers of passenger vehicles, SUVs and light pick-up trucks were included, thereby excluding pedestrians, passengers and drivers of motorcycles and larger, most likely commercial vehicles. Second, drivers under the age of 20 were excluded in order to address the issue of driver history. Third, all drivers were required to have been tested for both drugs and alcohol. Fourth, of those who tested positive for benzodiazepines, only those positive for a single half-life class of benzodiazepine were retained. Thus, subjects could be positive for multiple benzodiazepines as long as they were in the same half-life grouping (short, intermediate or long).

Study Design and Statistical Analyses

First, descriptive statistics were used to obtain demographic information for the four groups: 1) alcohol- and benzodiazepine-free, 2) alcohol only, 3) benzodiazepines only (stratified by half-life) and 4) alcohol plus benzodiazepines (stratified by half-life). Half-life was classified as either short ($\leq$6 hours), intermediate (>6 and $\leq$24) or long (>24). Groups were then compared for differences in sex (using a one-way ANOVA) and age. Differences in previous driver history were also compared using records of previous driving convictions within the three years preceding the crash. FARS includes drivers' previous records of crashes, DWI, speeding, license suspensions and a category for any other harmful moving convictions. The number of convictions (one, two and three or more) was also included in the comparison between groups. Finally, groups were compared for their use of other medications (licit and illicit). Detections of depressants,

narcotics, stimulants, cannabinoids and category of other miscellaneous agents (including such agents as inhalants, hallucinogens, and PCP) were analyzed for each of the study groups. Age, previous driver history and other medication detections were all compared using the Pearson Chi Square test.

Next, detections of benzodiazepines only and benzodiazepines in combination with alcohol were sorted by year. This was performed to achieve a better understanding of how the use of these agents is changing over time.

Finally, drivers were examined using a case control design. Those for which at least one unsafe driver action was recorded related to the crash (for example weaving or speeding) were considered cases. Appendix A includes a complete list of all possible unsafe driver actions (UDAs) recorded in the FARS database. Drivers without a record of an UDA in relation to the crash were classified as controls. After running a series of logistic regression test models, a final model was developed that included benzodiazepine exposure, BAC and a BAC squared term (to include the possibility of quadratic effects). It controlled for sex, age, age squared (again, to identify quadratic effects), previous driver history and other medication usage, and included a number of two-way interactions. The final model was centered at age 45 years, which was approximately the average age of the sample, and generally considered a benchmark as it is one of the safest groups of drivers.

To form an overall baseline, the odds of performing an UDA for the alcohol plus benzodiazepine group were calculated in reference to the alcohol- and benzodiazepine-free group. Benzodiazepine groups were again stratified by half-life, and alcohol was broken down into 0.02 mg/100 ml intervals. To address the possibility of additive or

synergistic effects, the odds of performing an UDA for the alcohol plus benzodiazepine group were calculated for two additional referents: 1) alcohol (at respective BAC levels), and 2) respective benzodiazepine.

All analyses were performed using SPSS Version 15.0. Due to limitations in the software, confidence intervals at various BAC / benzodiazepine half-life levels were obtained using the Delta method (Oehlert, 1992; B. Weaver, personal communication, February 12, 2008).

Results

Descriptive Statistics

A breakdown of descriptive information by alcohol and benzodiazepine group is included in Table 4.

A total of 116,510 drivers were included in the analysis, of whom 71.6% were male and the average age was 41.88 years. Sex and age significantly differed between groups. Although they made up the majority in all categories, the highest proportion of males was found in the alcohol only (82.8%) and all three alcohol plus benzodiazepine groups (86.7%, 74.3% and 77.7% for short, intermediate and long combinations, respectively). These same four alcohol-positive groups also had an average age (35.33 for alcohol only; 36.17 for short plus alcohol; 38.87 for intermediate plus alcohol; 37.61 for long plus alcohol) just under 10 years younger than the four remaining alcohol-free categories.

A look at previous driver history revealed that drivers positive for intermediate only (57.5%) or long benzodiazepines only (50.4%) were slightly more likely to have a poor driving record than the alcohol- and benzodiazepine-free group or short

benzodiazepine only group (both 42.5%), and were most similar to the alcohol only group (54.3%). Rates of a prior driving record increased between 7-9% in all three benzodiazepine groups in the presence of alcohol.

In general, those drivers positive for benzodiazepines (with or without alcohol) were more likely to be positive for other medications when compared to their benzodiazepine-free counterparts. Those who were positive for a long benzodiazepine, particularly in combination with alcohol, had the highest proportion of drivers positive for other medications (80.7%). Detections of depressants were especially high in this group; 62.6% of those drivers positive for long benzodiazepines plus alcohol were also positive for depressants.

Prevalence over time. The prevalence of benzodiazepine only and alcohol plus benzodiazepine detections over time was examined, and is illustrated in Figure 1. While detections of long benzodiazepines overall are falling, they continue to constitute most frequently detected benzodiazepines in the FARS database when combined with alcohol. Short and intermediate benzodiazepines make up smaller portions of the overall detection prevalence over time, however their detection rate is increasing. In fact, detections of intermediate benzodiazepines alone surpassed long benzodiazepines alone in 2006.

Combination Effects

To achieve a baseline view, the alcohol plus benzodiazepine groups were compared to the alcohol and benzodiazepine-free group at BAC levels ranging from 0.00 (to show the effects of benzodiazepines only) to 0.10 mg/100ml. With the exception of non-significant findings for short benzodiazepines in combination with BACs of 0.00 (i.e., benzodiazepine only) through 0.04 mg/100ml, significantly increased odds ratios

were reported at every BAC / benzodiazepine combination. The full results of this analysis are presented in Table 5. Figure 2 illustrates these same odds ratios for committing an UDA for each of the combination groups as well as the alcohol only group as compared to the alcohol- and benzodiazepine- free group.

As mentioned previously, additive or synergistic effects are observed when the effects of a combination of agents are greater than that which can be explained by either agent alone. Thus, the odds ratios for committing an UDA for each alcohol plus benzodiazepine combination were calculated in reference to each agent alone. Only significant odds ratios in relation to both referents would suggest an additive or synergistic interaction. Such was the case for long benzodiazepines when combined with alcohol at two low BAC levels: first at a BAC level of 0.02 where the odds ratio for performing an UDA were 1.14 (95% CI=1.08, 1.20) and 1.35 (95% CI=1.17, 1.52) for the long benzodiazepine only and alcohol only referents, respectively; second at a BAC level of 0.04 where the odds ratio for performing an UDA were 1.28 (95% CI=1.18, 1.39) and 1.25 (95% CI=1.07, 1.43) for the long benzodiazepine only and alcohol only referents, respectively. Results are displayed in Table 6.

Results from the full regression are displayed in Table 7. Appendix C includes the worksheets used to complete the calculation of confidence intervals for various alcohol and benzodiazepine combinations utilizing the Delta method, with results verified using predicted odds from the fitted line method.

Age and Sex

Sex was significant in the model, and showed that males were slightly less likely to commit an UDA than women, OR=.938 (95% CI=.901; .977), noting that this result is

based on the model being centered at age 45. Although the age term was non significant, OR=1.01 (95% CI=.994; 1.02), the age squared term was, OR=1.08 (95% CI=1.07; 1.08), indicating a quadratic effect. Figure 3 illustrates how the effects of age were quadratic for the alcohol plus benzodiazepine interaction at a BAC of 0.04 mg/100 ml. Overall, this interaction was significant for long benzodiazepines (Wald(1)=13.5, p >.005), but not short (Wald(1)=.06, p=.799) or intermediate (Wald(1)=.30, p=.583). Generally, the odds ratios for committing an UDA on long benzodiazepines in combination with alcohol revealed an inversed U-shaped curve, with peak odds at the approximate age of 45 years.

Previous Driver History

Drivers with a prior driving record demonstrated significantly higher odds ratios for committing an UDA, ranging from 1.05 (95% CI=1.01; 1.09) for one record of speeding, to 1.26 (95% CI=1.19; 1.33) for one record of license suspension. Odds ratios increased with the number of incidents recorded, to a high of 1.43 (95% CI=1.19; 1.72) for three or more previous car crashes. The only non-significant term was DWI. For full results, refer to Table 8.

Other Medications

The odds of committing an UDA was significantly increased for drivers positive for depressants, OR=1.58 (95% CI=1.42; 1.77), narcotics, OR=1.32 (95% CI=1.22; 1.43), stimulants, OR=1.85 (95% CI=1.75; 1.97), and drugs in the miscellaneous drugs category, OR=1.10 (95% CI=1.04, 1.17), but not for those positive for cannabinoids, OR=1.05 (95% CI=0.99; 1.12).

Discussion

Prior to this research, only a handful of studies addressed the issue of the combined effects of alcohol and benzodiazepines on driving. Although their collective findings suggested the possibility of dangerous, additive effects, their methodologies have been questionable, yielding results that were far from conclusive. It is clear from the literature that certain variables need to be taken into consideration when studying this combination, including BAC level (Hemmelgarn et al., 1997; Moskowitz & Fiorentino, 2000; Moskowitz & Robinson, 1998; Zador, 1991) and benzodiazepine half-life (Barbone et al., 1998; Brookhuis et al., 1990; Ingrum et al., 1992; O'Hanlon & Volkerts 1986; Verster et al., 2004; Willumeit et al., 1994). Sample size is an important factor in any study, as is the generalizability of the results to real life situations. Such considerations were often overlooked in these previous studies.

By stratifying results by BAC and benzodiazepine half-life, employing a large sample and utilizing epidemiological data containing culpability information, the current study took these important factors into consideration. By doing so, a much clearer picture of the combined effects of alcohol and benzodiazepines on driving has evolved.

As was expected, the combination of alcohol and benzodiazepines was significantly more likely to lead to an unsafe driver action when compared to the alcohol- and benzodiazepine-free referent group at almost every BAC / half-life combination. The only non-significant findings occurred when short half-life benzodiazepines were combined with alcohol at the relatively low BAC levels of 0.02 and 0.04 mg/100 ml. This is not surprising considering the effects of short benzodiazepines on their own, which, although non-significant, revealed an odds ratio of 0.85. This finding in line with

previous research which demonstrated that short benzodiazepines do not affect driving ability (Hemmelgarn et al., 1997; Verster et al., 2004). It has even been suggested by some to yield a protective effect (Willumeit et al., 1984), although the present study did not show short benzodiazepines to have any statistically significant protective effects in any combination compared to any referent.

The investigation at the heart of this study looked at possible additive or synergistic effects resulting from the combination of alcohol and benzodiazepines. Although the first analysis described above yielded significantly increased odds for the combination, using an alcohol- and benzodiazepine-free group as a referent cannot rule out the possibility that one agent alone is driving the result. Several researchers have claimed that alcohol and benzodiazepines combine to create an effect no greater than alcohol alone because alcohol was the stronger agent (Longo et al., 2000a; Palval & Linnoila, 1978; Terhune et al., 1992; Willumeit et al., 1994).

To determine if this was the case, odds of committing an UDA were calculated for the combination group in referent to the alcohol only group. Results showed that short benzodiazepines did not differ from the referent at any BAC level, ruling out an additive or synergistic effect. Nevertheless, significantly increased odds for intermediate benzodiazepines in combination with alcohol up to a BAC of 0.04 mg/100 ml, and for long benzodiazepines up to 0.06 mg/100ml were reported. Yet once again, this alone did not establish an additive effect, as it could not rule out the possibility that the benzodiazepine was the stronger agent. Consider that based on the analysis using the alcohol- and benzodiazepine-free referent, an intermediate or long benzodiazepine in the absence of alcohol has an odds ratio approximately equivalent to a BAC of 0.05 mg/100

ml and 0.04 mg/100 ml, respectively. Given the powerfully detrimental effects of both intermediate and long benzodiazepines in the absence of alcohol, it should be assumed that they are the stronger agent when combined with alcohol at low BAC levels. And this, in fact, was what the results suggested. Intermediate benzodiazepines in combination with alcohol were not significantly different from the effects of intermediate benzodiazepines alone, ruling out an additive or synergistic effect. Long benzodiazepines in combination with alcohol, on the other hand, did differ significantly from long benzodiazepines alone at BACs of 0.02 and 0.04 mg/100 ml. Because the analysis using the alcohol only referent had also shown significantly increased odds at these BAC levels, an additive or synergistic effect is implied.

Although tests (such as the Interaction Contrast Ratio, the Attributable Proportion due to Interaction, and the Synergy Index) do exist to measure additive and synergistic effects (Kaliani & Atashili, 2006), their reliance on dosage information makes them unsuited for this application. Thus, the effect's status as either additive or synergistic cannot be classified.

In addition to yielding information on the detrimental effects of alcohol and benzodiazepines on driving, this research provided a better look at the type of person likely to drive and experience the most detrimental outcomes under the effects of the combination. On average, the average combination user was younger (around 37), and more likely to be male than drivers in the benzodiazepine only groups, and in fact, most similar to the those in the alcohol only group. This typical combination user also appears to have a slightly worse driving record than his benzodiazepine only counterpart, suggesting that he may be a greater risk taker. He does not, however, appear to be more

likely to be under the effects of additional drugs when compared to this same referent. The most common type of benzodiazepine found in combination with alcohol seems to be on the verge of changing, as the prevalence of long benzodiazepine detections fall and intermediate benzodiazepine detections rise. This shift is most likely due to physicians becoming increasingly aware of the body of knowledge surrounding the dangers of benzodiazepines, and prescribing the shortest acting benzodiazepines possible to meet their patients' needs (Tu et al., 1991).

It should be noted that the description above identifies the person most likely to combine alcohol and benzodiazepines; it is not necessarily the person at greatest risk given the situation. This study has shown that risks differ for drivers across age groups; those positive for alcohol in combination with long benzodiazepines and are around the age 45 years show the highest odds of committing an UDA. All of this information is important for the development of targeted strategies to address this public health issue.

The results of this study also allow for the extrapolation of simple, straightforward concepts, which can translate the effects of the combination of alcohol and benzodiazepines on driving into concrete, easily understandable terms for the average benzodiazepine user. For example, it is interesting to note the different points at which alcohol and benzodiazepines comfort combine to create detriments equivalent to those which would be considered the legal drinking limit for alcohol alone. Using 0.08 mg/100 ml as a benchmark (the legal limit in much of North America), the findings in this study suggest that this equivalence is reached with: short benzodiazepines in combination with a BAC of approximately 0.07 mg/100 ml; intermediate benzodiazepines in combination with a BAC of approximately 0.05 mg/100 ml; and long benzodiazepines in combination

with a BAC of approximately 0.06 mg/100 ml. To give an example of how this may work using a BAC formula (Lawlor, 1998), consider the very simplified example of an average male weighing 180 lbs. He would need to consume approximately four standard alcoholic beverages over a period of 40 minutes to reach a BAC of 0.08 mg/ml. If he were under the effect of an intermediate benzodiazepine, he would only need to consume just over two drinks to reach that same level of impairment within the same time period.

It is important to address the limitations of this study. First, FARS data limited the classification of benzodiazepines to dichotomous variables, (i.e., present and not present). Had drug blood concentration levels been available, drivers positive for very low or sub-therapeutic amounts of benzodiazepines could have been separated from those at therapeutic and above therapeutic levels. Much like Drummer and colleagues demonstrated in 2004, removing sub-therapeutic concentrations from the analysis may have revealed much higher levels of culpability for the remaining drivers. This same benzodiazepine concentration information may also have made the classification of additive versus synergistic effects possible.

Second, information on the drivers' tolerance to benzodiazepines was unknown. As discovered by previous research on benzodiazepines, detrimental effects appear greatest in the initial period after filling a benzodiazepine prescription (Engeland, Skurtveit & Mørland, 2007; Hemmelgarn, et al., 1997; Neutel, 1996; Oster et al., 1987). Because odds ratios could only be calculated for a combination of all users, it is likely that the results of this study are an over-estimation of risk for long-term users, and an under-estimation for new users.

Third, the data in the sample only represent those involved in fatal crashes, and further, only those that were selected to be tested for alcohol and drugs, and as such, may represent those most unfit to drive. This makes generalizing these results to the general population more difficult.

Finally, any underlying medical conditions for which benzodiazepine may have been prescribed to the drivers in this study is unknown. Although previous research has suggested that anxious (O'Hanlon et al., 1995) and insomniac (Staner et al., 2005) patients do not differ from healthy controls when it comes to driving ability under the effects of benzodiazepines, the possibility of these conditions confounding the data cannot be completely ruled out.

Even with these limitations noted, it is clear that this study on the combined effects of alcohol and benzodiazepines on driving was a step in the right direction. Additive, possibly synergistic effects have been identified under specific conditions; conditions that could expand if issues such as benzodiazepine concentration levels and tolerance were taken into consideration. As such, additional research needs to be performed, perhaps utilizing a combination of laboratory experiments and epidemiological studies. Such investigations would provide much needed, concrete information for benzodiazepine prescribers and users, and as such be very valuable from a public health and safety standpoint.

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Appendix A

Unsafe Driver Actions

20. Leaving Vehicle Unattended with Engine Running; Leaving Vehicle Unattended in Roadway
21. Overloading or Improper Loading of Vehicle with Passenger or Cargo
22. Towing or Pushing Vehicle Improperly
23. Failing to Dim Lights or to Have Lights on When Required
24. Operating Without Required Equipment
25. Creating Unlawful Noise or Using Equipment Prohibited byLaw
26. Following Improperly
27. Improper or Erratic Lane Changing
28. Failure to Keep in Proper Lane or Running off Road
29. Illegal Driving on Road Shoulder, in Ditch, or Sidewalk, or on Median
30. Making Improper Entry to or Exit from Trafficway
33. Passing Where Prohibited by Posted Signs, Pavement Markings, Hill or Curve, or School Bus Displaying Warning Not to Pass
34. Passing on Wrong Side
35. Passing with Insufficient Distance or Inadequate Visibility or Failing to Yield to Overtaking Vehicle
36. Operating the Vehicle in an Erratic, Reckless, Careless or Negligent Manner or Operating at Erratic or Suddenly Changing Speeds
37. High-Speed Chase with Police in Pursuit

38. Failure to Yield Right of Way
39. Failure to Obey Traffic Actual Signs, Traffic Control Devices or Traffic Officers, Failure to Observe Safety Zone Traffic Laws
40. Passing Through or Around Barrier
41. Failure to Observe Warnings or Instructions on Vehicle Displaying Them
42. Failure to Signal Intentions
43. Giving Wrong Signal
44. Driving too Fast for Conditions or in Excess of Posted Speed Limit
45. Driving Less than Posted Maximum
46. Operating at Erratic or Suddenly Changing Speeds
47. Making Right Turn from Left-Turn Lane or Making Left Turn from Right-Turn Lane
48. Making Improper Turn
50. Driving Wrong Way on One-Way Trafficway
51. Driving on Wrong Side of Road (*Intentionally or Unintentionally*)
52. Operator Inexperience
53. Unfamiliar with Roadway
54. Stopping in Roadway (*Vehicle Not Abandoned*)
55. Underriding a Parked Truck
56. Improper Tire Pressure
57. Locked Wheel
58. Over Correcting
59. Getting Off/Out of or On/In to Moving Vehicle
60. Getting Off/Out of or On/In to Non-Moving Vehicle

Appendix C

Validation of the Delta Method – Referent = No Alcohol, No Benzodiazepines

Referent = No BZDS, BAC = 0

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																
Columns 1 - 5					Columns 6 - 10					Columns 11 - 15					Columns 16 - 18	
-0.166349	0.13058	0.399856	0.641478	0.855447	1.041761	0.592404	0.649997	0.710922	0.77518	0.842771	0.913694	0.371985	0.503702	0.622552	0.728535	0.821651	0.9019

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-0.166349	0.85	0.2224	0.41	1.28
0.02	Short	0.13058	1.14	0.2596	0.63	1.65
0.04	Short	0.399856	1.49	0.3507	0.80	2.18
0.06	Short	0.641478	1.90	0.4348	1.05	2.75
0.08	Short	0.855447	2.35	0.4941	1.38	3.32
0.1	Short	1.041761	2.83	0.5275	1.80	3.87
0	Intermedial	0.592404	1.81	0.1452	1.52	2.09
0.02	Intermedial	0.649997	1.92	0.1487	1.62	2.21
0.04	Intermedial	0.710922	2.04	0.1785	1.69	2.39
0.06	Intermedial	0.77518	2.17	0.2124	1.75	2.59
0.08	Intermedial	0.842771	2.32	0.2410	1.85	2.80
0.1	Intermedial	0.913694	2.49	0.2610	1.98	3.01
0	Long	0.371985	1.45	0.0958	1.26	1.64
0.02	Long	0.503702	1.65	0.0892	1.48	1.83
0.04	Long	0.622552	1.86	0.0905	1.69	2.04
0.06	Long	0.728535	2.07	0.0964	1.88	2.26
0.08	Long	0.821651	2.27	0.1039	2.07	2.48
0.1	Long	0.9019	2.46	0.1110	2.25	2.68

Predicted Odds from Fitted Line Method

	Y-Log None	Short	ntermediat	Long	Odds Ratio = exp(ylog_b - ylog_a) Short	Difference
0	-0.56	-0.72	0.03	-0.19	0.85	0.01
0.02	-0.35	-0.43	0.09	-0.05	1.14	0.00
0.04	-0.16	-0.16	0.15	0.06	1.49	0.00
0.06	0.02	0.08	0.22	0.17	1.90	0.00
0.08	0.2	0.3	0.28	0.26	2.36	0.01
0.1	0.36	0.48	0.36	0.34	2.83	0.00
					Intermediate	
	-0.56	-0.72	0.03	-0.19	1.80	0.00
	-0.35	-0.43	0.09	-0.05	1.92	0.00
	-0.16	-0.16	0.15	0.06	2.03	0.00
	0.02	0.08	0.22	0.17	2.18	0.01
	0.2	0.3	0.28	0.26	2.32	-0.01
	0.36	0.48	0.36	0.34	2.51	0.02
					Long	
	-0.56	-0.72	0.03	-0.19	1.45	0.00
	-0.35	-0.43	0.09	-0.05	1.67	0.01
	-0.16	-0.16	0.15	0.06	1.86	0.00
	0.02	0.08	0.22	0.17	2.08	0.00
	0.2	0.3	0.28	0.26	2.27	0.00
	0.36	0.48	0.36	0.34	2.46	0.00

Matrix Output of SE's - Use Diagonal

		Columns 1 - 5				Columns 6 - 10					Columns 11 - 15					Columns 16 - 18			
0	Short	0.222371	0.20883	0.195846	0.183536	0.172047	0.161552	0.013455	0.013424	0.013401	0.013386	0.013379	0.01338	0.015004	0.014925	0.014863	0.014821	0.014797	0.014793
0.02	Short	0.20883	0.25955	0.292759	0.314061	0.325801	0.329003	0.013482	0.013736	0.013972	0.014189	0.014388	0.014571	0.014365	0.014435	0.014521	0.014622	0.014739	0.014871
0.04	Short	0.195846	0.292759	0.350715	0.387602	0.409158	0.417763	0.013506	0.014008	0.01446	0.014866	0.01523	0.015554	0.013814	0.014027	0.014251	0.014486	0.01473	0.014984
0.06	Short	0.183536	0.314061	0.387602	0.434151	0.461943	0.474286	0.013526	0.014242	0.014875	0.015436	0.015931	0.016368	0.013361	0.013709	0.01406	0.014414	0.014771	0.015131
0.08	Short	0.172047	0.325801	0.409158	0.461943	0.494056	0.50942	0.013543	0.014439	0.015222	0.015908	0.01651	0.017036	0.013016	0.013485	0.013949	0.014407	0.014861	0.01531
0.1	Short	0.161552	0.329003	0.417763	0.474286	0.50942	0.527454	0.013556	0.014601	0.015505	0.016292	0.016979	0.017575	0.012789	0.013362	0.013921	0.014466	0.014999	0.015521
0	Intermedial	0.013455	0.013482	0.013506	0.013526	0.013543	0.013556	0.14522	0.136143	0.127353	0.118912	0.110901	0.103419	0.019425	0.019085	0.018778	0.018504	0.018266	0.018065
0.02	Intermedial	0.013424	0.013736	0.014008	0.014242	0.014439	0.014601	0.136143	0.148732	0.157725	0.163715	0.167026	0.167818	0.019035	0.018818	0.018633	0.01848	0.018362	0.018278
0.04	Intermedial	0.013401	0.013972	0.01446	0.014875	0.015222	0.015505	0.127353	0.157725	0.178461	0.192697	0.201814	0.206491	0.01869	0.01859	0.01852	0.018481	0.018472	0.018495
0.06	Intermedial	0.013386	0.014189	0.014866	0.015436	0.015908	0.016292	0.118912	0.163715	0.192697	0.212435	0.225371	0.232643	0.018391	0.018401	0.01844	0.018505	0.018597	0.018716
0.08	Intermedial	0.013379	0.014388	0.01523	0.015931	0.01651	0.016979	0.110901	0.167026	0.201814	0.225371	0.241014	0.250231	0.018141	0.018255	0.018393	0.018553	0.018737	0.018942
0.1	Intermedial	0.01338	0.014571	0.015554	0.016368	0.017036	0.017575	0.103419	0.167818	0.206491	0.232643	0.250231	0.260991	0.017943	0.018151	0.018379	0.018626	0.01889	0.019172
0	Long	0.015004	0.014365	0.013814	0.013361	0.013016	0.012789	0.019425	0.019035	0.01869	0.018391	0.018141	0.017943	0.095837	0.090186	0.084667	0.079307	0.074142	0.069214
0.02	Long	0.014925	0.014435	0.014027	0.013709	0.013485	0.013362	0.019085	0.018818	0.01859	0.018401	0.018255	0.018151	0.090186	0.089187	0.087997	0.086608	0.085011	0.083192
0.04	Long	0.014863	0.014521	0.014251	0.01406	0.013949	0.013921	0.018778	0.018633	0.01852	0.01844	0.018393	0.018379	0.084667	0.087997	0.090488	0.092207	0.093198	0.093483
0.06	Long	0.014821	0.014622	0.014486	0.014414	0.014407	0.014466	0.018504	0.01848	0.018481	0.018505	0.018553	0.018626	0.079307	0.086608	0.092207	0.096402	0.099369	0.101218
0.08	Long	0.014797	0.014739	0.01473	0.014771	0.014861	0.014999	0.018266	0.018362	0.018472	0.018597	0.018737	0.01889	0.074142	0.085011	0.093198	0.099369	0.103884	0.106952
0.1	Long	0.014793	0.014871	0.014984	0.015131	0.01531	0.015521	0.018065	0.018278	0.018495	0.018716	0.018942	0.019172	0.069214	0.083192	0.093483	0.101218	0.106952	0.110997

Validation of the Delta Method: Referent = Respective Benzodiazepine

Referent = Either Short, Intermediate or Long BZDS, BAC = 0

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																	
Columns 1 - 5						Columns 6 - 10						Columns 11 - 15					
0	0.29693	0.566205	0.807827	1.021796	1.208111	0	0.057593	0.118519	0.182777	0.250367	0.32129	0	0.131717	0.250567	0.35655	0.449666	0.529915

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	0	1.00	0.0000	1.00	1.00
0.02	Short	0.29693	1.35	0.1720	1.01	1.68
0.04	Short	0.566205	1.76	0.3094	1.16	2.37
0.06	Short	0.807827	2.24	0.4348	1.39	3.10
0.08	Short	1.021796	2.78	0.4841	1.83	3.73
0.1	Short	1.208111	3.35	0.5248	2.32	4.38
0	Intermediat	0	1.00	0.0000	1.00	1.00
0.02	Intermediat	0.057593	1.06	0.0784	0.91	1.21
0.04	Intermediat	0.118519	1.13	0.1432	0.85	1.41
0.06	Intermediat	0.182777	1.20	0.1948	0.82	1.58
0.08	Intermediat	0.250367	1.28	0.2336	0.83	1.74
0.1	Intermediat	0.32129	1.38	0.2604	0.87	1.89
0	Long	0	1.00	0.0000	1.00	1.00
0.02	Long	0.131717	1.14	0.0295	1.08	1.20
0.04	Long	0.250567	1.28	0.0551	1.18	1.39
0.06	Long	0.35655	1.43	0.0768	1.28	1.58
0.08	Long	0.449666	1.57	0.0948	1.38	1.75
0.1	Long	0.529915	1.70	0.1092	1.48	1.91

Predicted Odds from Fitted Line Method

	Y-Log				Odds Ratio = exp(ylog_b - ylog_a)	
	None	Short	ntermediat	Long	Short	Difference
0	-0.56	-0.72	0.03	-0.19	1.00	0.00
0.02	-0.35	-0.43	0.09	-0.05	1.34	-0.01
0.04	-0.16	-0.16	0.15	0.06	1.75	-0.01
0.06	0.02	0.08	0.22	0.17	2.23	-0.02
0.08	0.2	0.3	0.28	0.26	2.77	0.00
0.1	0.36	0.48	0.36	0.34	3.32	-0.03
					Intermediate	
	-0.56	-0.72	0.03	-0.19	1.00	0.00
	-0.35	-0.43	0.09	-0.05	1.06	0.00
	-0.16	-0.16	0.15	0.06	1.13	0.00
	0.02	0.08	0.22	0.17	1.21	0.01
	0.2	0.3	0.28	0.26	1.28	0.00
	0.36	0.48	0.36	0.34	1.39	0.01
					Long	
	-0.56	-0.72	0.03	-0.19	1.00	0.00
	-0.35	-0.43	0.09	-0.05	1.15	0.01
	-0.16	-0.16	0.15	0.06	1.28	0.00
	0.02	0.08	0.22	0.17	1.43	0.00
	0.2	0.3	0.28	0.26	1.57	0.00
	0.36	0.48	0.36	0.34	1.70	0.00

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5					Columns 6 - 10						Columns 11 - 15						Columns 16 - 18					
0 Short	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.02 Short	0	0.172033	0.230632	0.26606	0.287028	0.296619	0	0.002785	0.003859	0.004627	0.005224	0.005706	0	0.002096	0.00295	0.003594	0.004129	0.004592
0.04 Short	0	0.230632	0.309417	0.357271	0.38588	0.3994	0	0.003829	0.005306	0.006361	0.007183	0.007845	0	0.002886	0.004062	0.004949	0.005686	0.006325
0.06 Short	0	0.26606	0.357271	0.412995	0.446716	0.463262	0	0.004552	0.006307	0.007561	0.008538	0.009326	0	0.003437	0.004836	0.005894	0.006771	0.007532
0.08 Short	0	0.287028	0.38588	0.446716	0.484087	0.503248	0	0.005091	0.007054	0.008457	0.009551	0.010433	0	0.003851	0.00542	0.006606	0.00759	0.008443
0.1 Short	0	0.296619	0.3994	0.463262	0.503248	0.524842	0	0.005501	0.007623	0.00914	0.010322	0.011276	0	0.004171	0.00587	0.007155	0.008221	0.009146
0 Intermediat	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.02 Intermediat	0	0.002785	0.003829	0.004552	0.005091	0.005501	0	0.078358	0.105887	0.123355	0.134732	0.141496	0	0.002204	0.003091	0.003755	0.0043	0.004766
0.04 Intermediat	0	0.003859	0.005306	0.006307	0.007054	0.007623	0	0.105887	0.143176	0.16692	0.182483	0.191867	0	0.003057	0.004288	0.005209	0.005965	0.006613
0.06 Intermediat	0	0.004627	0.006361	0.007561	0.008457	0.00914	0	0.123355	0.16692	0.194775	0.213171	0.224446	0	0.003669	0.005148	0.006254	0.007162	0.007941
0.08 Intermediat	0	0.005224	0.007183	0.008538	0.009551	0.010322	0	0.134732	0.182483	0.213171	0.23362	0.246393	0	0.004149	0.005822	0.007073	0.008101	0.008982
0.1 Intermediat	0	0.005706	0.007845	0.009326	0.010433	0.011276	0	0.141496	0.191867	0.224446	0.246393	0.260412	0	0.004538	0.006368	0.007738	0.008864	0.009829
0 Long	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0.02 Long	0	0.002096	0.002886	0.003437	0.003851	0.004171	0	0.002204	0.003057	0.003669	0.004149	0.004538	0	0.029531	0.040327	0.047567	0.052736	0.056406
0.04 Long	0	0.00295	0.004062	0.004836	0.00542	0.00587	0	0.003091	0.004288	0.005148	0.005822	0.006368	0	0.040327	0.055099	0.06503	0.072147	0.077232
0.06 Long	0	0.003594	0.004949	0.005894	0.006606	0.007155	0	0.003755	0.005209	0.006254	0.007073	0.007738	0	0.047567	0.06503	0.076804	0.085278	0.091376
0.08 Long	0	0.004129	0.005686	0.006771	0.00759	0.008221	0	0.0043	0.005965	0.007162	0.008101	0.008864	0	0.052736	0.072147	0.085278	0.094776	0.101666
0.1 Long	0	0.004592	0.006325	0.007532	0.008443	0.009146	0	0.004766	0.006613	0.007941	0.008982	0.009829	0	0.056406	0.077232	0.091376	0.101666	0.109196

Validation of the Delta Method: Referent = Alcohol at 0.02 BAC

Referent = No BZDS, BAC = .02

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																	
Columns 1 - 5					Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
-0.370662	-0.073731981	0.195544	0.437165974	0.651134397	0.837449	0.388091	0.445684	0.50661	0.57	0.638	0.70938132	0.17	0.299389	0.418239	0.524222363	0.617338	0.697588

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-0.370662	0.69	0.2224	0.25	1.13
0.02	Short	-0.073732	0.93	0.2595	0.42	1.44
0.04	Short	0.195544	1.22	0.3507	0.53	1.90
0.06	Short	0.437166	1.55	0.4348	0.70	2.40
0.08	Short	0.651134	1.92	0.4940	0.95	2.89
0.1	Short	0.837449	2.31	0.5274	1.28	3.34
0	Intermediate	0.388091	1.47	0.1452	1.19	1.76
0.02	Intermediate	0.445684	1.56	0.1487	1.27	1.85
0.04	Intermediate	0.50661	1.66	0.1784	1.31	2.01
0.06	Intermediate	0.570868	1.77	0.2124	1.35	2.19
0.08	Intermediate	0.638458	1.89	0.2409	1.42	2.37
0.1	Intermediate	0.709381	2.03	0.2609	1.52	2.54
0	Long	0.167672	1.18	0.0958	0.99	1.37
0.02	Long	0.299389	1.35	0.0892	1.17	1.52
0.04	Long	0.418239	1.52	0.0904	1.34	1.70
0.06	Long	0.524222	1.69	0.0963	1.50	1.88
0.08	Long	0.617338	1.85	0.1038	1.65	2.06
0.1	Long	0.697588	2.01	0.1109	1.79	2.23

Predicted Odds from Fitted Line Method

	Y-Log				Odds Ratio = exp(ylog_b - ylog_a)	
	None	Short	Intermediate	Long	Short	Difference
0	-0.56	-0.72	0.03	-0.2	0.69	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.92	-0.01
0.04	-0.16	-0.16	0.15	0.06	1.21	-0.01
0.06	0.02	0.08	0.22	0.17	1.54	-0.01
0.08	0.2	0.3	0.28	0.26	1.92	0.00
0.1	0.36	0.48	0.36	0.34	2.29	-0.02
					Intermediate	
0	-0.56	-0.72	0.03	-0.2	1.46	-0.01
0.02	-0.35	-0.43	0.09	-0.1	1.55	-0.01
0.04	-0.16	-0.16	0.15	0.06	1.65	-0.01
0.06	0.02	0.08	0.22	0.17	1.77	0.00
0.08	0.2	0.3	0.28	0.26	1.88	-0.02
0.1	0.36	0.48	0.36	0.34	2.03	0.00
					Long	
0	-0.56	-0.72	0.03	-0.2	1.17	-0.01
0.02	-0.35	-0.43	0.09	-0.1	1.35	0.00
0.04	-0.16	-0.16	0.15	0.06	1.51	-0.01
0.06	0.02	0.08	0.22	0.17	1.68	-0.01
0.08	0.2	0.3	0.28	0.26	1.84	-0.01
0.1	0.36	0.48	0.36	0.34	1.99	-0.02

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5				Columns 6 - 10					Columns 11 - 15					Columns 16 - 18			
0 Short	0.222355	0.208796417	0.195794527	0.183467	0.17196	0.161449	0.013311	0.01	0.013	0.01268129	0.01	0.012372	0.014912	0.014728011	0.014564	0.014419	0.014295	0.014191
0.02 Short	0.208796	0.259510203	0.292713217	0.31401	0.325745	0.328942	0.013083	0.01	0.013	0.0132733	0.01	0.013401	0.014029	0.013991979	0.013974	0.013975	0.013995	0.014034
0.04 Short	0.195795	0.292713217	0.35066822	0.387553	0.409106	0.417708	0.012876	0.01	0.014	0.01377933	0.01	0.014255	0.013239	0.013347953	0.013473	0.013613	0.013769	0.01394
0.06 Short	0.183467	0.314010175	0.387552597	0.434102	0.461892	0.474232	0.012692	0.01	0.014	0.01420855	0.01	0.014965	0.012559	0.012809817	0.013071	0.013342	0.013622	0.01391
0.08 Short	0.17196	0.325744735	0.409105699	0.461892	0.494003	0.509365	0.012533	0.01	0.014	0.01456777	0.02	0.01555	0.012007	0.012391375	0.012778	0.013166	0.013555	0.013945
0.1 Short	0.161449	0.328941873	0.41770752	0.474232	0.509365	0.527398	0.012398	0.01	0.014	0.01486205	0.02	0.016023	0.011601	0.012105045	0.012601	0.013089	0.01357	0.014045
0 Intermediate	0.013311	0.013082629	0.012875873	0.012692	0.012533	0.012398	0.145218	0.14	0.127	0.11884908	0.11	0.10331	0.01944	0.019020754	0.018632	0.018277	0.017955	0.017671
0.02 Intermediate	0.013081	0.013146065	0.013204462	0.013256	0.0133	0.013338	0.136122	0.15	0.158	0.16365316	0.17	0.167735	0.018912	0.0186119	0.018343	0.018108	0.017906	0.017741
0.04 Intermediate	0.01287	0.013209623	0.013505001	0.013759	0.013974	0.014152	0.127311	0.16	0.178	0.19263185	0.2	0.206412	0.018434	0.018248863	0.018095	0.017974	0.017885	0.017829
0.06 Intermediate	0.012681	0.013273301	0.013779326	0.014209	0.014568	0.014862	0.118849	0.16	0.193	0.21236556	0.23	0.232563	0.018008	0.017934425	0.01789	0.017876	0.017891	0.017936
0.08 Intermediate	0.012515	0.013337097	0.014028975	0.014609	0.015091	0.015482	0.110815	0.17	0.202	0.22529681	0.24	0.250148	0.01764	0.017671181	0.017729	0.017814	0.017925	0.018061
0.1 Intermediate	0.012372	0.013401009	0.014255244	0.014965	0.01555	0.016023	0.10331	0.17	0.206	0.23256311	0.25	0.260906	0.017333	0.017461447	0.017613	0.017788	0.017985	0.018204
0 Long	0.014912	0.0140294	0.01323932	0.012559	0.012007	0.011601	0.01944	0.02	0.018	0.01800849	0.02	0.017333	0.095846	0.090178076	0.084641	0.079261	0.074073	0.06912
0.02 Long	0.014728	0.013991979	0.013347953	0.01281	0.012391	0.012105	0.019021	0.02	0.018	0.01793442	0.02	0.017461	0.090178	0.089162096	0.087955	0.086548	0.084933	0.083096
0.04 Long	0.014564	0.013973664	0.013472753	0.013071	0.012778	0.012601	0.018632	0.02	0.018	0.01789003	0.02	0.017613	0.084641	0.087954855	0.09043	0.092135	0.093111	0.093381
0.06 Long	0.014419	0.013974531	0.013613276	0.013342	0.013166	0.013089	0.018277	0.02	0.018	0.01787553	0.02	0.017788	0.079261	0.086548351	0.092135	0.096317	0.099273	0.101109
0.08 Long	0.014295	0.013994576	0.013769041	0.013622	0.013555	0.01357	0.017955	0.02	0.018	0.01789099	0.02	0.017985	0.074073	0.084932684	0.093111	0.099273	0.103778	0.106836
0.1 Long	0.014191	0.014033716	0.013939535	0.01391	0.013945	0.014045	0.017671	0.02	0.018	0.01793635	0.02	0.018204	0.06912	0.083095656	0.093381	0.101109	0.106836	0.110872

Validation of the Delta Method: Referent = Alcohol at 0.04 BAC

Referent = No BZDS, BAC = .04

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																	
Columns 1 - 5					Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
-0.56456	-0.267630422	0.001645	0.243267534	0.457235957	0.643551	0.194193	0.251786	0.312711	0.38	0.445	0.51548288	-0	0.105491	0.224341	0.330323923	0.42344	0.503689

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-0.56456	0.57	0.2224	0.13	1.00
0.02	Short	-0.26763	0.77	0.2595	0.26	1.27
0.04	Short	0.001645	1.00	0.3507	0.31	1.69
0.06	Short	0.243268	1.28	0.4348	0.42	2.13
0.08	Short	0.457236	1.58	0.4940	0.61	2.55
0.1	Short	0.643551	1.90	0.5274	0.87	2.94
0	Intermediate	0.194193	1.21	0.1453	0.93	1.50
0.02	Intermediate	0.251786	1.29	0.1488	0.99	1.58
0.04	Intermediate	0.312711	1.37	0.1784	1.02	1.72
0.06	Intermediate	0.376969	1.46	0.2124	1.04	1.87
0.08	Intermediate	0.44456	1.56	0.2409	1.09	2.03
0.1	Intermediate	0.515483	1.67	0.2609	1.16	2.19
0	Long	-0.026226	0.97	0.0960	0.79	1.16
0.02	Long	0.105491	1.11	0.0893	0.94	1.29
0.04	Long	0.224341	1.25	0.0905	1.07	1.43
0.06	Long	0.330324	1.39	0.0964	1.20	1.58
0.08	Long	0.42344	1.53	0.1038	1.32	1.73
0.1	Long	0.503689	1.65	0.1109	1.44	1.87

Predicted Odds from Fitted Line Method

	Y-Log				Odds Ratio = exp(ylog_b - ylog_a)	
	None	Short	Intermediate	Long	Short	Difference
0	-0.56	-0.72	0.03	-0.2	0.57	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.76	0.00
0.04	-0.16	-0.16	0.15	0.06	1.00	0.00
0.06	0.02	0.08	0.22	0.17	1.27	0.00
0.08	0.2	0.3	0.28	0.26	1.58	0.00
0.1	0.36	0.48	0.36	0.34	1.90	-0.01
					Intermediate	
0	-0.56	-0.72	0.03	-0.2	1.21	-0.01
0.02	-0.35	-0.43	0.09	-0.1	1.28	0.00
0.04	-0.16	-0.16	0.15	0.06	1.36	0.00
0.06	0.02	0.08	0.22	0.17	1.46	0.00
0.08	0.2	0.3	0.28	0.26	1.55	-0.01
0.1	0.36	0.48	0.36	0.34	1.68	0.01
					Long	
0	-0.56	-0.72	0.03	-0.2	0.97	0.00
0.02	-0.35	-0.43	0.09	-0.1	1.12	0.01
0.04	-0.16	-0.16	0.15	0.06	1.25	-0.01
0.06	0.02	0.08	0.22	0.17	1.39	0.00
0.08	0.2	0.3	0.28	0.26	1.52	-0.01
0.1	0.36	0.48	0.36	0.34	1.65	-0.01

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5				Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
0 Short	0.222403	0.208832127	0.195817659	0.183478	0.171959	0.161436	0.014213	0.01	0.013	0.013094	0.01	0.012502	0.015755	0.01548563	0.015234	0.015	0.014786	0.014592
0.02 Short	0.208832	0.259526226	0.292717422	0.314006	0.325734	0.328926	0.013761	0.01	0.014	0.01342465	0.01	0.013275	0.0147	0.014562583	0.014444	0.014345	0.014267	0.014208
0.04 Short	0.195818	0.292717422	0.350663381	0.387542	0.40909	0.417688	0.013347	0.01	0.014	0.01371333	0.01	0.013928	0.013737	0.013733395	0.013749	0.013783	0.013835	0.013906
0.06 Short	0.183478	0.314005953	0.387541622	0.434086	0.461872	0.474209	0.012975	0.01	0.014	0.01396265	0.01	0.014478	0.012885	0.013016018	0.013163	0.013324	0.013501	0.013691
0.08 Short	0.171959	0.325733956	0.40908996	0.461872	0.49398	0.509339	0.012647	0.01	0.014	0.01417468	0.01	0.014936	0.012169	0.012429824	0.0127	0.012981	0.01327	0.013567
0.1 Short	0.161436	0.328925682	0.417687761	0.474209	0.509339	0.52737	0.012368	0.01	0.014	0.01435107	0.01	0.01531	0.011614	0.011994064	0.012377	0.012761	0.013148	0.013536
0 Intermediate	0.014213	0.01376112	0.013347146	0.012975	0.012647	0.012368	0.145315	0.14	0.127	0.1189077	0.11	0.103341	0.020176	0.019697182	0.019246	0.018826	0.018439	0.018086
0.02 Intermediate	0.013812	0.013634555	0.013475341	0.013335	0.013215	0.013115	0.136207	0.15	0.158	0.16368006	0.17	0.167739	0.019537	0.019169286	0.018831	0.018524	0.018251	0.018012
0.04 Intermediate	0.013439	0.013522277	0.013597347	0.013664	0.013722	0.013772	0.127383	0.16	0.178	0.19264245	0.2	0.206404	0.01895	0.018691054	0.018462	0.018265	0.0181	0.017968
0.06 Intermediate	0.013094	0.013424645	0.013713328	0.013963	0.014175	0.014351	0.118908	0.16	0.193	0.212365	0.23	0.232547	0.01842	0.018266385	0.018142	0.018049	0.017986	0.017955
0.08 Intermediate	0.012781	0.01334198	0.013823435	0.014233	0.014578	0.014861	0.11086	0.17	0.202	0.22528761	0.24	0.250125	0.017952	0.017899095	0.017875	0.017878	0.017911	0.017971
0.1 Intermediate	0.012502	0.013274561	0.01392781	0.014478	0.014936	0.01531	0.103341	0.17	0.206	0.23254667	0.25	0.260877	0.01755	0.017592775	0.017661	0.017755	0.017874	0.018017
0 Long	0.015755	0.014700277	0.013736762	0.012885	0.012169	0.011614	0.020176	0.02	0.019	0.0184202	0.02	0.01755	0.096003	0.090329044	0.084784	0.079396	0.074199	0.069235
0.02 Long	0.015486	0.014562583	0.013733395	0.013016	0.01243	0.011994	0.019697	0.02	0.019	0.01826639	0.02	0.017593	0.090329	0.089298092	0.088076	0.086655	0.085025	0.083173
0.04 Long	0.015234	0.014444087	0.01374876	0.013163	0.0127	0.012377	0.019246	0.02	0.018	0.01814236	0.02	0.017661	0.084784	0.088076112	0.090532	0.092219	0.093179	0.093435
0.06 Long	0.015	0.014345265	0.013782792	0.013324	0.012981	0.012761	0.018826	0.02	0.018	0.01804875	0.02	0.017755	0.079396	0.086655022	0.092219	0.096383	0.099322	0.101144
0.08 Long	0.014786	0.014266526	0.013835355	0.013501	0.01327	0.013148	0.018439	0.02	0.018	0.01798603	0.02	0.017874	0.074199	0.085024838	0.093179	0.099322	0.103812	0.106856
0.1 Long	0.014592	0.014208203	0.013906238	0.013691	0.013567	0.013536	0.018086	0.02	0.018	0.01795451	0.02	0.018017	0.069235	0.083173268	0.093435	0.101144	0.106856	0.110879

Validation of the Delta Method: Referent = Alcohol at 0.06 BAC

Referent = No BZDS, BAC = .06

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																
Columns 1 - 5					Columns 6 - 10					Columns 11 - 15				Columns 16 - 18		
-0.748045	-0.451115039	-0.181839	0.059782917	0.273751339	0.460066	0.010708	0.068301	0.129227	0.19	0.261	0.33199827	-0.2	-0.077994	0.040856	0.146839306	0.239955	0.320205

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-0.748045	0.47	0.2225	0.04	0.91
0.02	Short	-0.451115	0.64	0.2596	0.13	1.15
0.04	Short	-0.181839	0.83	0.3507	0.15	1.52
0.06	Short	0.059783	1.06	0.4348	0.21	1.91
0.08	Short	0.273751	1.31	0.4940	0.35	2.28
0.1	Short	0.460066	1.58	0.5274	0.55	2.62
0	Intermediate	0.010708	1.01	0.1455	0.73	1.30
0.02	Intermediate	0.068301	1.07	0.1489	0.78	1.36
0.04	Intermediate	0.129227	1.14	0.1785	0.79	1.49
0.06	Intermediate	0.193485	1.21	0.2124	0.80	1.63
0.08	Intermediate	0.261075	1.30	0.2409	0.83	1.77
0.1	Intermediate	0.331998	1.39	0.2609	0.88	1.91
0	Long	-0.209711	0.81	0.0963	0.62	1.00
0.02	Long	-0.077994	0.92	0.0895	0.75	1.10
0.04	Long	0.040856	1.04	0.0907	0.86	1.22
0.06	Long	0.146839	1.16	0.0966	0.97	1.35
0.08	Long	0.239955	1.27	0.1039	1.07	1.47
0.1	Long	0.320205	1.38	0.1110	1.16	1.59

Predicted Odds from Fitted Line Method

Y-Log					Odds Ratio = exp(ylog_b - ylog_a)	
None	Short	Intermediate	Long		Short	Difference
0	-0.56	-0.72	0.03	-0.2	0.48	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.64	0.00
0.04	-0.16	-0.16	0.15	0.06	0.84	0.00
0.06	0.02	0.08	0.22	0.17	1.06	0.00
0.08	0.2	0.3	0.28	0.26	1.32	0.01
0.1	0.36	0.48	0.36	0.34	1.58	0.00
					Intermediate	
0	-0.56	-0.72	0.03	-0.2	1.01	0.00
0.02	-0.35	-0.43	0.09	-0.1	1.07	0.00
0.04	-0.16	-0.16	0.15	0.06	1.14	0.00
0.06	0.02	0.08	0.22	0.17	1.22	0.01
0.08	0.2	0.3	0.28	0.26	1.30	0.00
0.1	0.36	0.48	0.36	0.34	1.40	0.01
					Long	
0	-0.56	-0.72	0.03	-0.2	0.81	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.93	0.01
0.04	-0.16	-0.16	0.15	0.06	1.04	0.00
0.06	0.02	0.08	0.22	0.17	1.16	0.00
0.08	0.2	0.3	0.28	0.26	1.27	0.00
0.1	0.36	0.48	0.36	0.34	1.38	0.00

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5				Columns 6 - 10					Columns 11 - 15				Columns 16 - 18			
0 Short	0.222496	0.208915686	0.1958922	0.183544	0.172017	0.161487	0.015702	0.02	0.015	0.01421924	0.01	0.013409	0.017142	0.016807811	0.016489	0.016187	0.015903	0.015637
0.02 Short	0.208916	0.259581085	0.292756313	0.314034	0.325755	0.328941	0.015083	0.01	0.015	0.01430126	0.01	0.013903	0.015977	0.015758732	0.015558	0.015375	0.015212	0.015068
0.04 Short	0.195892	0.292756313	0.350687708	0.387557	0.4091	0.417693	0.014511	0.01	0.014	0.01437541	0.01	0.01433	0.014905	0.014804292	0.014722	0.014658	0.014614	0.014589
0.06 Short	0.183544	0.314034268	0.387557201	0.434094	0.461875	0.474209	0.013992	0.01	0.014	0.01444181	0.01	0.014696	0.013947	0.013963912	0.013999	0.014052	0.014122	0.01421
0.08 Short	0.172017	0.325754704	0.409099504	0.461875	0.493979	0.509334	0.013532	0.01	0.014	0.01450055	0.01	0.015006	0.013127	0.013259296	0.013407	0.01357	0.013747	0.013938
0.1 Short	0.161487	0.328940841	0.417692866	0.474209	0.509334	0.527362	0.013137	0.01	0.014	0.01455175	0.01	0.015263	0.012472	0.01271304	0.012965	0.013227	0.013499	0.01378
0 Intermediate	0.015702	0.015083056	0.014510982	0.013992	0.013532	0.013137	0.14548	0.14	0.128	0.11905041	0.11	0.103471	0.021352	0.02083028	0.020334	0.019867	0.019429	0.019024
0.02 Intermediate	0.015177	0.014799551	0.014456921	0.014151	0.013885	0.013661	0.136364	0.15	0.158	0.16376848	0.17	0.167804	0.020629	0.020208379	0.019816	0.019453	0.019121	0.018821
0.04 Intermediate	0.014681	0.014538542	0.014411703	0.014301	0.014207	0.014131	0.127533	0.16	0.179	0.19270562	0.2	0.206445	0.019958	0.019638333	0.019347	0.019085	0.018855	0.018656
0.06 Intermediate	0.014219	0.01430126	0.01437541	0.014442	0.014501	0.014552	0.11905	0.16	0.193	0.2124124	0.23	0.232574	0.019347	0.01912478	0.018931	0.018767	0.018633	0.01853
0.08 Intermediate	0.013794	0.014088905	0.014348111	0.014573	0.014766	0.014928	0.110996	0.17	0.202	0.22532382	0.24	0.250144	0.018801	0.018672381	0.018572	0.0185	0.018457	0.018443
0.1 Intermediate	0.013409	0.013902618	0.014329857	0.014696	0.015006	0.015263	0.103471	0.17	0.206	0.23257439	0.25	0.260888	0.018324	0.018285676	0.018273	0.018288	0.018328	0.018395
0 Long	0.017142	0.015977431	0.014905398	0.013947	0.013127	0.012472	0.021352	0.02	0.02	0.01934713	0.02	0.018324	0.096263	0.090588673	0.085044	0.079656	0.074458	0.069494
0.02 Long	0.016808	0.015758732	0.014804292	0.013964	0.013259	0.012713	0.02083	0.02	0.02	0.01912478	0.02	0.018286	0.090589	0.089544455	0.08831	0.086876	0.085234	0.083371
0.04 Long	0.016489	0.015557726	0.01472181	0.013999	0.013407	0.012965	0.020334	0.02	0.019	0.01893104	0.02	0.018273	0.085044	0.088309706	0.090744	0.092412	0.093355	0.093595
0.06 Long	0.016187	0.015375108	0.014658267	0.014052	0.01357	0.013227	0.019867	0.02	0.019	0.01876679	0.02	0.018288	0.079656	0.0868763	0.092412	0.096553	0.099473	0.101279
0.08 Long	0.015903	0.01521154	0.01461391	0.014122	0.013747	0.013499	0.019429	0.02	0.019	0.01863282	0.02	0.018328	0.074458	0.085234217	0.093355	0.099473	0.103943	0.106971
0.1 Long	0.015637	0.015067643	0.014588913	0.01421	0.013938	0.01378	0.019024	0.02	0.019	0.01852978	0.02	0.018395	0.069494	0.083371127	0.093595	0.101279	0.106971	0.110978

Validation of the Delta Method: Referent = Alcohol at 0.08 BAC

Referent = No BZDS, BAC = .08

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)																	
Columns 1 - 5					Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
-0.921115	-0.624185833	-0.35491	-0.11328788	0.100680545	0.286995	-0.162363	-0.10477	-0.043844	0.02	0.088	0.15892747	-0.4	-0.251065	-0.132215	-0.026231488	0.066885	0.147134

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-0.921115	0.40	0.2226	-0.04	0.83
0.02	Short	-0.624186	0.54	0.2597	0.03	1.04
0.04	Short	-0.35491	0.70	0.3507	0.01	1.39
0.06	Short	-0.113288	0.89	0.4348	0.04	1.75
0.08	Short	0.100681	1.11	0.4940	0.14	2.07
0.1	Short	0.286995	1.33	0.5274	0.30	2.37
0	Intermediate	-0.162363	0.85	0.1457	0.56	1.14
0.02	Intermediate	-0.10477	0.90	0.1491	0.61	1.19
0.04	Intermediate	-0.043844	0.96	0.1786	0.61	1.31
0.06	Intermediate	0.020414	1.02	0.2125	0.60	1.44
0.08	Intermediate	0.088005	1.09	0.2410	0.62	1.56
0.1	Intermediate	0.158927	1.17	0.2609	0.66	1.68
0	Long	-0.382782	0.68	0.0966	0.49	0.87
0.02	Long	-0.251065	0.78	0.0899	0.60	0.95
0.04	Long	-0.132215	0.88	0.0910	0.70	1.05
0.06	Long	-0.026231	0.97	0.0968	0.78	1.16
0.08	Long	0.066885	1.07	0.1041	0.87	1.27
0.1	Long	0.147134	1.16	0.1111	0.94	1.38

Predicted Odds from Fitted Line Method

	Y-Log				Odds Ratio = exp(ylog_b - ylog_a)	
	None	Short	Intermediate	Long	Short	Difference
0	-0.56	-0.72	0.03	-0.2	0.40	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.53	0.00
0.04	-0.16	-0.16	0.15	0.06	0.70	0.00
0.06	0.02	0.08	0.22	0.17	0.89	-0.01
0.08	0.2	0.3	0.28	0.26	1.11	0.00
0.1	0.36	0.48	0.36	0.34	1.32	-0.01
					Intermediate	
0	-0.56	-0.72	0.03	-0.2	0.84	-0.01
0.02	-0.35	-0.43	0.09	-0.1	0.90	0.00
0.04	-0.16	-0.16	0.15	0.06	0.95	-0.01
0.06	0.02	0.08	0.22	0.17	1.02	0.00
0.08	0.2	0.3	0.28	0.26	1.08	-0.01
0.1	0.36	0.48	0.36	0.34	1.17	0.00
					Long	
0	-0.56	-0.72	0.03	-0.2	0.68	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.78	0.00
0.04	-0.16	-0.16	0.15	0.06	0.87	-0.01
0.06	0.02	0.08	0.22	0.17	0.97	0.00
0.08	0.2	0.3	0.28	0.26	1.06	-0.01
0.1	0.36	0.48	0.36	0.34	1.15	-0.01

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5				Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
0 Short	0.222617	0.209029913	0.195999832	0.183646	0.172113	0.161579	0.017427	0.02	0.016	0.01567988	0.02	0.014711	0.018762	0.01838068	0.018013	0.017659	0.017321	0.017
0.02 Short	0.20903	0.25966097	0.292817653	0.314084	0.325796	0.328976	0.016685	0.02	0.016	0.01555433	0.02	0.014954	0.017527	0.017245973	0.016981	0.016732	0.0165	0.016287
0.04 Short	0.196	0.292817653	0.35073099	0.38759	0.409126	0.417714	0.015997	0.02	0.016	0.01544353	0.02	0.01517	0.016387	0.016207785	0.016046	0.015902	0.015776	0.015669
0.06 Short	0.183646	0.314083715	0.387590095	0.434118	0.461893	0.474222	0.01537	0.02	0.015	0.01534782	0.02	0.015359	0.015363	0.015285793	0.015226	0.015185	0.015162	0.015157
0.08 Short	0.172113	0.325795987	0.409125582	0.461893	0.493991	0.509343	0.014813	0.01	0.015	0.01526746	0.02	0.015523	0.01448	0.014502178	0.014542	0.014599	0.014672	0.014762
0.1 Short	0.161579	0.328976465	0.417714265	0.474222	0.509343	0.527367	0.014333	0.01	0.015	0.01520271	0.02	0.015661	0.013764	0.013880394	0.014012	0.014159	0.014319	0.014494
0 Intermediate	0.017427	0.016684944	0.01599677	0.01537	0.014813	0.014333	0.145687	0.14	0.128	0.11924689	0.11	0.103662	0.022743	0.022189987	0.021661	0.021158	0.020683	0.020237
0.02 Intermediate	0.016811	0.016279976	0.015794073	0.015357	0.014974	0.014649	0.136567	0.15	0.158	0.16389648	0.17	0.167907	0.021954	0.021494084	0.021059	0.020652	0.020273	0.019925
0.04 Intermediate	0.016227	0.015902438	0.015609445	0.01535	0.015126	0.014938	0.127732	0.16	0.179	0.19280277	0.2	0.206519	0.02122	0.020851585	0.020509	0.020195	0.01991	0.019655
0.06 Intermediate	0.01568	0.015554327	0.015443533	0.015348	0.015267	0.015203	0.119247	0.16	0.193	0.21249087	0.23	0.232631	0.020547	0.02026757	0.020015	0.019791	0.019595	0.01943
0.08 Intermediate	0.015173	0.015237661	0.015296948	0.015351	0.0154	0.015443	0.11119	0.17	0.202	0.22538954	0.24	0.250189	0.01994	0.019747228	0.019581	0.019443	0.019332	0.01925
0.1 Intermediate	0.014711	0.014954436	0.015170249	0.015359	0.015523	0.015661	0.103662	0.17	0.207	0.23263089	0.25	0.260925	0.019406	0.019295711	0.019212	0.019154	0.019122	0.019118
0 Long	0.018762	0.017527299	0.016387131	0.015363	0.01448	0.013764	0.022743	0.02	0.021	0.02054679	0.02	0.019406	0.096586	0.090916675	0.085377	0.079994	0.074802	0.069843
0.02 Long	0.018381	0.017245973	0.016207785	0.015286	0.014502	0.01388	0.02219	0.02	0.021	0.02026757	0.02	0.019296	0.090917	0.089860456	0.088614	0.08717	0.085518	0.083646
0.04 Long	0.018013	0.016980535	0.016045769	0.015226	0.014542	0.014012	0.021661	0.02	0.021	0.02001527	0.02	0.019212	0.085377	0.088614367	0.091025	0.092673	0.093599	0.093825
0.06 Long	0.017659	0.016731742	0.015901613	0.015185	0.014599	0.014159	0.021158	0.02	0.02	0.01979093	0.02	0.019154	0.079994	0.087170264	0.092673	0.096789	0.099689	0.101478
0.08 Long	0.017321	0.016500347	0.015775808	0.015162	0.014672	0.014319	0.020683	0.02	0.02	0.0195955	0.02	0.019122	0.074802	0.085518117	0.093599	0.099689	0.104136	0.107147
0.1 Long	0.017	0.016287091	0.015668795	0.015157	0.014762	0.014494	0.020237	0.02	0.02	0.01942986	0.02	0.019118	0.069843	0.0836456	0.093825	0.101478	0.107147	0.111135

Validation of the Delta Method: Referent = Alcohol at 0.10 BAC

Referent = No BZDS, BAC = .10

Log of Odds Ratio taken from Matrix Output

log of odds (B^D)

Columns 1 - 5					Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
-1.083772	-0.786842804	-0.517567	-0.27594485	-0.06197643	0.124338	-0.32502	-0.267426	-0.206501	-0.14	-0.07	-0.0037295	-0.5	-0.413722	-0.294872	-0.188888459	-0.095772	-0.015523

Odds Ratios and SE/CI's from Delta Method (Uses above and below Matrix Output)

		Odds Ratio	S.E.	Lower	Upper
0	Short	-1.083772	0.34	0.2228	-0.10	0.77
0.02	Short	-0.786843	0.46	0.2598	-0.05	0.96
0.04	Short	-0.517567	0.60	0.3508	-0.09	1.28
0.06	Short	-0.275945	0.76	0.4348	-0.09	1.61
0.08	Short	-0.061976	0.94	0.4940	-0.03	1.91
0.1	Short	0.124338	1.13	0.5274	0.10	2.17
0	Intermediate	-0.32502	0.72	0.1459	0.44	1.01
0.02	Intermediate	-0.267426	0.77	0.1492	0.47	1.06
0.04	Intermediate	-0.206501	0.81	0.1788	0.46	1.16
0.06	Intermediate	-0.142243	0.87	0.2126	0.45	1.28
0.08	Intermediate	-0.074652	0.93	0.2411	0.46	1.40
0.1	Intermediate	-0.00373	1.00	0.2610	0.48	1.51
0	Long	-0.545439	0.58	0.0969	0.39	0.77
0.02	Long	-0.413722	0.66	0.0902	0.48	0.84
0.04	Long	-0.294872	0.74	0.0913	0.57	0.92
0.06	Long	-0.188888	0.83	0.0971	0.64	1.02
0.08	Long	-0.095772	0.91	0.1044	0.70	1.11
0.1	Long	-0.015523	0.98	0.1113	0.77	1.20

Predicted Odds from Fitted Line Method

Y-Log					Odds Ratio = exp(ylog_b - ylog_a)	
None	Short	Intermediate	Long		Short	Difference
0	-0.56	-0.72	0.03	-0.2	0.34	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.45	0.00
0.04	-0.16	-0.16	0.15	0.06	0.59	0.00
0.06	0.02	0.08	0.22	0.17	0.76	0.00
0.08	0.2	0.3	0.28	0.26	0.94	0.00
0.1	0.36	0.48	0.36	0.34	1.13	0.00
					Intermediate	
0	-0.56	-0.72	0.03	-0.2	0.72	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.76	0.00
0.04	-0.16	-0.16	0.15	0.06	0.81	0.00
0.06	0.02	0.08	0.22	0.17	0.87	0.00
0.08	0.2	0.3	0.28	0.26	0.92	0.00
0.1	0.36	0.48	0.36	0.34	1.00	0.00
					Long	
0	-0.56	-0.72	0.03	-0.2	0.58	0.00
0.02	-0.35	-0.43	0.09	-0.1	0.66	0.00
0.04	-0.16	-0.16	0.15	0.06	0.74	0.00
0.06	0.02	0.08	0.22	0.17	0.83	0.00
0.08	0.2	0.3	0.28	0.26	0.90	0.00
0.1	0.36	0.48	0.36	0.34	0.98	0.00

Matrix Output of SE's - Use Diagonal

	Columns 1 - 5				Columns 6 - 10					Columns 11 - 15					Columns 16 - 18		
0 Short	0.222755	0.209161834	0.196126716	0.183768	0.172232	0.161695	0.019185	0.02	0.018	0.01723548	0.02	0.016147	0.02043	0.020010958	0.019604	0.019211	0.018831	0.018466
0.02 Short	0.209162	0.259755452	0.292892198	0.314146	0.32585	0.329024	0.018347	0.02	0.017	0.01694247	0.02	0.016182	0.019144	0.018812758	0.018496	0.018195	0.017909	0.01764
0.04 Short	0.196127	0.292892198	0.350785512	0.387633	0.409162	0.417745	0.017571	0.02	0.017	0.01667931	0.02	0.016216	0.017955	0.017713694	0.017488	0.017279	0.017086	0.016912
0.06 Short	0.183768	0.314145678	0.387633326	0.434151	0.46192	0.474245	0.016862	0.02	0.017	0.01644742	0.02	0.016248	0.016886	0.016733313	0.016597	0.016478	0.016377	0.016294
0.08 Short	0.172232	0.325849502	0.409161582	0.46192	0.494012	0.50936	0.016231	0.02	0.016	0.01624815	0.02	0.016278	0.01596	0.015893592	0.015844	0.015812	0.015797	0.015799
0.1 Short	0.161695	0.329024332	0.417745485	0.474245	0.50936	0.52738	0.015688	0.02	0.016	0.01608271	0.02	0.016307	0.015203	0.015217835	0.015249	0.015297	0.01536	0.01544
0 Intermediate	0.019185	0.018347423	0.017570532	0.016862	0.016231	0.015688	0.145918	0.14	0.128	0.11947425	0.11	0.103891	0.024201	0.023623229	0.023068	0.022537	0.022032	0.021555
0.02 Intermediate	0.018498	0.017847323	0.017249013	0.016709	0.016233	0.015927	0.136796	0.15	0.158	0.1640475	0.17	0.168034	0.02336	0.022867134	0.022398	0.021955	0.021538	0.02115
0.04 Intermediate	0.017847	0.01737815	0.016951511	0.016571	0.016239	0.015959	0.12796	0.16	0.179	0.19291981	0.2	0.206611	0.022575	0.022165785	0.021782	0.021424	0.021093	0.020791
0.06 Intermediate	0.017235	0.016942472	0.01667931	0.016447	0.016248	0.016083	0.119474	0.16	0.193	0.21258766	0.23	0.232705	0.021851	0.021524533	0.021223	0.020948	0.0207	0.020481
0.08 Intermediate	0.016667	0.016542936	0.016433669	0.01634	0.016261	0.016199	0.111418	0.17	0.202	0.22547275	0.24	0.25025	0.021196	0.020948898	0.020727	0.020531	0.020362	0.020221
0.1 Intermediate	0.016147	0.01618222	0.016215793	0.016248	0.016278	0.016307	0.103891	0.17	0.207	0.23270453	0.25	0.260977	0.020616	0.020444423	0.020298	0.020177	0.020082	0.020014
0 Long	0.02043	0.019143538	0.017955314	0.016886	0.01596	0.015203	0.024201	0.02	0.023	0.02185119	0.02	0.020616	0.096945	0.091282701	0.085751	0.080376	0.075193	0.070243
0.02 Long	0.020011	0.018812758	0.017713694	0.016733	0.015894	0.015218	0.023623	0.02	0.022	0.02152453	0.02	0.020444	0.091283	0.090215402	0.088959	0.087505	0.085844	0.083964
0.04 Long	0.019604	0.01849627	0.017487896	0.016597	0.015844	0.015249	0.023068	0.02	0.022	0.02122309	0.02	0.020298	0.085751	0.088958981	0.091346	0.092974	0.093883	0.094094
0.06 Long	0.019211	0.018194821	0.017278542	0.016478	0.015812	0.015297	0.022537	0.02	0.021	0.02094794	0.02	0.020177	0.080376	0.087505292	0.092974	0.097063	0.099942	0.101714
0.08 Long	0.018831	0.01790917	0.017086236	0.016377	0.015797	0.01536	0.022032	0.02	0.021	0.02070013	0.02	0.020082	0.075193	0.085844314	0.093883	0.099942	0.104366	0.107358
0.1 Long	0.018466	0.017640085	0.016911559	0.016294	0.015799	0.01544	0.021555	0.02	0.021	0.02048066	0.02	0.020014	0.070243	0.083963745	0.094094	0.101714	0.107358	0.111327

Table 1

Behavioural Areas and Tasks Affected by Alcohol

Domain	Included Tasks	No. of Studies	Sensitivity
Cognitive Tasks	Digit-symbol substitution, mathematical and verbal reasoning, memory, pattern recognition, visual backward masking, card sorting	31 (diverse)	0.005 mg/100 ml
Critical Flicker Fusion	Critical Flicker Fusion		0.1 mg/100 ml
Divided Attention	Simultaneous performance of two or more tasks such as tracking, visual search, number monitoring, and detection of auditory stimuli.	18	0.005 mg/100 ml
Driving Skills	Actual and simulated driving	25	0.001 mg/100 ml
Drowsiness	Multiple sleep latency test, repeated test of sustained wakefulness.		0.01 mg/100 ml
Perception	Detection of visual and/or auditory stimuli, time estimation, traffic hazard perception, anticipation time		0.037 mg/100 ml
Psychomotor tasks	Finger tapping, body balance, hand steadiness, drill press operation, assembly of electronic parts	18	0.06 mg/100 ml (finger tapping); 0.04 mg/100 ml (body balance); 0.049 mg/100 ml (skilled physical tasks)
Reaction time - Choice	Choice reaction time, choice reaction time with auditory distraction.		0.06 mg/100 ml

Domain	Included Tasks	No. of Studies	Sensitivity
Reaction time - Simple	Single known stimulus with a single response	5	Concluded to be an insensitive measure due to inconsistent results.
Tracking	Pursuit tracking, compensatory tracking, critical tracking		Ranging from 0.018 (adaptive tracking) to 0.054 (pursuit tracking)
Vigilance	Sustained attention (including some auditory and visual tests)		0.03 mg/100 ml
Visual Functions	Contrast sensitivity, depth perception, smooth pursuit, saccadic peak velocity, saccadic latency, saccadic inaccuracy, nystagmus, etc.	19	0.03 mg/100 ml

Note. From "A Review of the Literature on the Effects of Low Doses of Alcohol on Driving-Related Skills," by H. Moskowitz and D. Fiorentino, 2000, *National Highway Traffic Safety Administration* (Report No. DOT HS 809 028).

Table 2

Benzodiazepine Detections Amongst Drivers Apprehended under the Suspicion of Impairment

Authors, Year	Country	Sample Size	Rate of positive BZD detections
Appenzeller et al., 2002	Luxemburg	210	10.9%
Augsberger et al., 2005	Switzerland	440	13%
Augsberger & Rivier, 1997	Switzerland	641	15%
Christopherson et al., 1999	Scandinavia	800	9.5% – 24%
Ledingham, 1999	Scotland	75	40%
Lillsunde et al., 1996	Finland	298 (in 1979) 332 (in 1993)	6% (in 1979) 23% (in 1993)
Seymour & Oliver, 1999	Scotland	752	48%
Skurtveit et al., 2002	Norway	3343	30%

Table 3

Commonly Prescribed Benzodiazepines

BZD	Market Aim	Half-Life in Hours [Active Metabolite]
Alprazolam	Anxiolytic	6-12
Clonazepam	Anxiolytic	10-20
Clorazepate	Anxiolytic; Anticonvulsant	[36-100]
Diazepam	Anxiolytic; Hypnotic; Anticonvulsant; Muscle Relaxant	20-100 [36-200]
Estazolam	Hypnotic	10-24
Flunitrazepam	Hypnotic	18-26 [36-200]
Flurazepam	Hypnotic	[40-250]
Lorazepam	Anxiolytic; Anticonvulsant	10-20
Midazolam	Hypnotic	3 [1.8-6]
Oxazepam	Anxiolytic	4-15
Pinazepam	Sedative	[40-100]
Prazepam	Anxiolytic	[36-200]
Quazepam	Hypnotic	25-100
Temazepam	Hypnotic	8-33

Note.
Adapted from *Benzodiazepines: How They Work and How to Withdrawal. AKA the Ashton Manual*, by C. H. Ashton, 2002, Retrieved February 2, 2007, from http://www.benzo.org.uk/ bzequiv.htm. Copyright 2007 by C. H. Ashton.

Adapted from "Benzodiazepines—Effect on Human Performance and Behaviour," by O. H. Drummer, 2002, *Forensic Science Review, 14*, p. 2. Copyright 2002 by Central Police University Press.

Table 4

Demographic Information by Group

Characteristic	Alcohol and BZD Free (N=70,440)	Alcohol Only (N=43,366)	BZDs Only			BZDs + Alcohol			F/χ^2 **	*p* Value
			Short (N=174)	Intermediate (N=419)	Long (N=932)	Short (N=60)	Intermediate (N=210)	Long (N=909)		
Age, Mean	45.95	35.33	43.73	42.77	43.79	36.17	37.87	37.61	1497.66	<.001
Male, No (%)	45,622 (64.8)	35,887 (82.8)	114 (65.5)	256 (61.1)	595 (63.8)	52 (86.7)	156 (74.3)	706 (77.7)	4344.19	<.001
Previous Driver History, No. (%)										
Crashes	10,276 (14.6)	6,953 (16.0)	15 (8.6)	87 (20.8)	195 (20.9)	4 (6.7)	39 (18.6)	218 (24.0)	142.12	<.001
DWI	1,191 (1.7)	4,508 (10.4)	5 (2.9)	35 (8.4)	77 (8.3)	4 (6.7)	34 (16.2)	138 (15.2)	4442.90	<.001
Other Convictions	11,081 (15.7)	10,006 (23.2)	30 (17.2)	118 (28.2)	176 (18.9)	17 (28.3)	58 (27.6)	185 (20.4)	1032.16	<.001
Speeding	13,303 (18.9)	10,333 (23.8)	42 (24.1)	119 (28.4)	192 (20.6)	13 (21.7)	58 (27.6)	200 (22.0)	420.27	<.001
License Suspension	7,023 (10.0)	11,266 (26.0)	17 (9.8)	90 (21.5)	184 (19.7)	14 (23.3)	68 (32.4)	250 (27.5)	5210.87	<.001
Any of Above	27,634 (42.5)	23,559 (54.3)	74 (42.5)	241 (57.5)	470 (50.4)	31 (51.7)	135 (64.3)	534 (58.7)	2607.02	<.001
Other Medications, No (%)										
Depressant	1,354 (1.9)	749 (1.7)	15 (8.6)	15 (8.6)	80 (19.1)	2 (3.3)	40 (19.0)	569 (62.6)	23280.06	<.001
Narcotic	2,265 (3.2)	868 (2.0)	16 (9.2)	128 (30.5)	204 (21.9)	9 (15.0)	26 (12.4)	84 (9.2)	2555.69	<.001
Stimulant	3,975 (5.6)	4,163 (9.6)	16 (9.2)	81 (19.3)	108 (11.6)	11 (18.3)	24 (11.4)	115 (12.7)	796.14	<.001
Cannabinoid	2,778 (3.9)	3,592 (8.3)	9 (5.2)	34 (8.1)	63 (6.8)	2 (3.3)	33 (15.7)	74 (8.1)	1006.42	<.001
Other	5,230 (7.4)	3,165 (7.3)	56 (32.2)	133 (31.7)	631 (67.7)	23 (38.3)	70 (33.3)	614 (67.5)	9096.49	<.001
Any of Above	11,877 (16.9)	10,025 (23.1)	85 (48.9)	296 (70.6)	789 (84.7)	27 (61.7)	123 (58.6)	734 (80.7)	6098.62	<.001

**F-statistic given for age; Chi Square value given for sex

Table 5

Alcohol Plus Benzodiazepine Baseline Effects: Odds Ratios with 95% CI for Performing an UDA Compared to an Alcohol- and Benzodiazepine-Free Referent Group

BAC					
0.00	0.02	0.04	0.06	0.08	0.10
Short BZDs Plus Alcohol					
0.85 (0.41; 1.28)	1.14 (0.63; 1.65)	1.49 (0.80; 2.18)	1.90 (1.05; 2.75)	2.35 (1.38; 3.32)	2.83 (1.80; 3.87)
Intermediate BZDs Plus Alcohol					
1.81 (1.52; 2.09)	1.92 (1.62; 2.21)	2.04 (1.69; 2.39)	2.17 (1.75; 2.59)	2.32 (1.85; 2.80)	2.49 (1.98; 3.01)
Long BZDs Plus Alcohol					
1.45 (1.26; 1.64)	1.65 (1.48; 1.83)	1.86 (1.69; 2.04)	2.07 (1.88; 2.26)	2.27 (2.07; 2.48)	2.46 (2.25; 2.68)

Table 6

Alcohol Plus Benzodiazepine Additive Effects: Odds Ratios with 95% CI for Performing an UDA Compared to Alcohol Only and Benzodiazepine Only Referent Groups

	BAC					
Referent	0.00	0.02	0.04	0.06	0.08	0.10
	Short BZDs Plus Alcohol					
Alcohol	0.85 (0.41; 1.28)	0.93 (0.42; 1.44)	1.00 (0.31; 1.69)	1.06 (0.21; 1.91)	1.11 (0.14; 2.07)	1.13 (0.10; 2.17)
Short BZDs	1.00 (1.00; 1.00)	1.35 (1.01; 1.68)	1.76 (1.16; 2.37)	2.24 (1.39; 3.10)	2.78 (1.83; 3.73)	3.35 (2.32; 4.38)
	Intermediate BZDs Plus Alcohol					
Alcohol	1.81 (1.52; 2.09)	1.56 (1.27; 1.85)	1.37 (1.02; 1.72)	1.21 (0.80; 1.63)	1.09 (0.62; 1.56)	1.00 (0.48; 1.51)
Intermediate BZDs	1.00 (1.00; 1.00)	1.06 (0.91; 1.21)	1.13 (0.85; 1.41)	1.20 (0.82; 1.58)	1.28 (0.83; 1.74)	1.38 (0.87; 1.89)
	Long BZDs Plus Alcohol					
Alcohol	1.45 (1.26; 1.64)	1.35 (1.17; 1.52)	1.25 (1.07; 1.43)	1.16 (0.97; 1.35)	1.07 (0.87; 1.27)	0.98 (0.77; 1.20)
Long BZDs	1.00 (1.00; 1.00)	1.14 (1.08; 1.20)	1.28 (1.18; 1.39)	1.43 (1.28; 1.58)	1.57 (1.38; 1.75)	1.70 (1.48; 1.91)

Table 8

Regression Model

	B	S.E.	Wald	df	Sig.	Exp(B)	95.0% C.I.for EXP(B)	
	Lower	Upper	Lower	Upper	Lower	Upper	Lower	Upper
BZD			31.527	3	0.000			
BZD (Short)	-0.166	0.222	0.560	1	0.454	0.847	0.548	1.309
BZD (Intermediate)	0.592	0.145	16.641	1	0.000	1.808	1.360	2.404
BZD (Long)	0.372	0.096	15.066	1	0.000	1.451	1.202	1.750
BAC	0.105	0.002	2318.162	1	0.000	1.110	1.106	1.115
BAC2	-0.001	0.000	371.522	1	0.000	0.999	0.999	0.999
Sex	-0.064	0.021	9.376	1	0.002	0.938	0.901	0.977
Age	0.009	0.008	1.242	1	0.265	1.009	0.994	1.024
Ag 2	0.076	0.004	399.357	1	0.000	1.079	1.071	1.087
BAC x BZD			8.548	3	0.036			
BAC x BZD (Short)	0.051	0.095	0.285	1	0.593	1.052	0.874	1.267
BAC x BZD (Intermediate)	-0.077	0.043	3.246	1	0.072	0.926	0.852	1.007
BAC x BZD (Long)	-0.036	0.016	5.056	1	0.025	0.965	0.935	0.995
BAC x Age	-0.003	0.001	13.947	1	0.000	0.997	0.996	0.999
BAC x Age 2	-0.003	0.000	56.706	1	0.000	0.997	0.996	0.998
BAC2 x BZD			1.428	3	0.699			
BAC2 x BZD (Short)	-0.002	0.005	0.219	1	0.640	0.998	0.989	1.007
BAC2 x BZD (Intermediate)	0.002	0.002	0.894	1	0.344	1.002	0.998	1.005
BAC2 x BZD (Long)	0.000	0.001	0.310	1	0.577	1.000	0.999	1.001
Age x Sex	-0.078	0.009	72.278	1	0.000	0.925	0.909	0.942
Age2 x Sex	0.017	0.005	13.858	1	0.000	1.017	1.008	1.026
Age x BZD			1.483	3	0.686			
Age x BZD (Short)	0.027	0.091	0.088	1	0.767	1.027	0.860	1.227
Age x BZD (Intermediate)	0.083	0.071	1.344	1	0.246	1.086	0.945	1.249
Age x BZD (Long)	-0.009	0.040	0.049	1	0.824	0.991	0.916	1.072
Age2 x BZD			13.852	3	0.003			
Age2 x BZD (Short)	0.012	0.048	0.065	1	0.799	1.012	0.921	1.112
Age2 x BZD (Intermediate)	-0.020	0.036	0.301	1	0.583	0.980	0.913	1.053
Age2 x BZD (Long)	-0.077	0.021	13.503	1	0.000	0.926	0.888	0.965
Depressant	0.460	0.057	66.205	1	0.000	1.584	1.418	1.769
Narcotic	0.278	0.041	46.188	1	0.000	1.321	1.219	1.431
Stimulant	0.617	0.031	401.205	1	0.000	1.854	1.745	1.969
Cannabinoid	0.053	0.032	2.734	1	0.098	1.055	0.990	1.124
Other Medications	0.095	0.030	10.126	1	0.001	1.100	1.037	1.166
Prev Accident (any)			75.504	3	0.000			
Prev Accident (1)	0.133	0.022	38.074	1	0.000	1.142	1.095	1.192
Prev Accident (2)	0.268	0.049	30.310	1	0.000	1.307	1.188	1.438
Prev Accident (3+)	0.357	0.095	14.061	1	0.000	1.429	1.186	1.723
Prev DWI (any number)			1.345	3	0.719			
Prev DWI (1)	-0.047	0.045	1.123	1	0.289	0.954	0.874	1.041
Prev DWI (2)	-0.058	0.107	0.295	1	0.587	0.944	0.766	1.163
Prev DWI (3 or more)	-0.050	0.242	0.042	1	0.837	0.952	0.592	1.529
Prev Speeding (any)			19.759	3	0.000			
Prev Speeding (1)	0.048	0.020	5.491	1	0.019	1.049	1.008	1.091
Prev Speeding (2)	0.078	0.035	4.880	1	0.027	1.082	1.009	1.159
Prev Speeding (3+)	0.180	0.051	12.622	1	0.000	1.197	1.084	1.323
Prev License Suspension (any)			126.846	3	0.000			
Prev License Suspension (1)	0.228	0.029	61.049	1	0.000	1.256	1.186	1.330
Prev License Suspension (2)	0.294	0.045	43.457	1	0.000	1.342	1.230	1.465
Prev License Suspension (3+)	0.347	0.044	60.751	1	0.000	1.414	1.296	1.543
Prev Other Driver History (any)			30.453	3	0.000			
Prev Other Driver History (1)	0.085	0.022	15.311	1	0.000	1.089	1.043	1.137
Prev Other Driver History (2)	0.110	0.041	7.282	1	0.007	1.116	1.031	1.209
Prev Other Driver History (3+)	0.205	0.055	13.728		0.000	1.227	1.101	1.368
Constant	0.095	0.018	28.471		0.000	1.100		

Table 7

Previous Driver History: Odds Ratios with 95% CI for Performing an UDA Based on Driving Record

	Number of Records		
		2	3+
Crashes	1.14 (1.09; 1.19)	1.30 (1.19; 1.44)	1.43 (1.19; 1.72)
DWI	0.95 (0.87; 1.04)	0.94 (0.77; 1.16)	0.95 (0.59; 1.53)
Other Convictions	1.09 (1.04; 1.14)	1.12 (1.03; 1.21)	1.23 (1.10; 1.37)
Speeding	1.05 (1.01; 1.09)	1.08 (1.01; 1.16)	1.20 (1.08; 1.32)
License Suspension	1.26 (1.19; 1.33)	1.34 (1.23; 1.47)	1.41 (1.30; 1.54)

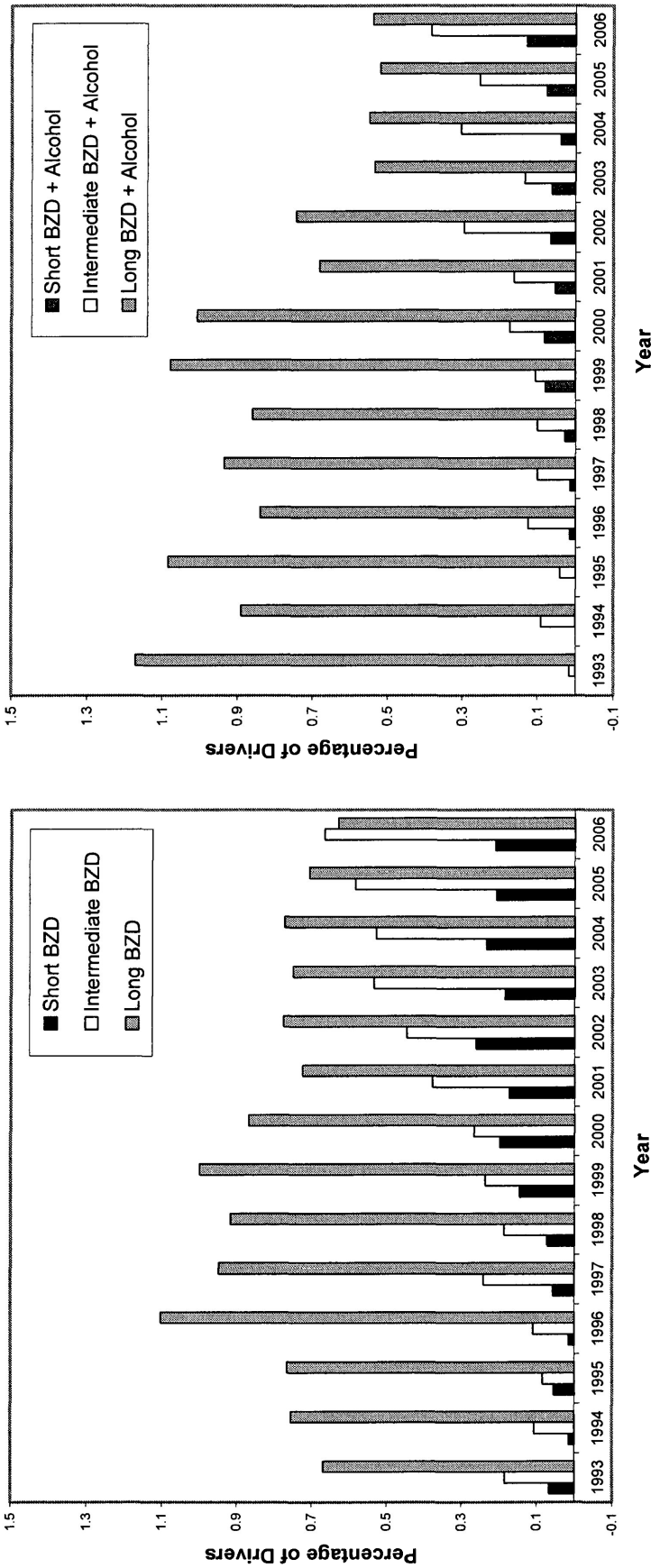

Figure 1. The Prevalence of Benzodiazepine and Alcohol Plus Benzodiazepine Detections over Time

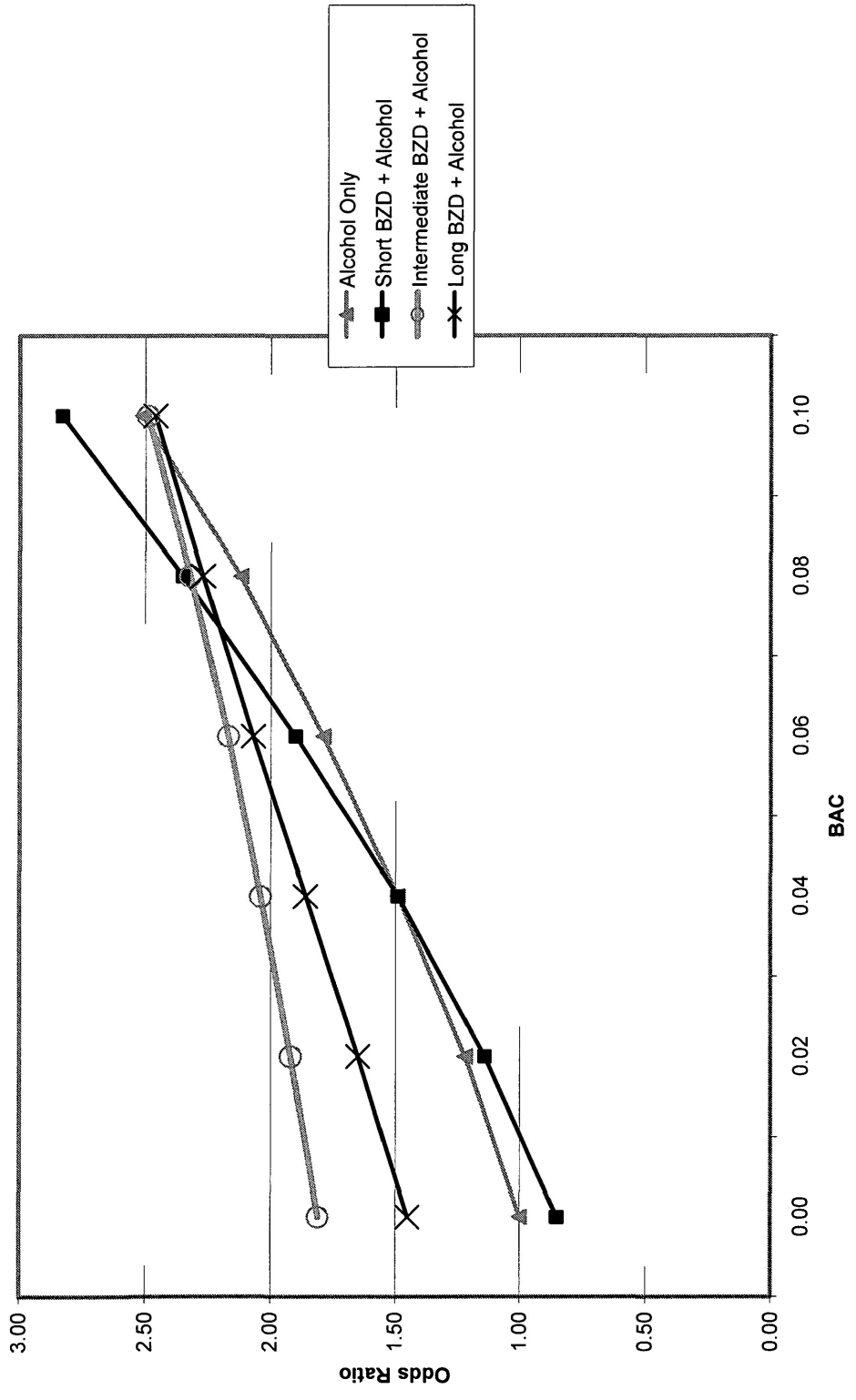

Figure 2. Odds Ratios for Committing an UDA Compared to the Alcohol- and Benzodiazepine-Free Referent Group

Figure 3. The Odds of Committing an UDA at 0.04 BAC Plus Benzodiazepines for Various Age Groups Compared to the Alcohol- and Benzodiazepine-Free Referent Group.