Supplementary Information

The Impact of Untreated Attention-Deficit/Hyperactivity Disorder on Motor Vehicle Accidents: A Systematic Review and Meta-analysis

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Methodology

Primary Objective

Research Question: What is the association between driving with untreated ADHD and traffic accidents?

Research Design: Systematic Literature Review

Primary Independent Variable: Untreated ADHD drivers versus a "normal" cohort (the general driving population).

Primary Dependent Variable: Odds ratio associated with having a traffic accident.

Studies were included in a systematic literature review that observed populations of individuals between the ages of 18 and 65 with diagnosed, but untreated, ADHD being compared with normal controls.

The systematic literature review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

We conducted an online PubMed search with the following primary MeSH terms:

"Attention Deficit Disorder with Hyperactivity" "Sleepiness", "Epidemiology", "Automobile Driving" "Distracted Driving" OR "Driving Under the Influence" "Aggressive Driving" OR "Automobiles" ("accidents, traffic"), "Odds Ratio" AND "female" OR "male".

A total of 57 studies were obtained from PubMed when the following filters were applied:

- Male and Female
- Age: Adult: 18-44 years
- Middle Aged + Aged: 45+ years
- Middle Aged: 45-65 years

We also searched additional databases including Simon Fraser University Library https://www.lib.sfu.ca/, and Google Scholar (15/Nov/2023) with keywords ADHD AND driving AND Accidents AND Risk. A total of 125 articles from SFU library and 7 records were identified through Google Scholar and from searching reference lists of included studies and relevant reviews. After removing duplicates (24), citations were then screened by title and abstract. We included case-control observational studies that reported the number of untreated ADHD population who were involved in car accidents compared to those without ADHD in the general population.

Exclusions were made according to the following criteria:

- Absence of comparative control (e.g., comparing to the general population).
- Abstract was not available.

- Studies published in languages other than English.
- Inability to extract or calculate the number of untreated ADHD/accident or control population/accident.
- Inclusion of subjects younger than 18 years old and older than 65.
- Studies reporting all male or all female subjects.

A total of 23 citations were retrieved using this method. After conducting a final thorough quality review of these 23 complex articles, we made further exclusions based on the following:

- Studies where a small percentage of the ADHD cohort was taking ADHD medications, and the data from untreated patients were not separated. Other medications, including anti-depression or substance use, were not excluded.
- Studies not stating physician/clinically diagnosed ADHD, a history of one or more previous diagnoses, or diagnosis based on DSM or ICD criteria.
- Studies reporting *only* ADHD self-diagnosis with the validated and frequently used Adult ADHD Self-Report Scale (ASRS) questionnaire, even if the results were evaluated by a trained researcher.

A total of 4 studies satisfied all criteria and were included in the meta-analysis.

Secondary Objective

We followed the same process as we did for untreated ADHD to determine the increased incidence of auto accidents associated with the well-known risk factors of cannabis use, sleepiness/fatigue, use of illicit drugs, alcohol consumption, speeding, and the distractions caused by cell phone use and texting.

Search from PubMed was done using Accidents, Traffic Mesh for each of the following individual risk factors: “Driving Under the Influence"; "Distracted Driving"; "Cell Phone”; “Alcoholic Intoxication"; “Illicit Drugs”; “Marijuana Abuse”; “Cannabis”; “Marijuana”; “Prescriptions”; “Medications”; Fatigue"; “Drowsiness”; and “Speeding**”.**

A total of 555 articles were retrieved using this method. After removing the duplicates, articles were initially screened based on title and abstract and 191 articles kept for further examination. We included systematic reviews and meta-analysis with the following inclusion criteria:

- Male and female from the general population
- Age 18-65 years
- Worldwide publications from 1990 to present
- Odds ratios with confidence intervals reported as statistical measurements, and car accidents associated with risk factors as the outcome.

In the first screening round, a total of 190 articles remained for further examination.

Studies were excluded based on the following criteria:

- Unavailable abstract
- Language other than English

In the second screening, a total of 83 articles remained for examination, and after removing more studies with the wrong design and/or methodology (e.g. observational studies, randomized controlled trials, OR (95% CI) not reported, or not associated with risk factors for car accidents), 21 articles remained and screened further for all inclusion criteria.

Alcohol Sub-Analysis

Articles were obtained by searching several databases on Sep 6th, 2024, including PubMed, SFU Library, Google Scholar, the Accident & Analysis Prevention journal, Traffic Injury Prevention, Journal of Safety Research, Transportation Research, Drug and Alcohol Dependence (through ScienceDirect), Centers for Disease Control and Prevention (CDC), and the National Highway Traffic Safety Administration (NHTSA).

Search from PubMed was done using the following Mesh and keywords:

- **"Accidents, Traffic"[Mesh] AND "Alcoholic Intoxication" OR "Blood Alcohol Content"[Mesh] OR "Driving Under the Influence"[Mesh]**
- **"Accidents, Traffic"[Mesh] OR driving AND "Alcoholic Intoxication" OR "Blood Alcohol Content"[Mesh] OR "Driving Under the Influence"[Mesh] OR AUD**
- **"Accidents, Traffic"[Mesh] AND "Alcoholic Intoxication"[Mesh]**
- **"Accidents, Traffic"[Mesh] AND drunk driving**
- **"Accidents, Traffic"[Mesh] AND "Blood Alcohol Content"[Mesh]**
- **"Accidents, Traffic"[Mesh] AND "Driving Under the Influence"[Mesh]**
- **Alcohol-Related Traffic Accident**
- **Ethyl alcohol AND Ethanol AND Impaired driving**
- **Alcohol Use Disorder AND Driving AND Accidents**
- **"Accidents, Traffic"[Mesh] AND Alcohol Use Disorder**

Filters *initially* applied were as follows:

- Systematic review
- Review
- Meta-analysis

- Male and Female
- Age: Adult: 19-44 years
- Middle Aged + Aged: 45+ years
- Middle Aged: 45-64 years
- Year:1990 – 2024
- English language

A combination of keywords was used to search other databases as follows: **Drunk; drunkenness; alcohol; Motor Vehicle Crash (MVC); ethyl alcohol; ethanol; Alcohol-Related Traffic Accident; Blood Alcohol Concentration (BAC); Driving License; Drunk Driving, Alcohol-Impaired Driving; alcohol use disorder (AUD); crash; fatal; injury; accident; Driving While Intoxicated (DWI); meta-analysis**
A total of 553 articles were retrieved using this method. After removing the duplicates, we made the initial selection by titles. Studies whose titles clearly indicated they were not related to the subject were discarded. This led to 68 articles that were retained for further examination.

In the second step, the analysis of the abstracts excluded studies with the wrong design (e.g., prevalence, RTC, cross-sectional), and 57 review papers were kept for further examination. The references of these review papers were also examined so that other papers that had not been identified through the employed search strategy could be located. We removed review articles (17) and included ONLY systematic reviews where authors performed meta-analysis (40). The inclusion criteria were as follows:

- Male and female from the general population
- Age 21-65 years
- Worldwide publications from 1990 to present
- Systematic reviews with meta-analysis reported odd ratios (OR) with a 95% confidence interval (95% CI) as statistical measurement and car accidents associated with alcohol risk factor as the outcome.
- Studies having a control group without the risk factor

Following the inclusion criteria, we identified **2 systematic reviews with meta-analysis** and **chose 3 observational studies** from them that met the age range of 21-65 and control group requirements.

References
Systematic reviews and meta-analysis:
1. Pelletti G, Boscolo-Berto R, Anniballi L, Giorgetti A, Pirani F, Cavallaro M, Giorgini L, Fais P, Pascali JP, Pelotti S. Prevalence of alcohol-impaired driving: a systematic review with a

gender-driven approach and meta-analysis of gender differences. Int J Legal Med. 2024 Jul 26. doi: 10.1007/s00414-024-03291-3. Epub ahead of print. PMID: 39060442.
2. Taylor B, Rehm J. The relationship between alcohol consumption and fatal motor vehicle injury: high risk at low alcohol levels. Alcohol Clin Exp Res. 2012 Oct;36(10):1827-34. doi: 10.1111/j.1530-0277.2012.01785.x. Epub 2012 May 7. PMID: 22563862; PMCID: PMC3433627.

Observational studies used in our analysis:

1. Kuypers KP, Legrand SA, Ramaekers JG, Verstraete AG. A case-control study estimating accident risk for alcohol, medicines and illegal drugs. PLoS One. 2012;7(8):e43496. doi: 10.1371/journal.pone.0043496. Epub 2012 Aug 28. PMID: 22952694; PMCID: PMC3429508.
2. Santoyo-Castillo D, Pérez-Núñez R, Borges G, Híjar M. Estimating the drink driving attributable fraction of road traffic deaths in Mexico. Addiction. 2018 May;113(5):828-835. doi: 10.1111/add.14153. Epub 2018 Feb 1. PMID: 29274185.
3. Zador PL, Krawchuk SA, Voas RB. Alcohol-related relative risk of driver fatalities and driver involvement in fatal crashes in relation to driver age and gender: an update using 1996 data. J Stud Alcohol. 2000 May;61(3):387-95. doi: 10.15288/jsa.2000.61.387. PMID: 10807209.

Additional Background Information on Risk Factors

Alcohol

Several studies have shown that, in addition to its psychopharmacological effects, alcohol interacts with existing personality factors, such as hostility, resulting in a greater expression of aberrant behaviors, and hence, increases the risk of accidents [51-53]. Consistently, problem drinkers and alcoholics were found to drive more recklessly after drinking than social drinkers [54] and drinking habits and attitudes were found to be stable determinants of drunken driving [55].

Speeding

Excessive speeding causes others using the road to misjudge the intentions of the speeding driver. Several aspects should be considered in the relationship between speed and auto accidents. One of the most important is that, as speed increases, so does the distance traveled

during the driver's reaction time and the distance needed to avoid an obstacle or stop. Moreover, higher speeds increase instability and risk when approaching a curve. At an intersection higher speed decreases the likelihood that the driver will be able to take evasive action in an emergency situation when another vehicle is in the way [1].

Cell Phone Use

A wealth of research has shown that driver distraction, and in particular, mobile phone use, raises the risk of road traffic collisions [56-58]. Driver distraction is a risk factor for crash injury and death, and cell phones are a major cause of such distraction. Most adolescents, for example, own a cell phone and use it frequently. A recent study estimated that 63% of teens report exchanging daily text messages and 30% report sending and receiving 100 or more text messages each day. Cell phone use during driving causes visual, manual, and cognitive distraction and slows driver reaction time. Despite perceiving that using a cell phone while driving is hazardous, both younger and older adolescents continue to engage in this behavior. An estimated 75% of college students report using a cell phone while driving [59].

Chi-square tests and logistic regression analyses showed that the frequency, not the duration, of drivers' talking while driving was related to accidents or near accidents [7].

Texting

Texting is a related technology that further compromises the driver. Pew Research Center studies reveal that the median number of teen texts per day is 50, and a third of teens text more than 100 times per day. In comparison with cell phone use while driving, 47% of adults and more than 50% of teens admit to texting while driving [6].

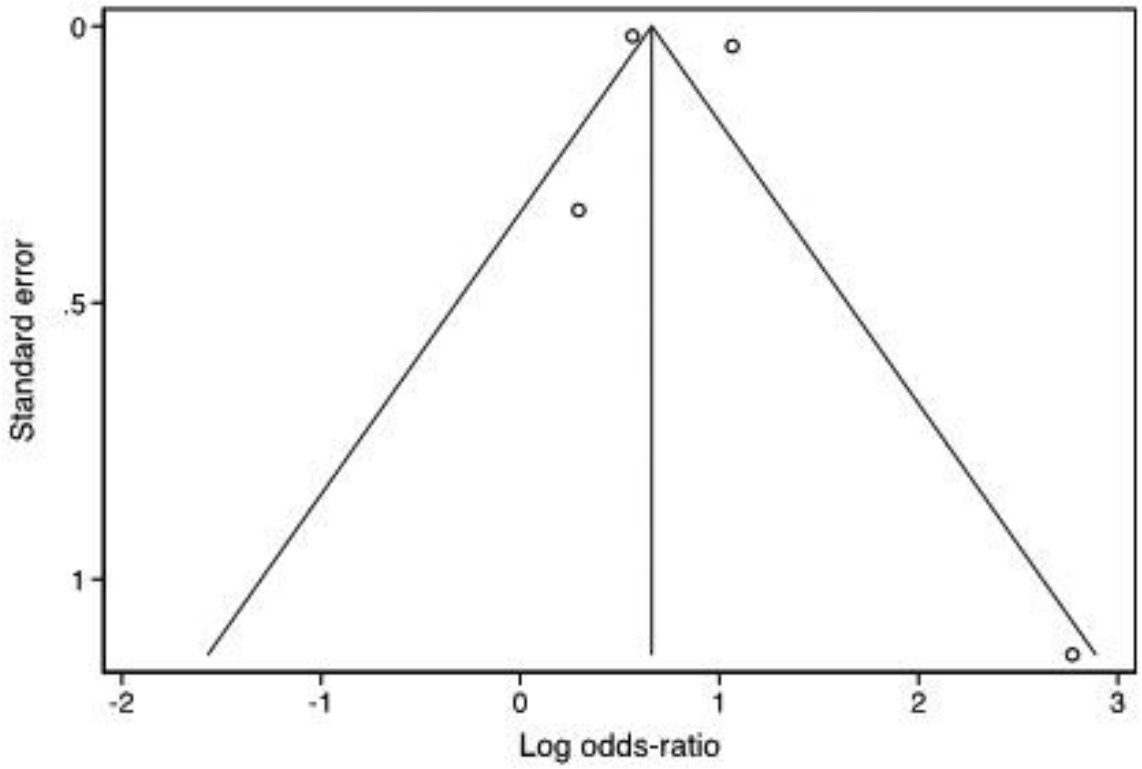
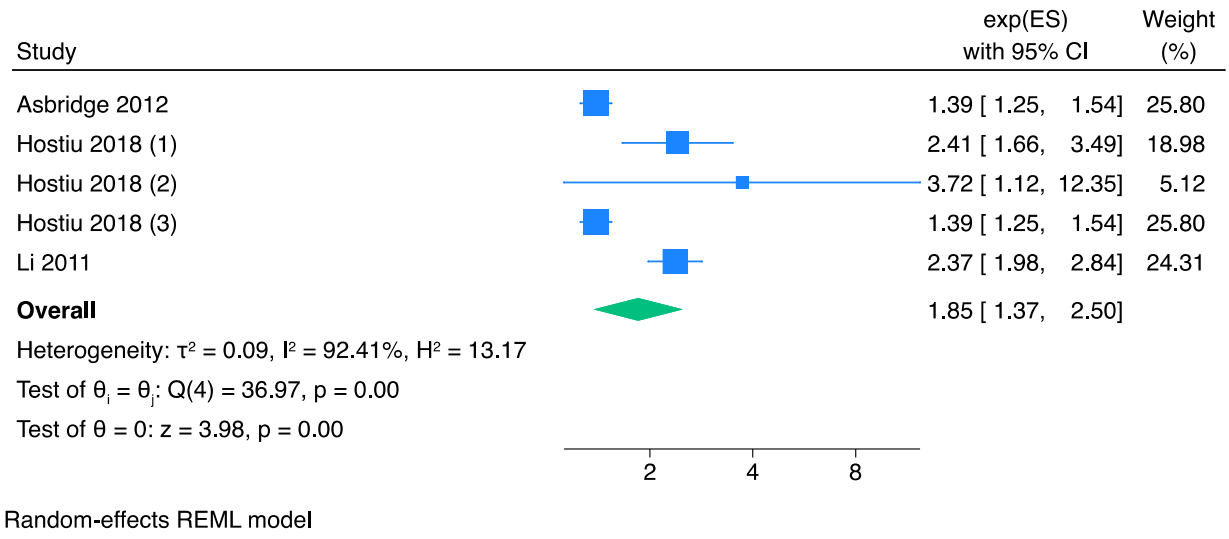


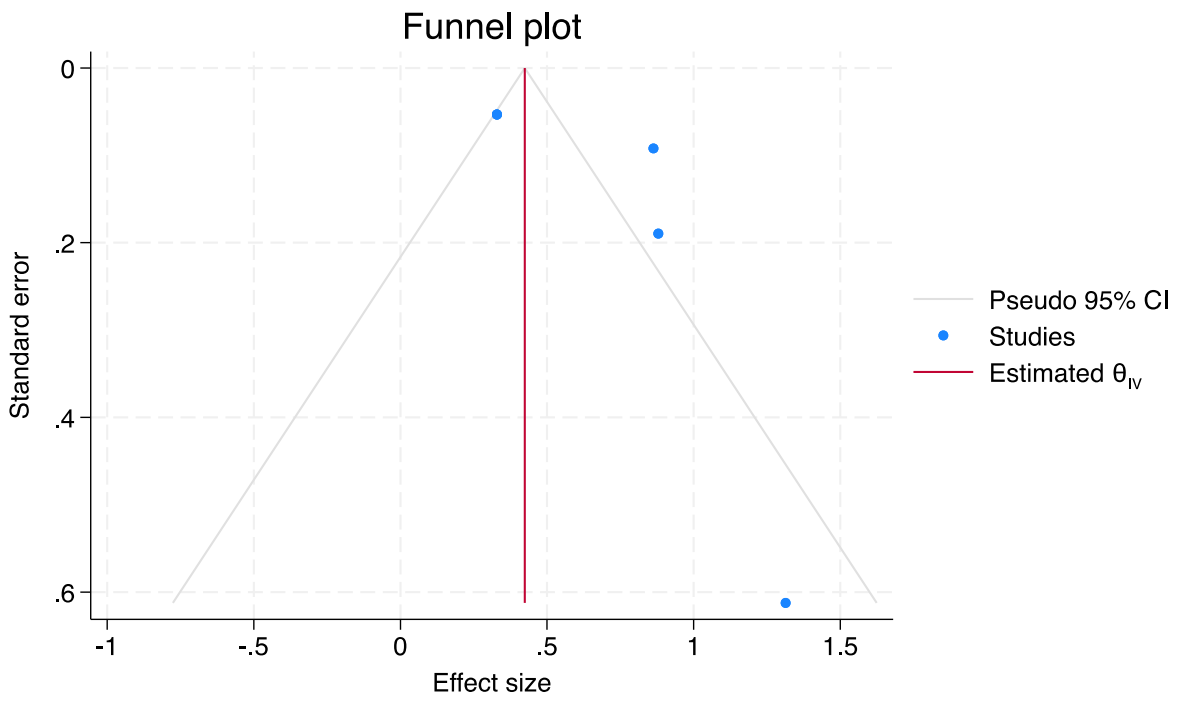
Figure 1. Funnel Plot of Heterogeneity of Results Across Studies

The funnel plot deals with publication bias. Circles represent each study included in the analysis. The vertical line represents the overall effect from the meta-analysis, and the diagonal lines display the confidence intervals. The top 2 circles represent the Chang articles, having the largest study populations and the greatest statistical power. With four studies included in the analysis, and the two Chang articles representing 99% of the pooled effect, there is no publication bias.

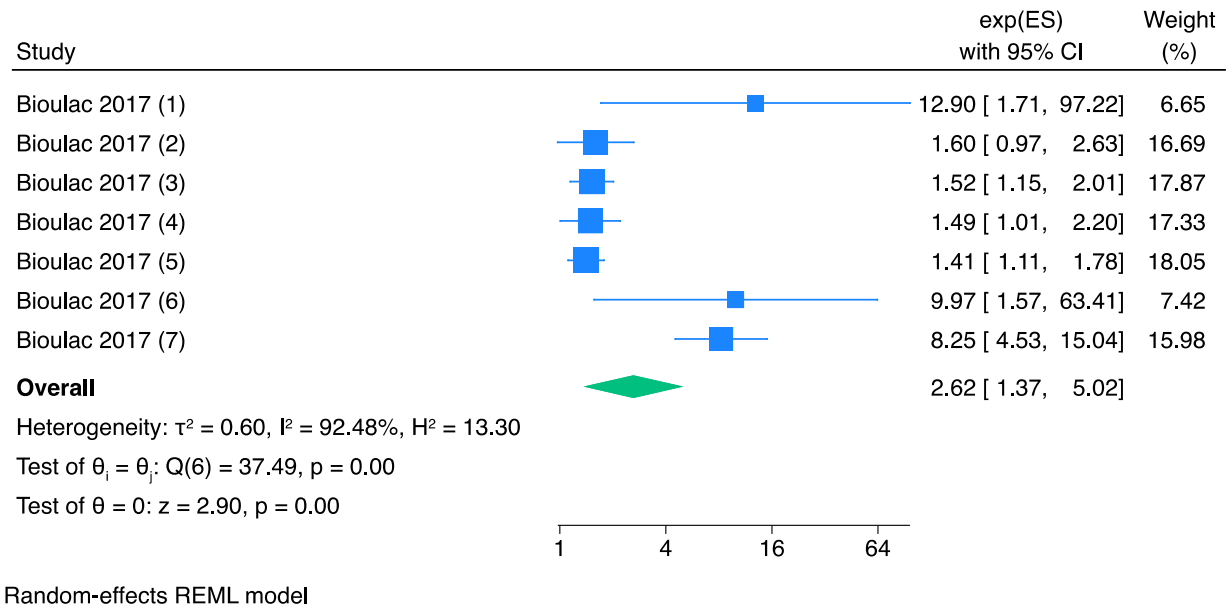


Drivers using THC/cannabis had 1.85 times higher odds of an accident (95% CI 1.37-2.50)

Supplemental Figure 2. THC/Cannabis Use Forest Plot.

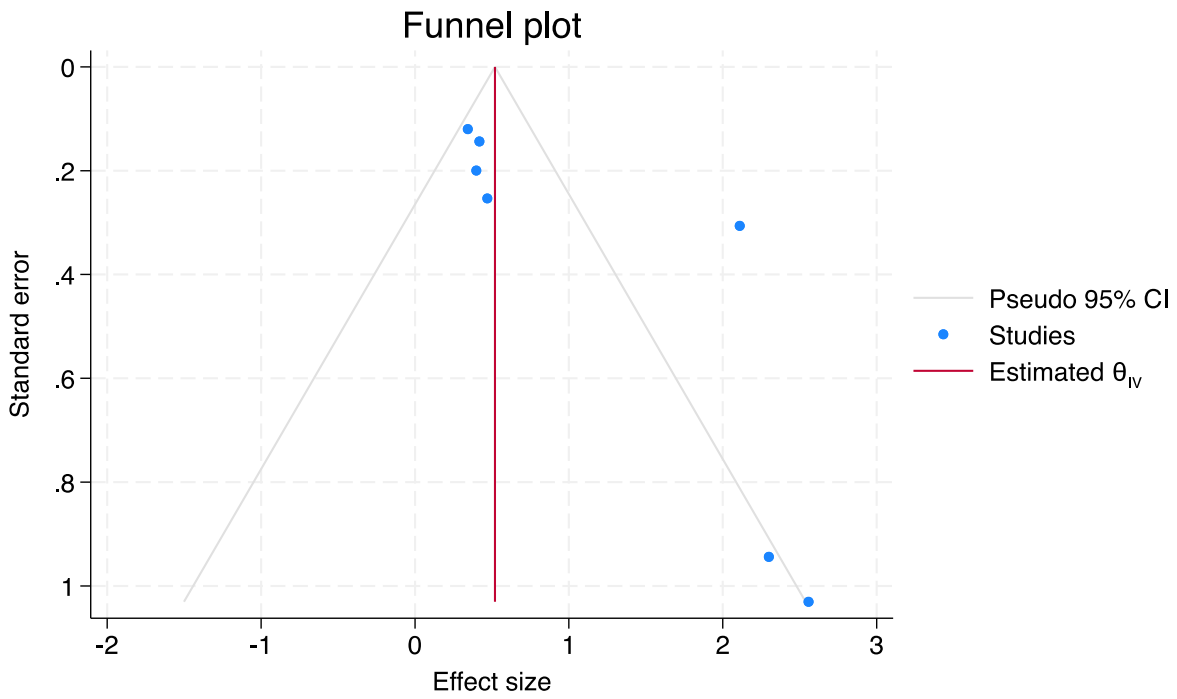


Supplemental Figure 3. THC/Cannabis Use Funnel Plot

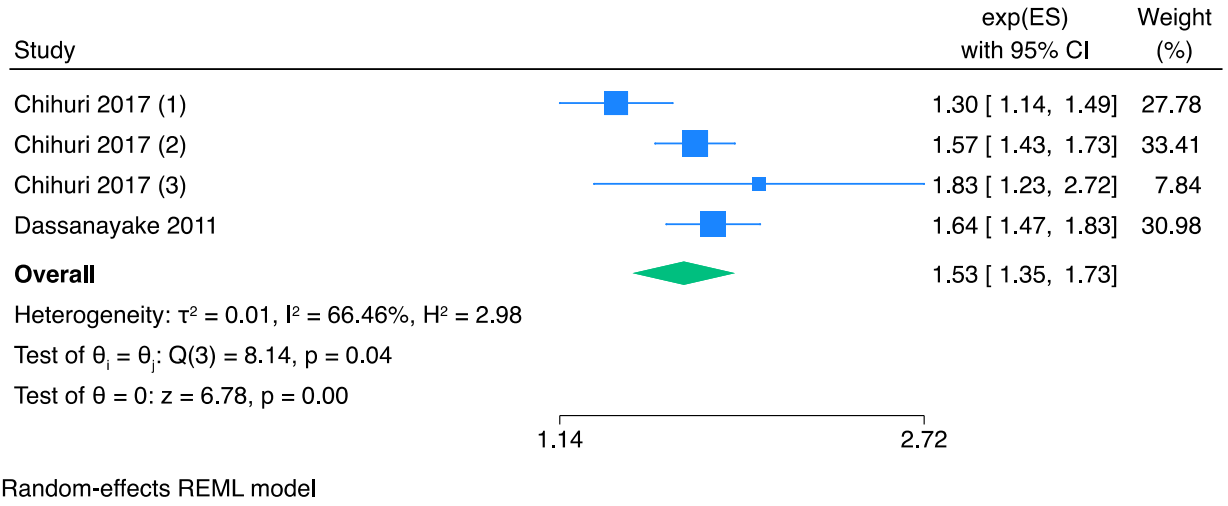


Sleepy/fatigued drivers had 2.62 higher odds of an accident (95% CI 1,37-5.02)

Supplemental Figure 4. Sleepiness/Fatigue Forest Plot

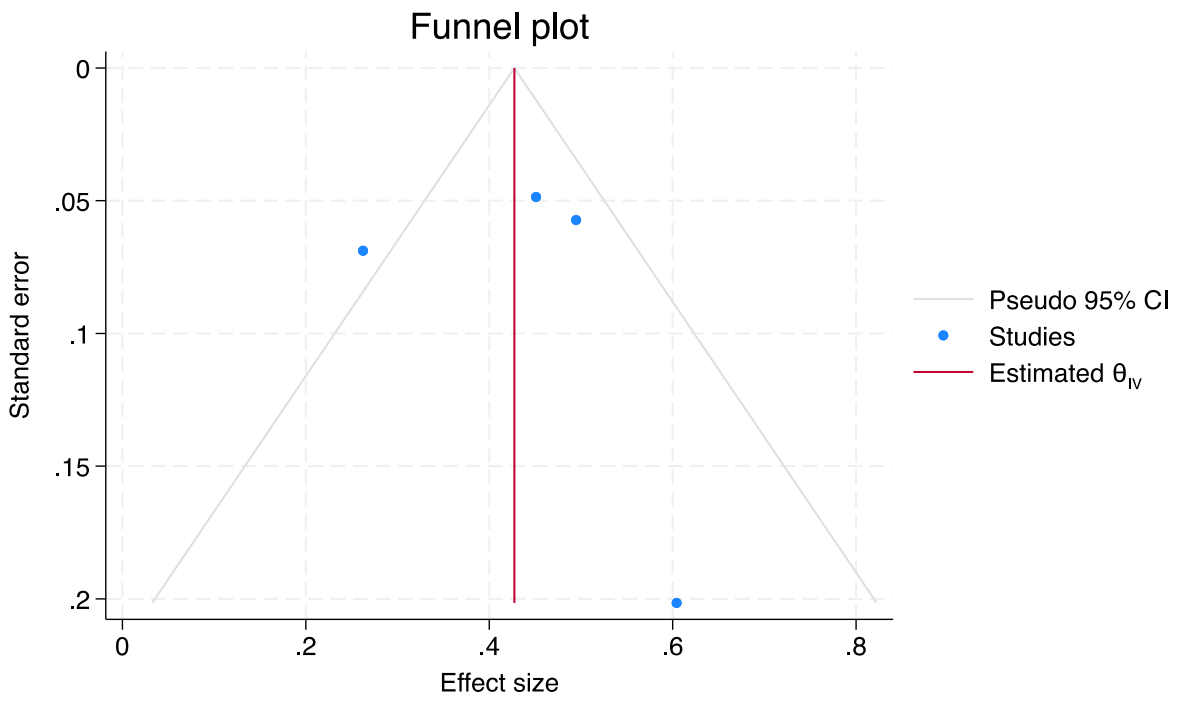


Supplemental Figure 5. Sleepiness/Fatigue Funnel Plot

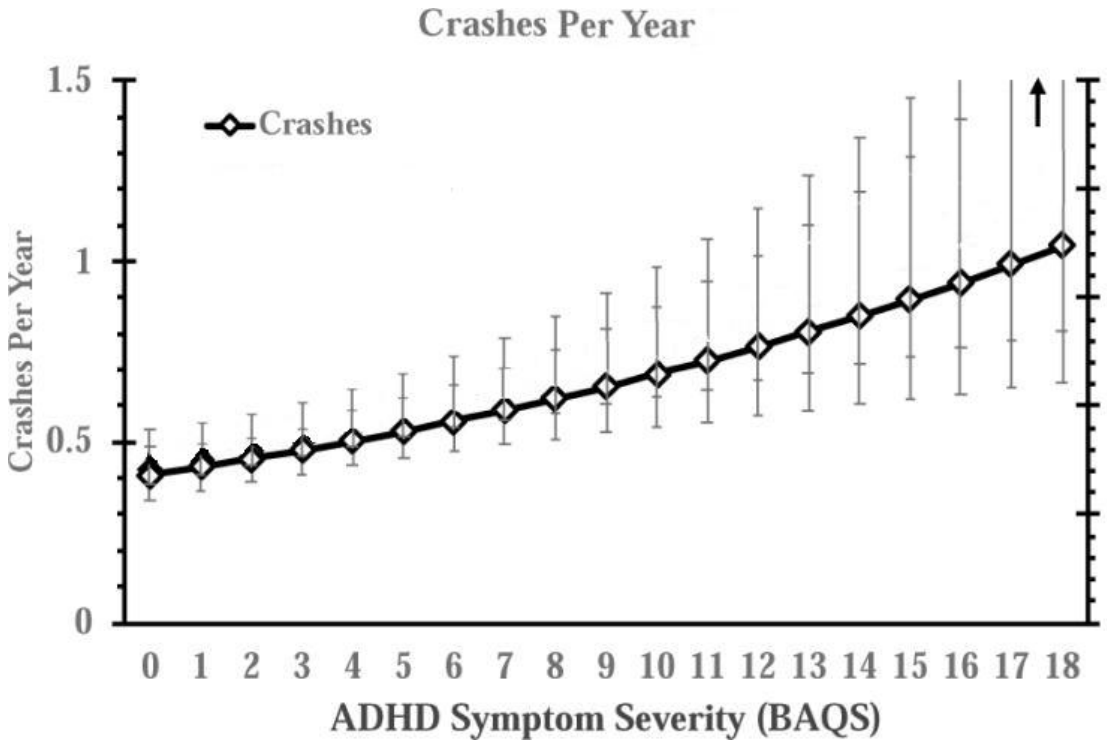


Drivers taking opioids/benzodiazepines had 1.53 times higher odds of an accident (95% CI 1.35-1.73)

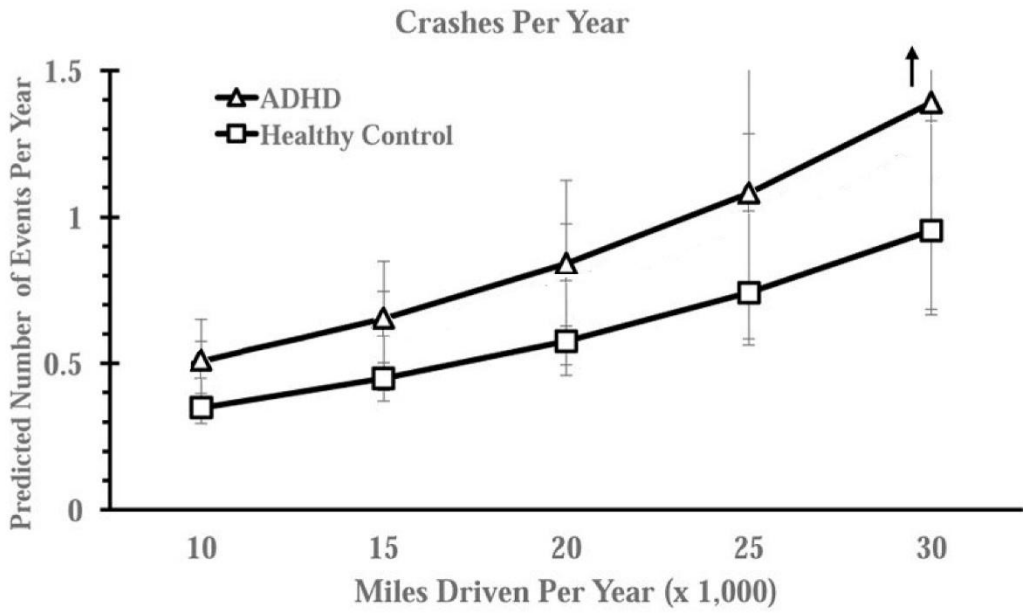
Supplemental Figure 6. Opioids/Benzodiazepines Forest Plot



Supplemental Figure 7. Opioids/Benzodiazepines Funnel Plot



Supplemental Figure 8. Crash risk as a function of BAQS ADHD symptom severity scores. Values reflect estimated marginal means for crashes per year, controlled for age, gender, education, and marital status. Per year was defined for days of continuous monitoring=365.25. Error bars reflect 95% Wald confidence intervals (CIs). (Aduen, 2018)



Supplemental Figure 9. Crash risk as a function of clinical group and exposure (miles driven per year), controlled for age, gender, education, and marital status. Values reflect estimated marginal means for incidents per year, defined for days of continuous monitoring=365.25. Error bars reflect 95% Wald CIs. (Aduen, 2018)