ACOEM Practice Guidelines: Opioids and Safety-Sensitive Work

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Objective: ACOEM has updated the treatment guidelines concerning opioids. This report highlights the safety-sensitive work recommendation that has been developed. **Methods:** Comprehensive literature reviews were accomplished with article abstraction, critiquing, grading, evidence table compilation, and guideline finalization by a multidisciplinary expert panel to develop evidence-based guidance. A total of 12 moderate-quality studies were identified to address motor vehicle crash risk, and none regarding other work among opioid-using patients. **Results:** Acute or chronic opioid use is not recommended for patients who perform safety-sensitive jobs. These jobs include operating motor vehicles, other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation and tasks involving high levels of cognitive function and judgment. **Conclusion:** Quality evidence consistently demonstrates increased risk of vehicle crashes and is recommended as the surrogate for other safety-sensitive work tasks.

Keywords: guidelines, opioids, opiates, narcotics, motor vehicle crashes, safety, occupation, work

INTRODUCTION

Driving simulator and experimental studies suggest that acute opioid exposures are associated with driving-related impairments,[1–3] with self-reported adverse effects markedly declining over days to weeks after initiation of an ongoing opioid prescription.[4,5] However, most of the driving simulator and experimental studies that looked at chronic opioid exposures reported no indirect evidence of increased risk of crash.[6–18] Other evidence suggests cognitive compromise among those with chronic opioid use, especially decision-making.[19–21] It has been theorized that chronic pain itself causes cognitive decline, thus potentially confounding opioid use. However, the evidence does not appear to support this theory.[22–26] Many researchers who have reviewed the literature have concluded there is no increased risk of motor vehicle crash with chronic opioid use.[7,27–31]

In response to the rise in opioids use, the American College of Occupational and Environmental Medicine (ACOEM) updated its opioid guidelines from the third edition of the ACOEM *Practice Guidelines*. This report summarizes the safety-sensitive recommendation developed for this update. The *ACOEM Opioids Guideline* is designed to provide health care providers, who are the primary target users, with evidence-based guidance for the use of opioids in treating working-age adults who have acute, subacute, chronic, or post-operative pain.

A 2009 guideline statement of the American Pain Society/American Academy of Pain Medicine on driving and work safety states that: "Clinicians should counsel patients on chronic opioid therapy about transient or lasting cognitive impairment that may affect driving and work safety. Patients should be counseled not to drive or engage in potentially dangerous activities when impaired or if they describe or demonstrate signs of impairment."[32] It also states that: "In the absence of signs or symptoms of impairment, there is no evidence that patients maintained on stable doses of COT (chronic opioid therapy) should be restricted from driving."[32] However, that guideline is now several years old and provides no references for original epidemiological studies, instead identifying two supportive review articles from one author[27,28] plus some of the experimental studies.

In contrast, there are long-standing recommendations against the use of narcotics, particularly including opioids in safety-sensitive work such as in the transportation sector.[33–35] Thus, whether opioids impair safety-sensitive work is unclear and prior evidence-based guidance is weak.

METHODS

A detailed methodology document used for development of this guideline (including evidence selection, scoring, incorporation of cost considerations,[36] and formulation of recommendations) is available on the Internet[37] and summarized elsewhere.[38,39] Noteworthy additions pertaining to this guideline are inclusion of large epidemiological studies for evidence of harms used for guidance and a change in the databases searched. All evidence related to opioids in prior ACOEM *Practice Guidelines*[40–48] after searching seven databases was included in this guideline (Medline, EBM Online, Cochrane, TRIP, CINAHL, EMBASE, PEDro). Comprehensive searches for epidemiological evidence were performed with both Pubmed and Google Scholar up through October 2013 to help assure complete capture. There was no limit on year of publication. All identified studies were scored for quality.

Guidance was then drafted using a table of evidence that abstracted the epidemiological evidence. Draft text and tables were forwarded to the multi-disciplinary Evidence-based Practice Opioids Panel which reviewed the evidence and finalized the text and recommendations. This guideline achieved 100% Panel agreement.

Guidance is developed with sufficient detail to facilitate assessment of compliance (Institute of Medicine (IOM)) and auditing/monitoring (Appraisal of Guidelines for Research and Evaluation [AGREE]).[36,49] Alternative options to manage conditions are provided in other ACOEM guidelines when comparative trials are available; however, alternative management strategies are provided in greater detail in other guidelines.[40–48]

The only AGREE[36] and IOM criterion not adhered to is incorporation of the views of the target population. Patients taking opioids, those in therapy or recovered from opioid dependence or addiction, or other affected patient groups were not involved on the Panel or external review process, nor were advocates for or against use of opioids. In accordance with the IOM's Trustworthy Guidelines, this guideline underwent external peer review and detailed records are kept, including responses to external peer reviewers.[49]

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While the primary patient population target is working adults, it is recognized that the principles may apply more broadly. The Evidence-based Practice Opioids Panel and the Research Team have complete editorial independence from the American College of Occupational and Environmental Medicine and Reed Group, neither of which has influenced the Guideline. The literature is routinely monitored and formally searched at least annually for evidence that would overturn this guidance. This guideline is planned to be updated at least every three years or more frequently should evidence require it.

This report summarizes the key findings for safety-sensitive work associated with use of opioids in ACOEM's *Practice Guidelines*.[50] All treatment recommendations are guidance-based on synthesis of the evidence plus expert consensus. These are recommendations for practitioners and decisions to adopt a particular course of action must be made by trained practitioners on the basis of available resources and the particular circumstances presented by the individual patient.

RESULTS

The search strategies identified 21,478 article abstracts (176 PubMed, 1552 EBSCO, 19,750 Google Scholar) of epidemiological studies. All articles were evaluated and 12 were included in these analyses (Table 1).[51–62] No epidemiological studies were identified addressing forklift driving, overhead crane operation, heavy equipment operation, cognitive function, and judgment. Disclosed conflicts of interest appear negligible among the authors of these studies (Table 1).

The identified studies included four population-based studies.[51–53,55] These studies utilized databases for prescriptions and crashes. The largest included two studies including over 3.1 million people in Norway[51,53] and 549,000 in Ontario, Canada.[55] One study was limited to codeine and tramadol,[51] one addressed risk from natural opium alkaloids,[53] one aggregated opioid types,[53,55] and one study focused on 4,626 methadone maintenance program participants.[52] All of these population-based studies found elevated risks of crash associated with opioid use (Fig. 1 and Table 1). Sub-analyses for tramadol also appear positive but underpowered (Standardized Incidence Ratio 1.5; 95% CI: 0.9–2.3).[51] Three studies were not included in Figure 1 as the risk estimates were comparisons with low dose opioid use rather than no use,[55–57] thus likely underestimating the risk estimates of any opioid use. Dose response relationships are suggested from both of the two studies evaluating those potential relationships.[51,55]

There were three case-crossover studies,[54,56,57] including one from the United Kingdom with 49,821 patients.[54] One study found increased risk with acute opioid use (0–4 weeks), continued increased risk throughout the opioid treatment period, and reversal of the elevated risks on opioid cessation.[54] One study suggesting increased risks did not clearly separate licit from illicit use.[57]

There were four case-control[58,59,61,62] and one cross sectional studies.[60] All reported an elevated risk of crash, except for a small case-control study (n = 8 cases, n = 20 controls) that reported an odds ratio for crash associated with opioids of 2.3 (95% C.I.0.87–6.32)[61] and thus appears underpowered. One case-control study found elevated crash risk from use of buprenorphine and methadone.[58] An elevated risk of fatal crash associated with opioids was reported from the USA's Fatality Analysis Reporting System of 75,026 drivers.[59] The latter study also found an association with unsafe driving actions (especially failure to stay in the lane) that preceded fatal crashes.[59]

Based on the available evidence, the following recommendation is developed by the Evidence-based Practice Opioids Panel:

> Acute or chronic opioid use is not recommended for patients who perform safety-sensitive jobs. These jobs include operating motor vehicles, other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation, sharps work (eg, knives, box cutters, needles), work with injury risks (eg, heights) and tasks involving high levels of cognitive function and judgment. The rating level is "C." Confidence in the recommendation is moderate. Panel agreement with this guideline recommendation is 100%.

Among those treated with opioids, including tramadol, sufficient time after the last dose is recommended to eliminate approximately 90% of the drug and active metabolites from their system. Caution is also warranted for those consuming other depressant medications such as benzodiazepines and sedating antihistamines. Provider and organizational barriers to implement this recommendation are relatively few. However, there may be some patients taking opioids while employed in safety-sensitive jobs, and there are no validated tools to assess whether they can perform their job safely.

Benefits of this guideline include potential reductions in accidents and injury risks to self, public and coworkers. Potential harms of this guideline may include preclusion of someone from working who is theoretically not at increased risk, although there is no validated method to demonstrate an individual's safety while consuming opioids.

DISCUSSION

Acute or chronic opioid use is not recommended for patients who perform safety-sensitive jobs. By analogy, this recommendation is extended beyond operation of motor vehicles to include other modes of transportation, forklift driving, overhead crane operation, heavy equipment operation, work with sharps, work with risk of injury (eg, heights) and tasks involving high levels of cognitive function.[19–21,22–26]

Both weak and strong opioids have been consistently associated with increased risk of motor vehicle crashes (MVC) in all large epidemiological studies of working age adults sufficiently powered to detect motor vehicle crash risk with the risk estimates ranging from 29% to more than 800% increased risk.[51–56,58–60] There also is some evidence suggestive of a dose-response relationship.[51,55]

Strengths of this guideline include a relatively large database of studies. This evidence also includes consistent findings involving large populations, different study designs and different countries. Only one study did not find statistical significance of increased risk,[61] yet has a small sample size with a point estimate suggesting increased risk that appears underpowered. Therefore, the overall evidence base is strongly supportive of this guideline's recommendation. The "C" rating instead of a higher rating is due to the reliance on epidemiological studies rather than randomized controlled trials.

Weaknesses of this guideline include the theoretical possibility that there are patients without increased risk. Presumably if such exist, they are on very low doses of opioids. Yet, this guideline did not find either absence of, or lower risk among those on either lower doses or weaker opioids, suggesting if there is a threshold for no increased risk, that threshold is apparently at a very low morphine equivalent dosage. Further epidemiological research investigating those possibilities may be helpful. However, in summary, the ACOEM Evidence-based Practice Opioids Panel recommends preclusion of opioid use in safety-sensitive jobs.

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TABLE 1. Included Epidemiological Studies of Motor Vehicle Crash Risk among Opioid-using Drivers

Name/Year Location Potential Conflict of Interest	Score*	Study Design	Exposure	Population Age Range Dropout Rate Case Definition	Results	Conclusion	Comments
Bachs 2009 Norway Work was funded by the Norwegian Institute of Health. Authors declared no conflict of interest.	II	Population-based cohort design	Prescription of codeine or tramadol in national prescription database.	N = 3.1 million followed from age 18 or Jan 7, 2004, until accident or age 70 or death. Age 18–70 Examined whether driver with filled prescription for codeine or tramadol is at increased risk or standardized incidence ratio (SIR) for road accident resulting in injury to persons.	N = 181 accidents with injury and drivers on codeine (defined as within 7 days after dispensing date); 20 on tramadol. SIR gender and all age groups combined: 1.9; 95% CI: 1.6–2.2. High codeine SIR 2.9 (2.3–3.6). SIR for tramadol (1.5; 95% CI: 0.9–2.3) not significant, but suggests trend.	"[W]e found an increased SIR of motor vehicle accidents that resulted in injury and involved drivers exposed to Codeine."	Study used drug databases. Under-powered for tramadol (non-significant 50% increased risk). Data suggest higher risk if higher codeine consumed.
Engeland 2007 Norway No mention of industry sponsorship or conflict of interest.	II	Population-based cohort study	Born between April 1934 – Sep 1987, living in Norway 2004–05. Information on prescriptions and road traffic accidents.	N = 3,115,322 drivers followed 1.5 years. Age 19–69 Drop-out rate not reported. Examined risk of driver involvement in road traffic accident while using prescription drugs.	Accident risk increased in users of (any) prescribed drugs; OR = 1.4, 95% CI, 1.3–1.5. Risk increased in users of natural opium alkaloids (OR = 2.0; 1.7–2.4), tranquilizing benzodiazepines (2.9; 2.5–3.5), hypnotic benzodiazepines (3.3; 2.1–4.7).	"The increased risk of being involved in a road accident as driver while receiving prescribed opiates and benzodiazepines supported the results from other studies."	Large sample size. Study evaluated risk after initial prescription over 7 and 14 days, finding significantly increased risks.
Bramness 2012 Norway Funded by internal funds at Norwegian Institute of Public Health. Authors declared no conflict of interest.	II	Population-based cohort study	Patients on methadone maintenance treatment April 1, 2004, or from 18th birthday until first accident as driver.	N = 4,626 patients exposed to methadone. Age 18–69 Investigated whether exposure to methadone affects risk of motor vehicle accident with personal injury.	N = 26 methadone-exposed drivers in accidents with personal injury. Males had increased accident risk of 2.4, 95% CI: 1.5–3.6, when exposed to methadone; females had no increased risk, SIR 1.1, 95% CI: 0.2–3.1.	"Men exposed to methadone appear to have an increased risk of being involved in motor vehicle accidents involving personal injuries."	Prescription database; data suggest increased risk of crash for males on methadone. Results negative for females, but underpowered. Combined male/female risk 2.1 (95% CI 1.4, 3.1) for relationship between methadone and traffic accident.
Gomes 2013 Ontario, Canada Supported by grant from Ontario Ministry of Health and Long-term Care Drug Innovation Fund and Institute for Clinical Evaluative Sciences.	II	Population-based study with nested case-control	April 1, 2003 through March 31, 2011. Computerized medical records tool.	N = 549,878 given at least 1 prescription of opioid and involved in a MVC; 5,300 were matched with a control; of these 2,428 (45.81%) were drivers, 840 (15.85%)	Drivers prescribed very low doses vs. low and moderate doses of opioid had a 21% vs. 29% increased odds of road trauma (1.21 [95% CI: 1.02–1.42] vs. 1.29 [1.06–1.57]).	"Among drivers prescribed opioids, a significant relationship exists between drug dose and risk of road trauma. This association is distinct and does not appear with passengers, pedestrians, and others injured in road trauma."	Data suggest opioids associated with increased risk of road trauma (relationship appears dose-response). Data may substantially underestimate risk as comparison is low dose rather than "0" dose.

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TABLE 1. (*Continued*)

Name/Year Location Potential Conflict of Interest	Score*	Study Design	Exposure	Population Age Range Dropout Rate Case Definition	Results	Conclusion	Comments
Dr. Mamdani reported honoraria from Bayer, Boehringer Ingelheim, Bristol-Myers Squibb, Pfizer.				passengers, 579 (10.92%) pedestrians, and 1453 (27.42%) unknown or in miscellaneous position. Age 18–64	Drivers prescribed high and very high doses vs. low and moderate had a 42% vs. 23% increased odds of road trauma (1.42 [95% CI, 1.15–1.76] and 1.23 [1.02–1.49]).		
Gibson 2009 United Kingdom No mention of industry sponsorship or conflict of interest.	II	Case-crossover and case-series analyses	1986–2004 – 255 GP clinic medical records of The Health Improvement Network, and prescription for any benzodiazepines, nonbenzodiazepine hypnotics, beta-blockers, selective serotonin reuptake inhibitors, tricyclic antidepressants, opioids, and antihistamines.	N = 49,821 in MVC using benzodiazepines, nonbenzodiazepine hypnotics, beta-blockers, selective serotonin reuptake inhibitors, tricyclic antidepressants, opioids, and antihistamines. Age 18–74	Opioid treatment associated with increased risk of MVC (IRR acute period up to 4 weeks = 10.9, 99% CI 9.96–11.93; IRR 4 weeks after opioid began = 1.70, 99% CI: 1.39, 2.08), persisted throughout treatment (IRR = 1.29, 99% CI: 1.08, 1.54). This was not observed when opioids were withdrawn.	"[T]he risk of motor vehicle crash is increased by the use of benzodiazepines, opioids, and compound analgesic preparations containing acetaminophen and an opioid for the duration of their usage, the risk decreasing once the medication is discontinued."	Data suggest increased crash risk associated with opioids. Increased risk reversed on opioid cessation.
Majdzadeh 2009 Iran Study funded by Institute of Public Health Research, Tehran University of Medical Sciences. No COIs disclosed.	II	Case-crossover	Study conducted in Shaheed Bahonar Hospital ER in Kerman province, only trauma center for 400,000.	N = 75 involved in MVC and regular opium users. Age ≥18 Driving under influence of opium before accident and overlap between driving hours and hours after opium consumption until accident considered as person-hours exposed for hazard period.	Relative risk for opioid consumption 6 hours before accident 3.2 ($p = 0.05$) and 3 hours before accident 4.29, $p = 0.05$.	"These results suggest a heightened risk of traffic injuries after opium consumption in regular users."	Data suggest opioids associated with increased risk of crash. Data only regarding opioid users, which may underestimate risks compared with non-use.
Mørland 2011 Denmark, Finland, Iceland, Norway, Sweden No mention of industry sponsorship. No conflicts of interest disclosed.	II	Case-crossover and case-series analyses	Jan 2001- Dec 2002. Participating labs collected biological samples from medico-legal autopsies and in some cases from drivers still alive shortly after accident.	(N = 501) Denmark, (N = 463) Finland, (N = 23) Iceland, (N = 344) Norway, and (N = 590) Sweden. Age not specified Study aim to find which drugs/drug combinations most common in drivers who died, in particular (single vehicle crashes where crash responsibility referred to driver killed).	60% of drivers in single vehicle crashes with alcohol and/or drug in blood samples vs. 30% of drivers killed in collisions with other vehicles. 40% non-alcohol drugs in blood; illicit-drugs in 24% who had non-alcohol drug in their sample. Drug range 36–41% in single vehicle crashes; 68–71% in multiple vehicle crashes.	"[I]n Northern European countries, alcohol and impairing non-alcohol drugs are frequently detected in killed vehicle drivers, and very frequently in younger drivers killed in single vehicle accidents."	Data not stratified for opioids into illicit and licit. Risk comparisons are low rather than non-use of opioids.

(*Continued*)

TABLE 1. (*Continued*)

Name/Year Location Potential Conflict of Interest	Score*	Study Design	Exposure	Population Age Range Dropout Rate Case Definition	Results	Conclusion	Comments
Corsenac 2012 France Supported by French Health Products Agency, French National Research Agency, French National Medical Research Institute, French Medical Research Foundation, and French Direction Générale de la Santé. All authors declare no competing interests.	III	Population-based case-control using three databases: police reports, health care, insurance databases	Use of buprenorphine and methadone.	N = 72,685 drivers involved in injurious crash in France July 2005 – May 2008. Age <29–49 Study objective to investigate association between risk of being responsible for road traffic crash and use of buprenorphine and methadone.	N = 196; drivers exposed to buprenorphine or methadone on day of crash young, largely male (29–38) and using level 2 and 3 medicines or highest level risk. 387 drivers taking at least 1 dispensation of buprenorphine/ methadone in 6 months preceding crash showed increased responsibility risk, OR = 1.70, 95% CI: 1.36 2.14. Excluding 159 drivers with dispensation in prior 8 days before crash, OR = 1.52, 95% CI: 1.14–2.03. Adjusted OR for crash = 2.02, 95% CI 1.40–2.91.	"Users of methadone and buprenorphine were at increased risk of being responsible for injurious road traffic crashes."	Increased risk of crash if buprenorphine or methadone on day of crash. Considerable use of other medications may have (partially) confounded.
Dubois 2010 U.S.A., District of Columbia, Puerto Rico No mention of industry sponsorship or conflict of interest.	III	Population-based case-control design based on data from U.S. NHTSA Fatality Analysis Reporting System	1993–2006, those involved in fatal crashes.	N = 75,026 drivers tested for both alcohol and drugs had a blood alcohol level of 0. Mean age 46 Examinee impact of opioid analgesics on drivers involved in fatal accidents.	N = 2,109/75,026 positive for opioids; 380/75,026 positive for 2 opioids. Females had increased odds of performing unsafe driving actions (UDA) from age 25 (OR: 1.35) to 55 (OR: 1.30); for males age 25–65 (OR: 1.66, 1.39 respectively). Testing positive for opioids increased odds of UDA associated with crash by 57%.	"[T]he results of our study suggest that opioids negatively affect safe driving."	Study eliminated confounding by alcohol. Data suggest opioids associated with unsafe driving prior to fatal crash. Findings not found in elderly.
Mura 2003 France Financial support from French Ministry of Health, in framework of "Programme Hospitalier de Recherche Clinique National." No COIs disclosed.	III	Case-control study	Prevalence of: alcohol, cannabinoids, opiates, cocaine metabolites, amphetamines and therapeutic psychoactive drugs.	N = 900–1,800 drivers in non-fatal accident; 900 controls in same ER for non-traumatic reason. Age 18->50 Blood samples from drivers injured in road accidents vs. controls used to screen for alcohol, cannabinoids, cocaine metabolites, opiates, amphetamines, and therapeutic psychoactive drugs.	Morphine prevalence between drivers 2.7%; patients 0.03%, with highly significant, p < 0:001, with OR = 8.2. Psychoactive therapeutic drugs in 142 drivers (15.8%) and 107 controls (11.9%) p < 0.05. Benzodiazepines found alone in 9.4% of drivers and 5.8% of patients, OR = 1.7, p < 0.01.	"[A] higher prevalence of opiates, alcohol, cannabinoids and the combination of these last two compounds in blood samples from drivers involved in road accidents than in those from controls, which suggests a causal role for these compounds in road crashes."	Large sample size. Opioids associated with higher risk of crash (OR = 8.2). Licit vs. illicit use unclear.

(*Continued*)

TABLE 1. (*Continued*)

Name/Year Location Potential Conflict of Interest	Score*	Study Design	Exposure	Population Age Range Dropout Rate Case Definition	Results	Conclusion	Comments
Movig 2004 Tilburg, region of The Netherlands No mention of industry sponsorship. No COIs disclosed.	III	Prospective case-control study	Use of alcohol and/or licit and illicit drugs	N = 110 injured car or van drivers admitted to ER; N = 816 randomly selected from moving traffic during 20 roadside survey sessions. Age 18–50 To assess relationship between drug use and trauma injuries requiring hospitalization caused by motor vehicle accidents.	74% males; 40% of all cases positive for 1 or more drugs and/or alcohol vs. 14% controls. Benzodiazepines, adjusted OR = 5.1 (95% CI: 1.8–14.0) and alcohol significantly associated with accidents. Those concomitantly exposed to alcohol/1 or more drugs had highest accident risk, adjusted OR = 112.2 (95% CI: 14.1–892.9). Crash risk with injuries not statistically significantly related to opiates, adjusted OR = 2.35 (95% CI 0.87, 6.32).	"[Drug] use, especially alcohol, benzodiazepines and multiple drug use and drug–alcohol combinations, among vehicle drivers increases the risk for a road trauma accident requiring hospitalization."	Likely underpowered for opioids with OR = 2.3, n = 28.
Howard 2004 Australia Supported by grants from Vicroads and Roads and Traffic Authority of New South Wales. All authors declare no competing interests.	III	Cross-sectional study	To measure prevalence of excessive sleepiness and sleep-disordered breathing and assess accident risk factors.	N = 2,342 commercial vehicle drivers who completed questionnaire and anthropomorphic measurements. N = 161 drivers who attend in lab polysomnography. Mean age (questionnaire) = 42.4; polysomnography = 47.8 Simple random sample: 98 workplaces selected from 395 on database of Australia Transport Workers Union.	59.6% of drivers had sleep-disordered breathing and 15.8% had obstructive sleep apnea syndrome. Odds ratio for reported crash in past 3 years associated with narcotics use OR = 2.40 (95% CI 1.46–3.92, p <0.01).	"Chronic excessive sleepiness and sleep-disordered breathing are common in Australian commercial vehicle drivers. Accident risk was related to increasing chronic sleepiness and antihistamine and narcotic analgesic use."	Data suggest an association between opioid use and risk of commercial motor vehicle accidents.

*Score "I" for high- or moderate-quality randomized controlled clinical trial (score of 0–11, with 8–11 high quality, 4–7.5 moderate quality and 0–3.5 low quality). For observational studies of harms, a score of "II" is for prospective cohort studies, prospective comparative studies, case-crossover and large, population-based studies. A score of "III" is for retrospective, case control or cross-sectional studies.

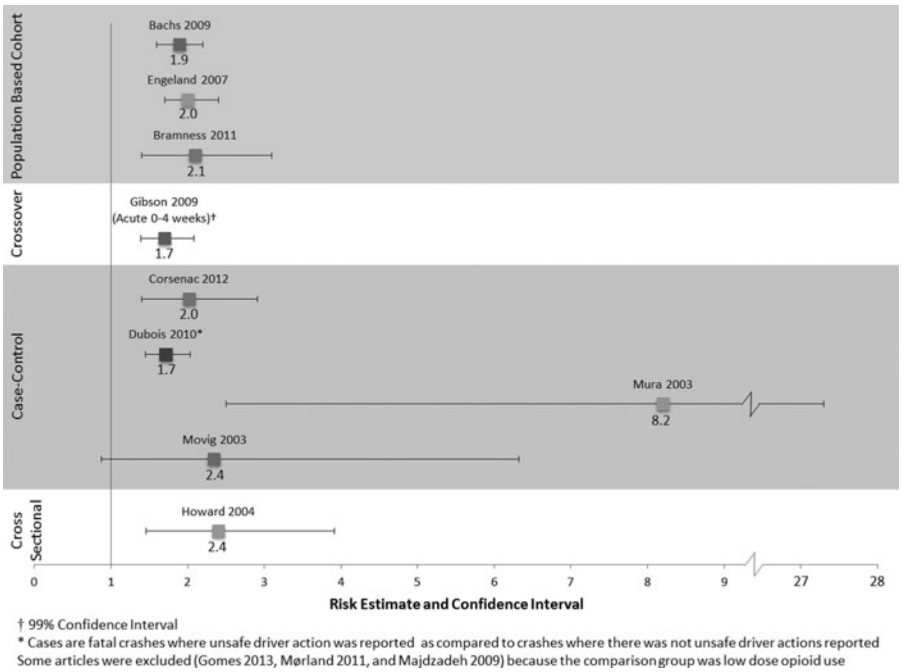

FIGURE 1. Risk Estimates and Confidence Intervals of Included Studies Assessing Relationships Between Opioid Use and Crashes.

and Jeremiah L. Dortch, BS. Drs. Hegmann and Thiese also conducted research for this guideline. Dr. Harris served as the Opioids Panel methodologist.

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