Evidence Report

Psychiatric Disorders and Commercial Motor Vehicle Driver Safety

Presented to

The Federal Motor Carrier Safety Administration

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Prepared for

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Evidence reports are sent to the Federal Motor Carrier Safety Administration's (FMCSA) Medical Review Board (MRB) and Medical Expert Panels (MEP). MRB and MEP make recommendations on medical topics of concern to the FMCSA.

The FMCSA will consider all MRB and MEP recommendations; however, all proposed changes to current standards and guidance (guidelines) will be subject to public notice and comment and relevant rule-making processes.

Policy Statement

This report was prepared by ECRI Institute under subcontract to MANILA Consulting Group, Inc., which holds prime GS-10F-0177N/DTMC75-06-F-00039 with the Department of Transportation's Federal Motor Carrier Safety Administration. ECRI Institute is an independent, nonprofit health services research agency and a Collaborating Center for Health Technology Assessment of the World Health Organization. ECRI Institute has been designated an Evidence-based Practice Center by the United States Agency for Healthcare Research and Quality. ECRI Institute's mission is to provide information and technical assistance to the healthcare community worldwide to support safe and cost-effective patient care. The results of ECRI Institute's research and experience are available through its publications, information systems, databases, technical assistance programs, laboratory services, seminars, and fellowships. The purpose of this evidence report is to provide information regarding the current state of knowledge on this topic. It is not intended as instruction for medical practice or for making decisions regarding individual patients.

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Executive Summary

Purpose of Evidence Report

Of all occupations in the United States, trucking industry workers experience the third highest fatality rate, accounting for 12% of all worker deaths. About two-thirds of fatally injured truck workers were involved in highway crashes. According to statistics from the U.S. Department of Transportation, there were 4,932 fatal crashes involving a large truck in 2005 for a total of 5,212 fatalities. In addition, there were 137,144 nonfatal crashes; 59,405 of these crashes resulted in an injury to at least one individual (for a total of 89,681 injuries).

The purpose of this evidence report is to summarize the available data pertaining to the relationship between a number of psychiatric disorders and commercial motor vehicle (CMV) driver safety. Driving is a complicated psychomotor performance that depends on fine coordination between the sensory and motor systems. It is influenced by factors such as arousal, perception, learning, memory, attention, concentration, emotion, reflex speed, time estimation, auditory and visual functions, decision making, and personality. Complex feedback systems interact to produce the appropriate coordinated behavioral response. Anything that interferes with any of these factors to a significant degree may impair driving ability. Psychiatric illnesses may affect thinking, mood, and/or perception, resulting in a wide range of types and degrees of cognitive impairment. Insight is critical for drivers to drive within their limitations and to know how and when these limitations change. Poor insight in patients with psychiatric illness may be evidenced by noncompliance with treatment, trivializing their role in a crash, or repeated involuntary admissions to hospital (often as a result of discontinuing prescribed medication).

To meet the aims of the evidence report, we addressed the following three key questions:

Key Question 1: Are individuals with a psychiatric disorder at an increased risk for motor vehicle crash? If so, are there specific psychiatric disorders that present a particularly high risk?

Key Question 2: Are individuals using psychotherapeutics for a psychiatric disorder at an increased risk for crash when compared to comparable individuals who are not using psychotherapeutics?

Key Question 3: What traits associated with personality disorders are associated with reductions in motor vehicle driver safety?

Thus, the primary aims of this report are to examine the relationship between psychiatric disorders and driver safety and to examine the impact of psychopharmacotherapy on driver safety.

Identification of Evidence Bases

Separate evidence bases for each of the key questions addressed by this evidence report were identified using a process consisting of a comprehensive search of the literature, examination of abstracts of identified studies in order to determine which articles would be retrieved, and the selection of the actual articles that would be included in each evidence base.

A total of seven electronic databases (MEDLINE, PubMed (preMEDLINE), EMBASE, PsycINFO, CINAHL, TRIS, the Cochrane Library) were searched (through January 28, 2008). In addition, we

examined the reference lists of all obtained articles with the aim of identifying relevant articles not identified by our electronic searches. Hand searches of the "gray literature" were also performed. Admission of an article into an evidence base was determined by formal retrieval and inclusion criteria that were determined *a priori*.

Grading the Strength of Evidence

Our assessment of the quality of the evidence took into account not only the quality of the individual studies that compose the evidence base for each key question; we also considered the interplay between the quality, quantity, robustness, and consistency of the overall body of evidence.

Analytic Methods

The set of analytic techniques used in this evidence report was extensive. Random-effects meta-analyses were used to pool data from different studies. Differences in the findings of studies (heterogeneity) were identified using the Q-statistic and I^2. Sensitivity analyses, aimed at testing the robustness of our findings, included the use of cumulative random-effects meta-analysis.

Presentation of Findings

In presenting our findings, we made a clear distinction between qualitative and quantitative conclusions and we assigned a separate "strength-of-evidence" rating to each conclusion format. The strength-of-evidence ratings assigned to these different types of conclusion are defined in Table 1.

Table 1. Strength-of-Evidence Ratings for Qualitative and Quantitative Conclusions

Strength of Evidence	Interpretation
Qualitative Conclusion	
Strong	Evidence supporting the qualitative conclusion is convincing. It is highly unlikely that new evidence will lead to a change in this conclusion.
Moderate	Evidence supporting the qualitative conclusion is somewhat convincing. There is a small chance that new evidence will overturn or strengthen our conclusion. ECRI Institute recommends regular monitoring of the relevant literature for moderate-strength conclusions.
Minimally Acceptable	Although some evidence exists to support the qualitative conclusion, this evidence is tentative and perishable. There is a reasonable chance that new evidence will either overturn or strengthen our conclusions. ECRI Institute recommends frequent monitoring of the relevant literature.
Insufficient	Although some evidence exists, the evidence is insufficient to warrant drawing an evidence-based conclusion. ECRI Institute recommends frequent monitoring of the relevant literature.
Quantitative Conclusion (Stability of Effect-size Estimate)	
High	The estimate of treatment effect in the conclusion is stable. It is highly unlikely that the magnitude of this estimate will change substantially as a result of the publication of new evidence.
Moderate	The estimate of treatment effect the conclusion is somewhat stable. There is a small chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI Institute recommends regular monitoring of the relevant literature.
Low	The estimate of treatment effect included in the conclusion is likely to be unstable. There is a reasonable chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI Institute recommends frequent monitoring of the relevant literature.
Unstable	Estimates of the treatment effect are too unstable to allow a quantitative conclusion to be drawn at this time. ECRI Institute recommends frequent monitoring of the relevant literature.

Evidence-based Conclusions

The findings of our analysis of the best available data addressing each of the questions asked by the Federal Motor Carrier Safety Administration are presented below.

Key Question 1: Are individuals with a psychiatric disorder at an increased risk for motor vehicle crash? If so, are there specific psychiatric disorders that present a particularly high risk?

- **The evidence concerning crash risk for drivers with psychiatric disorders is inconclusive. The possibility of an increased risk of crash for some drivers with psychiatric disorders cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

Our searches identified eight direct crash risk studies with a total of 1,931 individuals with psychiatric disorders. The quality assessment was low for six studies and moderate for two studies. None of the study participants were specifically identified as CMV drivers, so the generalizability of findings to the CMV driver population is unclear.

The findings of seven studies could be combined in a quantitative analysis. Pooling of the data from these studies found no statistically significant difference in crash risk between drivers with psychiatric disorders and drivers without psychiatric disorders. However, the possibility of an increased crash risk for some drivers with psychiatric disorders could not be ruled out. We note that the patient populations enrolled in these studies were unlikely to have included individuals with severe symptoms who would be more likely to have impaired driving ability.

Subgroup Analyses: Specific Psychiatric Disorders and Crash Risk

- **Psychotic Disorders: Currently available evidence does not suggest an increased crash risk for individuals with psychotic disorders compared to individuals without these disorders, but an increased crash risk cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

- **Mood Disorders: Although evidence suggests the possibility that individuals with mood disorders are at an increased risk for a motor vehicle crash compared with drivers who do not have mood disorders, more evidence is needed to reach a firm conclusion.**

- **Anxiety Disorders: A paucity of evidence prevents us from being able to draw an evidence-based conclusion about the effects of anxiety disorders on the risk of motor vehicle crash.**

- **Personality Disorders: Due to inconsistencies in the available evidence, we are precluded from drawing an evidence-based conclusion pertaining to the strength of the relationship between personality disorders and crash risk at this time.**

Our searches identified four studies with a total of 332 individuals with psychotic disorders, three studies with a total of 377 individuals with mood disorders, one study with 95 individuals with anxiety disorders, and three studies with 217 individuals with personality disorders. The median quality assessment for each subgroup analysis was low. Even when pooling of data was possible, none of these analyses found a statistically significant increase in crash risk for any of the four types of disorders compared to patients

without psychiatric disorders. However, the possibility of increased crash risk could not be ruled out in any of these subgroup analyses.

Key Question 2: Are individuals using psychotherapeutics for a psychiatric disorder at an increased risk for crash when compared to comparable individuals who are not using psychotherapeutics?

Analysis 1: Benzodiazepine Use and Crash Risk

- **Benzodiazepine use is associated with an increased risk for a motor vehicle crash (Strength of Evidence: Moderate).**
    - **Benzodiazepine anxiolytic use is associated with an increased risk for a motor vehicle crash (Strength of Evidence: Minimally Acceptable).**
    - **Crash risk may be greater during the first week of an index prescription of benzodiazepines (Strength of Evidence: Minimally Acceptable).**
    - **Crash risk may be greater among benzodiazepine users ≤40 years of age (Strength of Evidence: Minimally Acceptable).**

Our searches identified nine direct crash risk studies with a total of approximately 235,000 individuals using benzodiazepines. The average quality of these studies was moderate. None of the study participants were specifically identified as CMV drivers, so the generalizability of the findings to the CMV driver population is unclear. The findings of the nine studies were inconsistent. However, pooling of the data from each study found elevated odds of crash associated with benzodiazepine use. This finding was statistically significant and robust.

Because benzodiazepine anxiolytics are more likely to be used than hypnotics in patients with psychiatric disorders, we performed a subgroup analysis of five studies that presented separate crash data for users of anxiolytics. The pooled data analysis found that the odds of crash were significantly increased in users of benzodiazepine anxiolytics.

Further analysis to identify factors that may lead to increased risk for benzodiazepine users identified timing of exposure and patient age as potential risk factors. Two studies found the highest risk of crash to occur during the first week of the index prescription, and two studies found that crash risk was higher in benzodiazepine users ≤40 years of age.

Analysis 2: Antipsychotic Use and Crash Risk

- **The evidence concerning crash risk associated with antipsychotic use is inconclusive. The possibility of an increased crash risk associated with antipsychotic use cannot be ruled out.**

One study addressed the potential association between antipsychotic drugs and crash risk. This study found no excess risk of crash associated with antipsychotic agents within two weeks or four weeks of the index prescription. As this is a single moderate-quality study and the 95% confidence intervals around the effect estimates do not rule out the possibility of increased risk, more evidence is needed to confirm these findings.

Analysis 3: Antidepressant Use and Crash Risk

- **The evidence concerning crash risk associated with antidepressant use is inconclusive. The possibility of an increased crash risk associated with antidepressant use (particularly tricyclic antidepressant [TCA] use) cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

Our searches identified seven direct crash risk studies with an unknown number of individuals using antidepressants—the number is not reportable because the raw data needed to calculate the total study population using antidepressants was not reported in all studies. Because these are seven of the nine studies identified under benzodiazepines, the generalizability issues and quality assessments are described in the earlier summary.

The findings of six of the seven studies could be combined to obtain a summary estimate of the relative odds of crash associated with antidepressant use. Pooling of the data from these studies found that the odds of crash was not significantly different for drivers using antidepressants compared to drivers not using antidepressants. However, there was a trend toward elevated risk associated with antidepressants, and the wide confidence interval around the summary estimate means that the possibility of increased crash risk cannot be ruled out. The same finding was shown for a subgroup meta-analysis of studies that separately reported data on TCA use.

Key Question 3: What traits associated with personality disorders are associated with reductions in motor vehicle driver safety?

- **The evidence suggests that individuals with traits associated with personality disorders are at an increased risk for a motor vehicle crash compared to comparable drivers who do not have traits associated with personality disorders. These traits include aggression, hostility, impulsivity, disregard for law (i.e., attitude toward traffic law violations), and various psychological symptoms. However, inconsistencies in the methodologies of the included studies preclude us from drawing an evidence-based conclusion pertaining to the strength of the relationship between traits associated with personality disorders and crash risk at this time.**

Our searches identified 21 direct crash risk studies with a total study population of 164,539 individuals, 512 of whom were CMV drivers. The quality assessment of 14 of the included studies was low; the quality assessment of the remaining 7 studies was moderate. Methodological limitations of these studies include the lack of uniformity in the definition of the traits, behaviors, and outcomes as well as the use of scales that may not have been age or gender appropriate. Since most of the studies did not include CMV drivers, the generalizability of the findings to the CMV driver population is unclear.

Because the studies used a number of different scales and methodologies to measure the traits and behaviors and the outcome measures could not be assumed to be uniform, we were precluded from combining them for quantitative analysis. Instead, we have provided a qualitative summary of the findings.

Overall, the studies suggest that traits such as aggression, hostility, impulsivity, disregard for laws (i.e., attitude toward traffic law violations), and various psychological symptoms are associated with an increase in crash risk. The same can be said of behaviors such as risky driving and violation of traffic

laws. In turn, behaviors such as risky driving are associated with aggression, impulsivity, and psychological symptoms such as anxiety, depression, and psychosis. Violation of traffic laws is associated with risky driving and aggression. Table 2 provides a quick summary of the associations between factors and outcomes.

Table 2. Associations between Factors and Outcomes for Key Question 3

	Aggression	Hostility	Impulsivity	Attitude toward Traffic Law Violations	Psychological Symptoms*	Behaviors	
						Risky Driving	Violations of Traffic Law(s)
Crash	●	●	●	●	●	●	●
Risky Driving	●	NA	●	●	●	—	●
Violations of Traffic Laws	●	NA	NA	NA	NA	●	—
Aggression	—	NA	NA	NA	●	●	●

● Factor has a negative impact on this outcome such that crash risk is increased.

* Psychological symptoms include anxiety, paranoid ideation, depression, psychosis, personality disorder, irritability, negativism, and antisocial tendencies.

NA: Not applicable. (This factor was not examined in relationship to the outcome of interest.)

Overall Summary

This report did not find conclusive evidence of an association between increased crash risk and any of four classes of psychiatric disorders (psychotic disorders, mood disorders, anxiety disorders, and personality disorders). However, given the limitations of the available studies and the likelihood that patients with severe symptoms would not be driving and thus would not be enrolled, the possibility of increased crash risk for some patients with psychiatric disorders cannot be ruled out. In contrast, the evidence was sufficient to show an association between use of at least one class of psychotherapeutic medications (benzodiazepines) and increased crash risk. This association held in a subgroup analysis of benzodiazepine anxiolytics that are likely to be used by patients with anxiety disorders. Further evidence suggested that the risk of crash was highest during the first week of index treatment and that benzodiazepine users aged <40 years were at higher risk than other age groups. The evidence was unclear about whether any type of antipsychotic or antidepressant was associated with increased crash risk. The available evidence also suggested an association between certain traits of patients with personality disorders (including aggression, hostility, impulsivity, disregard for law, and various psychological symptoms) and increased crash risk.

Preface

Organization of Report

This evidence report contains three major sections: (1) *Background*, (2) *Methods*, and (3) *Synthesis of Findings*. These major sections are supplemented by extensive use of appendices.

In the *Background* section, we provide background information about psychiatric disorders and driving. Also included in the background section is information pertaining to current regulatory standards and guidelines from the Federal Motor Carrier Safety Administration (FMCSA) and three other government transportation safety agencies; the Federal Aviation Administration, the Federal Railroads Administration, and the Maritime Administration. In addition, we summarize equivalent information from other countries that are generally considered to have well-developed medical fitness programs. In the *Methods* section, we detail how we identified and analyzed information for this report. The section covers the key questions addressed, details of literature searching, criteria for including studies in our analyses, evaluation of study quality, assessment of the strength of the evidence base for each question, and methods for abstracting and synthesis of clinical study results. The *Synthesis of Results* section of this report is organized by key question. For each question, we report on the quality and quantity of the studies that provided relevant evidence. We then summarize available data extracted from included studies either qualitatively or, when the data permit, qualitatively and quantitatively (using meta-analysis). Each section in the Synthesis of Results section closes with our conclusions that are based on our assessment of the available evidence.

Scope

The purpose of this evidence report is to address several key questions that pertain to the potential association between psychiatric disease and crash risk. Each of these key questions was formulated by the FMCSA in such a way that its answer will provide information necessary for the process of updating its current physical qualification standards and guidance to medical examiners. The key questions addressed in this evidence report are as follows:

Key Question 1: Are individuals with a psychiatric disorder at an increased risk for motor vehicle crash? If so, are there specific psychiatric disorders that present a particularly high risk?

Key Question 2: Are individuals using psychotherapeutics for a psychiatric disorder at an increased risk for crash when compared to comparable individuals who are not using psychotherapeutics?

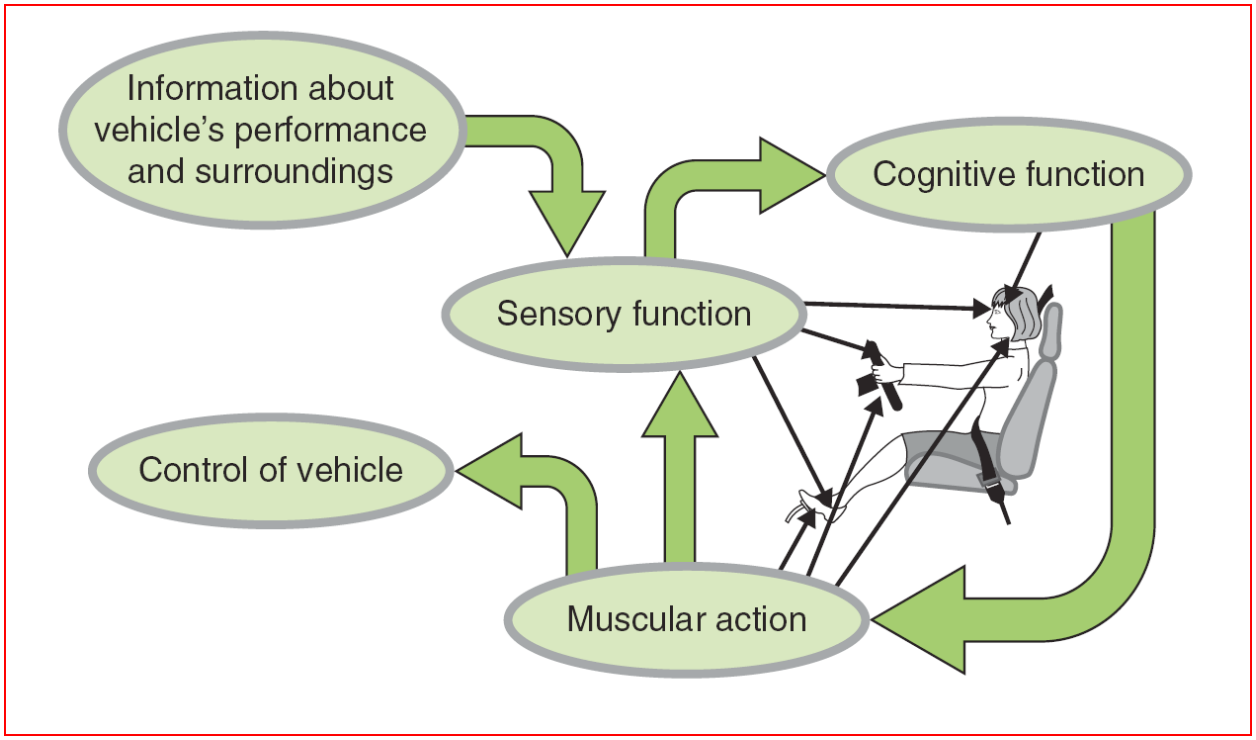
Key Question 3: What traits associated with personality disorders are associated with reductions in motor vehicle driver safety?

Background

Safe driving requires that the driver be able to maintain effective and reliable control of his or her vehicle; have the capability to respond to the road, traffic, and other external clues; and be able to follow the "rules of the road." Drivers consciously learn all these skills and demonstrate them as part of obtaining their commercial driver's license to pass the driving test, and the vast majority of people have the ability to achieve a satisfactory standard. Driving performance generally improves with experience, and driving ultimately becomes an "overlearned" skill that is subconsciously retained and can readily be used as required. Impairments caused by health problems can interfere with driving performance.

The task of driving can be thought of as a continuous loop, in which information about the road, other drivers, and the vehicle is processed by the brain; this leads to the driver taking action to adjust the speed and direction of the vehicle and to direct his or her gaze to likely danger areas (Figure 1). The results of these actions then feed back into a further round of adjustments. The loop is dynamic, and timing is critical for making continuous adjustments in the light of new perceptions. Within this loop, vision is the dominant sense involved. Visual and other perceptions convey information such as speed, location of vehicles, and other obstacles. The driver analyzes current perceptions based on prior training and experience about safety risks, vehicle characteristics, and the anticipated behavior of other road users. The intent of the journey in terms of route and destination is also used to decide the actions required, especially at junctions. Current perceptions, learned responses, and intentions about the journey all interact, largely at a subconscious level in an experienced driver. They are converted into musculoskeletal actions so that the driver can adjust the vehicle controls using his or her hands and feet and into head and eye movements to direct his or her gaze. The loop is closed by the driver observing the effects of very recent decisions about the control of the vehicle and adjusting the next ones, while also taking into account new information about the surroundings. Any condition that impairs perception, cognition (including alertness, attitude to risk, recall), or motor function has the potential to interfere with the whole loop and thus impair driving and make it less safe. This interference may be constant, as with a defect in vision. It may be episodic, as in a sudden loss of consciousness. In the longer term, the time course and prognosis of the impairing condition, whether fluctuating, progressive, remitting, or a mixed picture, will determine the pattern of future risk.(1)

Figure 1. The Driving Task



Source: Carter, 2006 (see: http://www.dft.gov.uk/pgr/roadsafety/drs/fitnesstodrive/fitnesstodrive)

The purpose of this evidence report is to summarize the available data pertaining to the relationship between a number of psychiatric disorders and commercial motor vehicle (CMV) driver safety. Driving is a complicated psychomotor performance, which depends on fine coordination between the sensory and motor systems. It is influenced by factors such as arousal, perception, learning, memory, attention, concentration, emotion, reflex speed, time estimation, auditory and visual functions, decision making, and personality. Complex feedback systems interact to produce the appropriate coordinated behavioral response. Anything that interferes with any of these factors to a significant degree may impair driving ability. Psychiatric illnesses may affect thinking, mood, and/or perception, resulting in a wide range of types and degrees of cognitive impairment. Insight is critical for drivers to drive within their limitations and to know how and when these limitations change. Poor insight in patients with psychiatric illness may be evidenced by noncompliance with treatment, trivializing their role in a crash, or repeated involuntary admissions to hospital (often as a result of discontinuing prescribed medication).

The Classification of Psychiatric Disorders

The Diagnostic and Statistical Manual of Mental Disorders (DSM), published by the American Psychiatric Association, is the standard classification of mental disorders used by mental health professionals in the United States. It is intended to be applicable in a wide array of contexts and used by clinicians and researchers of many different orientations (e.g., biological, psychodynamic, cognitive, behavioral, interpersonal, family systems). It also contains diagnostic codes taken from the World Health Organization's International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) that can be used for record keeping and reimbursement (see: http://www.psychnet-uk.com/dsm_iv/_misc/complete_tables.htm). Since all the diagnostic codes are valid ICD-9-CM codes,

DSM users automatically satisfy diagnostic coding requirements under the Health Insurance Portability and Accountability Act of 1996.

DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition), published in 1994, was the most recent major revision of the DSM. It was the culmination of a six-year effort that involved more than 1,000 individuals and numerous professional organizations. Much of the effort involved a comprehensive review of the literature to establish a firm empirical basis for making modifications. Numerous changes were made to the classifications (i.e., disorders were added, deleted, and reorganized), to the diagnostic criteria sets, and to the descriptive text, based on careful consideration of the available research about the various mental disorders.

In anticipation of the fact that the next major revision of the DSM (i.e., DSM-V) will not appear until 2011 or later (at least 16 years after DSM-IV), a text revision of the DSM-IV called DSM-IV-TR was published in May 2000. The primary goal of the DSM-IV-TR was to maintain the currency of the DSM-IV text, which reflected the empirical literature up to 1992. Thus, most of the major changes in DSM-IV-TR were confined to the descriptive text. Changes were made to a handful of criteria sets to correct errors identified in DSM-IV. In addition, some of the diagnostic codes were changed to reflect updates to the ICD-9-CM coding system adopted by the U.S. government.

1. Disorders usually first diagnosed in infancy, childhood, or adolescence
    - Mental retardation
    - Learning disorders
    - Motor skills disorders
    - Communication disorders
    - Pervasive developmental disorders
    - Attention deficit and disruptive behavior disorders
    - Feeding and eating disorders of infancy or early childhood
    - Tic disorders
    - Elimination disorders
    - Other disorders of infancy, childhood, or adolescence
2. Delirium, dementia, amnesia and other cognitive disorders
    - Delirium
    - Dementia
    - Amnestic disorders
    - Other cognitive disorders
3. Mental disorders caused by a general medical condition not elsewhere classified
4. Substance-related disorders
    - Alcohol-related disorders
    - Amphetamine (or amphetamine-like)-related disorders
    - Caffeine-related disorders
    - Cannabis-related disorders
    - Cocaine-related disorders

- Hallucinogen-related disorders
- Inhalant-related disorders
- Nicotine-related disorders
- Opioid-related disorders
- Phencyclidine (or phencyclidine-like)-related disorders
- Sedative-, hypnotic-, or anxiolytic-related disorders
- Polysubstance-related disorders
- Other (or unknown) substance-related disorders

5. Schizophrenia and other psychotic disorders
6. Mood disorders
    - Major depressive disorder
    - Dysthymic disorder
    - Bipolar disorder
7. Anxiety disorders
    - Acute stress disorder
    - Agoraphobia (with or without a history of panic disorder)
    - Generalized anxiety disorder (GAD)
    - Obsessive-compulsive disorder (OCD)
    - Panic disorder (with or without agoraphobia)
    - Phobias (including social phobia)
    - Post-traumatic stress disorder (PTSD)
8. Somatoform disorders
9. Factitious disorders
10. Dissociative disorders
11. Sexual and gender identity disorder
    - Sexual dysfunctions
    - Paraphilias
    - Gender identity disorders
12. Eating disorders
13. Sleep disorders
    - Primary sleep disorders
    - Parasomnias
    - Other sleep disorders
14. Impulse-control disorders not elsewhere classified
15. Adjustment disorders
16. Personality disorders
    a. *Cluster A* (odd or eccentric disorders)
        i. Paranoid personality disorder
        ii. Schizoid personality disorder
        iii. Schizotypal personality disorder

b. *Cluster B* (dramatic, emotional, or erratic disorders)
    i. Antisocial personality disorder
    ii. Borderline personality disorder
    iii. Histrionic personality disorder
    iv. Narcissistic personality disorder
c. *Cluster C* (anxious or fearful disorders)
    i. Avoidant personality disorder
    ii. Dependent personality disorder (*not* the same as Dysthymia)
    iii. Obsessive-compulsive personality disorder (*not* the same as OCD)

Psychiatric Disorders Considered in Present Evidence Report

Not all of the psychiatric disorders identified in the previous section are examined in this evidence report. The psychiatric disorders considered for consideration in the present evidence report (as defined by DSM-IV) are listed below:

- Cognitive disorders
- Substance-related disorders
- Schizophrenia and other psychotic disorders
- Mood disorders
- Anxiety disorders
- Personality disorders

The six disorders listed above are considered in this evidence report because they are of particular concern to the FMCSA and the medical examiners responsible for certifying individuals as being medically qualified to drive a CMV. On further discussion with the FMCSA, it was decided that two of the six disorders listed above would not be considered further in the current evidence report; these are cognitive disorders and substance-related disorders.

Why Are Cognitive Disorders not Considered Further in this Evidence Report?

Psychiatric disorders that are included in this diagnostic category include the following disorders:

- Delirium (consequent to a general medical condition, substance intoxication, substance withdrawal, multiple etiologies)
- Dementia (consequent to Alzheimer's disease, Creutzfeldt-Jakob disease, head trauma, Huntington's disease, HIV disease, Parkinson's disease, Pick's disease, substance-induced [persisting], vascular disease, and other general medical diseases)
- Amnestic disorders (consequent to a general medical condition, substance abuse [persistent], unspecified causes)

The impact of cognitive impairment (particularly dementia) on driver safety has been well studied and is being considered by the FMCSA as the subject of a future evidence report that will fall under the auspices of a neurological expert panel. Preliminary research on the impact of delirium and amnestic disorders on driver safety found that studies have not been performed. Consequently, we do not address cognitive disorders further in this evidence report.

Why Are Substance-related Disorders not Considered Further in this Evidence Report?

Substance abuse refers to the use of any substances that cause a detriment to the individual's physical health or causes the user legal, social, financial, or other problems, including endangering their lives or the lives of others. Substance abuse is not specific to illegal substances, but people can also abuse legal substances that are bought or prescribed. Substance abuse is an old-fashioned term; the term problematic substance use is now more widely used. There are 11 groups of substances specifically discussed in DSM-IV: alcohol, amphetamines and related sympathomimetics, caffeine, cannabis, cocaine, hallucinogens, inhalants, nicotine, opiates, phencyclidine and related drugs, and sedatives, hypnotics, or anxiolytics.

Preliminary research by the FMCSA identified more than 1,000 articles on the impact of substance abuse and the impact of interventions for substance abusers on driver safety. As a consequence, it was decided that should the FMCSA wish to examine the impact of substance-related disorders on driver safety, this should be carried out in a separate evidence report specific to this disorder.

Key Features of the Disorders Considered in Present Evidence Report

In this section of the evidence report, we provide the reader with a brief description of the primary features of the four psychiatric disorders that we consider in this evidence report.

Psychotic Disorders

The disorders included in this category of psychiatric disorders include schizophrenia, schizophreniform disorder, schizoaffective disorder, delusional disorder, brief psychotic disorder, shared psychotic disorder, psychotic disorder owing to a general medical condition, substance-induced psychotic disorder, and psychotic disorder not otherwise specified. All of these disorders potentially impact driver safety because they are associated with cognitive impairment, slowed reaction times, and a variable degree of distraction that may depend on the perceptual distortions present at any time.

DSM-IV–TR Diagnostic Criteria for Psychotic Disorders

We present the current DSM diagnostic criteria (DSM-IV-TR) for schizophrenia and other psychotic disorders below.

Schizophrenia

A. *Characteristic symptoms:* Two (or more) of the following, each present for a significant portion of time during a one-month period (or less if successfully treated):
    1. Delusions
    2. Hallucinations
    3. Disorganized speech (e.g., frequent derailment or incoherence)
    4. Grossly disorganized or catatonic behavior
    5. Negative symptoms, (i.e., affective flattening, alogia, or avolition)

    Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behavior or thoughts or two or more voices conversing with each other.

B. *Social/occupational dysfunction:* For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning, such as work, interpersonal relations, or self-care are markedly below the level achieved prior the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. *Duration:* Continuous signs of the disturbance persist for at least six months. This six-month period must include at least one month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. *Schizoaffective and mood disorder exclusion:* Schizoaffective disorder and mood disorder with psychotic features have been ruled out because either (1) no major depressive, manic, or mixed episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active-phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. *Substance/general medical condition exclusion:* The disturbance is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. *Relationship to a pervasive developmental disorder:* If there is a history of autistic disorder or another pervasive developmental disorder, the additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

Schizophreniform Disorder

A. Criteria A, D, and E of schizophrenia are met.

B. An episode of the disorder (including prodromal, active, and residual phases) lasts at least one month but less than six months. (When the diagnosis must be made without waiting for recovery, it should be qualified as "Provisional.")

Schizoaffective Disorder

A. An uninterrupted period of illness during which, at some time, there is either a major depressive episode, a manic episode, or a mixed episode concurrent with symptoms that meet Criterion A for schizophrenia.
Note: The major depressive episode must include Criterion A1: depressed mood (see below).
During the same period of illness, there have been delusions or hallucinations for at least two weeks in the absence of prominent mood symptoms.

B. Symptoms that meet criteria for a mood episode are present for a substantial portion of the total duration of the active and residual periods of the illness.

C. The disturbance is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Delusional Disorder

A. Nonbizarre delusions (i.e., involving situations that occur in real life, such as being followed, poisoned, infected, loved at a distance, deceived by spouse or lover, or having a disease) of at least one month's duration.

B. Criterion A for schizophrenia has never been met. Note: Tactile and olfactory hallucinations may be present in delusional disorder if they are related to the delusional theme.

C. Apart from the impact of the delusion(s) or its ramifications, functioning is not markedly impaired and behavior is not obviously odd or bizarre.

D. If mood episodes have occurred concurrently with delusions, their total duration has been brief relative to the duration of the delusional periods.

E. The disturbance is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Brief Psychotic Disorder

A. Presence of one (or more) of the following symptoms:

   1. Delusions
   2. Hallucinations
   3. Disorganized speech (e.g., frequent derailment, incoherence)
   4. Grossly disorganized or catatonic behavior (Note: Do not include a symptom if it is a culturally sanctioned response pattern.)

B. Duration of an episode of the disturbance is at least one day but less than one month, with eventual full return to premorbid level of functioning.

C. The disturbance is not better accounted for by a mood disorder with psychotic features, schizoaffective disorder, or schizophrenia and is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Shared Psychotic Disorder

A. A delusion develops in an individual in the context of a close relationship with another person(s), who has an already-established delusion.

B. The delusion is similar in content to that of the person who already has the established delusion.

C. The disturbance is not better accounted for by another psychotic disorder (e.g., schizophrenia) or a mood disorder with psychotic features and is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Psychotic Disorder Caused by a General Medical Condition

A. Prominent hallucinations or delusions

B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct physiological consequence of a general medical condition.

C. The disturbance is not better accounted for by another mental disorder.

D. The disturbance does not occur exclusively during the course of a delirium.

Substance-induced Psychotic Disorder

A. Prominent hallucinations or delusions (Note: Does not include hallucinations if the person has insight that they are substance-induced.)

B. There is evidence from the history, physical examination, or laboratory findings of either of the following:

   1. The symptoms in Criterion A developed during, or within a month of, substance intoxication or withdrawal.

   2. Medication use is etiologically related to the disturbance.

C. The disturbance is not better accounted for by a psychotic disorder that is not substance-induced. Evidence that the symptoms are better accounted for by a psychotic disorder that is not substance-induced might include the following: the symptoms precede the onset of the substance use (or medication use); the symptoms persist for a substantial period of time (e.g., about a month) after the cessation of acute withdrawal or severe intoxication or are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use; or other evidence suggests the existence of an independent non-substance-induced psychotic disorder (e.g., a history of recurrent non-substance-related episodes).

D. The disturbance does not occur exclusively during the course of a delirium. (Note: This diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms are in excess of those usually associated with the intoxication or withdrawal syndrome and when the symptoms are sufficiently severe to warrant independent clinical attention.)

Epidemiology

Approximately 2.4 million American adults, or about 1.1% of the population aged 18 and older in a given year, have schizophrenia. Schizophrenia affects men and women with equal frequency. Schizophrenia often first appears in men in their late teens or early 20s. In contrast, women are generally affected in their 20s or early 30s.

Mood Disorders

A mood disorder is a condition whereby the prevailing emotional mood is distorted or inappropriate to the circumstances. The two major types of mood disorders are depression (or unipolar depression) and bipolar disorder. All mood disorders have the potential to deleteriously impact driver safety. Depression is known to impair cognitive function, and some individuals with mood disorders, even when treated to full remission, demonstrate residual nonprogressive cognitive dysfunction in short-term memory, concentration, and mental processing speed.

DSM-IV–TR Diagnostic Criteria for Mood Disorders

Major Depressive Disorder, Single Episode

An individual meets the DSM-IV criteria for major depression disorder, single episode, if the following criteria are met:

A. Presence of a single major depressive episode.

B. The major depressive episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

C. There has never been a manic episode, a mixed episode, or a hypomanic episode. (Note: This exclusion does not apply if all the manic-like, mixed-like, or hypomanic-like episodes are substance- or treatment-induced or caused by the direct physiological effects of a general medical condition.)

Major Depressive Disorder, Recurrent

An individual meets the DSM-IV criteria for major depression disorder, recurrent, if the following criteria are met:

A. Presence of two or more major depressive episodes.

B. The major depressive episodes are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

C. There has never been a manic episode, a mixed episode, or a hypomanic episode. (Note: This exclusion does not apply if all of the manic-like, mixed-like, or hypomanic-like episodes are substance- or treatment-induced or caused by the direct physiological effects of a general medical condition.)

Dysthymic Disorder

An individual meets the DSM-IV criteria for dysthymic disorder if the following criteria are met:

A. Depressed mood for most of the day, for more days than not, as indicated either by subjective account or observation by others, for at least two years. (Note: In children and adolescents, mood can be irritable and duration must be at least one year.)

B. Presence, while depressed, of two (or more) of the following:

1. Poor appetite or overeating
2. Insomnia or hypersomnia
3. Low energy or fatigue
4. Low self-esteem
5. Poor concentration or difficulty making decisions
6. Feelings of hopelessness

C. During the two-year period (one year for children or adolescents) of the disturbance, the person has never been without the symptoms in Criteria A and B for more than two months at a time.

D. No major depressive episode has been present during the first two years of the disturbance (one year for children and adolescents); i.e., the disturbance is not better accounted for by chronic major depressive disorder or major depressive disorder in partial remission. (Note: There may have been a previous major depressive episode provided there was a full remission [no significant signs or symptoms for two months] before development of the dysthymic disorder. In addition, after the initial two years [one year in children or adolescents] of dysthymic disorder, there may be superimposed episodes of major depressive disorder, in which case both diagnoses may be given when the criteria are met for a major depressive episode.)

E. There has never been a manic episode, a mixed episode, or a hypomanic episode, and criteria have never been met for cyclothymic disorder.

F. The disturbance does not occur exclusively during the course of a chronic psychotic disorder, such as schizophrenia or delusional disorder.

G. The symptoms are not caused by the direct physiological effects of a substance (e.g., drug of abuse, medication) or a general medical condition (e.g., hypothyroidism).

H. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Cyclothymic Disorder

An individual meets the DSM-IV criteria for cyclothymic disorder if the following criteria are met:

A. For at least two years, the presence of numerous periods with hypomanic symptoms and numerous periods with depressive symptoms that do not meet criteria for a major depressive episode. (**Note**: In children and adolescents, the duration must be at least one year.)

B. During the above two-year period (one year in children and adolescents), the person has not been without the symptoms in Criterion A for more than two months at a time.

C. No major depressive episode, manic episode, or mixed episode has been present during the first two years of the disturbance.
Note: After the initial two years (one year in children and adolescents) of cyclothymic disorder, there may be superimposed manic or mixed episodes (in which case both bipolar I disorder and cyclothymic disorder may be diagnosed) or major depressive episodes (in which case both bipolar II disorder and cyclothymic disorder may be diagnosed).

D. The symptoms in Criterion A are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

E. The symptoms are not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

F. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Bipolar II Disorder

An individual meets the DSM-IV criteria for bipolar II disorder if the following criteria are met:

A. Presence (or history) of one or more major depressive episodes.

B. Presence (or history) of at least one hypomanic episode.

C. There has never been a manic episode or a mixed episode.

D. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

E. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Bipolar I Disorder, Single Manic Episode

An individual meets the DSM-IV criteria for bipolar I disorder, single manic episode, if the following criteria are met:

A. Presence of only one manic episode and no past major depressive episodes. (**Note**: Recurrence is defined as either a change in polarity from depression or an interval of at least two months without manic symptoms.)

B. The manic episode is not better accounted for by schizoaffective disorder and is not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

Bipolar I Disorder, Most Recent Episode Hypomanic

An individual meets the DSM-IV criteria for bipolar I disorder, most recent episode hypomania, if the following criteria are met:

A. Currently (or most recently) in a hypomanic episode.

B. There has previously been at least one manic episode or mixed episode.

C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

Bipolar I Disorder, Most Recent Episode Manic

An individual meets the DSM-IV criteria for bipolar I disorder, most recent episode manic, if the following criteria are met:

A. Currently (or most recently) in a manic episode.

B. There has previously been at least one major depressive episode, manic episode, or mixed episode.

C. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

Bipolar I Disorder, Most Recent Episode Mixed

An individual meets the DSM-IV criteria for bipolar I disorder, most recent episode mixed, if the following criteria are met:

A. Currently (or most recently) in a mixed episode.

B. There has previously been at least one major depressive episode, manic episode or mixed episode.

C. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

Bipolar I Disorder, Most Recent Episode Depressed

An individual meets the DSM-IV criteria for bipolar I disorder, most recent episode depressed, if the following criteria are met:

A. Currently (or most recently) in a major depressive episode.

B. There has previously been at least one manic episode or mixed episode.

C. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

Bipolar I Disorder, Most Recent Episode Unspecified

An individual meets the DSM-IV criteria for bipolar I disorder, most recent episode unspecified, if the following criteria are met:

A. Criteria, except for duration, are currently (or most recently) met for a manic, a hypomanic, a mixed, or a major depressive episode.

B. There has previously been at least one manic episode or mixed episode.

C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The mood symptoms in Criteria A and B are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder, delusional disorder, or psychotic disorder not otherwise specified.

E. The mood symptoms in Criteria A and B are not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication, other treatment) or a general medical condition (e.g., hyperthyroidism).

Epidemiology

Mood disorders include major depressive disorder, dysthymic disorder, cyclothymic disorder, and bipolar disorder. Approximately 20.9 million American adults, or about 9.5% of the U.S. population aged 18 and older in a given year, have a mood disorder. The median age of onset for mood disorders is 30 years. Depressive disorders often co-occur with anxiety disorders and substance abuse.

Major Depressive Disorder

- Major depressive disorder is the leading cause of disability in the United States for ages of 15–44.
- Major depressive disorder affects approximately 14.8 million American adults, or about 6.7% of the U.S. population aged 18 and older in a given year.
- While major depressive disorder can develop at any age, the median age at onset is 32.
- Major depressive disorder is more prevalent in women than in men.

Dysthymic Disorder

- Dysthymic disorder affects approximately 3.3 million American adults. This figure translates to about 1.5% of the U.S. population aged 18 and older in a given year.
- The median age of onset of dysthymic disorder is 31.

Cyclothymic Disorder

- Studies reported a lifetime prevalence of cyclothymic disorder from 0.4% to 1%.
- Prevalence in mood disorders clinics may range from 3% to 5%.

Bipolar Disorder

- Bipolar disorder affects approximately 5.7 million American adults, or about 2.6% of the U.S. population aged 18 and older in a given year.
- The median age of onset for bipolar disorders is 25 years.

Anxiety Disorders

Anxiety disorders include panic disorder, obsessive-compulsive disorder (OCD), post-traumatic stress disorder (PTSD), generalized anxiety disorder (GAD), and phobias (social phobia, agoraphobia, and specific phobia). Anxiety disorders may cause motor vehicle crashes when the level of driver anxiety interferes with concentration or causes "freezing" or perseverative errors.

Approximately 40 million American adults aged 18 and older, or about 18.1% of people in this age group in a given year, have an anxiety disorder. Anxiety disorders frequently co-occur with depressive disorders or substance abuse. Most people with one anxiety disorder also have another anxiety disorder. Nearly three-quarters of those with an anxiety disorder have their first episode by age 21.5.

Generalized Anxiety Disorder (GAD)

GAD is a common chronic disorder that affects twice as many women as men and can lead to considerable impairment. As the name implies, GAD is characterized by long-lasting anxiety that is not focused on any particular object or situation. In other words it is unspecific or free-floating. People with this disorder feel afraid of something but are unable to articulate the specific fear. They fret constantly

and have a hard time controlling their worries. Because of persistent muscle tension and autonomic fear reactions, they may develop headaches, heart palpitations, dizziness, and insomnia. These physical complaints, combined with the intense, long-term anxiety, make it difficult to cope with normal daily activities.

DSM-IV-RT Diagnostic Criteria

A. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least six months, about a number of events or activities (such as work or school performance).

B. The person finds it difficult to control the worry.

C. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms present for more days than not for the past six months). (Note: Only one item is required in children.)

1. Restlessness or feeling keyed up or on edge
2. Being easily fatigued
3. Difficulty concentrating or mind going blank
4. Irritability
5. Muscle tension
6. Sleep disturbance (difficulty falling or staying asleep or restless unsatisfying sleep)

D. The focus of the anxiety and worry is not confined to features of an Axis I disorder (e.g., the anxiety or worry is not about having a panic attack [as in panic disorder], being embarrassed in public [as in social phobia], being contaminated [as in OCD], being away from home or close relatives [as in separation anxiety disorder], gaining weight [as in anorexia nervosa], having multiple physical complaints [as in somatization disorder], or having a serious illness [as in hypochondriasis]), and the anxiety and worry do not occur exclusively during PTSD.

E. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Epidemiology

- Approximately 6.8 million American adults, or about 3.1% of people aged 18 and over have GAD in a given year.
- GAD can begin across the life cycle, though the median age of onset is 31 years.

Panic Disorder

In panic disorder, a person suffers brief attacks of intense terror and apprehension that cause trembling and shaking, confusion, dizziness, nausea, difficulty breathing, and feelings of impending doom or a situation that would be embarrassing. One who is often plagued by sudden bouts of intense anxiety might be said to be afflicted by this disorder.

Many people who have panic attacks (especially their first one) think they are having a heart attack and often end up at the doctor's office or emergency room. Even if the tests all come back normal, the person will still worry; the physical manifestations of anxiety reinforcing his or her fear that something is wrong

with his or her body. Heightened awareness (hypervigilance) of any change in the normal function of the body will be noticed and interpreted as a possible life-threatening illness by an individual suffering from panic attacks.

DSM-IV-RT Diagnostic Criteria

A. Both 1 and 2:

   1. Recurrent unexpected panic attacks.
   2. At least one of the attacks has been followed by one month (or more) of one (or more) of the following:
      a. Persistent concern about having additional attacks
      b. Worry about the implications of the attack or its consequences (e.g., losing control, having a heart attack, "going crazy")
      c. A significant change in behavior related to the attacks

B. Presence or absence of agoraphobia.

C. The panic attacks are not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g., hyperthyroidism).

D. The panic attacks are not better accounted for by another mental disorder, such as social phobia (e.g., occurring on exposure to feared social situations), specific phobia (e.g., on exposure to a specific phobic situation), OCD (e.g., on exposure to dirt in someone with an obsession about contamination), PTSD (e.g., in response to stimuli associated with a severe stressor), or separation anxiety disorder (e.g., in response to being away from home or close relatives).

Epidemiology

- Approximately 6 million American adults aged 18 and older, or about 2.7% of people in this age group have panic disorder in a given year.
- Panic disorder typically develops in early adulthood (median age of onset is 24 years), but the age of onset extends throughout adulthood.
- About one in three people with panic disorder develops agoraphobia, a condition in which the individual becomes afraid of being in any place or situation where escape might be difficult or help unavailable in the event of a panic attack.

Phobias

This category involves a strong, irrational fear and avoidance of an object or situation. The person knows the fear is irrational, yet the anxiety remains. Phobic disorders differ from GAD and panic disorder because there is a specific stimulus or situation that elicits a strong fear response. A person suffering from a phobia of spiders might feel so frightened by a spider that he or she would try to jump out of a speeding car to get away from one.

People with phobias have especially powerful imaginations, so they vividly anticipate terrifying consequences from encountering such feared objects as knives, bridges, blood, enclosed places, certain

animals, or situations. These individuals generally recognize that their fears are excessive and unreasonable but are generally unable to control their anxiety.

Epidemiology

Social Phobia

- Approximately 15 million American adults aged 18 and over, or about 6.8% of people in this age group have social phobia in a given year.
- Social phobia begins in childhood or adolescence, typically around age 13.

Agoraphobia

- Approximately 1.8 million American adults aged 18 and over, or about 0.8% of people in this age group have agoraphobia without a history of panic disorder in a given year.
- The median age of onset of agoraphobia is 20.

Specific Phobia

- Approximately 19.2 million American adults age 18 and over, or about 8.7% of people in this age group in a given year, have some type of specific phobia.
- Specific phobia typically begins in childhood; the median age of onset is seven years.

Obsessive-Compulsive Disorder

OCD is a type of anxiety disorder primarily characterized by obsessions or compulsions. Obsessions are distressing, repetitive, intrusive thoughts or images that the individual often realizes are senseless. Compulsions are repetitive behaviors that the person feels forced or compelled to do to relieve anxiety.

DSM-IV-RT Diagnostic Criteria

A. Either obsessions or compulsions:

Obsessions as defined by 1, 2, 3, and 4:

1. Recurrent and persistent thoughts, impulses, or images that are experienced at some time during the disturbance as intrusive and inappropriate and that cause marked anxiety or distress.
2. The thoughts, impulses, or images are not simply excessive worries about real-life problems.
3. The person attempts to ignore or suppress such thoughts, impulses, or images or to neutralize them with some other thought or action.
4. The person recognizes that the obsessional thoughts, impulses, or images are a product of his or her own mind (not imposed from without as in thought insertion).

Compulsions as defined by 1 and 2:

1. Repetitive behaviors (e.g., hand washing, ordering, checking) or mental acts (e.g., praying, counting, repeating words silently) that the person feels driven to perform in response to an obsession or according to rules that must be applied rigidly.

2. The behaviors or mental acts are aimed at preventing or reducing distress or preventing some dreaded event or situation; however, these behaviors or mental acts either are not connected in a realistic way with what they are designed to neutralize or prevent or are clearly excessive.

B. At some point during the course of the disorder, the person has recognized that the obsessions or compulsions are excessive or unreasonable. (Note: This does not apply to children.)

C. The obsessions or compulsions cause marked distress, are time-consuming (take more than an hour a day), or significantly interfere with the person's normal routine, occupational (or academic) functioning, or usual social activities or relationships.

D. If another Axis I disorder is present, the content of the obsessions or compulsions is not restricted to it (e.g., preoccupation with food in the presence of an eating disorder; hair pulling in the presence of trichotillomania; concern with appearance in the presence of body dysmorphic disorder; preoccupation with drugs in the presence of a substance use disorder; preoccupation with having a serious illness in the presence of hypochondriasis; preoccupation with sexual urges or fantasies in the presence of a paraphilia; or guilty ruminations in the presence of major depressive disorder).

E. The disturbance is not caused by the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

Epidemiology

- Approximately 2.2 million American adults aged 18 and older, or about 1% of people in this age group in a given year, have OCD.
- The first symptoms of OCD often begin during childhood or adolescence; however, the median age of onset is 19.

Post-traumatic Stress Disorder

PTSD is an anxiety disorder that results from a traumatic experience. Post-traumatic stress can result from an extreme situation, such as being involved in warfare, rape, a hostage situation, or a serious accident. It can also result from long-term (chronic) exposure to a severe stressor: for example, soldiers who endure individual battles but cannot cope with an unceasing sequence of battles. The sufferer may experience flashbacks, avoidant behavior, and other symptoms.

DSM-IV-RT Diagnostic Criteria

A. The person has been exposed to a traumatic event in which both of the following were present:

1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury or a threat to the physical integrity of self or others.

B. The person's response involved intense fear, helplessness, or horror.

C. The traumatic event is persistently reexperienced in one (or more) of the following ways:

1. Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions

2. Recurrent distressing dreams of the event
3. Acting or feeling as if the traumatic event were recurring, including a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated (Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event)
4. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

D. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

1. Efforts to avoid thoughts, feelings, or conversations associated with the trauma
2. Efforts to avoid activities, places, or people that arouse recollections of the trauma
3. Inability to recall an important aspect of the trauma
4. Markedly diminished interest or participation in significant activities
5. Feeling of detachment or estrangement from others
6. Restricted range of affect (e.g., unable to have loving feelings)
7. Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

E. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

1. Difficulty falling or staying asleep
2. Irritability or outbursts of anger
3. Difficulty concentrating
4. Hypervigilance
5. Exaggerated startle response

F. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than one month.

G. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Epidemiology

- Approximately 7.7 million American adults aged 18 and older, or about 3.5% of people in this age group have PTSD in a given year.
- PTSD can develop at any age, including childhood, but research shows that the median age of onset is 23 years.
- About 19% of Vietnam veterans experienced PTSD at some point after the war. The proportion of veterans returning from the current conflicts in Afghanistan and Iraq with PTSD is not clear. The disorder also frequently occurs after violent personal assaults, such as rape, mugging, or domestic violence; terrorism; natural or human-caused disasters; and accidents.

Personality Disorders

Personality disorder, formerly referred to as a *characterological disorder*, is a class of mental disorder characterized by rigid and on-going patterns of thought and action. The underlying belief systems informing these patterns are referred to as fixed fantasies. The inflexibility and pervasiveness of these behavioral patterns often cause serious personal and social difficulties, as well as general impairment of functioning. Individuals with personality disorders (including antisocial personality disorder, borderline personality disorder, histrionic personality disorder, and narcissistic personality disorder) are of concern to those involved in driver safety because the disorders are known to be associated with behaviors such as aggression, egocentricity, impulsiveness, resentment of authority, intolerance of frustration, and irresponsibility.

DSM-IV–TR Diagnostic Criteria

Diagnosis of a personality disorder must satisfy the following general criteria in addition to the specific criteria listed under the specific personality disorder under consideration.

A. Experience and behavior that deviates markedly from the expectations of the individual's culture. This pattern is manifested in two (or more) of the following areas:
    1. Cognition (perception and interpretation of self, others, and events)
    2. Affect (the range, intensity, lability, and appropriateness of emotional response)
    3. Interpersonal functioning
    4. Impulse control

B. The enduring pattern is inflexible and pervasive across a broad range of personal and social situations.

C. The enduring pattern leads to clinically significant distress or impairment in social, occupational, or other important areas of functioning.

D. The pattern is stable and of long duration, and its onset can be traced back at least to adolescence or early adulthood.

E. The enduring pattern is not better accounted for as a manifestation or consequence of another mental disorder.

F. The enduring pattern is not caused by the direct physiological effects of a substance or a general medical condition such as head injury.

People under 18 years old who fit the criteria of a personality disorder are usually not diagnosed with such a disorder, although they may be diagnosed with a related disorder. In order to diagnose an individual under the age of 18 with a personality disorder, symptoms must be present for at least one year. Antisocial personality disorder, by definition, cannot be diagnosed at all in persons under 18.

Cluster A Personality Disorders (Odd or Eccentric Disorders)

Paranoid Personality Disorder

The DSM-IV-TR characterizes paranoid personality disorder as follows:

A. A pervasive distrust and suspiciousness of others such that their motives are interpreted as malevolent, beginning by early adulthood and present in a variety of contexts, as indicated by four (or more) of the following:

    1. Suspects, without sufficient basis, that others are exploiting, harming, or deceiving him or her.
    2. Is preoccupied with unjustified doubts about the loyalty or trustworthiness of friends or associates.
    3. Is reluctant to confide in others because of unwarranted fear that the information will be used maliciously against him or her.
    4. Reads hidden demeaning or threatening meanings in benign remarks or events.
    5. Persistently bears grudges (i.e., is unforgiving of insults, injuries, or slights).
    6. Perceives attacks on his or her character or reputation that are not apparent to others and is quick to react angrily or to counterattack.
    7. Has a recurrent suspicion, without justification, regarding the fidelity of a spouse or sexual partner.

Exclusionary conditions:

    1. Does not occur exclusively during the course of a mood disorder with psychotic features, schizophrenia, or another psychotic disorder.
    2. Is not caused by the direct physiological effects of a general medical condition.

Schizoid Personality Disorder

The DSM-IV-TR defines schizoid personality disorder as:

A. A pervasive pattern of detachment from social relationships and a restricted range of expression of emotions in interpersonal settings, beginning by early adulthood and present in a variety of contexts, as indicated by four (or more) of the following:

    1. Neither desires nor enjoys close relationships, including being part of a family.
    2. Almost always chooses solitary activities.
    3. Has little, if any, interest in having sexual experiences with another person.

4. Takes pleasure in few, if any, activities.
5. Lacks close friends or confidants other than first-degree relatives.
6. Appears indifferent to the praise or criticism of others.
7. Shows emotional coldness, detachment, or flattened affectivity.

B. Does not occur exclusively during the course of schizophrenia, a mood disorder with psychotic features, another psychotic disorder, or a pervasive developmental disorder, and is not caused by the direct physiological effects of a general medical condition.

Note: DSM-IV states that a person with schizoid personality disorder may feel sensitive to the opinions of others and may even feel lonely but cannot do anything about the loneliness caused by the disorder.

Schizotypal Personality Disorder

The DSM-IV-TR defines schizoid personality disorder as follows:

A. A pervasive pattern of social and interpersonal deficits marked by acute discomfort with and reduced capacity for close relationships as well as by cognitive or perceptual distortions and eccentricities of behavior, beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

1. Ideas of reference (excluding delusions of reference)
2. Odd beliefs or magical thinking that influences behavior and is inconsistent with sub-cultural norms (e.g., superstition; belief in clairvoyance, telepathy, or "sixth sense"; in children and adolescents, bizarre fantasies or preoccupations)
3. Unusual perceptual experiences, including bodily illusions
4. Odd thinking and speech (e.g., vague, circumstantial, metaphorical, overelaborate, or stereotyped)
5. Suspiciousness or paranoid ideation
6. Inappropriate or constricted affect
7. Behavior or appearance that is odd, eccentric, or peculiar
8. Lack of close friends or confidants other than first-degree relatives
9. Excessive social anxiety that does not diminish with familiarity and tends to be associated with paranoid fears rather than negative judgments about self

B. Does not occur exclusively during the course of schizophrenia, a mood disorder with psychotic features, another psychotic disorder, or a pervasive developmental disorder.

Cluster B – Personality Disorders (Dramatic, Emotional, or Erratic Disorders)

Antisocial Personality Disorder

The DSM-IV-TR defines antisocial personality disorder as a pervasive pattern of disregard for and violation of the rights of others occurring since age 15, as indicated by three (or more) of the following:

1. Failure to conform to social norms with respect to lawful behaviors as indicated by repeatedly performing acts that are grounds for arrest
2. Deceitfulness, as indicated by repeated lying, use of aliases, or conning others for personal profit or pleasure
3. Impulsivity or failure to plan ahead
4. Irritability and aggressiveness, as indicated by repeated physical fights or assaults
5. Reckless disregard for safety of self or others
6. Consistent irresponsibility, as indicated by repeated failure to sustain steady work or to honor financial obligations
7. Lack of remorse, as indicated by being indifferent to or rationalizing having hurt, mistreated, or stolen from another

The manual lists the following additional necessary criteria:

1. There is evidence of conduct disorder with onset before age 15.
2. The occurrence of antisocial behavior is not exclusively during the course of schizophrenia or a manic episode.

Borderline Personality Disorder

DSM-IV-TR defines borderline personality disorder as follows:

1. Frantic efforts to avoid real or imagined abandonment, such as lying, stealing, temper tantrums *(Not including suicidal or self-mutilating behavior covered in Criterion 5)*
2. A pattern of unstable and intense interpersonal relationships characterized by alternating between extremes of idealization and devaluation
3. Identity disturbance: markedly and persistently unstable self-image or sense of self
4. Impulsivity in at least two areas that are potentially self-damaging (e.g., promiscuous sex, eating disorders, substance abuse, reckless driving, overspending, stealing, binge eating) *(Again, not including suicidal or self-mutilating behavior covered in Criterion 5)*
5. Recurrent suicidal behavior, gestures, threats, or self-mutilating behavior
6. Affective instability caused by a marked reactivity of mood (e.g., intense episodic dysphoria, irritability, anxiety usually lasting a few hours and only rarely more than a few days)
7. Chronic feelings of emptiness, worthlessness
8. Inappropriate anger or difficulty controlling anger (e.g., frequent displays of temper, constant anger, recurrent physical fights, getting mad over something small)
9. Transient, stress-related paranoid ideation or severe dissociative symptoms

Histrionic Personality Disorder

DSM-IV-TR defines histrionic personality disorder as a pervasive pattern of excessive emotionality and attention seeking, beginning by early adulthood and present in a variety of contexts, as indicated by five (or more) of the following:

1. Is uncomfortable in situations in which he or she is not the center of attention
2. Interaction with others is often characterized by inappropriate sexually seductive or provocative behavior
3. Displays rapidly shifting and shallow expression of emotions
4. Consistently uses physical appearance to draw attention to self
5. Has a style of speech that is excessively impressionistic and lacking in detail
6. Shows self-dramatization, theatricality, and exaggerated expression of emotion
7. Is suggestible (i.e., easily influenced by others or circumstances)
8. Considers relationships to be more intimate than they actually are

Narcissistic Personality Disorder

The DSM-IV-TR requires that at least five of the following criteria are met:

1. Has a grandiose sense of self-importance
2. Is preoccupied with fantasies of unlimited success, power, brilliance, beauty, or ideal love
3. Believes that he or she is "special" and unique and can only be understood by other special people
4. Requires excessive admiration
5. Strong sense of entitlement
6. Takes advantage of others to achieve his or her own ends
7. Lacks empathy
8. Is often envious or believes others are envious of him or her
9. Arrogant affect

Cluster C – Personality Disorders (anxious or fearful disorders)

Avoidant Personality Disorder

The DSM-IV-TR defines avoidant personality disorder as a "pervasive pattern of social inhibition, feelings of inadequacy, and hypersensitivity to negative evaluation, beginning by early adulthood and present in a variety of contexts," as indicated by at least four of the following:

1. Avoids occupational activities that involve significant interpersonal contact because of fears of criticism, disapproval, or rejection
2. Is unwilling to get involved with people unless certain of being liked

3. Shows restraint within intimate relationships because of the fear of being shamed or ridiculed
4. Is preoccupied with being criticized or rejected in social situations
5. Is inhibited in new interpersonal situations because of feelings of inadequacy
6. Views self as socially inept, personally unappealing, or inferior to others
7. Is unusually reluctant to take personal risks or to engage in any new activities because they may prove embarrassing

Avoidant personality disorder is often confused with antisocial personality disorder; clinically, the term *anti-social* denotes sociopathy, not social inhibitions.

Dependent Personality Disorder

The DSM-IV-TR defines dependent personality disorder as a "pervasive and excessive need to be taken care of that leads to submissive and clinging behavior and fears of separation, beginning by early adulthood and present in a variety of contexts," as indicated by five (or more) of the following:

1. Has difficulty making everyday decisions without an excessive amount of advice and reassurance from others
2. Needs others to assume responsibility for most major areas of his or her life
3. Has difficulty expressing disagreement with others because of fear of loss of support or approval (this does not include realistic fears of retribution)
4. Has difficulty initiating projects or doing things on his or her own (because of a lack of self-confidence in judgment or abilities rather than a lack of motivation or energy)
5. Goes to excessive lengths to obtain nurturance and support from others, to the point of volunteering to do things that are unpleasant
6. Feels uncomfortable or helpless when alone because of exaggerated fears of being unable to care for himself or herself
7. Urgently seeks another relationship as a source of care and support when a close relationship ends
8. Is unrealistically preoccupied with fears of being left to take care of himself or herself

Many cases of dependent personality disorder also have roots in OCD, and instead of being afraid if they are alone when not in a relationship, tend to think everything is wrong.

Obsessive-Compulsive Personality Disorder

The DSM-IV-TR defines that for a diagnosis of obsessive-compulsive personality disorder, patients must exhibit at least four of the following:

1. Preoccupation with details, rules, lists, order, organization, bodily functions, or schedules, to the extent that the major point of the activity is lost
2. Perfectionism that interferes with task completion (e.g., is unable to complete a project because his or her own overly strict standards are not met)

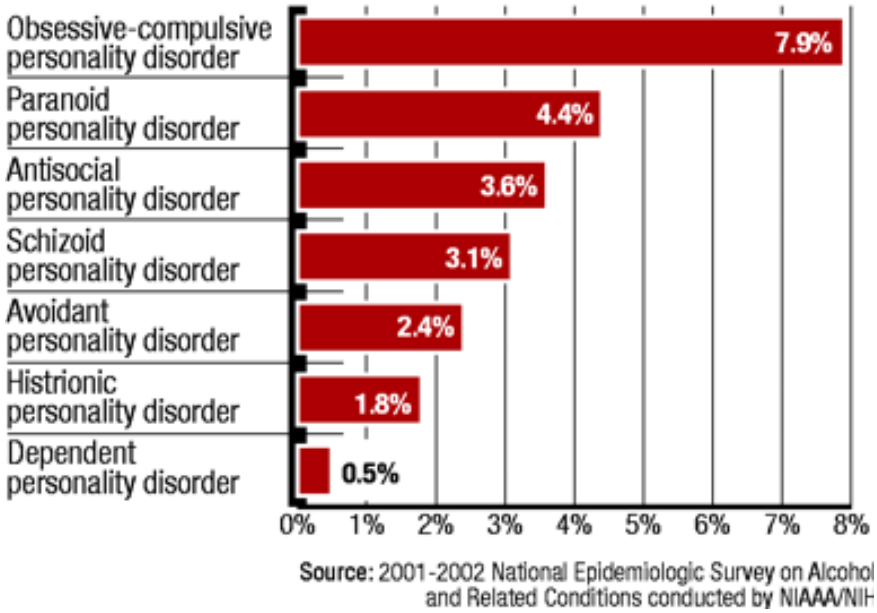
3. Excessive devotion to work and productivity to the exclusion of leisure activities and friendships (not accounted for by obvious economic necessity)
4. Overconscientious, scrupulous, and inflexible attitudes about matters of morality, ethics, or values (not accounted for by cultural or religious identification)
5. Inability to discard worn-out or worthless objects even when they have no sentimental value
6. Reluctance to delegate tasks or to work with others unless they submit to exactly his or her way of doing things
7. Adoption of a miserly spending style toward both self and others; money is viewed as something to be hoarded for future catastrophes
8. Rigidity and stubbornness
9. Urge to perfect every little thing

While a person may exhibit any or all of the characteristics of a personality disorder, it is not diagnosed as a disorder unless the person has trouble leading a normal life caused by these issues.

Epidemiology

According to results from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions, almost 15% of Americans, or 30.8 million adults, meet diagnostic criteria for at least one personality disorder (see Figure 2).

Figure 2. Prevalence of Personality Disorders in the United States



Source: 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions conducted by NIAAA/NIH

The Burden of Psychiatric Disorders

Worldwide, psychiatric disorders are considered a common cause of disability, although underreporting makes for limitations in obtaining data. The World Health Organization (WHO) estimated that neuropsychiatric conditions (which included unipolar depressive disorder, bipolar disorder, substance

disorders, primary insomnia, and dementia), account for 12% of the total proportion of disability life-adjusted years and 31% of the years of life lived with a disability.(2) A similar examination of the impact of mental disorders on employment behavior performed by Kessler et al. (1997) found that psychiatric disorders were associated with lost work days, with the average number of days missed varying by the type of disorder.(3) Moussavi et al. (2007) reported that the fourth leading cause of global disease burden was depression, with a one-year prevalence rate of 3.2%, compared to angina (4.5%), arthritis (4.1%), and diabetes (2%).(4) Given its comorbidity with chronic musculoskeletal and metabolic diseases such as arthritis and diabetes,(5,6) and the projected increases in the rates of these diseases with the overall aging of the population, depression is anticipated to become the second leading cause of global disease burden by 2020.(4) Information on psychiatric disease as calculated by WHO is featured in Table 3.

Table 3. Leading Causes of DALYs and YLDs in All Ages and Genders, estimated for 2000(2)

Condition	DALYs All Ages	YLDs All Ages	DALYs Ages 15–44	YLDs Ages 15–44
Unipolar Depressive Disorder	4.4%	11.9%	8.6%	16.4%
Schizophrenia	Not in top 20 causes	2.8%	2.6%	4.9%
Bipolar Affective Disorder	Not in top 20 causes	2.5%	2.5%	4.7%

DALYs: Disability life-adjusted years
YLDs: Years lived with disability

Treatments for Psychiatric Disorders

The treatments available for psychiatric disorders vary according to the disorder, its etiology, and severity. Most treatments are used primarily to relieve symptoms, prevent the progression of the disease, and allow the individual to function in the community.(7) Mental disorders can be chronic and recurrent, and are associated with decreasing functional ability over time. These factors suggest that treatment should begin as soon as the disorder is diagnosed, may embrace several different regimens over the course of an individual's lifetime, and is dependent on individual compliance. Treatments include:(2,8-10)

- Psychotherapy
- Psychotropic therapy
- Multimodal therapy
- Other therapeutic options

Psychotherapy

The psychotherapeutic (or "talk therapy") approach to mental health issues involves the communication of problems by the individual to a psychotherapist who then assists that individual in developing the skills needed to alter his or her current behavior, mood, and emotional modes of response to external factors.(11,12) Psychotherapeutic interventions include the following:

- Cognitive therapy
- Interpersonal therapy
- Behavior therapy
- Supportive therapy

Psychotropic Therapy

Psychotropic therapy (or pharmacotherapy) is often used to treat individuals with psychiatric disorders.(12) Drug therapies for psychiatric disorders fall into three basic categories:

- Antipsychotics
- Anxiolytics
- Antidepressants

More specific information on the psychotherapeutic agents that are currently used in the United States to treat individuals with a psychiatric disorder is presented in Table 4. All the drugs included in the table act by altering the status of the central nervous system. Common side effects associated with psychotropic drugs include drowsiness, impaired cognitive and/or psychomotor function, and changes in vision function. Consequently, all psychotropic drugs have the potential to affect driver safety. For a complete list of the potential adverse effects that have been observed in clinical trials, the reader is directed to the drugs' labeling information (a link to this information, which is available from the Federal Drug Administration web site) is provided in Table 4).

Table 4. Medications Commonly Used in the Treatment of Individuals with Psychiatric Disorders

Generic	Trade Names (US)	Psychotic Disorders	Mood Disorders	Anxiety Disorders	Personality Disorders	Specific Indication	Link to Labeling Information
Alprazolam	Xanax		✓	✓		Treatment of anxiety disorders; panic attacks	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a684001.html
Amitriptyline (TCA)	Elavil		✓			Treatment of symptoms of endogenous depression	http://www.rxlist.com/cgi/generic/amitrip_ids.htm
Amoxapine	Asendin	✓	✓	✓		Treatment of symptoms of depression with neurotic or reactive depressive disorders, endogenous, and psychotic depressions; depression accompanied by anxiety or agitation	http://www.rxlist.com/cgi/generic/amoxapine_ids.htm
Bupropion	Wellbutrin		✓			Treatment of depression and seasonal affective disorder (SAD)	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a695033.html
Buspirone	BuSpar		✓	✓		Treatment of anxiety disorders; short term treatment of symptoms of anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a688005.html
Carbamazepine	Tegretol		✓		✓	Treatment of mania or mixed episodes in bipolar I disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682237.html
Clorazepate	Azene, Tranxene			✓		Management of anxiety disorders; short term treatment of symptoms of anxiety disorders	http://www.rxlist.com/cgi/generic/clorazepate_ids.htm
Chlordiazepoxide	Librax, Libritabs, Librium			✓		Treatment of anxiety; control of agitation associated with alcohol withdrawal	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682078.html
Chlorpromazine	Thorazine	✓				Psychotic disorders; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682040.html
Chlorprothixene	Taractan	✓				Psychotic disorders; treatment of disorganized or psychotic thinking, hallucinations, and delusions	http://psyweb.com/Drughtm/jsp/chlorth.jsp
Citalopram (SSRI)	Celexa		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a699001.html
Clomipramine (TCA)	Anafranil		✓		✓	Treatment of depression and obsessive-compulsive disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a697002.html
Clonazepam	Klonopin			✓		Treatment of anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682279.html
Clozapine	Clozaril	✓				Psychotic disorders; treatment of schizophrenia with suicidal ideation or behavior	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a691001.html
Desipramine (TCA)	Norpramin, Pertofrane		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682387.html
Diazepam	Valium			✓		Treatment of anxiety; control of agitation associated with alcohol withdrawal	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682047.html

Generic	Trade Names (US)	Psychotic Disorders	Mood Disorders	Anxiety Disorders	Personality Disorders	Specific Indication	Link to Labeling Information
Divalproex sodium (valproic acid)	Depakote		✓		✓	Treatment of mania in bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682412.html
Doxepin (TCA)	Adapin, Sinequan		✓	✓		Treatment of depression and anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682390.html
Duloxetine	Cymbalta		✓	✓	✓	Treatment of depression and generalized anxiety disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a604030.html
Escitalopram (SSRI)	Lexapro		✓	✓		Treatment of depression and generalized anxiety disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a603005.html
Fluoxetine (SSRI)	Prozac		✓		✓	Treatment of depression; obsessive-compulsive disorder; eating disorders; panic attacks; treatment of symptoms of premenstrual dysphoric disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a689006.html
Fluphenazine	Permitil, Prolixin	✓				Schizophrenia; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682172.html
Fluvoxamine (SSRI)	Luvox				✓	Treatment of obsessive-compulsive disorder (OCD)	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a695004.html
Haloperidol	Haldol	✓				Psychotic disorders; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682180.html
Imipramine (TCA)	Tofranil		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682389.html
Isocarboxazid (MAOI)	Marplan		✓			Treatment of resistant depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a605036.html
Lamotrigine	Lamictal		✓		✓	Used to increase time between episodes of depression, mania, and other abnormal moods in bipolar I disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a695007.html
Lithium carbonate	Eskalith, Lithane, Lithobid		✓		✓	Treatment and prevention episodes of mania in bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a681039.html
Lithium citrate	Cibalith-S	✓	✓		✓	Treatment of acute manic and hypomanic episodes in bipolar disorder; maintenance therapy to diminish the intensity and frequency of subsequent manic episodes in individuals with a history of mania; maintenance in unipolar depression; acute and maintenance therapy in schizoaffective disorder; augments antidepressant effect of tricyclic or MAOI antidepressants in treatment of resistant major unipolar depression	http://www.drugs.com/mmx/lithium-citrate.html
Lorazepam	Ativan			✓		Treatment of anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682053.html

Generic	Trade Names (US)	Psychotic Disorders	Mood Disorders	Anxiety Disorders	Personality Disorders	Specific Indication	Link to Labeling Information
Loxapine	Loxitane	✓				Psychotic disorders; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682311.html
Maprotiline (TCA)	Ludiomil		✓	✓		Treatment of depression, bipolar disorder, anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682158.html
Mesoridazine	Serentil	✓		✓		Treatment of the symptoms of schizophrenia; reduction in restlessness, anxiety, and tension, hyperactivity and uncooperativeness	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682306.html
Mirtazapine	Remeron		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a697009.html
Molindone	Lidone, Moban	✓				Psychotic disorders; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682238.html
Nefazodone	Serzone		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a695005.html
Nortriptyline (TCA)	Aventyl, Pamelor		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682620.html
Olanzapine	Zyprexa	✓				Treatment of schizophrenia, bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a601213.html
Oxazepam	Serax			✓		Treatment of anxiety, control of agitation associated with alcohol withdrawal	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682050.html
Paroxetine (SSRI)	Paxil		✓	✓	✓	Treatment of depression; panic disorder; social anxiety disorder, OCD, generalized anxiety disorder (GAD), post-traumatic stress disorder (PTSD); premenstrual dysphoric disorder (PMDD)	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a698032.html
Perphenazine	Trilafon	✓				Schizophrenia; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682165.html
Phenelzine (MAOI)	Nardil		✓			Treatment of resistant depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682089.html
Pimozide	Orap	✓				Control of tics	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a686018.html
Prazepam	Centrax			✓		Treatment of anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a601100.html
Protriptyline (TCA)	Vivactil		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a604025.html
Quetiapine	Seroquel	✓	✓			Treatment of symptoms of schizophrenia; treatment of episodes of mania or depression in bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a698019.html
Risperidone	Risperdal	✓	✓			Treatment of symptoms of schizophrenia; treatment of episodes of mania or mixed episodes in bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a694015.html

Generic	Trade Names (US)	Psychotic Disorders	Mood Disorders	Anxiety Disorders	Personality Disorders	Specific Indication	Link to Labeling Information
Sertraline (SSRI)	Zoloft		✓	✓	✓	Treatment of depression, panic attacks, social anxiety disorder, OCD, PTSD, PMDD	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a697048.html
Thioridazine	Mellaril	✓				Schizophrenia; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682119.html
Thiothixene	Navane	✓				Schizophrenia; treatment of symptoms such as hallucinations, delusions, and hostility	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682867.html
Tranylcypromine (MAOI)	Parnate		✓			Treatment of resistant depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682088.html
Trazodone	Desyrel					Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a681038.html
Trifluoperazine	Stelazine	✓		✓		Schizophrenia; treatment of symptoms such as hallucinations, delusions, and hostility; short term treatment of anxiety	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a682121.html
Triflupromazine	Vesprin	✓				Psychotic disorders; treatment of symptoms such as hallucinations, delusions, and hostility	http://psyweb.com/Drughtm/jsp/trifup.jsp
Trimipramine (TCA)	Surmontil		✓			Treatment of depression	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a602010.html
Venlafaxine	Effexor		✓	✓		Treatment of depression; GAD; social anxiety disorder; panic disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a694020.html
Ziprasidone	Geodon	✓	✓			Treatment of symptoms of schizophrenia; treatment of episodes of mania or mixed episodes in bipolar disorder	http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a699062.html

MAOI: Monoamine oxidase inhibitor
SSRI: Selective serotonin reuptake inhibitor
TCA: Tricyclic antidepressant

Multimodal Therapy

Multimodal therapy brings together a variety of elements, including cognitive/behavioral therapy and pharmacotherapy, to provide optimal care through an approach that encompasses the etiology of the disorder and the psychological and social issues which interact within the individual's experience of illness.(8)

Other therapeutic options

When psychotherapy, pharmacotherapy, and multimodal therapy have failed to provide relief from psychiatric symptoms and quality of life has diminished, other treatment options for mental health disorders are available.(13-15) The decision to treat a psychiatric disorder with some of these therapies requires considering many factors, including the risks associated with surgical procedures, and the progression of the disease in the absence of these therapies. Other therapeutic options to treat psychiatric disorders include the following:

- Deep brain stimulation (DBS)
- Electroconvulsive therapy (ECT)
- Transcranial magnetic stimulation

It is important to note that approximately 50% of individuals in the United States who have a severe mental illness (e.g., depression) do not attempt to obtain treatment because of the stigma attached to psychiatric disorders.(8,16,17) When treatment for a psychiatric disorder is sought, it is usually administered through a general practitioner; this may be the result of a lack of trained professionals or reduced availability of specialized services or a reluctance to associate with a mental health professional because of the "shame" associated with mental disorders.(2) Overall, the use of mental health services worldwide corresponded to the gross national product amount spent on healthcare of a particular country. In the 12 months preceding the Wang et al. study, approximately 2% of all Nigerians and 18% of all U.S. citizens used mental health care; of individuals with a severe mental disorder, 11% of Chinese and 61% of Belgians received any type of mental health care, and 10% of Nigerians and 42% of French received care which met minimum treatment standards.(18)

Medical Fitness-for-Duty Regulations

Several of the abnormal behaviors associated with the psychiatric disorders discussed above have the potential to adversely affect driver safety and increase the risk for a motor vehicle crash. To provide for public safety, U.S. federal and state laws have been created that set CMV operation standards for individuals with psychiatric disorders. Current U.S. federal regulatory criteria for CMV drivers are discussed in the sections below.

Current Federal Physical Qualification Standards

The FMCSA regulations, found in 49 Code of Federal Regulations (CFR) 301 through 399, cover businesses that operate CMVs in interstate commerce. The FMCSA regulations that pertain specifically to an individual's fitness to drive a CMV are covered by CFR 391.41. Only motor carriers engaged purely in intrastate commerce are not directly subject to these regulations. However, intrastate motor carriers are subject to state regulations, which must be identical to or compatible with the federal regulations in order

for states to receive motor carrier safety grants from the FMCSA. States have the option of exempting CMVs with a gross vehicle weight rating of less than 26,001 lbs.

The current medical qualification standards that pertain to individuals with a psychiatric disorder are presented below. Relevant subparts of CFR 391.41 that pertain directly to individuals with a psychiatric disease state the following:

A person is physically qualified to drive a CMV if he or she meets the following conditions:

- (b)(9) Has no mental, nervous, organic, or functional disease or psychiatric disorder likely to interfere with his/her ability to drive a commercial motor vehicle safely; and
- (b)(12)(i) Does not use a controlled substance identified in 21 CFR 1308.11 Schedule I, an amphetamine, a narcotic, or any other habit-forming drug.
- (b)(12)(ii) *Exception*. A driver may use such a substance or drug if the substance or drug is prescribed by a licensed medical practitioner who
    - (b)(12)(ii)(A) is familiar with the driver's medical history and assigned duties;
    - (b)(12)(ii)(B) has advised the driver that the prescribed substance or drug will not adversely affect the driver's ability to safely operate a commercial motor vehicle; and
    - (b)(13) has no current clinical diagnosis of alcoholism.

Current Guidance to Medical Examiners

While no official guidance to medical examiners exists, some recommendations on the certification of individuals with psychiatric disorders are available. These recommendations emanate from a 1991 conference report titled, "*Conference on Psychiatric Disorders and Commercial Drivers"* available online at http://www.fmcsa.dot.gov/rulesregs/medreports.htm. Recommendations pertinent to the four psychiatric disorders considered in this evidence report are presented below.(19)

Psychotic Disorders

The authors of the conference report made the following recommendations:

- Individuals with active psychosis who are experiencing significant symptoms related to such an illness (for example, impairment in judgment and/or attention or suicidal behaviors) should not be considered medically qualified to drive a CMV.
- All individuals with a history of a psychotic disorder should be referred to a psychiatrist for further evaluation.
    - Individuals with a history of psychotic disorder must be symptom-free for at least one year before reevaluation by a psychiatrist.
    - Individuals with a history of a brief reactive psychosis may be reevaluated sooner if their clinical conditions have significantly improved.
- Individuals with a history of psychotic disorder who are currently certified to drive a CMV should be required to report any psychotic symptoms within 30 days of onset.
- All individuals with a history of psychotic disorder who are currently certified to drive a CMV and who remain symptom-free should be reevaluated by a psychiatrist every two years.

Mood Disorders

The authors of the conference report made the following recommendations:

- All individuals who suffer from mania or a severe major depression or who are suicidal at the time of the evaluation are not medically qualified to drive commercially.
- All individuals with a history of mania or significant depressive symptomatology should be referred by the medical examiner to a psychiatrist for further evaluation.
- Individuals who have experienced a severe depressive episode, a suicide attempt, or manic episode should be symptom-free for one year before reevaluation by a psychiatrist. However, individuals who have experienced a nonpsychotic major depressive disorder unaccompanied by suicidal behavior and who are currently symptom-free may be reexamined within six months.
- Individuals with a history of mania or significant depressive symptomatology who are currently certified to drive a CMV should be required to report any manic or severe major depressive episode within 30 days of its onset.
- All individuals with a history of mania or significant depressive symptomatology, who remain symptom-free and are currently certified to drive a CMV, should be reevaluated by a psychiatrist every two years.

Personality Disorders

The authors of the conference report made the following recommendation pertaining to individuals with a personality disorder:

- Individuals with a history or who are suspected of having a personality disorder should be referred to a psychiatrist for an assessment of behaviors that might constitute a risk to driver safety. Decisions pertaining to whether an individual can be considered medically qualified to drive a CMV should be made on a case-by-case basis.

Medical Fitness Standards from Other Transportation Agencies in the United States

Current medical fitness standards and guidelines for individuals performing safety sensitive work within other transportation agencies within the United States are summarized in Table 5. Included in Table 5 are pertinent standards for pilots only. At the current time, no other federal agency within the Department of Transportation has medical qualification standards that speak specifically to psychiatric disorders.

Table 5. Medical Fitness for Duty Standards from U.S. Federal Aviation Agency

Standard

Medical qualification standards for a first-class airman medical certificate that pertain directly to psychiatric disorders are as follows:

- No established medical history or clinical diagnosis of any of the following:
  - A personality disorder that is severe enough to have repeatedly manifested itself by overt acts.
  - A psychosis. As used in this section, "psychosis" refers to a mental disorder in which:
    - The individual has manifested delusions, hallucinations, grossly bizarre or disorganized behavior, or other commonly accepted symptoms of this condition; or
    - The individual may reasonably be expected to manifest delusions, hallucinations, grossly bizarre or disorganized behavior, or other commonly accepted symptoms of this condition.
  - No other personality disorder, neurosis, or other mental condition that the Federal Air Surgeon, based on the case history and appropriate, qualified medical judgment relating to the condition involved, finds—
    - Makes the person unable to safely perform the duties or exercise the privileges of the airman certificate applied for or held; or
    - May reasonably be expected, for the maximum duration of the airman medical certificate applied for or held, to make the person unable to perform those duties or exercise those privileges.
  - A bipolar disorder.
  - Substance dependence, except where there is established clinical evidence, satisfactory to the Federal Air Surgeon, of recovery, including sustained total abstinence from the substance(s) for not less than the preceding 2 years. As used in this section—
    - "Substance" includes: Alcohol; other sedatives and hypnotics; anxiolytics; opioids; central nervous system stimulants such as cocaine, amphetamines, and similarly acting sympathomimetics; hallucinogens; phencyclidine or similarly acting arylcyclohexylamines; cannabis; inhalants; and other psychoactive drugs and chemicals; and
    - "Substance dependence" means a condition in which a person is dependent on a substance, other than tobacco or ordinary xanthine-containing (e.g., caffeine) beverages, as evidenced by—
      - Increased tolerance;
      - Manifestation of withdrawal symptoms;
      - Impaired control of use; or
      - Continued use despite damage to physical health or impairment of social, personal, or occupational functioning.
    - No substance abuse within the preceding 2 years defined as:
      - Use of a substance in a situation in which that use was physically hazardous, if there has been at any other time an instance of the use of a substance also in a situation in which that use was physically hazardous;
      - A verified positive drug test result, an alcohol test result of 0.04 or greater alcohol concentration, or a refusal to submit to a drug or alcohol test required by the U.S. Department of Transportation or an agency of the U.S. Department of Transportation; or
      - Misuse of a substance that the Federal Air Surgeon, based on case history and appropriate, qualified medical judgment relating to the substance involved, finds—
        - Makes the person unable to safely perform the duties or exercise the privileges of the airman certificate applied for or held; or
        - May reasonably be expected, for the maximum duration of the airman medical certificate applied for or held, to make the person unable to perform those duties or exercise those privileges.

*Source of information for FAA Regulations and Guidelines:

http://www.faa.gov/about/office_org/headquarters_offices/avs/offices/aam/ame/guide/app_process/exam_tech/item47/amd/
http://www.faa.gov/about/office_org/headquarters_offices/avs/offices/aam/ame/guide/app_process/exam_tech/item47/amd/table/

Regulatory Medical Fitness Standards for CMV Drivers in Other Countries

Regulatory medical fitness standards for the protection and safety of the public interest (including licensed drivers) have been established globally. The medical standards of these countries are used to assess and determine the fitness of drivers operating CMVs. Likewise, psychiatric disorders are defined, and criteria for establishing these standards are constructed. Each country demonstrates its interpretation of psychiatric disorders through definition and by determining whom it affects.

Regulatory Standards and Certification Guidelines from Select Countries

Regulatory standards and guidelines that pertain directly to psychological disorders and CMV driver safety from selected countries other than the United States are summarized in Table 6.

Table 6. Standards and Guidelines for CMV Drivers in Other Countries

Country/ Consortium	Source	Standard or Guideline
Australia	Assessing Fitness to Drive (For Commercial and Private Vehicle Drivers) Medical Standards for Licensing and Clinical Management Guidelines. Austroads and NTC (National Transport Commission) Australia (2006) Medical Standards for Licensing – Psychiatric Disorders	The criteria for an *unconditional license* are NOT met: ○ If the person has an acute or chronic psychosis, whether schizophrenic, bipolar (manic or depressive phase), or other depressive psychosis; or ○ If the person has a personality or psychiatric disorder with features such as aggression, violence, etc., which are hazardous to driving; or ○ If the person is taking psychoactive drugs which will impair driving performance on a long-term basis; or ○ If the person's judgment or perceptual, cognitive, or motor function is affected by mental disorder; or ○ If the examining doctor believes that there is a significant risk of a previous psychotic condition relapsing. A *conditional license* may be granted by the Driver Licensing Authority, taking into account the opinion of a psychiatrist and the nature of the driving task, and subject to periodic review: ○ If the condition is well controlled and the person is compliant with treatment over a substantial period; and ○ The person is taking medication that minimizes the risk of cognitive or other side effects that might affect driving Individuals on antipsychotics should be warned against driving while being stabilized.
Canada	Determining Medical Fitness to Operate Motor Vehicles. CMA (Canadian Medical Association) Driver's Guide 7th edition. (2006)	In general, drivers with a psychiatric illness may be considered fit to drive if: ○ The psychiatric condition is stable (not in the acute phase) ○ Functional cognitive impairment assessed is minimal (adequate alertness, memory, attention and executive function abilities) ○ The patient is compliant and consistent with prescribed psychotropic medication ○ The maintenance dose of medication does not cause noticeable sedation ○ The patient has the insight to self-limit at times of symptom relapse and to seek assessment promptly ○ The patient's family is supportive of his or her driving Further psychiatric assessment should be considered if: ○ A family member reports a concern ○ An at-fault crash occurs ○ There is uncertainty about the degree of cognitive impairment Immediate contraindications to driving include the following: ○ Acute psychosis ○ Condition relapses sufficient to impair perceptions, mood or thinking ○ Medication with potentially sedating effects initiated or dose increased ○ Lack of insight or lack of cooperation with treatment ○ Lack of compliance with any conditional licensing limitations imposed by motor vehicle licensing authority ○ Suicidal plan involving crashing a vehicle ○ Intent to use vehicle to harm others A person seen to have, or who is reported to have, any of these problems should be advised not to drive until the condition is evaluated and treated. ○ <u>Depression and bipolar disorder:</u> ○ A manic episode is a contraindication to driving; fitness to return to driving will depend on response to treatment and the patient's level of insight and degree of inter-episode functioning. If a patient with bipolar disorder is advised not to drive, consent should be sought to notify a

Country/ Consortium	Source	Standard or Guideline
		family member. Non compliance with medical advice not to drive shall be reported to licensing authorities. ○ Most treatment of depression is with newer generation drugs rather than the older tricyclic agents. Tricyclic have been associated with an increased risk of crash, especially at higher doses, or if multiple agents are used. Selective serotonin reuptake inhibitors (SSRIs) are less likely to cause impairment. ○ Electroconvulsive therapy (ECT) can induce sustained confusion in 1 in 200 patients. Those receiving outpatient ECT need to comply with standard guidelines for not driving after anesthesia and take extra time if they are experiencing any memory problems after ECT. ○ Rapid-rate transcranial magnetic stimulation (rTMS) is reported to produce no evidence of cognitive impairment. ○ Anxiety disorders: ○ Anxiety disorders may cause crashes when the level of driver anxiety interferes with concentration or causes "freezing" or perseverative errors. ○ Benzodiazepines may increase the risk of crash. ○ Psychotic episodes: ○ An acute episode is incompatible with safe driving. ○ Antidepressants and antipsychotics: ○ Patients taking antidepressants or antipsychotics should be carefully observed during the initial phase of dose adjustment and advised not to drive if they show any evidence of drowsiness or hypotension. Patients who are stable on maintenance doses can usually drive any class of motor vehicle if they are symptom free.
New Zealand	Medical aspects of fitness to drive: A Guide for Medical Practitioners. Land Transport Safety Authority. (May 2002) Section 8: Mental disorder	Individuals with severe chronic mental conditions should be given the recommended periods to refrain from driving as outlined below. ○ Recommendations do not imply that all individuals with anxiety, depression, schizophrenia or bi-polar disease should refrain from driving. This information applies to those individuals who: ○ Have an ongoing serious occurrence of their mental illness, which may include a regular pattern of episodes where their ability to drive safely may be affected by their mental condition ○ Do not respond well to treatment or are non-compliant with treatment over extended periods of time, such as over several months, and this may impair their ability to drive safely. Any severe and chronic mental condition that impairs an individual's ability to drive safely for an extended period will render the individual unfit to drive for a period, usually 12 months. In exceptional circumstances the return to commercial driving can be significantly less than 12 months but this will depend on: ○ A satisfactory period of being stable and symptom free ○ A full supportive relevant psychiatric opinion ○ A low risk of recurrence or relapse, and ○ Absence of residual impairment It is recommended that an individual be granted a driving restriction of less than 9 months, the medical practitioner may wish to discuss this with the Chief Medical Adviser by writing to him or her outlining the patient's circumstances, including the nature of the commercial driving that is generally undertaken, and the patient's prognosis.
Sweden	Swedish National Road Administration Statute Book Effective 1/1/99	Every mental disorder which manifests itself in seriously disturbed behavior, impulse control disorder or a pronounced lack of judgment or adaptability constitutes grounds for denial of possession unless the condition is stable and the risk of such manifestations has been assessed to be minimal. ○ The assessment of the risk shall be in light of the following: ○ The significance of the disorder with respect to traffic safety ○ The awareness of the disorder ○ Compliance and effect of the treatment ○ The absence of a relapse during the observation time The foregoing also applies if the condition is organic in nature. In this case, the assessment shall also include disturbances in attention, in a sense of judgment and in memory as well as visual-spatial function. In the case of schizophrenia and other psychotic syndromes, special attention should be paid to 1. Delusions 2. Hallucinations 3. Outbursts of anger and rage 4. Disorganized behavior 5. Defects remaining after an active phase of the disease 6. Excessive consumption of alcohol or use of other substances that influence the ability to drive a power-driven vehicle. In the case of a schizoaffective disorder, special attention shall be paid to symptoms resembling mania. ○ *Possession shall not be granted earlier than one year after the most recent active phase of the disease.* In the case of bipolar disorder, special attention shall be paid to 1. An initial appearance late in life

Country/ Consortium	Source	Standard or Guideline
		2. Multiple manic episodes 3. Repeated conditions of hypomania 4. Psycho-social stress 5. An excessive consumption of alcohol or use of other substances that influence the ability to drive a power-driven vehicle. *Possession of a license shall not be granted earlier than one year after the most recent relapse. In the case of a relapse, a shorter observation time can be accepted only in a depressive phase.* In the case of personality disorders, special attention shall be paid to anti-social personality disorders and borderline personality disorders. Reappraisals shall occur at intervals judged suitable in each individual case.
United Kingdom	At a glance Guide to the current Medical Standards of Fitness to Drive (for Medical Practitioners) Issued by Drivers Medical Group. DVLA, Swansea (February 2007)	Anxiety or depression (without significant memory or concentration problems, agitation, behavioral disturbance or suicidal thoughts): o Very minor short-lived illnesses need not be notified. More severe anxiety states of depressive illnesses (with significant memory or concentration problems, agitation, behavioral disturbances or suicidal thoughts): o *Driving is permitted when the person is well and stable for a period of 6 months.* Medication must not cause side effects, which would interfere with alertness or concentration. Driving is usually permitted if the anxiety or depression is long-standing, but maintained symptom-free on doses of psychotropic medication which do not impair. DVLA may require psychiatric reports. Acute psychotic disorders of any type: o *Driving must cease* pending the outcome of medical inquiry. It is normally a requirement that the person should be well and stable for 3 years (i.e., to have experienced a good level of functional recovery with insight into their illness and to be fully adherent to the agreed treatment plan, including engagement with the medical services) before driving can be resumed. In line with good practice, attempts should be made to achieve the minimum effective anti-psychotic dose; tolerability should be optimal and not associated with any deficits (i.e., in alertness, concentration and motor performance) that might impair driving ability. Where in patients with established illness the history suggests a likelihood of relapse, the risk should be appraised as low (either in the treated or untreated state). DVLA will normally require a consultant report that specifically addresses the relevant issues above before the license can be considered. o *Where psychiatric illness has been associated with substance misuse, continuing misuse is not acceptable for licensing.* Hypomania/Mania: o *Driving must cease* pending the outcome of medical inquiry. It is normally a requirement that the person should be well and stable for 3 years (i.e., to have experienced a good level of functional recovery with insight into their illness and to be fully adherent to the agreed treatment plan, including engagement with the medical services) before driving can be resumed. In line with good practice, attempts should be made to achieve the minimum effective dose of psychotropic medication; tolerability should be optimal and not associated with any deficits (i.e., in alertness, concentration and motor performance) that might impair driving ability. Where in patients with established illness the history suggests a likelihood of relapse, the risk should be appraised as low (either in the treated or untreated state). DVLA will normally require a consultant report that specifically addresses the relevant issues above before the license can be considered. Chronic schizophrenia and other chronic psychosis: o *Driving must cease* pending the outcome of medical inquiry. It is normally a requirement that the person should be well and stable for 3 years (i.e., to have experienced a good level of functional recovery with insight into their illness and to be fully adherent to the agreed treatment plan, including engagement with the medical services) before driving can be resumed. In line with good practice, attempts should be made to achieve the minimum effective dose of anti-psychotic dose; tolerability should be optimal and not associated with any deficits (i.e., in alertness, concentration and motor performance) that might impair driving ability. Where in patients with established illness the history suggests a likelihood of relapse, the risk should be appraised as low (either in the treated or untreated state). DVLA will normally require a consultant report that specifically addresses the relevant issues above before the license can be considered.

Methods

The *Methods* section provides a synopsis of how we identified and analyzed information for this report. The section briefly covers the key questions addressed; literature searches performed; the criteria used, including studies, evaluation of study quality, assessment of the strength of the evidence base for each key question; and the methods used for abstracting and analyzing available data. Specific details of literature searches, study quality assessment, statistical approaches used, and other factors are documented in the appendices.

Key Questions

This evidence report addresses three key questions. Each of these key questions was developed by the FMCSA in such a way that the answers to these questions provided information that would be useful in updating their current physical qualification standards and guidance to medical examiners. The three key questions addressed in this evidence report are as follows:

Key Question 1: Are individuals with a psychiatric disorder at an increased risk for motor vehicle crash? If so, are there specific psychiatric disorders that present a particularly high risk?

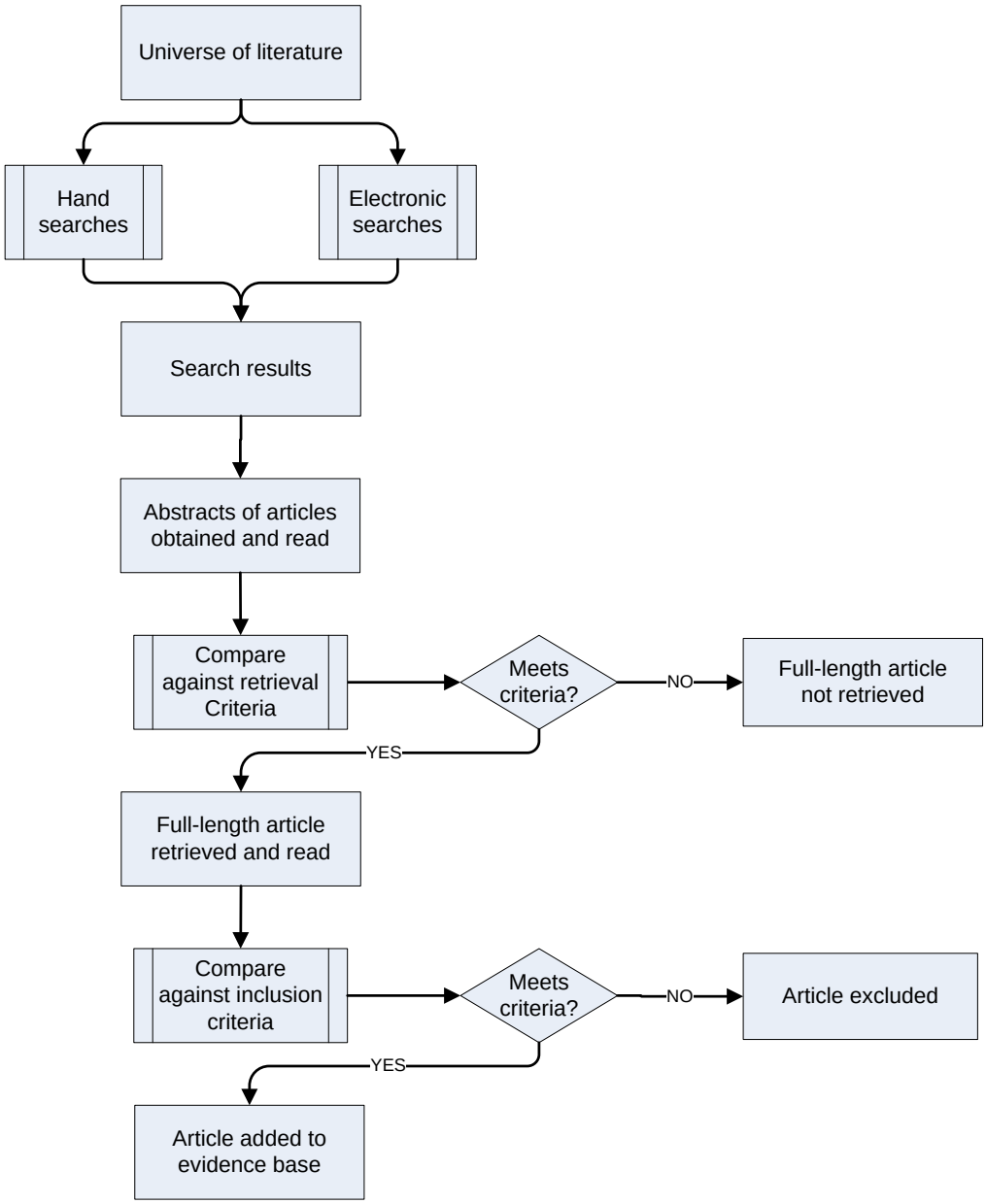
Key Question 2: Are individuals using psychotherapeutics for a psychiatric disorder at an increased risk for crash when compared to comparable individuals who are not using psychotherapeutics for a psychiatric disorder?

Key Question 3: What traits associated with personality disorders are associated with reductions in motor vehicle driver safety?

Identification of Evidence Bases

The individual evidence bases for each of the three key questions addressed in this evidence report were identified using the multistage process captured by the algorithm presented in Figure 3. The first stage of this process consists of a comprehensive search of the literature. The second stage of the process consists of the examination of abstracts of identified studies in order to determine which articles will be retrieved. The final stage of the process consists of the selection of the actual articles that will be included in the evidence base.

Figure 3. Evidence-base Identification Algorithm



Searches

One characteristic of a good evidence report is a systematic and comprehensive search for information. Such searches distinguish systematic reviews from traditional literature reviews that use a less rigorous approach to identifying and obtaining literature, thereby allowing a reviewer to include only articles that agree with a particular perspective and to ignore articles that do not. Our approach precludes this potential reviewer bias because we obtain and include articles according to explicitly determined *a priori* criteria. Full details of the search strategies used in this report are presented in Appendix A.

Electronic Searches

We performed comprehensive searches of the electronic databases listed in Table 7.

Table 7. Electronic Databases Searched

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	Through 2008, Issue 1	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2008, Issue 1	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2008, Issue 1	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2008, Issue 1	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment Database (HTA)	Through 2008, Issue 1	www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	Through January 28, 2008	OVID
TRIS (Transportation Research Information Services)	Searched December 13, 2007	
U.K. National Health Service Economic Evaluation Database (NHS EED)	Through 2008, Issue 1	www.thecochranelibrary.com
U.S. National Guideline Clearinghouse (NGC)	Searched December 13, 2007	www.ngc.gov

Manual Searches

We reviewed journals and supplements maintained in ECRI Institute's collections of more than 1,000 periodicals. Nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies were also screened. In addition, we examined the reference lists of all obtained articles with the aim of identifying relevant reports not identified by our electronic searches. In order to retrieve additional relevant information, we also performed hand searches of the "gray literature." Gray literature consists of reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. The latter documents do not appear in the peer-reviewed journal literature.

Retrieval Criteria

Retrieval criteria were used to determine whether a full-length version of an article identified by our searches should be ordered. Decisions pertaining to whether a full-length article should be retrieved are usually based on a review of available abstracts. For this project, retrieval criteria were determined *a priori* in conjunction with the FMCSA. The retrieval criteria are presented in Appendix B.

If an article did not meet the retrieval criteria for this evidence report, the full-length version of the article was not obtained. If it was unclear whether a potentially relevant article met our retrieval criteria (e.g., no abstract was available for evaluation), the full-length version of that article was obtained.

Inclusion and Exclusion Criteria

Each retrieved article was read in full by an ECRI Institute analyst who determined whether that article met a set of predetermined, question-specific inclusion criteria. As was the case for the retrieval criteria, the inclusion criteria for this evidence report were determined *a priori* in conjunction with the FMCSA. These inclusion and exclusion criteria are presented in Appendix C.

If, on reading an article, it was found not to meet the question-specific inclusion criteria listed in Appendix C, the article was excluded from the analysis. Each excluded article, along with the reason(s) for its exclusion, is presented in Appendix D.

Evaluation of Quality and Strength of Evidence

Rather than focus on the quality of the individual studies that compose an evidence base, our approach to assessing the quality of evidence focused on the overall *body* of the available evidence that was used to draw an evidence-based conclusion.(20) Using this approach, which is described briefly in Appendix E, we took into account not only the quality of the individual studies that compose the evidence base for each key question, we will also consider the interplay between the quality, quantity, robustness, and consistency of the overall body of evidence.

Our approach to assessing the strength of the body of evidence makes a clear distinction between a qualitative conclusion (e.g., "Individuals with psychiatric disorders are at increased risk for a motor vehicle crash") and a quantitative conclusion (e.g., "When compared to individuals who do not have psychiatric disorders, the risk ratio for a motor vehicle crash among individuals with the disorder is 1.37; 95% CI: 1.03–1.74; p <0.005."). As shown in Table 8, we assigned a separate strength-of-evidence rating to each of type of conclusion. Evidence underpinning a qualitative conclusion was rated according to its strength, and evidence underpinning quantitative conclusions was rated according to the stability of the effect-size estimate that was calculated.

Table 8. Strength-of-Evidence Ratings for Qualitative and Quantitative Conclusions

Strength of Evidence	Interpretation
Qualitative Conclusion	
Strong	Evidence supporting the qualitative conclusion is convincing. It is highly unlikely that new evidence will lead to a change in this conclusion.
Moderate	Evidence supporting the qualitative conclusion is somewhat convincing. There is a small chance that new evidence will overturn or strengthen our conclusion. ECRI Institute recommends regular monitoring of the relevant literature for moderate-strength conclusions.
Minimally Acceptable	Although some evidence exists to support the qualitative conclusion, this evidence is tentative and perishable. There is a reasonable chance that new evidence will either overturn or strengthen our conclusions. ECRI Institute recommends frequent monitoring of the relevant literature.
Insufficient	Although some evidence exists, the evidence is insufficient to warrant drawing an evidence-based conclusion. ECRI Institute recommends frequent monitoring of the relevant literature.

Strength of Evidence	Interpretation
Quantitative Conclusion (Stability of Effect-size Estimate)	
High	The estimate of treatment effect in the conclusion is stable. It is highly unlikely that the magnitude of this estimate will change substantially as a result of the publication of new evidence.
Moderate	The estimate of treatment effect the conclusion is somewhat stable. There is a small chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI Institute recommends regular monitoring of the relevant literature.
Low	The estimate of treatment effect included in the conclusion is likely to be unstable. There is a reasonable chance that the magnitude of this estimate will change substantially as a result of the publication of new evidence. ECRI Institute recommends frequent monitoring of the relevant literature.
Unstable	Estimates of the treatment effect are too unstable to allow a quantitative conclusion to be drawn at this time. ECRI Institute recommends frequent monitoring of the relevant literature.

The definitions presented in the table above are intuitive. Qualitative conclusions that are supported by strong evidence are less likely to be overturned by the publication of new data than conclusions supported by weak evidence. Likewise, quantitative effect-size estimates deemed to be stable are more unlikely to change significantly with the publication of new data than are unstable effect-size estimates.

Statistical Methods

The set of analytic techniques used in this report was extensive. In summary, random-effects meta-analyses were used to pool data from different studies.(21-30) Important differences in the findings of different studies (heterogeneity) were identified using the Q-statistic and I^2.(26,31-36) Whenever appropriate, heterogeneity was explored using meta-regression techniques.(37-39) Sensitivity analyses, aimed at testing the robustness of our findings, were performed using cumulative random-effects meta-analyses.(40-46) All meta-analyses in this evidence report were performed using Comprehensive Meta-Analysis software.(47-49)

We calculated several different estimates of effect. The choice of effect-size estimate depended on the purpose of the studies we assessed, their design, and whether reported outcome data were continuous or dichotomous. Between-group differences in outcome measured using continuous data were analyzed in their original metric (if all included studies reported on the same outcome using the same metric) or the data were standardized into a common metric known as the standardized mean difference. Dichotomous data were analyzed using the rate ratio (RR) or the odds ratio (OR). Time-to-event data were analyzed using the hazard ratio (HR). The formulae for these effect sizes and their variance are presented in Table 9. If means and standard deviations were not available for continuous data, every effort was made to determine an estimate of treatment effect from reported statistics (e.g., t-values, f-values) or from *p* values using methods described in detail elsewhere.(50)

Table 9. Effect-size Estimates Used in Evidence Report and Their Variance

Effect size	Formula (Effect size)	Formula (Variance)
WMD	$\mu_{TG} - \mu_{CG}$	$\left(\sqrt{\frac{(n_{TG}-1)(s_{TG})^2+(n_{CG}-1)(s_{CG})^2}{n_{TG}+n_{CG}-2}}\right)\left(\frac{1}{n_{TG}}+\frac{1}{n_{cg}}\right)$
SMD	$\frac{\mu_{TG}-\mu_{CG}}{\left(\sqrt{\frac{(n_{TG}-1)(s_{TG})^2+(n_{CG}-1)(s_{CG})^2}{n_{TG}+n_{CG}-2}}\right)}$	$\frac{n_{TG}+n_{CG}}{n_{TG}n_{CG}}+\frac{SMD^2}{2(n_{TG}+n_{CG})}$
Where: μ_{TG} = mean (treatment group); μ_{CG} = mean (control group); S_{TG} = standard deviation (treatment group); S_{CG} = standard deviation (control group); n_{TG} = enrollees (treatment group); n_{CG} = enrollees (control group)		
Event Rate	$a/a+b$	$\ln\left[\frac{1}{a}+\frac{1}{a+b}\right]$
Where: a = number of individuals in cohort experiencing an event; b = number of individuals in cohort who did not experience an event		
RR (incidence)	$\left(\frac{a_{msd}}{pt_{msd}}\right) \Big/ \left(\frac{b_{control}}{pt_{control}}\right)$	$\ln\left[\frac{1}{a_{msd}}+\frac{1}{b_{control}}\right]$
Where: a = number of individuals with psychiatric disorders / using psychotherapeutics who crashed; pt_{msd} = rate denominator (psychiatric disorder grp); b = number of individuals without psychiatric disorders / using psychotherapeutics who crashed; $pt_{control}$ = rate denominator (control grp)		
OR	$\left(\frac{a}{b}\right) \Big/ \left(\frac{c}{d}\right) = \left(\frac{ad}{bc}\right)$	$\frac{1}{a}+\frac{1}{b}+\frac{1}{c}+\frac{1}{d}$
RR	$\left(\frac{a}{a+c}\right) \Big/ \left(\frac{b}{b+d}\right)$	$\frac{1}{a}+\frac{1}{a+c}+\frac{1}{b}+\frac{1}{b+d}$
Where: a = number of individuals with psychiatric disorders / using psychotherapeutics who crashed; b = number of individuals without psychiatric disorders / using psychotherapeutics who crashed; c = number of individuals with psychiatric disorders / using psychotherapeutics who did not crash; d = number of individuals without psychiatric disorders / using psychotherapeutics who did not crash.		
HR	$\frac{O_{pi}/E_{pi}}{O_{ci}/E_{ci}}$	$\exp\left(\ln\left[\frac{1}{E_{pi}}+\frac{1}{E_{ci}}\right]\right)$
Where O_{pi} = observed number of events in treatment group; O_{ci} = observed number of events in control group; E_{pi} = log rank expected number of events in treatment group; E_{ci} = log rank expected number of events in control group		

HR: Hazard ratio; OR: Odds ratio; RR: Rate ratio; SMD: Standardized mean difference; WMD: Weighted mean difference

Evidence Synthesis

This section summarizes the findings of our systematic review of the evidence pertaining to each of the key questions asked by the FMCSA.

Key Question 1: Are individuals with a psychiatric disorder at an increased risk for motor vehicle crash? If so, are there specific psychiatric disorders that present a particularly high risk?

As noted in the background section, psychiatric disorders are of considerable concern to those responsible for road safety because of disorder-associated disruptions to an individual's thinking, mood, and judgment. The primary purpose of this section of the evidence report is to evaluate the best available evidence pertaining to the possible association between psychiatric disorders (i.e., psychotic, mood, anxiety, personality) and crash risk. If such an association is found, the secondary purpose of this section is to determine whether specific types of psychiatric disorder pose a particular risk to driver safety.

Identification of Evidence Base

To meet the aims of this section of the evidence report, we searched for studies that compared the crash risk observed among individuals with a diagnosed psychiatric disorder and crash risk observed among otherwise comparable individuals who do not have a psychiatric disorder (cohort studies). We also looked for studies that compared the prevalence of psychiatric disorders among a cohort of individuals who have experienced a crash within a specified time frame and a cohort of individuals who had not experienced a crash (case-control studies).

The evidence-base identification pathway for Key Question 1 is summarized in Figure 4. Our searches[1] identified a total of 10,217 articles that appeared relevant to this key question. Following an examination of the abstracts for these articles, 130 full-length articles were retrieved and read in full. Eight of these 130 retrieved articles were ultimately found to meet the inclusion criteria[2] for Key Question 1. These eight studies are listed in Table 10. Appendix D lists the 121 articles that were retrieved, read in full, and then excluded.

[1] See Appendix A for search strategies.
[2] See Appendix C for inclusion criteria.

Figure 4. Development of Evidence Base for Key Question 1

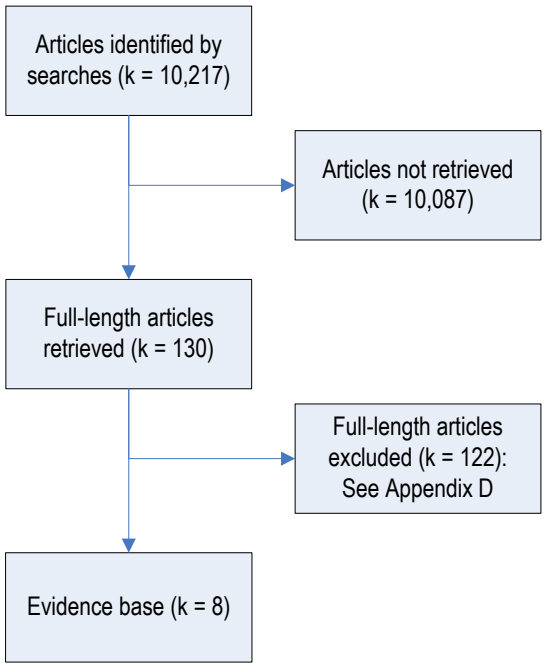


Table 10. Evidence Base for Key Question 1

Reference	Year	Study Location	Country
Armstrong and Whitlock(51)	1980	Queensland	Australia
Buttiglieri and Guenette(52)	1967	California	USA
Crancer and Quiring(53)	1969	Washington	USA
Edlund et al.(54)	1989	NR	USA
Foley et al.(55)	1995	Iowa	USA
Koepsell et al.(56)	1994	Washington	USA
Wear(57)	1985	Wyoming	USA
Waller(58)	1965	California	USA

Evidence Base

This subsection provides a brief description of the key attributes of the eight studies that compose the evidence base for Key Question 1. Here we discuss applicable information pertaining to the quality of the included studies and the generalizability of each study's findings to CMV drivers.

Characteristics of Included Studies

The key characteristics of the eight included studies that address Key Question 1 are presented in Table 11. Seven of the included studies utilized a cohort study design in which the crash rate among individuals with a history of a psychiatric disorder were compared to the crash risk of individuals who had been involved in a crash (cases) and a comparable group of individuals with no history of such a disorder. The result of this study design is usually presented as a crash RR. These studies are asking a very straightforward question:

what is the ratio of the incidence of crash among a cohort of individuals with a history of a psychiatric disorder compared to the incidence of crash observed among a group of comparable individuals who do not have a history of a psychiatric disorder?

The remaining study utilized a case-control study design in which the prevalence of individuals with a psychiatric disorder was compared in two groups of individuals; those who experienced a motor vehicle crash (cases) and those who did not (controls). The results of studies of this type are usually presented as an OR. That is, these studies ask the question: what is the ratio of the odds of having a history of a psychiatric disorder among those who have crashed within a certain time frame and those who have not crashed?

In most studies, information on whether an individual included in a study had been involved in a crash came from police or insurance company databases. Crash data reported in three of the included studies were based on self-report. In most cases, the definition of what constituted a "crash" in the study was not defined. Only two of the nine included studies provided this information. Both of these studies only considered crashes in which the driver was injured. In no case was it clear whether only crashes in which the driver was considered to be at fault were considered.

One important limitation to the evidence base for Key Question 1 is that one cannot draw conclusions from these studies about the association between active psychiatric disorder and crash risk. None of the studies make a distinction between crashes that occurred among individuals who had active symptomology at the time of a crash and crashes that occurred among individuals who were not experiencing symptoms at the time of a crash. The best that one can hope to obtain from these studies is an indication whether individuals with a history of psychiatric disease are at an increased risk for a crash.

Table 11. Key Study Design Characteristics of Studies That Address Key Question 1

Reference	Year	Study Design	Comparison	Disorder(s)					Driving Exposure Controlled For?	Definition of Crash	Outcome(s) Self-reported?
				Psychotic	Mood	Anxiety	PD*	Not Specified			
Armstrong and Whitlock(51)	1980	Cohort	Psychiatric illness vs. physical Illness	✓	✓	✓			Yes	NR	Yes
Buttiglieri and Guenette(52)	1967	Cohort	Psychiatric illness admitted to hospital vs. male California drivers					✓	No	NR	No: records from CA Dept. Motor Vehicles
Crancer and Quiring(53)	1969	Cohort	Psychiatric illness admitted to hospital vs. drivers; King County, Washington	✓	✓	✓	✓		No	NR	No: records from WA Dept. Motor Vehicles
Edlund et al.(54)	1989	Cohort	Outpatient schizophrenic population vs. medical center staff	✓					Yes	Injurious crash	Yes
Foley et al.(55)	1995	Cohort	Individuals reporting depression vs. individuals NR depression		✓				No	NR	No: records from IA Dept. Motor Vehicles
Koepsell et al.(56)	1994	Case-control	Individuals who crashed (cases) vs. individuals who did not (controls)		✓				No	Injurious crash	No: police records
Wear(57)	1985	Cohort	Psychiatric illness admitted to hospital vs. general Wyoming drivers	✓			✓		No	NR	No: Wyoming Highway Safety Branch
Waller(58)	1965	Cohort	Individuals with a psychiatric disorder vs. general CA drivers	✓	✓				Yes	NR	No: CA Dept. Motor Vehicles

*Personality disorders

NR: Not reporting

Quality of Evidence Base

The findings of our assessment of the quality of the studies that compose the evidence base for Key Question 1 are summarized in Table 12. Our assessment found that the quality of the eight included studies ranged from low (k = 6 studies) to moderate (k = 2 studies). Issues that contributed to low quality assessment ratings included possible selection bias, in that some of the psychiatric populations of study were made up solely of individuals who had been admitted to a psychiatric inpatient clinic for care, meaning that they may represent one end of the disorder spectrum and may not be representative of the disorder(s) of study overall. An unknown number of individuals in the psychiatric population may have been using psychotropic medications that may have affected their cognitive and psychomotor abilities, introducing a potential confounder variable that was not always accounted for in the study design. Finally, the failure to control for driving exposure in five of the studies presents another potential source of bias.

Table 12. Quality of the Studies That Assess Key Question 1

Reference	Year	Quality Scale Used	Quality
Armstrong and Whitlock(51)	1980	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Buttiglieri and Guenette(52)	1967	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Crancer and Quiring(53)	1969	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Edlund et al.(54)	1989	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Foley et al.(55)	1995	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Koepsell et al.(56)	1994	Revised Newcastle-Ottawa Quality Assessment Scale – Case-control Studies	Moderate
Wear(57)	1985	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Waller(58)	1965	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the eight studies that compose the evidence base for Key Question 1 are presented in Table 13. As noted in the table, direct evidence pertaining to the impact of psychiatric disorders on crash risk among CMV drivers does not exist. Consequently, our conclusions must be based on information obtained from studies of private motor vehicle license holders, an unknown number of whom may have held commercial driver licenses.

The generalizability of the findings of these latter studies to CMV drivers is unclear. Exposure to risk is far lower among noncommercial vehicle drivers because their driving exposure is lower than that of CMV drivers. This is of particular concern because drivers with psychiatric disorders may not feel like driving on certain days, but CMV drivers will be under extra pressure to keep driving regardless of symptoms because their livelihood depends upon it. Thus, studies of non-CMV drivers with psychiatric disorders may underestimate the level of risk experienced by CMV drivers with psychiatric disorders. Women tend to be overrepresented in studies of general driver populations. The ages of the private motor vehicle license holders included in most of these studies are similar to those of CMV drivers, with the exception of two studies that selected individuals age 65 or older. It is unclear whether the ethnicity of the private motor vehicle license holders included in these studies is representative of CMV drivers, due to lack of reporting.

Table 13. Individuals with Psychiatric Disorders Enrolled in Studies That Address Key Question 1

Study	Year	n =	% CMV Drivers	Patient Selection	Characteristics of Individuals with Psychiatric Disorders				Generalizability to Target Population
					Age - Years	% Male	Ethnicity	Comorbid Conditions	
Foley et al.(55)	1995	Psychiatric: 322	NR	Psychiatric: Individuals who scored >80th percentile for abbreviated CES-D scale	Range: ≥68	49	NR	Functional limitations Hearing disorders Visual disorders Cardiovascular disorders Back pain Chest pain Respiratory disorders Urinary system disorders	Unclear
		Controls: 1,532	NR	Controls: Individuals who scored <80th percentile for abbreviated CES-D scale			NR		
Koepsell et al.(56)	1994	Crash: 234	NR	Members of Group Health Cooperative of Puget Sound (HMO)	65-69: 38% 70-74: 28% 75-79: 21% >80: 12%	50	Nonwhite: 8%	Cardiovascular disorders Neurological disorders Asthma Arthritis Diabetes mellitus Pulmonary disorders	Unclear
		No crash: 446	NR	Members of Group Health Cooperative of Puget Sound (HMO)	65-69: 39% 70-74: 29% 75-79: 20% >80: 13%	50	Nonwhite: 3%		
Edlund et al.(54)	1989	Psychiatric: 70	NR	Psychiatric: Schizophrenic outpatients from psychiatric clinic	Mean: 36.8 (SD 10.3)	ND	NR	NR	Unclear
		Controls: 122	NR	Controls: Staff recruited from medical center	Mean 33 (SD 12.8)	40	NR	NR	
Wear(57)	1985	Cases: 281	NR	Cases: Individuals hospitalized for psychiatric disorder in Wyoming	16-19: 10.4% 20-24: 14.9% 25-34: 22.3% 35-44: 23.4% 45-54: 19% 55-60: 10%	65	NR	NR	Unclear
		Controls: NR	NR	Controls: Individuals from Wyoming Highway Safety Branch Records					
Armstrong and Whitlock(51)	1980	Psychiatric: 100	NR	Psychiatric: Patients admitted to a psychiatric hospital	Mean: 38.5 (SD 13.06)	49	NR	NR	Unclear
		Controls: 100	NR	Physically ill: Patients admitted to a private general hospital for nonpsychiatric disorders	Mean: 40.2 (SD 13.18)	49	NR		
Crancer and Quiring(53)	1969	Psychiatric: 271	NR	Psychiatric: Admitted to Kings County Hospital and diagnosed with a psychiatric disorder	Mean: 36.8	48	NR	NR	Unclear
		Controls: 687,228	NR	Controls: Currently licensed drivers in Kings County, Washington	NR	58	NR		

Study	Year	n =	% CMV Drivers	Patient Selection	Characteristics of Individuals with Psychiatric Disorders				Generalizability to Target Population
					Age - Years	% Male	Ethnicity	Comorbid Conditions	
Buttiglieri and Guenette(52)	1967	Psychiatric: 361	NR	Psychiatric: Patients admitted to psychiatric ward at Sepulveda Veterans Administration Hospital	Modal patient: 40	100	Modal patient: Caucasian	NR	Unclear
		Controls: 86,717	NR	Controls: Male drivers in California	NR	100	NR		
Waller(58)	1965	Cases: 292	NR	Cases: Individuals with records under review with California Department of Motor Vehicles	Males: 36.7 Females: 40	66	NR	NR	Unclear
		Controls: 1,646	NR	Controls: Randomly sampled volunteers from license renewal pool at California Department of Motor Vehicles					

CES-D: Center for Epidemiologic Studies Depression scale, reduced from 20 items to 11
ND: Data reported for drivers and nondrivers
NR: Not reported
SD: Standard deviation

Findings

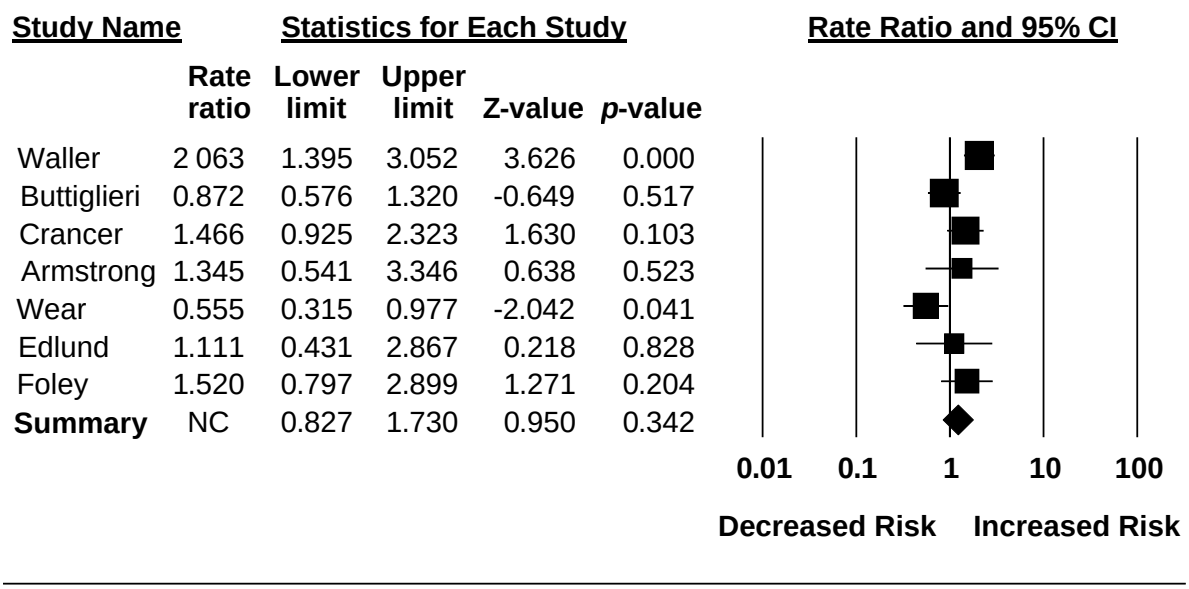
The findings of the eight included studies are presented in Table 14. The majority of studies presented data on the rate of crashes experienced by a group of individuals with a psychiatric disorder compared with a group of individuals who did not have a psychiatric disorder. Relevant data extracted from these studies are presented in Table 14 and in Figure 5.

Table 14. Crash Rate Ratio for Drivers with History of a Psychiatric Disorder

Reference	Year	Psychiatric Disorder Studied	Rate Ratio (95% CI)*	*P* =	Evidence of Increased Crash Risk
Armstrong and Whitlock(51)	1980	Psychiatric disorders (not specific disorder)	1.345 (0.541 – 3.346)	0.638	No
Buttiglieri and Guenette(52)	1967	Psychiatric disorders (not specific disorder)	0.872 (0.576 – 1.320)	0.517	No
Crancer and Quiring(53)	1969	Psychiatric disorders (not specific disorder)	1.466 (0.925 – 2.323)	0.103	No
Edlund et al.(54)	1989	Schizophrenic disorder	1.111 (0.431 – 2.867)	0.828	No
Foley et al.(55)	1995	Mood disorder	1.520 (0.797 – 2.899)	0.204	No
Wear(57)	1985	Psychiatric disorders (not specific disorder)	0.555 (0.315 – 0.977)	0.041	No
Waller(58)	1965	Psychiatric disorders (not specific disorder)	2.063 (1.395 – 3.052)	0.000	Yes
Koepsell et al.(56)	1994	Mood disorder	Odds ratio: 1.7 (0.9 – 3.1)	NR	No

* Calculated by ECRI Institute.
CI: Confidence interval

Figure 5. Crash Risk for Individuals with a Psychiatric Disorder



NC: Not calculated

Six included studies reported more crashes among drivers with psychiatric disorders compared to other drivers (Edlund et al., Foley et al., Crancer and Quiring, Koepsell et al., Armstrong and Whitlock, and Waller); although only two of these studies showed a statistically significant difference between groups. Two included studies reported fewer crashes among drivers with psychiatric disorders (Buttiglieri and Guenette and Wear), but only the study by Wear showed a statistically significant difference. One study (Koepsell et al.) was a case-control study that reported an OR; as such, this study's data could not be combined with the cohort studies that presented rates of crash and allowed calculation of RRs. A formal assessment of these data for quantitative consistency (homogeneity testing) found that the findings of the seven cohort studies were not consistent (I^2 = 66.7%), which precluded obtaining a single estimate of effect. However, we combined the crash RR data in a random-effects meta-analysis in an attempt to determine whether an elevated crash risk was associated with psychiatric disorders. Because the 95% confidence interval (CI) of the summary effect estimate overlapped with 1 (indicating the possibility of no difference in crash risk between groups), the results are insufficient to determine whether a combined population of patients with psychiatric disorders is at an elevated risk of crash compared to individuals without psychiatric disorders.

Psychotic Disorders and Crash Risk

Four studies in the evidence base for Key Question 1 specifically addressed the effect of psychotic disorders on crash risk. Because these studies were included in the evidence base for all psychiatric disorders, the primary attributes, quality assessment scores, and generalizability tables for the studies in this subsection are found in Table 11, Table 12, and Table 13, respectively.

Findings

All four studies presented data on the ratio of crashes experienced by a group of individuals with psychotic disorders compared with a group of individuals without psychotic disorders. Relevant data extracted from these studies are presented in Table 15 and in Figure 6.

Table 15. Crash Risk in Drivers with Psychotic Disorders Compared to Drivers without Psychotic Disorders

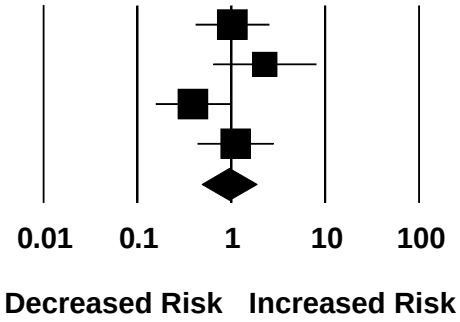
Reference	Year	Condition	Effect Size (95% CI)*	*P* =	Evidence of Increased Crash Risk
Edlund et al.(54)	1989	Schizophrenic disorder	RR = 1.111 (0.431 – 2.867)	0.828	No
Wear(57)	1985	Psychotic disorders	RR = 0.390 (0.155 – 0.979	0.045	No
Armstrong and Whitlock(51)	1980	Psychotic disorders	RR = 2.273 (0.634 – 8.146	0.208	No
Crancer and Quiring(53)	1969	Psychotic disorders	RR = 1.028 (0.411 – 2.576)	0.952	No
Overall effect size			RR = 0.933 (0.475 – 1.833)	0.841	No

* Calculated by ECRI Institute.

CI: Confidence interval
NR: Not reported
RR: Rate ratio

Figure 6. Crash Risk for Individuals with a Psychotic Disorder

Study Name	Rate ratio	Lower limit	Upper limit	Z-value	*p*-value
Crancer	1.028	0.411	2.576	0.060	0.952
Armstrong	2.273	0.634	8.146	1.260	0.208
Wear	0.390	0.155	0.979	-2.006	0.045
Edlund	1.111	0.431	2.867	0.218	0.828
Summary	0.933	0.475	1.833	-0.201	0.841



CI: Confidence interval

One included study reported fewer crashes among patients with a psychotic disorder compared to control drivers (Wear), while three included studies reported more crashes among drivers with a psychotic disorder (Crancer and Quiring, Armstrong and Whitlock, and Edlund et al.), although the latter three studies did not show a statistically significant between-group difference in crash risk. A formal assessment of these data for quantitative consistency (homogeneity testing) found that the findings of the four studies were consistent ($I^2 = 45.1\%$). We then combined the crash RR data in a random-effects meta-analysis in order to obtain a single estimate of crash risk associated with psychotic disorders.

The random-effects meta-analysis found that the 95% CI for the crash rate risk associated with psychotic disorders overlaps with 1 and the between-group difference in crash rate was not statistically significant. Because the 95% CI is too wide to rule out the possibility of a difference between groups, this finding is insufficient to determine whether crash risk is elevated among drivers with psychotic disorders compared to drivers without these disorders.

Mood Disorders and Crash Risk

A total of three studies in the evidence base for Key Question 1 specifically addressed the effect of mood disorders on crash risk. Since all of these studies were part of the larger evidence base for all psychiatric disorders, the primary attributes, quality assessment scores, and generalizability tables for the studies in this subsection are found in Table 11, Table 12, and Table 13, respectively.

A potential problem is that two of the three studies did not include patients clinically diagnosed with a mood disorder. In these studies, the Center for Epidemiological Studies Depression Scale was given to patients to estimate their level of depressive symptoms. Patients who scored within the 80th percentile or above were considered to have depression, but this is not the same as a clinical diagnosis of depression.

Findings

All three studies presented data on the ratio of crashes experienced by a group of individuals with depression (or at least symptoms of depression) compared with a group of individuals without mood disorders. Relevant data extracted from these studies are presented in Table 16.

Table 16. Crash Risk in Drivers with Mood Disorders Compared to Drivers without Mood Disorders

Reference	Year	Condition	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Foley et al.(55)	1995	Depressive score	RR = 1.520 (0.797 – 2.899)*	0.204	No
Koepsell et al.(56)	1994	Depressive score	OR = 1.7 (0.9 – 3.1)	NR	No
Armstrong and Whitlock(51)	1980	Diagnosis of manic-depression	RR = 1.069 (0.340-3.358)*	0.909	No

* Calculated by ECRI Institute.

CI: Confidence interval
NR: Not reported
OR: Odds ratio
RR: Rate ratio

All three included studies reported a higher crash rate among drivers with a mood disorder (specifically depression) compared to control drivers, although the difference did not reach statistical significance in any of these studies. Because the study by Koepsell et al. was a case-control study that could only report ORs, the data could not be combined with the data from the cohort studies that reported crash rates. Since the latter two studies were of low quality, we did not combine their data in a meta-analysis. Although all the studies showed a slightly higher crash rate among individuals with depression, no studies showed a statistically significant difference in crashes between these individuals and individuals without depression. Therefore, the evidence is insufficient to determine whether drivers with depression have an elevated risk of crash.

Anxiety Disorders and Crash Risk

Study of Crancer and Quiring

Crancer and Quiring(53) compared crash risk among drivers diagnosed with psychoneurotic disorders and a large reference population residing in the same county. “Psychoneurotic disorders” is an outdated term not used in DSM-IV, but the authors describe the patients in this category as having various types of anxiety. The crash RR was 1.47 (95% CI 0.67–3.19), which showed a slightly higher crash rate for psychoneurotic drivers; however, this difference was not statistically significant ($p = 0.334$). Because the CI is wide enough that an increased crash risk cannot be ruled out, the findings of this study are inconclusive.

One other study (Armstrong and Whitlock) reported the number of crashes for drivers with “neuroses,” a category that is not used in DSM-IV but could include patients with anxiety disorders. However, the authors did not define what type of patients were included in this category.(51) Because this broad category may include patients with disorders outside the scope of this report (e.g., somatoform disorders, sexual dysfunction disorders), we do not evaluate the data pertaining to drivers with neuroses.

Personality Disorders and Crash

A total of three studies in the evidence base for Key Question 1 specifically addressed the effect of personality disorders on crash risk. Since all of these studies were part of the larger evidence base for all psychiatric disorders, the primary attributes, quality assessment scores, and generalizability tables for the studies in this subsection are found in Table 11, Table 12, and Table 13, respectively.

Findings

All three studies presented data on the ratio of crashes experienced by a group of individuals with personality disorders compared with a group of individuals without personality disorders. Relevant data extracted from these studies are presented in Table 17 and in Figure 7.

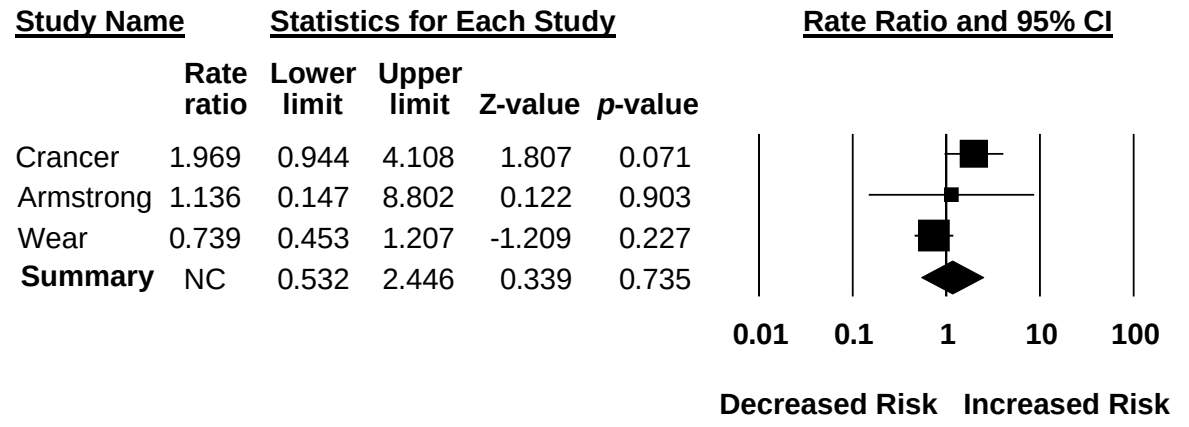
Table 17. Crash Risk in Drivers with Personality Disorders Compared to Drivers without Personality Disorders

Reference	Year	Condition	Effect Size (95% CI)*	*P* =	Evidence of Increased Crash Risk
Wear(57)	1985	Personality disorder	RR: 0.739 (0.453 – 1.207)	0.227	No
Armstrong and Whitlock(51)	1980	Personality disorder	RR: 1.136 (0.147 – 8.802)	0.903	No
Crancer and Quiring(53)	1965	Personality disorder	RR: 1.969 (0.944 – 4.108)	0.071	No
Overall Effect Size			RR: (0.532 – 2.446	0.735	No

* Calculated by ECRI Institute.

CI: Confidence interval
RR: Rate ratio

Figure 7. Crash Risk in Individuals with Personality Disorders



CI: Confidence interval
NC: Not calculated

Two included studies reported more crashes among drivers with a personality disorder compared to control drivers (Crancer and Quiring, Armstrong and Whitlock), while the remaining study (Wear) reported fewer crashes among drivers with a personality disorder. However, no studies found a statistically significant between-group difference in crash rates. A formal assessment of these data for quantitative consistency found that the findings of the three studies were inconsistent (I^2 = 57.8%). We then combined the crash RR data in a random-effects meta-analysis in order to determine the direction of effect and the range within which the effect size is likely to fall.

The random-effects meta-analysis found that the 95% CI of the crash RR associated with personality disorders is 0.532–2.446. Although this finding was not statistically significant (p = 0.182), the wide CI does not rule out the possibility of a between-group difference in crash rates. Therefore, the results are insufficient to determine whether drivers with personality disorders have an increased crash risk compared to other drivers.

Section Summary

- **The evidence concerning crash risk for drivers with psychiatric disorders is inconclusive. The possibility of an increased risk of crash for some drivers with psychiatric disorders cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

Our searches identified eight direct crash risk studies with a total of 1,931 individuals with psychiatric disorders. The quality assessment was low for six studies and moderate for two studies. None of the study participants were specifically identified as CMV drivers, so the generalizability of findings to the CMV driver population is unclear.

The findings of seven studies could be combined in a quantitative analysis. Pooling of the data from these studies found no statistically significant difference in crash risk between drivers with psychiatric disorders and drivers without psychiatric disorders. However, the possibility of an increased crash risk for some drivers with psychiatric disorders could not be ruled out. We note that the patient populations enrolled in these studies were unlikely to have included individuals with severe symptoms who would be more likely to have impaired driving ability.

Subgroup Analyses: Specific Psychiatric Disorders and Crash Risk

- **Psychotic Disorders: Currently available evidence does not suggest an increased crash risk for individuals with psychotic disorders compared to individuals without these disorders, but an increased crash risk cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

- **Mood Disorders: Although evidence suggests the possibility that individuals with mood disorders are at an increased risk for a motor vehicle crash compared with drivers who do not have mood disorders, more evidence is needed to reach a firm conclusion.**

- **Anxiety Disorders: A paucity of evidence prevents us from being able to draw an evidence-based conclusion about the effects of anxiety disorders on the risk of motor vehicle crash.**

- **<u>Personality Disorders:</u> Due to inconsistencies in the available evidence, we are precluded from drawing an evidence-based conclusion pertaining to the strength of the relationship between personality disorders and crash risk at this time.**

Our searches identified four studies with a total of 332 individuals with psychotic disorders, three studies with a total of 377 individuals with mood disorders, one study with 95 individuals with anxiety disorders, and three studies with 217 individuals with personality disorders. The median quality assessment for each subgroup analysis was low. Even when pooling of data was possible, none of these analyses found a statistically significant increase in crash risk for any of the four types of disorders compared to patients without psychiatric disorders. However, the possibility of increased crash risk could not be ruled out in any of these subgroup analyses.

Key Question 2: Are individuals using psychotherapeutics for a psychiatric disorder at an increased risk for crash when compared to comparable individuals who are not using psychotherapeutics?

Pharmacotherapy for psychiatric disorders is a concern to those responsible for road safety because medication may have broad effects on cognitive and psychomotor abilities that can result in functional problems, contributing to an increased potential for a motor vehicle crash.

The three major categories of psychotropic drug therapies used to treat psychiatric disorders include antipsychotics, anxiolytics, and antidepressants (see Table 4 in the Background section of this report for a complete list of psychotherapeutic agents used in the United States). Antipsychotics are mostly used to treat symptoms of psychotic disorders, including psychotic thinking, hallucinations, delusions, hostility, suicidal behavior, and symptoms of schizophrenia. Some antipsychotics also may treat symptoms of mood disorders such as bipolar disorder. Anxiolytics primarily treat anxiety associated with anxiety disorders, but some also have antidepressant effects. Benzodiazepines comprise the largest class of anxiolytics, although not all benzodiazepines are considered anxiolytics (some are hypnotics used primarily for insomnia treatment). Antidepressants are primarily used to treat depression, but some antidepressants also may relieve symptoms of anxiety or certain personality disorders. Three major classes of antidepressants include tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and monoamine oxidase inhibitors. All of these agents have effects on the central nervous system with the potential to impair driving ability.

Prior research has shown potential associations between various psychotherapeutic agents and impaired driving ability. In short-term studies of patients with anxiety, benzodiazepine use has been associated with impairment in cognitive function and driving ability for up to three weeks.(59-62) Antipsychotics have been associated with impaired psychomotor function or simulated driving performance in patients with schizophrenia.(63-67) Some studies have also reported an association between certain antidepressants (usually TCAs) and impaired driving performance.(68-70)

In this section, we review the evidence pertaining to crash risk associated with psychotherapeutics. The purpose of this review is to determine whether psychotherapeutics pose a risk to road safety inasmuch as they may affect the ability to perform the functions required to safely operate a commercial motor vehicle.

Identification of Evidence Base

We searched for trials that compared crash risk among individuals with a psychiatric disorder who were using psychotherapeutic medications and individuals who were not using psychotherapeutic medications. In addition, we looked for studies that compared the prevalence of use of psychotherapeutic medications among cohorts of individuals with psychiatric disease who had or had not experienced a crash. If our searches could not identify studies that focused exclusively on individuals with psychiatric disease, we included studies that evaluated the effect of psychotherapeutic medications on crash risk in general or unspecified driver populations. Such studies would likely include a large proportion of patients with psychiatric disease, and the side effects of these medications that might contribute to crash risk should be similar for drivers with or without psychiatric disease.

The evidence base identification pathway for Key Question 2 is summarized in Figure 8. Our searches (Appendix A) identified a total of 1,952 articles that appeared relevant to this key question. Following application of a set of retrieval criteria (Appendix B), 98 full-length articles were retrieved and read in full. Of these 98 retrieved articles, nine were found to meet the inclusion criteria for Key Question 2 (Appendix C). Table 18 lists these nine included studies. Appendix D lists the 89 articles that were retrieved but then excluded from inclusion in the evidence base for Key Question 2 and provides the reason for their exclusion.

Figure 8. Development of Evidence Base for Key Question 2

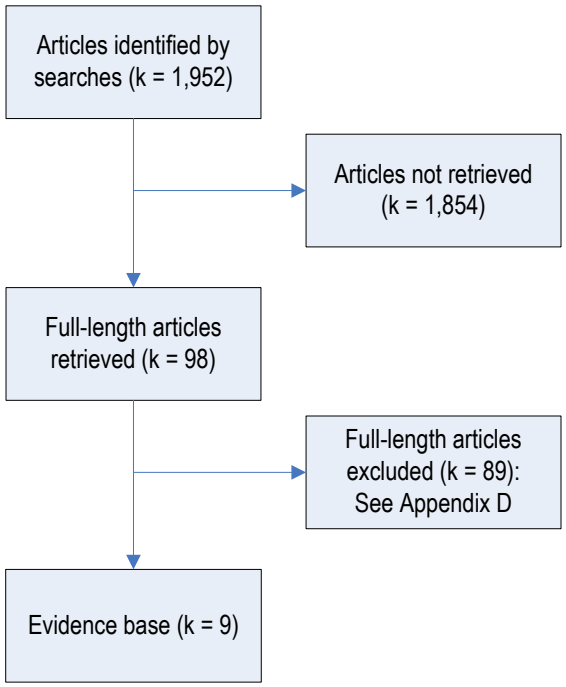


Table 18. Evidence Base for Key Question 2

Reference	Year	Study Location	Country
Barbone et al.(71)	1998	Tayside Region	UK
Hemmelgarn et al.(72)	1997	Quebec	Canada
Honkanen et al.(73)	1980	Helsinki	Finland
Leveille et al.(74)	1994	Washington	USA
McGwin et al.(75)	2000	Alabama	USA
Movig et al.(76)	2003	Tilburg	Netherlands
Neutel(77)	1995	Ontario	Canada
Ray et al.(78)	1992	Tennessee	USA
Wadsworth et al.(79)	2005	Cardiff	UK

Evidence Base

This subsection provides a brief description of the key attributes of the nine studies that comprise the evidence base for Key Question 2. Here we discuss information pertaining to the quality of the included studies and the generalizability of each study's findings to drivers of commercial vehicles. Key characteristics of the nine included studies that address Key Question 2 are presented in Table 19. None of the studies exclusively enrolled patients with psychiatric disorders. However, the psychotherapeutic medications used in these studies can be assumed to have similar effects on central nervous system functions important for driving ability in both psychiatric and nonpsychiatric patients.

Table 19. Key Study Design Characteristics of Studies That Address Key Question 2

Reference	Year	Study Design	Comparison	Pharmacotherapy			Driving Exposure Controlled For?	Primary Outcome	Definition of Crash	Outcome Self-reported?
				Benzodiazepines	Antipsychotics	Antidepressants				
Barbone et al.(71)	1998	Case crossover	Odds of having an accident while exposed to psychoactive drugs compared to odds of having an accident while unexposed	✓		✓	No	Crash	Road traffic crash attended by Tayside Police	No – Tayside police records
Hemmelgarn et al.(72)	1997	Nested case control	Individuals who had experienced a crash vs. individuals who had not experienced a crash	✓			No	Crash	Motor vehicle crash in which at least 1 person sustained bodily injury	No – Computerized crash records
Honkanen et al.(73)	1980	Case control	Individuals who had experienced a crash vs. individuals who had not experienced a crash	✓			No	Crash	Crash requiring visit to hospital emergency department within 6 hours of the crash	No – Crash-related injury recorded in hospital
Leveille et al.(74)	1994	Case control	Individuals who had experienced a crash vs. individuals who had not experienced a crash	✓		✓	Yes	Crash	Motor vehicle collision resulting in injuries for which drivers sought treatment within 7 days of the crash	No – Health plan case records
McGwin et al.(75)	2000	Case control	Individuals who had experienced a crash vs. individuals who had not experienced a crash	✓		✓	Yes	Crash	Listed as having had a crash by the Alabama Dept. of Public Safety	No – Alabama Dept. of Public Safety records
Movig et al.(76)	2003	Case control	Individuals injured in a crash vs. individuals who had not experienced a crash	✓		✓	No	Crash	Crash requiring hospitalization	No – Hospital records used to confirm crash
Neutel(77)	1995	Prospective cohort	Individuals who had received a benzodiazepine prescription vs. individuals who had not received a benzodiazepine prescription	✓	✓	✓	No	Crash	Crash registered with hospital inpatient data base records	No – Hospital records used to confirm crash
Ray et al.(78)	1992	Retrospective cohort	Individuals who had received a benzodiazepine or antidepressant prescription vs. individuals who had not received a benzodiazepine or antidepressant prescription	✓		✓	Yes	Crash	Crash with injury	No – Police report
Wadsworth et al.(79)	2005	Survey	Individuals who had experienced a crash vs. individuals who had not experienced a crash	✓		✓	No	Crash	Crash in which individual was the driver	Yes

Quality of Evidence Base

The results of our assessment of the overall quality of the evidence base for Key Question 2 are presented in Table 20. Our assessment found that the quality of the included studies was in the low-to-moderate range. Six of the nine included studies were graded as being of moderate quality. The remaining three studies were graded as low quality.

Table 20. Quality of Studies for Key Question 2

Reference	Year	Quality Scale Used	Quality
Barbone et al.(71)	1998	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low
Hemmelgarn et al.(72)	1997	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Moderate
Honkanen et al.(73)	1980	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low
Leveille et al.(74)	1994	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Moderate
McGwin et al.(75)	2000	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Moderate
Movig et al.(76)	2003	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Moderate
Neutel(77)	1995	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Ray et al.(78)	1992	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Wadsworth et al.(79)	2005	ECRI Institute Quality Scale VI – Surveys	Low

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the nine studies that compose the evidence base for Key Question 2 are presented in Table 21.

The generalizability of the findings of these latter studies to CMV drivers is unclear. All the studies included private motor vehicle license holders, an unknown number of whom may have held commercial driver licenses. Exposure to risk is lower among noncommercial vehicle drivers because their driving exposure is lower than that of CMV drivers. This is of particular concern because drivers taking pharmacotherapy for psychiatric disorders may not feel like driving on certain days, but CMV drivers will be under pressure to keep driving regardless of symptoms because their livelihood depends upon it. Thus, studies of non-CMV drivers with psychiatric disorders requiring pharmacotherapy may underestimate the level of risk experienced by CMV drivers with psychiatric disorders requiring pharmacotherapy. Women tend to be overrepresented in studies of general driver populations. In this case, the percentage of females included in the studies of private motor vehicle license holders ranged from 15% to 62%, meaning that gender may be an issue when considering generalizability of populations. The ages of the private motor vehicle license holders included in four of these studies were ≥65 years, which is older than the average age of CMV drivers. It is unclear whether the ethnicity of the private motor vehicle license holders included in these studies is representative of CMV drivers, due to lack of reporting.

Table 21. Individuals Using Psychotherapeutics Enrolled in Studies That Address Key Question 2

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age (%)	% Male	Ethnicity (%)	Comorbidity	
Barbone et al.(71)	1998	Cases: 1,731	NR	Cases: Drivers involved in a first road-traffic crash attended by Tayside police, who had used any psychoactive drug at some time during the study period.	<30 (22.0) 30–44 (33.9) 45–64 (31.6) >65 (12.5)	54.8	NR	NR	Unclear
Hemmelgarn et al.(72)	1997	Cases: 5,579	NR	Cases: Elderly drivers involved in a motor vehicle crash in which at least 1 person was injured.	67–70 (33.8) 71–74 (32.3) 75–79 (24.0) 80–84 (9.9)	80.0	NR	Chronic disease score, mean ±SD: 2.8 ±2.8	Unclear
		Controls: 55,790		Controls: Randomly selected from the cohort of all eligible elderly drivers who had not crashed during the study period.	67–70 (38.0) 71–74 (33.0) 75–79 (22.0) 80–84 (7.0)	72.2		2.6 ±2.8	Unclear
Honkanen et al.(73)	1980	Cases: 203	NR	Cases: All injured drivers who arrived at 5 emergency departments in Helsinki within six hours of crash.	Mean age: 34.2 years	82	NR	NR	Unclear
		Controls: 325		Controls: Random selection of drivers at 10 petrol stations in Helsinki during the study period.	35.5 years	89		NR	Unclear
Leveille et al.(74)	1994	Cases: 234	NR	Cases: Persons over age 65 who sought treatment for motor vehicle collision injuries within 7 days of a crash in which they were driving.	65–69 (40) 70–74 (29) 75–79 (20) ≥80 (11)	50	White (92) Black (3) Native American (2) Asian (3)	Diabetes treated with oral hypoglycemics or insulin: 9	Unclear
		Controls: 447		Controls: Matched persons from the same group health plan who did not seek treatment for crash injury during the study period.	65–69 (40) 70–74 (30) 75–79 (19) ≥80 (11)	50	White (97) Black (2) Native American (1) Asian (0.2)	Diabetes treated with oral hypoglycemics or insulin: 2	Unclear

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age (%)	% Male	Ethnicity (%)	Comorbidity	
McGwin et al.(75)	2000	At fault crashes: 249	NR	Total of 901 drivers aged 65 and older selected from Alabama Dept. of Public Safety driving records.	65–68 (21.3) 69–72 (25.4) 73–77 (25.8) 78–93 (27.5)	49.6	White (74.6) Black (23.0) Other (2.5)	Cardiovascular disease Renal disease Musculoskeletal Visual Cognitive Diabetes and complications Cancer	Unclear
		Not at fault crashes: 198			65–68 (39.6) 69–72 (23.6) 73–77 (23.6) 78–93 (13.2)	51.1	White (74.2) Black (22.5) Other (3.3)	As above	Unclear
		No crash: 454			65–68 (25.7) 69–72 (24.4) 73–77 (25.7) 78–93 (24.2)	49.1	White (80.0) Black (16.8) Other (0.8)	As above	Unclear
Movig et al.(76)	2003	Cases: 110	NR	Cases: Drivers involved in crashes needing hospitalization.	18–25 (28) 25–34 (32) 35–49 (26) ≥50 (14)	74	NR	NR	Unclear
		Controls: 816		Controls: Drivers recruited at random while driving on public roads.	18–25 (18) 25–34 (28) 35–49 (29) ≥50 (25)	74			
Neutel(77)	1995	Benzodiazepine anxiolytic users: 147,726	NR	Cases: Individuals who received a prescription for an anxiolytic in past 60 days.	20–39 (34.5) 40–59 (34.2) ≥60 (31.2)	36.8	NR	NR	Unclear
		Controls: 97,862		Controls: Individuals who had not received a prescription for an anxiolytic in the 6 months preceding the study.	20–39:16.9 40–59:30 ≥60 (53.2)	40			
Ray(78)	1992	16,262	NR	Individuals between the ages of 65–85 years old, enrolled in the Tennessee Medicaid program with a valid driver's license during the study period.	NR*	NR	NR	NR	Unclear

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age (%)	% Male	Ethnicity (%)	Comorbidity	
Wadsworth et al.(79)	2005	7,979	NR	Respondents to a postal questionnaire conducted among individuals randomly selected from the electoral registers of Cardiff and Merthyr Tydfil, Wales.	Mean: 45.6 (SD: 18.0, Range 16–97)	42	White (97)	NR	Unclear

* Data reported in person-years, no population numbers supplied.

NR: Not reported
SD: Standard deviation

Findings

The only psychotherapeutics that were consistently reported and evaluated in the available studies were benzodiazepines and antidepressants (including TCAs and SSRIs). Because all studies separately evaluated benzodiazepines and antidepressants, we did not perform a combined analysis of all psychotherapeutic drugs but instead performed separate analyses of benzodiazepines and antidepressants.

Benzodiazepines and Crash Risk

All nine studies in the evidence base presented data on the ratio of crashes experienced by a group of individuals using benzodiazepines compared with a group of individuals who did not use benzodiazepines. Relevant data extracted from these studies are presented in Table 22 and in Figure 9. An important observation is that only a subset of benzodiazepines (anxiolytics) is generally prescribed for anxiety or anxiety-related psychiatric disorders. Another subset (hypnotics) is prescribed primarily for relief of insomnia. Although insomnia is actually a common symptom in patients with mental disorders, it is also fairly common in the general population.(1) Thus, a substantial proportion of hypnotic prescriptions are for patients without psychiatric disorders. Only four of the nine crash studies distinguished between these two subsets in their data analyses or allowed an independent analysis to be performed. However, since benzodiazepines as a class have similar mechanisms of action, we have included studies that analyzed all benzodiazepines as a class. We subsequently perform a separate subgroup analysis of benzodiazepine anxiolytics, which are more likely to be used by patients with psychiatric disorders.

Table 22. Crash Risk in Drivers using Benzodiazepines Compared to Drivers not Using Benzodiazepines

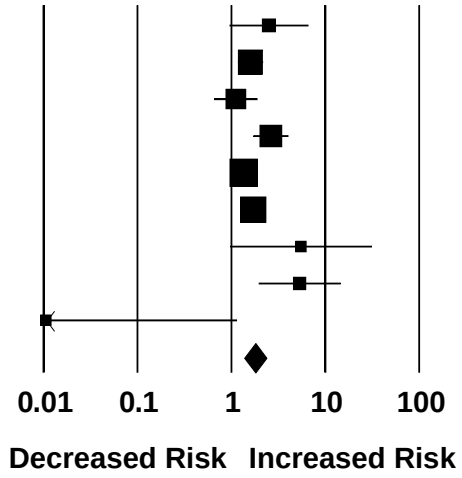
Reference	Year	Condition	Crash Data				Evidence of Increased Crash Risk
			% with Condition (Crash)	% with Condition (No Crash)	Effect Size (95% CI)	*P* =	
Barbone et al.(71)	1998	Benzodiazepine use	NR	NR	OR: 1.62 (1.24 – 2.12)	NR	Yes
Hemmelgarn et al.(72)	1997	Benzodiazepine use	Long half-life: 10.1	7.6	Adjusted OR: 1.28 (1.12 – 1.45)	NR	Yes
			Short half-life: 19.1	18.7	Adjusted OR: 0.96 (0.88 – 1.05)	NR	No
Honkanen et al.(73)	1980	Benzodiazepine use	5.0	2.2	OR: 2.378 (0.891 – 6.353)*	0.084	No
Leveille et al.(74)	1994	Benzodiazepine use	9.4	8.9	OR: 1.056 (0.612 – 1.823)*	0.845	No
McGwin et al.(75)	2000	Benzodiazepine use	1.6	0.4	OR: 5.200 (0.901 – 30.022)*	0.065	No
Movig et al.(76)	2003	Benzodiazepine use	10	1.5	OR: 5.05 (1.82 – 14.04)	0.002	Yes
Neutel(77)	1995	Benzodiazepine use	0.08	0.02	OR: 2.488 (1.598 – 3.875)*	0.000	Yes
Ray et al.(78)	1992	Benzodiazepine use	NR	NR	OR: 1.509 (1.092 – 2.085)*	0.013	Yes
Wadsworth et al.(79)	2005	Benzodiazepine use	NR	NR	OR: 0.010 (0.000 – 1.100)	0.055	No

* Calculated by ECRI Institute.

CI: Confidence interval
NR: Not reported
OR: Odds ratio

Figure 9. Crash Risk in Drivers using Benzodiazepines

Study Name	Odds ratio	Lower limit	Upper limit	Z-value	*p*-value
Honkanen	2.378	0.891	6.353	1.729	0.084
Ray	1.509	1.092	2.085	2.494	0.013
Leveille	1.056	0.612	1.823	0.195	0.845
Neutel	2.488	1.598	3.875	4.034	0.000
Hemmelgarn	1.280	1.125	1.456	3.747	0.000
Barbone	1.620	1.239	2.118	3.526	0.000
McGwin	5.200	0.901	30.022	1.843	0.065
Movig	5.050	1.818	14.026	3.107	0.002
Wadsworth	0.010	0.000	1.100	-1.920	0.055
Summary	NC	1.283	2.204	3.762	0.000



CI: Confidence interval
NC: Not calculated

Eight included studies reported more crashes among drivers using benzodiazepines compared to drivers who were not using benzodiazepines, although not all of these studies showed a statistically significant difference between groups. One study found a decreased risk of crash among drivers using benzodiazepines compared to drivers who were not using benzodiazepines (Wadsworth et al.). A formal assessment of these data for quantitative consistency (homogeneity testing) found that the findings of the eight studies were inconsistent (I^2 = 66.9%). Because there were so few studies, we did not perform meta-regression to explore the differences among study results.

Due to these unexplained differences, we did not attempt to obtain a summary estimate of the pooled effect sizes. Instead, we performed a random-effects meta-analysis to determine the direction of effect and the 95% CI within which the effect size is likely to fall. Pooling of the data from the included studies using a random-effects meta-analysis found that the crash OR associated with benzodiazepine use is 1.28 – 2.20, p <0.0001, suggesting that the crash risk associated with benzodiazepine use is between 1.3 and 2.2 times greater than the crash risk for comparable individuals who do not use benzodiazepines. The results of the meta-analysis were found to be robust; removal of each study separately and cumulative analysis by year of publication did not alter the findings (see Appendix G for these analyses).

The results of this meta-analysis concur with the findings of a systematic review by Thomas, who concluded that the use of benzodiazepines approximately doubled the risk of crashes.(80)

However, these findings do not necessarily mean that benzodiazepine use leads to an increased crash risk in all drivers under all circumstances. The effects could potentially be influenced by type of benzodiazepine (anxiolytic vs. hypnotic), dose, duration of exposure (e.g., first-time use vs. repeat use),

duration of effect (short half-life vs. long half-life), and possibly driver age. Accordingly, we examined the evidence further in an attempt to determine whether any of these factors influence the risk level of benzodiazepine use.

Four studies separately reported data concerning crash risk associated with use of benzodiazepine anxiolytics and use of benzodiazepine hypnotics, and a fifth study reported that at least 92% of the benzodiazepines used were anxiolytics (Table 23). The studies by Barbone et al., Neutel, and Ray et al. showed a statistically significant elevation in the odds of crash associated with use of anxiolytics. Our independent calculation of the data in the study by Honkanen found an OR in the same direction that did not quite reach statistical significance (the only benzodiazepines used by drivers in this study were anxiolytics). The study by Leveille found an OR in the opposite direction (suggesting lower risk for anxiolytic users), although this finding did not reach statistical significance. Only one of the three studies that evaluated hypnotics showed significantly elevated odds of crash associated with hypnotics, although another study showed a nonstatistically significant trend toward elevated crash risk.

Table 23. Benzodiazepine Therapeutic Subsets (Anxiolytic or Hypnotic) and Crash Risk

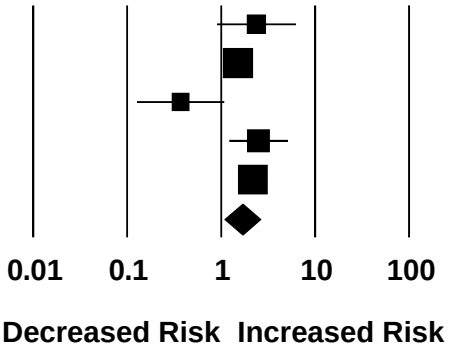
Reference	Year	Condition	Benzodiazepine Therapeutic Subset	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Barbone et al.(71)	1998	Benzodiazepine use	Anxiolytic Hypnotic	OR: 2.18 (1.52 – 3.13) 1.19 (0.83 – 1.70)	≤0.05 NS	Yes No
Honkanen et al.(73)	1980	Benzodiazepine use	Anxiolytic (Diazepam or Oxazepam)	OR: 2.378 (0.891 – 6.353)*	0.084	No
Leveille et al.(74)	1994	Benzodiazepine use	Anxiolytic Hypnotic	OR: 0.37 (0.13 – 1.10)* 1.87 (0.94 – 3.70)*	NS NS	No No
Neutel(77)	1995	Benzodiazepine use	Anxiolytic Hypnotic	OR: 2.5 (1.2 – 5.2) 3.9 (1.9 – 8.3)	≤0.05 ≤0.05	Yes Yes
Ray(78)	1992	Benzodiazepine use	Anxiolytic (at least 92% of benzodiazepines used)	OR: 1.509 (1.092 – 2.085)*	0.013	Yes

* Calculated by ECRI Institute.

CI: Confidence interval
NS: Not statistically significant
OR: Odds ratio

Figure 10. Benzodiazepine Anxiolytics and Crash Risk

Study Name	Odds ratio	Lower limit	Upper limit	Z-value	*p*-value
Honkanen	2.378	0.891	6.350	1.729	0.084
Ray	1.509	1.092	2.085	2.494	0.013
Leveille	0.371	0.125	1.099	-1.789	0.074
Neutel	2.500	1.201	5.204	2.450	0.014
Barbone	2.180	1.519	3.128	4.229	0.000
Summary	NC	1.072	2.576	2.271	0.023



CI: Confidence interval
NC: Not calculated

Because benzodiazepine anxiolytics are more likely to be used than hypnotics in patients with psychiatric disorders, we performed a subgroup meta-analysis of the five studies that reported data separately on anxiolytics (Figure 10). Because the findings of the studies were inconsistent (I^2 = 64.8%), the meta-analysis attempted to determine only whether crash risk was elevated rather than to determine an accurate estimate of the size of the risk. The findings indicate that the odds of crash were significantly higher for drivers exposed to benzodiazepine anxiolytics compared to unexposed drivers (p = 0.023). Removal of a single study showed that the findings were not robust (Appendix G). However, the evidence is minimally sufficient to support an increased crash risk associated with anxiolytic use.

Five studies reported separate data for benzodiazepine use based on the half-life (long, intermediate, or short) of the drugs (Table 24). Three of the five studies reported statistically significant ORs indicating increased odds of crash associated with long half-life benzodiazepines. The remaining two studies (Honkanen et al., Leveille et al.) did not show a statistically increased risk for long half-life benzodiazepines, although the study by Honkanen et al. was on the borderline (p = 0.051). In one study (Barbone et al.) that further separated the analysis by anxiolytics and hypnotics, the increased odds for long half-life drugs was associated with anxiolytics but not hypnotics. This was the only study that reported an OR for intermediate half-life benzodiazepines, and it did not show a statistically significant increase in odds of crash. Two studies (Barbone et al., Neutel) reported statistically significant ORs indicating an increased odds of crash associated with specific short half-life benzodiazepines (the hypnotics zopiclone and triazolam and the anxiolytic lorazepam); one short half-life drug (the anxiolytic oxazepam) was not associated with increased crash risk in the study by Neutel. Two studies (Hemmelgarn et al. and Leveille et al.) did not show an increased odds of crash with short half-life benzodiazepines; those used in the study by Hemmelgarn et al. included alprazolam, bromazepam, lorazepam, oxazepam, temazepam, and triazolam.

Table 24. Benzodiazepine Half-life and Crash Risk

Reference	Year	Condition	Half-life	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Barbone et al.(71)	1998	Benzodiazepine use (all types)	Long Intermediate Short	OR: 2.03 (1.41 – 2.93) 1.19 (0.82 – 1.73) 4.00 (1.31 – 12.2)	≤0.05 NS ≤0.05)	Yes No Yes
		Benzodiazepine use (Anxiolytics)	Long Intermediate	OR: 2.22 (1.47 – 3.37) 1.59 (0.71 – 3.57)	≤0.05 NS	Yes No
		Benzodiazepine use (Hypnotics)	Long Intermediate Short: Zopiclone	OR: 0.88 (0.41 – 1.87) 1.10 (0.73 – 1.64) 4.00 (1.31 – 12.2)	NS NS ≤0.05	No No Yes
Hemmelgarn et al.(72)	1997	Benzodiazepine use	Long Short	Adjusted OR: 1.28 (1.12 – 1.45) 0.96 (0.88 – 1.05)	≤0.05 NS	Yes No
Honkanen et al.(73)	1980	Benzodiazepine use (Anxiolytics)	Long: Diazepam	OR: 2.784 (0.996 – 7.781)*	0.051	No
Leveille et al.(74)	1994	Benzodiazepine use (All types)	Long Short	OR: 0.84 (0.36 – 1.97)* 1.15 (0.55 – 2.40)*	NS NS	No No
		Benzodiazepine use (Anxiolytics)	Long: Chlordiazepoxide Diazepam Short: Alprazolam	OR: 0.96 (0.09 – 10.59)* 0.38 (0.08 – 1.73)* 0.24 (0.03 – 1.89)*	NS NS NS	No No No
		Benzodiazepine use (Hypnotics)	Long: Flurazepam Short: Triazolam	OR: 1.93 (0.62 – 6.07)* 1.79 (0.78 – 4.12)*	NS NS	No No
Neutel(81)	1998	Benzodiazepine use (Anxiolytics)	Long: Diazepam Short: Lorazepam Oxazepam	Adjusted OR: 3.1 (1.4 – 6.5) 2.4 (1.0 – 6.3) 1.0 (0.3 – 3.7)	≤0.05 ≤0.05 NS	Yes Yes No
		Benzodiazepine use (Hypnotics)	Long: Flurazepam Short: Triazolam	Adjusted OR: 5.1 (2.3 – 11.6) 3.2 (1.4 – 7.3)	≤0.05 ≤0.05	Yes Yes

* Calculated by ECRI Institute.

CI: Confidence interval
NS: Not statistically significant
OR: Odds ratio

Four studies commented on the effect of benzodiazepine dose on crash risk, but only two of these studies presented numbers related to this issue (Table 25). The two studies that reported ORs both showed significantly greater odds of crash associated with higher doses of benzodiazepines. However, the two studies that only commented on dose both reported that no dose-related differences in crash risk were observed.

Table 25. Benzodiazepine Dose and Crash Risk

Reference	Year	Condition	Dose	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Barbone et al.(71)	1998	Benzodiazepine use (all types)	Low Intermediate High	OR: 1.27 (0.80 – 2.07) 1.68 (1.13 – 2.49) 2.67 (1.33 – 5.39)	NS ≤0.05 ≤0.05	No Yes Yes
		Benzodiazepine use (Anxiolytics)	Low Intermediate High	OR: 0.79 (0.25 – 2.49) 2.65 (1.64 – 4.29) NC	NS ≤0.05	No Yes
		Benzodiazepine use (Hypnotics)	Low Intermediate High	OR: 1.26 (0.76 – 2.11) 0.89 (0.50 – 1.61) 1.84 (0.90 – 3.74)	NS NS NS	No No No
Hemmelgarn et al.(72)	1997	Benzodiazepine use	NR	No numbers reported. Authors reported "no dose effects.	NR	NR
Leveille et al.(74)	1994	Benzodiazepine use	NR	No numbers presented. Authors reported no difference between high and low dose-equivalences.	NR	NR
Ray(78)	1992	Benzodiazepine use	≤4 mg 8 mg 12 - 16 mg ≥20 mg	OR: 1.1 (0.5 – 2.2) 1.2 1.8 2.4 (1.3 – 4.4)	NS NS ≤0.05 ≤0.05	No No Yes Yes

CI: Confidence interval
NC: Not calculable; too few cases
NR: Not reported
NS: Not statistically significant
OR: Odds ratio

The study by Ray et al. also reported that the risk of crash increased for benzodiazepine users if they were taking more than one benzodiazepine. The relative risk for one benzodiazepine was 1.5 (95% CI: 1.1 – 2.0), but the risk increased to 4.8 (95% CI 1.6 – 14.5) for those using more than one benzodiazepine. However, the findings of this single study require confirmation.

Four studies reported data on duration of benzodiazepine exposure and crash risk from index use (Table 26), although they did not examine exactly the same time intervals. Two of the studies (Hemmelgarn et al., Neutel) evaluated crash risk during the first week of benzodiazepine use; both found significantly elevated odds of crash among benzodiazepine users compared to nonusers within the first week of use. In the Hemmelgarn et al. study, this increased risk was associated with use of long half-life benzodiazepines but not short half-life benzodiazepines. Both studies found in general that the risk of crash decreased over subsequent weeks of use. However, in the Neutel study, the risk was still statistically significant during the second week of use for benzodiazepine hypnotics (but not anxiolytics), and in the Hemmelgarn et al. study, the risk associated with long half-life drugs became

significant again after 60 days (this may be simply due to greater statistical power as there were more patients in that particular time frame). The suggestion of decreasing risk with longer exposure could be a result of tolerance as patients may adjust to the effects of benzodiazepines over time. Of the two remaining studies, Leveille et al. only compared the first 60 days of use with the next 120 days of use and did not find a significantly elevated risk for either time frame. Similarly, Ray examined the first 30 days of use, 30 to 90 days of use, and greater than 90 days of use. Although all intervals showed a slightly elevated risk with benzodiazepine use, the only statistically significant finding was for greater than 90 days of use.

Table 26. Duration of Benzodiazepine Exposure and Crash Risk

Reference	Year	Condition	Duration of Exposure	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Hemmelgarn et al.(72)	1997	Benzodiazepine use (Long half-life)		Adjusted OR:		
			1–7 days	1.45 (1.04 – 2.03)	≤0.05	Yes
			8–30 days	1.16 (0.90 – 1.50)	NS	No
			31–60 days	1.22 (0.84 – 1.79)	NS	No
			61–365 days	1.26 (1.09 – 1.45)	≤0.05	Yes
		Benzodiazepine use (Short half-life)		Adjusted OR:		
			1–7 days	1.04 (0.81 – 1.34)	NS	No
			8–30 days	1.06 (0.90 – 1.26)	NS	No
			31–60 days	0.99 (0.77 – 1.28)	NS	No
			61–365 days	0.91 (0.8 – 1.01)	NS	No
Leveille et al.(74)	1994	Benzodiazepine use		Adjusted OR:		
			1–60 days	0.9 (0.4 – 2.0)	NS	No
			61–182 days	1.2 (0.5 – 2.7)	NS	No
Neutel(77)	1995	Benzodiazepine use (Anxiolytics)		OR:		
			1–14 days	5.6 (1.7 – 18.4)	≤0.05	Yes
			1–30 days	2.5 (1.2 – 5.2)	≤0.05	Yes
			1–7 days	13.5	≤0.05	Yes
			8–14 days	1.9	NS	No
			15–21 days	1.4	NS	No
			22–28 days	0.8	NS	No
			29–60 days	1.2	NS	No
		Benzodiazepine use (Hypnotics)		OR:		
			1–14 days	6.5 (1.9 – 22.4)	≤0.05	Yes
			1–30 days	3.9 (1.9 – 8.3)	≤0.05	Yes
			1–7 days	9.1	≤0.05	Yes
			8–14 days	5.0	≤0.05	Yes
			15–21 days	2.8	NS	No
			22–28 days	2.7	NS	No
			29–60 days	1.4	NS	No
		Benzodiazepine use (Anxiolytics + Hypnotics)		OR:		
			New	3.4 (1.7 – 6.8)	≤0.05	Yes
			Repeat	1.4 (0.4 – 5.4)	NS	No
Ray(78)	1992	Benzodiazepine use		RR:		
			1–30 days	1.3 (0.6 – 2.9)	NS	No
			31–90 days	1.6 (0.7 – 3.8)	NS	No
			>90 days	1.6 (1.1 – 2.2)	≤0.05	Yes

CI: Confidence interval
NS: Not statistically significant
OR: Odds ratio
RR: Risk ratio

Two studies (Barbone et al., Neutel) reported the risk of crash associated with benzodiazepine use in different age groups (Table 27). When all types of benzodiazepines were analyzed together, both studies found an elevated risk of crash that was statistically significant in drivers age 40 or younger. Drivers in the age range of 40 to 60 did not quite show a statistically significant increase in risk. The studies differed on the findings for the age group >60 years; although the Barbone et al. study did not find an elevated crash risk for this group, the Neutel study found a statistically significant increase in crash risk. The studies also differed when separate analyses were done for benzodiazepine anxiolytics and hypnotics. The Barbone et al. study found a greater crash risk associated with anxiolytics rather than hypnotics in younger age groups, whereas the Neutel study found a greater crash risk associated with hypnotics rather than anxiolytics in younger age groups.

Table 27. Benzodiazepine Use and Crash Risk in Different Age Groups

Reference	Year	Condition	Patient Age Groups	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Barbone et al.(71)	1998	Benzodiazepine use (All types)	<30 years 30–44 years 45–64 years ≥65 years	OR: 2.66 (1.35 – 5.25) 2.18 (1.30 – 3.64) 1.48 (0.97 – 2.27) 0.93 (0.53 – 1.66)	≤0.05 ≤0.05 NS NS	Yes Yes No No
		Benzodiazepine use (Anxiolytics)	<30 years 30–44 years 45–64 years ≥65 years	OR: 3.59 (1.67 – 7.72) 3.29 (1.70 – 6.39) 1.67 (0.93 – 2.99) 0.78 (0.27 – 2.24)	≤0.05 ≤0.05 NS NS	Yes Yes No No
		Benzodiazepine use (Hypnotics)	<30 years 30–44 years 45–64 years ≥65 years	OR: 1.00 (0.31 – 3.23) 1.42 (0.71 – 2.85) 1.37 (0.76 – 2.48) 0.89 (0.46 – 1.72)	NS NS NS NS	No No No No
Neutel(77)	1995	Benzodiazepine use (All types)	20–39 40–59 ≥60	OR: 2.46 (1.06 – 5.68) 2.14 (0.95 – 4.79) 2.03 (1.00 – 4.14)	≤0.05 NS ≤0.05	Yes No Yes
		Benzodiazepine use (Anxiolytics)	20–39 40–59 ≥60	OR: 1.99 (0.84 – 4.72) 1.82 (0.78 – 4.26) 2.03 (0.94 – 4.40)	NS NS NS	No No No
		Benzodiazepine use (Hypnotics)	20–39 40–59 ≥60	OR: 3.74 (1.54 – 9.13) 2.80 (1.15 – 6.81) 2.04 (0.91 – 4.59)	≤0.05 ≤0.05 NS	Yes Yes No

CI: Confidence interval
NS: Not statistically significant
OR: Odds ratio

Van Laar and Volkerts(59) examined a similar group of studies and made a series of recommendations for minimizing impaired driving in individuals who are using benzodiazepines. These recommendations include the following:

- The lowest effective dose should be prescribed.
- Use of single doses up to temazepam 20 mg, lormetazepam 1 mg, oxazepam 30 mg, loprazolam 1 mg, triazolam 0.245 mg, nitrazepam 5 mg, flunitrazepam 1 mg and diazepam 10 mg have been associated with little residual impairment in the morning, 10 to 11 hours after nocturnal intake. Higher doses are expected to produce more serious and prolonged impairment.
- After a single dose of lorazepam 2.5 mg, patients are advised to refrain from driving for up to 24 hours. For a single dose of diazepam up to 10 mg, a recovery time of 7 hours may be sufficient.
- Use of more than one benzodiazepine at a time should be avoided, as should sudden dose increases.
- Prescription of nonbenzodiazepine alternative drugs with a lower sedative potential (e.g., buspirone) may be considered.
- Patients should be educated about the risk of driving impairment during benzodiazepine therapy. They may not be aware of these effects because subjective feelings of sedation do not always correspond with performance impairment. Patients should be warned about acute peak effects for rapidly acting benzodiazepines such as diazepam and about additive effects with concomitant use of central nervous system depressant drugs, such as alcohol. Patients must be aware that partial tolerance may develop during the course of long-term therapy, but their performance may not return to the premedication level.

Antipsychotics and Crash Risk

Only one study addressed the potential association between antipsychotic drugs and crash risk. Neutel found no excess risk of crash associated with antipsychotic agents within two weeks (OR 0.7, 95% CI: 0.2 – 2.9) or four weeks (OR 0.6, 95% CI: 0.2–1.9) of the index prescription.(77) Because this is a single moderate-quality study and the 95% CIs do not rule out the possibility of increased risk, more evidence is needed to confirm these findings.

Antidepressants and Crash Risk

A total of seven studies in the evidence base for Key Question 2 specifically addressed the effect of antidepressants on crash risk. The primary attributes, quality assessment scores, and generalizability tables for the studies in this subsection are found in Table 19, Table 20, and Table 21 respectively, of the general psychotherapeutics section.

Findings

Seven studies presented data on the ratio of crashes experienced by a group of individuals using antidepressants compared with crashes experienced by a group of individuals who did not use antidepressants. Relevant data extracted from these studies are presented in Table 28 and in Figure 11.

Table 28. Crash Risk in Drivers using Antidepressants Compared to Drivers not Using Antidepressants

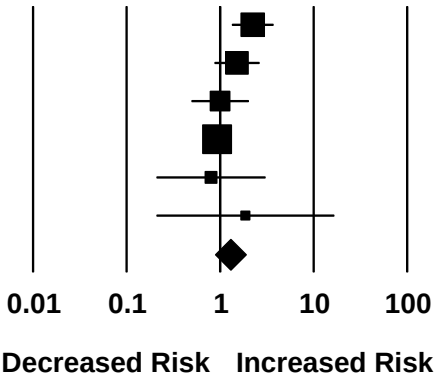
Reference	Year	Condition	Crash Rate Data				Evidence of Increased Crash Risk
			% with Condition (Crash)	% with Condition (No Crash)	Effect Size (95% CI)	*P* =	
Barbone et al.(71)	1998	Antidepressant use (SSRI or TCA)	NR	NR	SSRI OR: 0.85 (0.55 – 1.33) TCA OR: 0.93 (0.72 – 1.21)	NS	No
Leveille et al.(74)	1994	Antidepressant use (TCA)	9.8	6.7	OR: 1.515 (0.859 – 2.674)*	0.152	No
McGwin et al.(75)	2000	Antidepressant use (class not specified)	1.2	1.9	OR: 0.800 (0.207 – 3.098)	0.747	No
Movig et al.(76)	2003	Antidepressant use (TCA)	1	0.5	OR: 1.862 (0.206 – 16.823)*	0.580	No
Neutel(77)	1995	Antidepressant use (class not specified)	NR	NR	OR: 1.00 (0.488 – 2.049)*	1.000	No
Ray et al.(78)	1992	Antidepressant use (TCA)	NR	NR	OR: 2.223 (1.322 – 3.762)*	0.003	Yes
Wadsworth et al.(79)	2005	Antidepressant use (SSRI or TCA)	NR	NR	SSRI OR: 1.410 (0.511 – 3.889) TCA OR: 0.00 (0.00 – 3.96)	0.507	No

* Calculated by ECRI Institute.

CI: Confidence interval
NR: Not reported
NS: Not statistically significant
OR: Odds ratio
SSRI: Selective serotonin reuptake inhibitor
TCA: Tricyclic antidepressant

Figure 11. Crash Risk in Drivers Using Antidepressants

Study Name	Odds ratio	Lower limit	Upper limit	Z-value	*p*-value
Ray	2.230	1.322	3.762	3.006	0.003
Leveille	1.515	0.859	2.674	1.434	0.152
Neutel	1.000	0.488	2.049	0.000	1.000
Barbone	0.930	0.717	1.206	-0.548	0.584
McGwin	0.800	0.207	3.098	-0.323	0.747
Movig	1.862	0.206	16.823	0.554	0.580
Summary	NC	0.873	1.854	1.252	0.211



NC: Not calculated

Three included studies reported more crashes among drivers using antidepressants compared to control drivers (Ray et al., Leveille et al., and Movig, et al.), although the difference was statistically significant only in the study by Ray et al. All three of these studies specifically evaluated TCAs. One study reported no difference in crash risk (Neutel). Two other studies reported a decrease in crash risk in individuals using antidepressants when compared to individuals not using antidepressants, although the difference was not statistically significant. In one of the two studies (Barbone et al.), an adjunct publication reported that 70% of TCA users received subtherapeutic doses.(82) The results of the remaining study (Wadsworth et al.) are more difficult to clarify. This study reported separate ORs for SSRIs and TCAs. Although the findings for both categories of depressant were not statistically significant, the trends were in opposite directions: SSRIs were associated with a slight elevation in number of crashes (OR = 1.4), while TCAs were associated with a reduced number of crashes (OR = 0.00). This latter finding is inconsistent with the findings of the studies by Movig et al. and Ray et al.

In evaluating the potential for a pooled data analysis, we determined that the data from Wadsworth et al. should not be pooled with the results of the other studies for several reasons. First, the data from the TCA group were unusable; the OR that was presented was not accurate enough to be used in a pooled analysis. Also for this reason, the data from the two categories of antidepressants could not be combined, and the number of patients who received antidepressants was not reported in the study. It would have been possible to use the OR for the SSRI category in a meta-analysis, but we chose not to use it because it was not representative of the findings for TCAs within that study. Also, we could only confirm that one of the other six studies included SSRIs in its assessment of antidepressants.

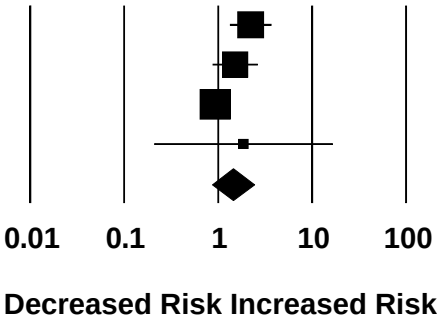
Accordingly, our quantitative analysis includes data from only six studies (Ray et al., Leveille et al., Barbone et al., Movig et al., McGwin et al., and Neutel). A formal assessment of these data for quantitative consistency (homogeneity testing) found that the findings of the six studies were inconsistent (I^2 = 51.1%). Although this precluded a quantitative effect estimate, we combined the crash OR data in a

random-effects meta-analysis in an attempt to determine the general direction of the effect (i.e., whether crash risk was increased).

The random-effects meta-analysis did not find a statistically significant increase in the odds of crash associated with antidepressant use (Figure 11). However, because the 95% CI around the summary effect is wide enough to encompass the possibility of an elevated crash risk with antidepressant use, this finding is inconclusive.

Figure 12. Crash Risk in Drivers Using Tricyclic Antidepressants

Study Name	Odds ratio	Lower limit	Upper limit	Z-value	*p*-value
Ray	2.223	1.318	3.750	2.994	0.003
Leveille	1.515	0.859	2.673	1.434	0.152
Barbone	0.930	0.717	1.206	-0.548	0.584
Movig	1.862	0.206	16.827	0.553	0.580
Summary	NC	0.849	2.384	1.340	0.180



CI: Confidence interval
NC: Not calculated

We performed a separate subgroup meta-analysis of studies that reported crash data associated with TCA use (Figure 12). However, the findings of this subgroup analysis were also inconclusive (i.e., an increased crash risk could be neither confirmed nor ruled out).

The findings of the two studies that separately evaluated SSRI use (Barbone et al., Wadsworth et al.) did not show an elevated crash risk associated with use of this category of antidepressants (Table 28). However, the results of these two low-quality studies are not sufficient evidence to rule out the possibility of increased crash risk.

To determine whether certain factors might have an influence on crash risk associated with antidepressant use, we further examined the available studies for information concerning crash risk in association with dose, number of prescribed antidepressants, duration and timing of exposure, and patient age.

Two studies (Barbone et al., Ray et al.) presented information regarding the effect of TCA dose on crash risk (Table 29). Barbone et al. did not find a statistically significant increase in crash for SSRI or TCA use at any dose level. In contrast, Ray et al. found that for TCA users the relative risk of crash increased from 0.8 (95% CI: 0.3 – 2.7) for the equivalent of 25 mg amitriptyline or less to 5.5 (95% CI: 2.6 – 11.6) for 125 mg or greater.

Table 29. Antidepressant Dose and Crash Risk

Reference	Year	Condition	Dose	Effect Size (95% CI)	*P* =	Evidence of Increased Crash Risk
Barbone et al.(71)	1998	SSRI use	Low Intermediate High	OR: 0.80 (0.50 – 1.30) 1.37 (0.47 – 3.97) NC	NS NS	No No
		TCA use	Low Intermediate High	OR: 0.90 (0.66 – 1.22) 0.90 (0.54 – 1.43) 1.39 (0.56 – 3.48)	NS NS NS	No No No
Ray(78)	1992	TCA use	≤25 mg 50 mg 75-100 mg ≥125 mg	OR: 0.8 (0.3 – 2.7) 2.5 1.8 5.5 (2.6 – 11.6)	NS NS NS ≤0.05	No No No Yes

CI: Confidence interval
NC: Not calculable; too few cases
NS: Not significant
OR: Odds ratio

The study by Ray et al. also examined the potential impact of using single versus multiple TCAs on crash risk. For single TCA users, the relative risk of crash was 2.0 (95% CI: 1.3 – 3.1); the risk increased to 9.8 (95% CI: 2.4 – 39.5) for users of more than one TCA.(78) However, the findings of this single study require confirmation.

Leveille et al. evaluated crash risk based on time of exposure to TCAs. The authors reported that exposure within 60 days of the reference date led to a higher crash risk (adjusted OR 2.3, 95% CI: 1.1 – 4.8) than past exposure between 60 days and six months before to the reference date (adjusted OR 0.7, 95% CI: 0.2 – 1.9).(74) Again, these findings should be replicated in another study before conclusions are drawn.

Barbone et al. reported crash risk of TCA users and SSRI users according to age group. This study did not find a statistically significant increase in crash risk in any age group for either type of antidepressant, although there was a trend toward increased risk with TCAs in the under-30 and over-65 age groups.(71)

Section Summary

Analysis 1: Benzodiazepine Use and Crash Risk

- **Benzodiazepine use is associated with an increased risk for a motor vehicle crash (Strength of Evidence: Moderate).**
- **Benzodiazepine anxiolytic use is associated with an increased risk for a motor vehicle crash (Strength of Evidence: Minimally Acceptable).**
- **Crash risk may be greater during the first week of an index prescription of benzodiazepines (Strength of Evidence: Minimally Acceptable).**
- **Crash risk may be greater among benzodiazepine users ≤40 years of age (Strength of Evidence: Minimally Acceptable).**

Our searches identified nine direct crash risk studies with a total of approximately 235,000 individuals using benzodiazepines. The average quality of these studies was moderate. None of the study participants were specifically identified as CMV drivers, so the generalizability of the findings to the CMV driver population is unclear. The findings of the nine studies were inconsistent. However, pooling of the data from each study found elevated odds of crash associated with benzodiazepine use. This finding was statistically significant and robust.

Because benzodiazepine anxiolytics are more likely to be used than hypnotics in patients with psychiatric disorders, we performed a subgroup analysis of five studies that presented separate crash data for users of anxiolytics. The pooled data analysis found that the odds of crash were significantly increased in users of benzodiazepine anxiolytics.

Further analysis to identify factors that may lead to increased risk for benzodiazepine users identified timing of exposure and patient age as potential risk factors. Two studies found the highest risk of crash to occur during the first week of the index prescription, and two studies found that crash risk was higher in benzodiazepine users ≤40 years of age.

Analysis 2: Antipsychotic Use and Crash Risk

- **The evidence concerning crash risk associated with antipsychotic use is inconclusive. The possibility of an increased crash risk associated with antipsychotic use cannot be ruled out.**

One study addressed the potential association between antipsychotic drugs and crash risk. This study found no excess risk of crash associated with antipsychotic agents within two weeks or four weeks of the index prescription. As this is a single moderate-quality study and the 95% CIs around the effect estimates do not rule out the possibility of increased risk, more evidence is needed to confirm these findings.

Analysis 3: Antidepressant Use and Crash Risk

- **The evidence concerning crash risk associated with antidepressant use is inconclusive. The possibility of an increased crash risk associated with antidepressant use (particularly TCA use) cannot be ruled out (Strength of Evidence: Minimally Acceptable).**

Our searches identified seven direct crash risk studies with an unknown number of individuals using antidepressants—the number is not reportable because the raw data needed to calculate the total study population using antidepressants was not reported in all studies. Because these are seven of the nine studies identified under benzodiazepines, the generalizability issues and quality assessments are described in the earlier summary.

The findings of six of the seven studies could be combined to obtain a summary estimate of the relative odds of crash associated with antidepressant use. Pooling of the data from these studies found that the odds of crash was not significantly different for drivers using antidepressants compared to drivers not using antidepressants. However, there was a trend toward elevated risk associated with antidepressants, and the wide confidence interval around the summary estimate means that the possibility of increased crash risk cannot be ruled out. The same finding was shown for a subgroup meta-analysis of studies that separately reported data on TCA use.

Key Question 3: What traits associated with personality disorders are associated with reductions in motor vehicle driver safety?

There are many factors that contribute to the risk of a motor vehicle crash, including vehicle type and condition, the roadway type and condition, and the way that an individual chooses to operate a motor vehicle. The previous key questions of this report have demonstrated that not all individuals have the same risk of experiencing a crash: individuals who are using certain psychotherapeutic medications may have an increased risk of crash compared to individuals who do not use psychotherapeutic medications. When considering the risk of crash it is also important to understand the role an individual's psychological state and motivations may play in increasing or decreasing driver safety. In individuals with personality disorders, some personality traits that are part of the disorder may be related to behavior that may be associated with their risk of motor vehicle crash.

In this section we review the evidence pertaining to those traits found in personality disorders that may be associated with reductions in driver safety. The purpose of this review is to determine whether these traits pose a risk to road safety inasmuch as they may affect the ability to perform the functions required to safely operate a CMV.

Background

Human factors, specifically driving behaviors, make an important contribution to crashes.(83) The reports being produced under this subcontract with the FMCSA are in large part investigations of the human factors, specifically health-related factors, which may contribute to reductions in driver safety. There are other factors which may also affect safe driving, including driver attitude.(84-88)

Driver Attitude

Driver attitude is classified into the following two groups, each with a distinct psychological origin:

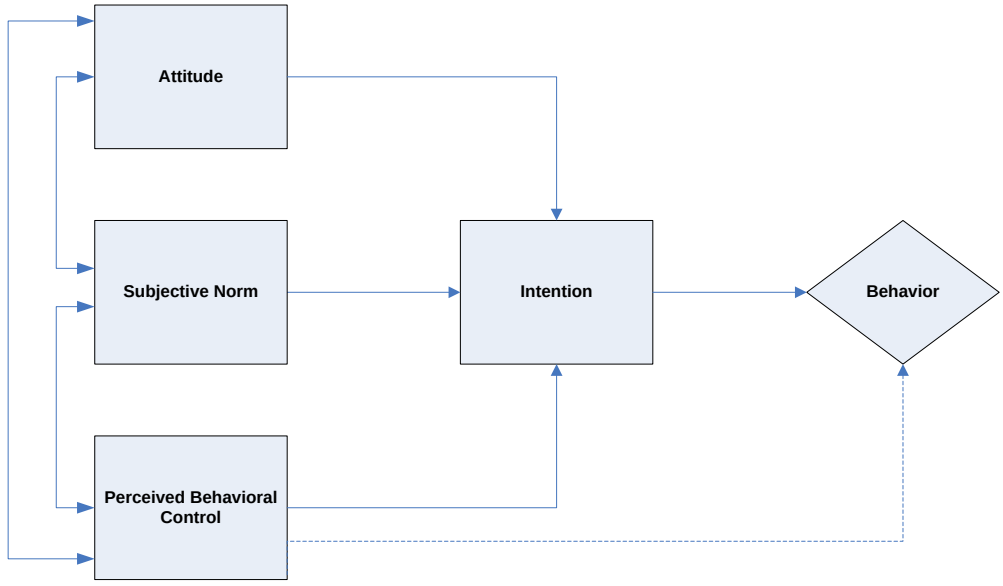
- Errors: When the actions that an individual plans to achieve a specific consequence fail to achieve the desired result, it is considered an error. Errors are internally related in that they deal with an individual's cognitive processes.
    - Straying: slips or lapses that constitute an individual's unconscious departure from the intended action
    - Mistakes: deviation from a method that would bring about the fulfilling of an individual's goal
        - Rule-based mistakes involve the use of an inappropriate condition—action rule, or the '**if** condition, **then** action' rule (i.e., if the condition holds, perform the action). The condition can be either true or false (Boolean logic), and the action may either be performed, or not.
        - Knowledge-based mistakes occur when an individual is required due to unique circumstances, to make a decision based on the information he or she currently has available, regardless of how incomplete that information may be.

- Violations: The "deliberate deviation from those practices believed necessary to maintain the safe operation of a potentially hazardous system." Violations are externally related in that they deal with rules, operating systems, codes of practice, and are governed by social context.(89)

In driving, Parker et al.(90,91) and Aberg and Rimmo(92) demonstrated that violations, but not errors, are a factor in crashes.

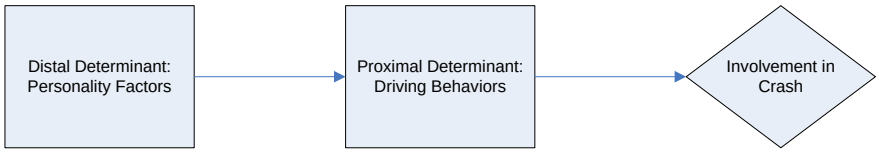
Bridging the gap between attitude and action is Ajzen's Theory of Planned Behavior (1985),(93) which states that behaviors can be predicted by intention and attitudes toward the act and the perceived behavioral control. A model to illustrate this concept is featured in Figure 13.(94)

Figure 13. Model of the Theory of Planned Behavior



Therefore, if crashes are related to violations of traffic rules or traffic codes of practice, and the individual who performs the violation has formed the intent not to follow a practice related to the safe operation of a motor vehicle based on attitudes toward the act, then they are making a choice to engage in risky driving behavior that may result in a crash. Their choice of action is related to the individual's personal characteristics and motivation.(86,92,95-97) Applying this model to driving, studies by Parker et al. have demonstrated that speeding and aggressive driving behavior are related to the intention part of the model in Figure 13.(84,98) A model combining all the concepts outlined thus far is featured in Figure 14.

Figure 14. Distal and Proximal Determinants of Behavior and Crash



Risky Driving and Aggressive Driving

Risky driving and aggressive driving are terms that are very broadly and, it has been argued, inconsistently defined.(99) The National Highway Transportation Safety Administration (NHTSA) defined aggressive driving as "the operation of a motor vehicle in a manner that endangers or is likely to endanger persons or property."(100) A review of the studies included in the evidence base for this key question reveals overlapping themes regarding aggressive driving, including:

- Speed violations
- Running red lights
- Stop sign violations
- Slow driving
- Tailgating
- Improper passing
- Verbal insults
- Physical assault
- Honking horn
- Flashing lights/high beams

Dula and Geller(99) proposed that the NHTSA definition of aggressive driving be viewed along a spectrum of dangerous driving behavior that is divided into the following three categories:

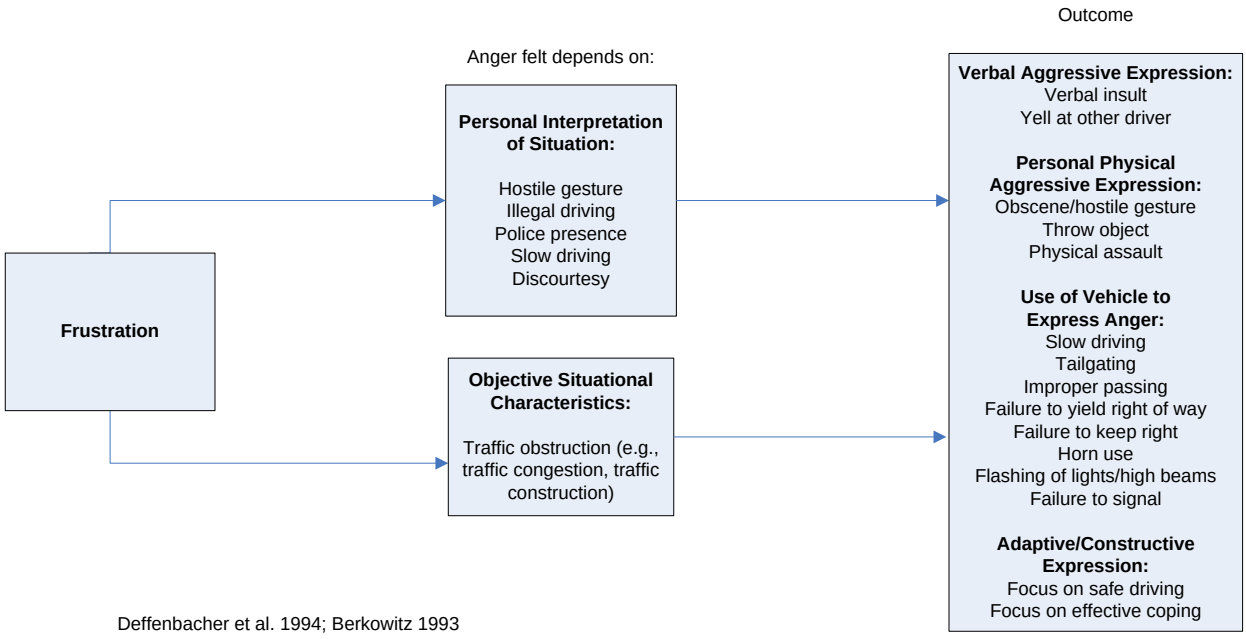
- Intentional acts of other-oriented aggression
- Experiencing negative emotions while driving
- Risk-taking actions while driving

The authors also recommended that the popular term "road rage" be abandoned in research due to inconsistencies in definition that were unlikely to be resolved in a way that would improve utility.(99,101)[3] Miles and Johnson (102) proposed that road rage and aggressive driving differed in several key ways, most notably in the severity of the aggressive behavior, the presence of trait anger, a sense of territoriality or entitlement in which the individual committing the act feels entitled to the roadway and sees others who are using it as an intrusion, and a sense of personal space which may include not only the automobile but the roadway.

A model of the factors involved in aggressive driving behavior based on the Deffenbacher et al. Driver Anger Scale)(103) and Berkowitz's (1993) research on the causes and consequences of aggression as related to frustration is featured in Figure 15.(104,105)

[3] Road rage is defined by NHTSA as a criminal offense involving "an assault with a motor vehicle or other dangerous weapon by the operator or passenger(s) of one motor vehicle on the operator or passenger(s) of another motor vehicle or is caused by an incident that occurred on a roadway."

Figure 15. Factors Involved in Aggressive Driving Behavior



Deffenbacher et al. 1994; Berkowitz 1993

As with aggressive driving, risky driving is loosely defined. It is considered distinctly separate from other forms of dangerous driving behavior (probably because it can include forms of nonaggressive behavior such as not wearing a seat belt while driving) and includes speeding, unsafe passing, tailgating, and entering an intersection when the light is turning red.(106) Risky driving may be related to sensation seeking, impulsivity (the inability on the part of the individual to control engaging in risk-taking behaviors), and low risk perception.(92,107-114) In a review of injury and risk-taking behavior by Turner et al. in 2004,(115) the authors defined risky behavior as "a socially unacceptable volitional behavior with a potentially negative outcome in which precautions are not taken (e.g., speeding, drinking and driving) or a socially acceptable behavior in which the danger is recognized (competitive sports, skydiving)."

Predicting Risky and Aggressive Driving Practices

There are several potential predicting factors for risky and aggressive driving practices. These factors are featured in Table 30.(116-121)

Table 30. Potential Predictive Factors for Risky and Aggressive Driving

Factor	Behavior
Age	Risky driving behavior differs between age groups. Compared to older drivers, younger drivers are more likely to • Speed; • Tailgate; • Engage in risky overtaking; • Allow too little time to merge; and/or • Fail to give way to pedestrians.
Gender	Males consistently engage in more risky driving behaviors than females, including • Speeding; • Driving under the influence of alcohol; and/or • Breaking rules associated with being on a restricted license.
Competitiveness (trait related to behavior in which the person views interactions with others as a contest)	Competitiveness may be related to on road competitive driving, and possibly speeding and tailgating. Drivers who report frequent racing of motor vehicles are more likely to be injured while driving.†
Openness, conscientiousness, extraversion, agreeableness, and neuroticism (OCEAN, or the Five Factor Model of Personality)	Crashes correlate to five-factor personality model.†
Aggression	Aggression has been associated with risky driving behavior.
Psychopathy	Antisocial personality has been associated with deviant behavior.†
Authority defiance	Authority defiance has not had sufficient research to be definitively considered a risky driving predictor.
Time saving/convenience	The desire to arrive on time for an appointment or at a destination has been associated with drowsy driving and speeding.†
Sensation seeking	Accepting risk in order to obtain new, different, and intense sensations and experiences is associated with risky driving such as speeding, racing other drivers, and passing in no-passing zones. It can be said to be the expression of a preference for novelty and willingness to take risks to satisfy this preference.
Driver attitudes and beliefs	An attitude toward a behavior is a key element in intentions to perform the behavior. Attitude itself comprises a belief about the outcome of a behavior. An attitude toward risky driving would play a part in determining whether the person engages in risky driving behavior.
Perceived risk	The individual's understanding of the risk of an undesirable outcome resulting from a behavior, for example, optimism bias (expecting a better outcome from an action than would be expected for the individual's peers).
Risk utility	The value or usefulness of a risk may be associated with risky driving behavior. For example, speeding may be useful if it saves the individual time, or if the individual enjoys speeding.

† Further research is needed to ascertain the role of this factor as a contributor to risky driving. (Fernandes et al., 2007)

From this table, it is obvious that a number of diverse and complicated factors contribute to risky driving behaviors.(106,116,122) Some of the factors seem obvious: a person who believes that he or she will be late for an appointment may choose to engage in a risky driving behavior (e.g., speeding, tailgating) in order to achieve the desired goal of arriving on time.(123,124) Not all these attitudinal factors and personality traits contribute to driving behavior in the same way, neither do they exist in a vacuum. A number of factors, individually but not necessarily equally, contribute to bring about risky driving behavior.(116)

Driving Behaviors and Risk of Crash

A number of studies and reviews have identified driving behaviors that were associated with an increased risk of crash.(106,117,118,125-128) Observations from three of these studies included the behaviors outlined in Table 31.(125,126)

Table 31. Driving Behaviors Associated with Increased Crash Risk

Factor	AAA Foundation for Traffic Safety (2006)	NHTSA* (2001)(2003)
Driver inattention	Driver inattention nearly doubled the risk of crash compared to driving while paying attention to the road (OR = 1.9, 95% CI: 1.4 – 2.5)	The most dominant component of crash causal factor pattern, contributing approximately 22.7% to the pattern Crash type: • Same direction, rear end • Turn, merge, path encroachment • Single driver, right or left roadside departure without traction loss • Intersecting paths, straight paths • Same traffic way, opposite directions • Other, miscellaneous
Speeding	Driving at inappropriate speeds nearly tripled the risk of crash compared to driving at an appropriate speed (OR = 2.9, 95% CI: 1.7 – 4.8).	The second most dominant component of crash causal factor pattern, contributing approximately 18.7% Crash type: • Same direction, rear end • Single driver, right or left roadside departure with traction loss • Same traffic way, opposite direction • Other, miscellaneous • Speed of vehicle directly correlated to severity of crash
Alcohol/drug consumption	ND	The third most dominant component of crash causal factor pattern, contributing approximately 18.2 to the pattern Relative frequency of alcohol/drugs related to crash severity
Perceptual errors	ND	The fourth most dominant component of crash causal factor pattern, contributing approximately 15.1% to the pattern
Decision errors	ND	The fifth most dominant component of crash causal factor pattern, contributing approximately 10.1% to the pattern
Drowsiness	Drowsiness nearly tripled the risk of crash compared to driving when not drowsy (OR = 2.9, 95% CI: 2.0 – 4.3)	The sixth most dominant component of crash causal factor pattern, contributing approximately 6.4% to the pattern (included blackouts and seizures) Crash type: • Single driver, right or left roadside departure without traction loss
Aggressive Driving	Aggressive driving more than doubled the risk of crash compared to nonaggressive driving behavior (OR = 2.1, 95% CI: 1.3 – 3.4)	Incidence rate of aggressive driving in this study was estimated at 9%, with a caution that selection bias may have been a factor in the geographic sampling

* National Highway Transportation Safety Administration

CI: Confidence interval
ND: Not discussed
OR: Odds ratio

Each of these behavioral factors contributes to the risk of crash and the type of crash that occurs. For example, the leading contributors to single-vehicle off-roadway crashes were speeding resulting in a loss of control, driver inattention, and driver use of alcohol/drugs. For a lane-changing crash, the leading behavioral contributors were driver inattention, speeding, and driver use of alcohol/drugs.

A survey to determine factors associated with "high risk" CMV drivers conducted among safety managers and others designated by the researchers as experts in this area (e.g., former drivers, fleet managers,

government regulatory and enforcement personnel, industry trade association representatives, researchers) found that aggressive/angry drivers were of most concern, followed by impatient/impulsive drivers; introverted/unsociable drivers were 15th on the list of 16 factors.(129)

Personality Disorders

Personality disorders constitute maladaptive personality traits that create difficulty in relating to others or in forming relationships due to rigidity of behavior, thinking, and perception that diminishes the ability to respond to change, affects interpersonal functioning on a day-to-day basis, and limits the ability to engage in social activities. Personality disorders are generally categorized in three clusters, with each disorder having distinct behaviors and symptoms. These disorders include the following:(130,131)

- Cluster A (odd or eccentric behavior): schizoid personality disorder; paranoid personality disorder; schizotypal personality disorder
- Cluster B (dramatic, emotional, or erratic behavior): antisocial personality disorder; borderline personality disorder; histrionic personality disorder; narcissistic personality disorder
- Cluster C (anxious, fearful behavior): avoidant personality disorder; dependent personality disorder; obsessive-compulsive personality disorder

There is no specific treatment for personality disorders; various forms of cognitive therapy and pharmacological therapy are used to treat concomitant psychiatric disorders such as anxiety and/or depression.

Traits Associated with Personality Disorders

Each personality disorder is defined by a unique, pervasive pattern of behavior and inner experience that is both sufficiently different from what is expected in the individual's social context and affects a minimum of two of the following areas: cognition, affect, social function, or the ability to control impulses. Table 32 provides signs and symptoms of personality disorders as defined by the Mayo Clinic.(132)

Table 32. Signs and Symptoms of Personality Disorders by Cluster

Personality Disorder	Signs and Symptoms
Cluster A	
Paranoid personality disorder	• Belief that others are lying, cheating, exploiting, or trying to harm • Perception of hidden, malicious meaning in benign comments • Inability to work collaboratively with others • Emotional detachment • Hostility toward others
Schizoid personality disorder	• Fantasizing • Extreme introversion • Emotional distance, even from family members • Fixation on own thoughts and feelings • Emotional detachment
Schizotypal personality disorder	• Indifference to and withdrawal from others • "Magical thinking"—the idea that individuals and events can be influenced by thoughts • Odd, elaborate style of dressing, speaking, and interacting with others • Belief that messages are hidden for the individual in public speeches and displays • Suspicious or paranoid ideas
Cluster B	
Histrionic personality disorder	• Excessive sensitivity to others' approval • Attention-grabbing, often sexually provocative clothing and behavior • Excessive concern with physical appearance • False sense of intimacy with others • Constant, sudden emotional shifts
Narcissistic personality disorder	• Inflated sense of—and preoccupation with—importance, achievements, and talents • Constant attention-grabbing and admiration-seeking behavior • Inability to empathize with others • Excessive anger or shame in response to criticism • Manipulation of others to further the individual's own desires
Antisocial (formerly, sociopathic) personality disorder	• Chronic irresponsibility and unreliability • Lack of regard for the law and for others' rights • Persistent lying and stealing • Aggressive, often violent behavior • Lack of remorse for hurting others • Lack of concern for the safety of self and others
Borderline personality disorder	• Difficulty controlling emotions or impulses (DSM –IV-TR examples include gambling, spending money recklessly, binge eating, engaging in unsafe sex, driving recklessly)(Verheul examples include sensation seeking(133)) • Frequent, dramatic changes in mood, opinions, and plans • Stormy relationships involving frequent, intense anger and possibly physical fights • Fear of being alone despite a tendency to push people away • Feeling of emptiness inside • Suicide attempts or self-mutilation
Cluster C	
Avoidant personality disorder	• Hypersensitivity to criticism or rejection • Self-imposed social isolation • Extreme shyness in social situations, though the individual may strongly desire close relationships
Dependent personality disorder	• Excessive dependence on others to meet physical and emotional needs • Tolerance of poor, even abusive treatment in order to stay in relationships • Unwillingness to independently voice opinions, make decisions, or initiate activities • Intense fear of being alone • Urgent need to start a new relationship when one has ended
Obsessive-compulsive personality disorder	• Excessive concern with order, rules, schedules, and lists • Perfectionism, often so pronounced that the individual can't complete tasks because personal standards are impossible to meet • Inability to throw out even broken, worthless object • Inability to share responsibility with others • Inflexibility about the "right" ethics, ideas, and methods • Compulsive devotion to work at the expense of recreation and relationships • Financial stinginess • Discomfort with emotions and aspects of personal relationships that the individual can't control

Personality Disorders and Reductions in Driver Safety

A violation constitutes the "deliberate deviation from those practices believed necessary to maintain the safe operation of a potentially hazardous system."(89) Parker et al. demonstrated that violations are a factor in crashes, but errors are not, and that speeding and aggressive driving behavior are related to intention and, therefore, behavior.(84,98) The driving behavior an individual practices is thus related to his/her personal traits and motivation.

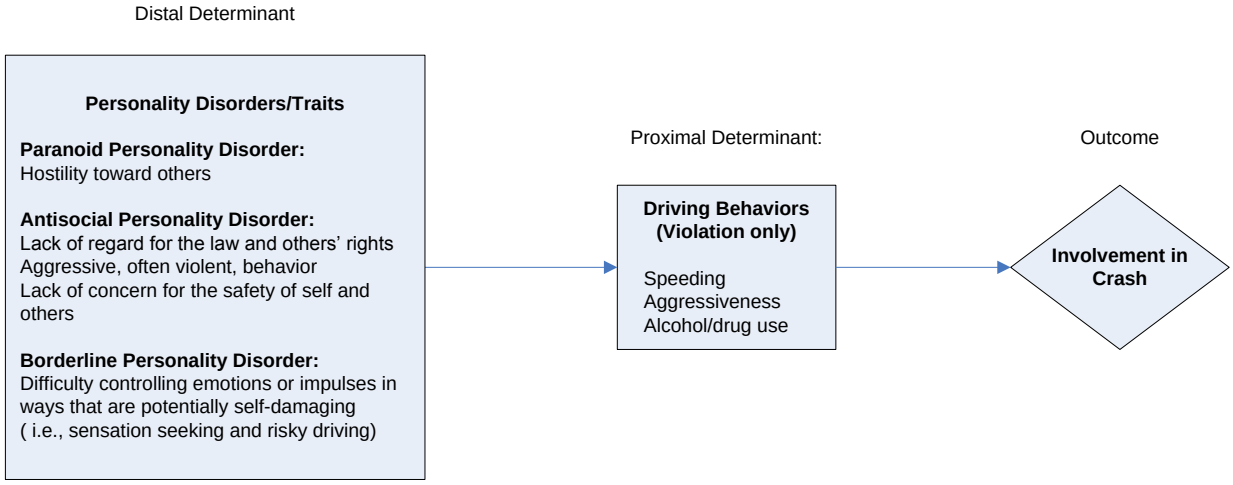
In the section of report on driving behaviors and the risk of crash, we identified seven types of driving behavior that increase the risk of a motor vehicle crash (or "risky driving behaviors"). These behaviors are as follows:

- Speeding
- Drowsiness
- Driver inattention
- Aggression
- Alcohol/drug use
- Perceptual error
- Decision error

Sumer (2003) proposed a contextually mediated model of personality factors and driving behaviors to distinguish between distal and proximal factors that might be involved in crash. Testing of the model found that psychological symptoms (anxiety, depression, hostility, and psychoticism) were correlated with sensation seeking (risk taking, novelty, and intensity) and aggression (anger, physical aggression, verbal aggression, and hostility), and that sensation seeking and aggression had significant and direct effects on aberrant driving behaviors (errors and violations). Altogether, distal factors such as sensation seeking and aggression explained 57% of the variance in aberrant driving behaviors, and aberrant driving behaviors and psychological symptoms significantly predicted the number of crashes that occurred. Sumer noted that the model may have underestimated the relationships between the potential predictors and crash because of the large number of individuals in the study population (49%) that did not report having experienced a crash.(134) Similar results were reported by Garrity and Demick (2001), who found that the mood states of anger/hostility, depression/dejection, and tension/anxiety were negatively associated with cautious driving behavior; personality traits such as neuroticism, extraversion, openness, agreeableness, and conscientiousness were not related to driving behavior. There were significant associations between the mood states and personality traits, with neuroticism and conscientiousness being correlated to all mood states, anger/hostility having significant positive correlations with tension/anxiety, neuroticism, and depression/dejection and a significant negative correlation to conscientiousness. It may be said that this study suggests that the personality traits acted as distal determinants and the mood states as proximal determinants of driving behavior.(135)

The signs and symptoms of recognized personality disorders were outlined and defined in Table 32 (DSM-IV-TR, 2000).(136) Combining the relationship of violation to crash, the types of driving behavior that increase the risk of crash, and personality disorder traits, we can create a model based on Sumer's contextually mediated model to explore the relationship of these traits to a reduction in driver safety (Figure 16).

Figure 16. Relationship of Violations, Driving Behavior, and Personality Disorders to Crash



From the model, we see that we have identified three personality disorders that are distinguished by traits that may be related to a reduction in the safe operation of a motor vehicle, as follows:

- Paranoid personality disorder
- Antisocial personality disorder
- Borderline personality disorder

Identification of Evidence Base

To meet the aims of this section of the evidence report, we searched for trials that compared crash risk among individuals with personality disorders and/or related traits and otherwise comparable individuals who did not have personality disorders and/or related traits. In addition, we looked for studies that compared the prevalence of personality disorders and/or related traits among cohorts of individuals who had or had not experienced a crash.

The evidence base identification pathway for Key Question 3 is summarized in Figure 17. Our searches (Appendix A) identified a total of 261 articles that appeared to be relevant to this key question. Following application of a set of retrieval criteria (Appendix B), 33 full-length articles were retrieved and read in full. Of these 33 retrieved articles, 21 were found to meet the inclusion criteria for Key Question 3 (Appendix C). Table 33 lists these 21 included studies. Table D-3 of Appendix D lists the 12 articles that were retrieved but then excluded from inclusion in the evidence base for Key Question 3 and provides the reason for their exclusion.

Figure 17. Development of Evidence Base for Key Question 3

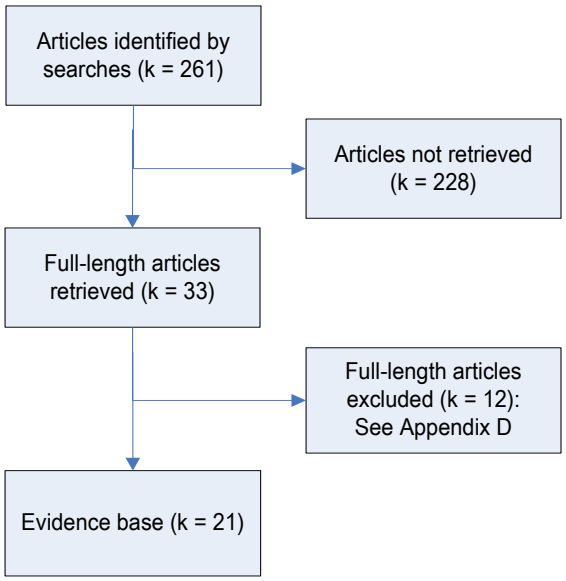


Table 33. Evidence Base for Key Question 3

Reference	Year	Study Location	Country
Professional Drivers			
Sumer(134)	2003	Ankara	Turkey
Sullman et al.(137)	2002	Multi-site	New Zealand
Lajunen et al.(138)	2001	Ankara	Turkey
Other Drivers			
Gulliver and Begg(139)	2007	Dunedin	New Zealand
Nabi et al.(140)	2007	St.Maurice	France
Verschuur and Hurts(141)	2007	Leiden	Netherlands
Schwebel et al.(110)	2007	Alabama	USA
Kontogiannis(142)	2006	Crete	Greece
Blows et al.(143)	2005	Auckland	New Zealand
Malta et al.(144)	2005	New York	USA
Nabi et al.(145)	2005	St.Maurice	France
Turner and McClure(146)	2004	Brisbane	Australia
Karlsson et al.(109)	2003	Stockholm	Sweden
Wells-Parker et al.(101)	2002	Multi-site	USA
Fong et al.(147)	2001	London	United Kingdom
Bell et al.(148)	2000	Multi-site	USA
Alparslan et al.(149)	1999	Aydin	Turkey
Deery and Fildes(150)	1999	Victoria	Australia
Parker et al.(91)	1995	Amsterdam	Netherlands
Rajalin(151)	1994	Helsinki	Finland
Mayer and Treat(152)	1977	Indiana	USA

Evidence Base

This subsection provides a brief description of the key attributes of the 21 studies that comprise the evidence base for Key Question 3. Here we discuss pertinent information pertaining to the quality of the included studies and the generalizability of each study's findings to CMV drivers. Key characteristics of the 21 included studies that address Key Question 3 are presented in Table 34. The testing instruments used in the included studies are presented in Table 35.

Table 34. Key Study Design Characteristics of Studies That Address Key Question 3

Reference	Year	Study Design	Comparison	Personality Disorder/Trait				Driving Exposure Controlled For?	Primary Outcome	Definition of Crash	Outcome Self-reported?
				Cluster A	Cluster B	Cluster C	Other*				
Professional Drivers											
Sumer(134)	2003	Survey	Drivers involved in crashes vs. drivers not involved in crashes	✓	✓	✓		Yes	Crash	NR	Yes
Sullman et al.(137)	2002	Survey	Drivers involved in crashes vs. drivers not involved in crashes		✓			Yes	Crash	Any incident that involved injury to another person (including the respondent), damage to property or vehicles	Yes
Lajunen et al.(138)	2001	Survey	Drivers involved in >1 crash vs. drivers involved in no crashes or a single crash	✓			✓	No	Crash	NR	Yes
Other Drivers											
Gulliver and Begg(139)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes		✓			Yes	Crash	NR	Yes
Nabi et al.(140)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		Yes	Crash	NR	Yes
Verschuur and Hurts(141)	2007	Survey	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		No	Crash	NR	Yes
Schwebel et al.(110)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes			✓		Yes	Crash	NR	No
Kontogiannis(142)	2006	Survey	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		No	Crash	NR	Yes
Blows et al.(143)	2005	Cohort	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		No	Crash	Crash with injury requiring treatment by physician	No
Malta et al.(144)	2005	Survey	Drivers involved in crashes vs. drivers not involved in crashes	✓	✓	✓	✓	No	Crash	NR	Yes
Nabi et al.(145)	2005	Cohort	Drivers involved in crashes vs. drivers not involved in crashes		✓			Yes	Crash	NR	Yes
Turner and McClure(146)	2004	Case-control	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		No	Crash	NR	Yes
Karlsson et al.(109)	2003	Cohort	Drivers involved in crashes vs. drivers not involved in crashes			✓		No	Crash	NR	Yes

Reference	Year	Study Design	Comparison	Personality Disorder/Trait				Driving Exposure Controlled For?	Primary Outcome	Definition of Crash	Outcome Self-reported?
				Cluster A	Cluster B	Cluster C	Other*				
Wells-Parker et al.(101)	2002	Survey	Drivers involved in crashes vs. drivers not involved in crashes		✓			No	Crash	NR	Yes
Fong et al.(147)	2001	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	✓	✓	✓		No	Crash	NR	Yes
Bell et al.(148)	2000	Cohort	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		Yes	Crash	NR	No
Alparslan et al.(149)	1999	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	✓	✓			No	Crash	NR	Yes
Deery and Fildes(150)	1999	Survey	Drivers involved in crashes vs. drivers not involved in crashes		✓	✓		Yes	Crash	NR	Yes
Parker et al.(91)	1995	Cohort	Drivers involved in crashes with violations vs. drivers involved in crashes with errors		✓			Yes	Crash	NR	Yes
Rajalin(151)	1994	Case-control	Drivers involved in fatal crashes vs. drivers not involved in crashes			✓		Yes	Crash	Fatal	No
Mayer and Treat(152)	1977	Case-control	Drivers involved in crashes vs. drivers not involved in crashes		✓		✓	No	Crash	NR	Yes

* Other may comprise negativity, passive-aggressive disorder, depression, anxiety, etc.

NR: Not reported

Table 35. Testing Instruments

Test	References																						
	Professional Driver	Sumer(134)	Sullman(137)	Lajunen et al.(138)	Private Motor Vehicle Drivers	Gulliver and Begg(139)	Nabi et al.(140)	Verschuur and Hurts(141)	Schwebel et al.(110)	Kontogiannis(142)	Blows et al.(143)	Malta et al.(144)	Nabi et al.(145)	Turner and McClure(146)	Karlsson et al.(109)	Wells-Parker et al.(101)	Fong et al.(147)	Bell et al.(148)	Alparslan et al.(149)	Deery and Fildes(150)	Parker et al.(91)	Mayer and Treat(152)	Test Totals
ADHD/ODD												✓											1
AISS		✓																					1
BDHQ													✓							✓			2
BPAQ		✓															✓						2
BSI		✓		✓																			2
CIS-R																	✓						1
DBQ		✓	✓					✓	✓	✓											✓		6
DBRS							✓																1
DMDATS														✓						✓	✓		3
DS																					✓		1
DSP												✓											1
HEA																					✓		1
IED												✓											1
In-depth Questionnaire																✓							1
In-house Questionnaire															✓			✓					2
LES																	✓						1
MPG						✓																	1
MSDS		✓																					1
NZBDHS											✓												1
Personal/Familial												✓											1
RLC																					✓		1
SCID-II												✓							✓				2
STCPD																	✓						1
ZSSS									✓												✓		2

ADHD/ODD: Attention Deficit Hyperactivity Disorder/Oppositional Defiant Disorder; AISS: Arnett Inventory of Sensation Seeking; BDHQ: Buss Durkee Hostility Query; BPAQ: Buss Perry Aggression Questionnaire; BSI: Brief Symptom Inventory; CIS-R: Clinical Interview Schedule; DBQ: Driver Behavior Questionnaire (Reason et al.1990); DBRS: Driver Behavior Road Safety Questionnaire; DMDATS: Donovan and Marlatt Driver Aggression and Thrill Seeking; DS: Driving Scenarios; DSP: Driver Stress Profile; HEA: Howarth Emotional Adjustment; In-depth Questionnaire: Questionnaire created by the author(s) of the study; In-house Questionnaire: Questionnaire created by the author(s) of the study; LES: Life Events Schedule; MPG: Multidimensional Personality Questionnaire; MSDS: Multidimensional Self Destructiveness Scale; NZBDHS: New Zealand Blood Donors Health Survey; Personal/Familial: Personal and Familial Psychiatric and Anger/Aggression History Interview; RLC: Rotter Locus of Control; SCID I and II: Structural Clinical Interview for DMS-III-R; STCPD: Screening Test for Comorbid Personality Disorders; ZSSS: Zuckerman Sensation Seeking Scale

Quality of Evidence Base

The results of our assessment of the overall quality of the evidence base for Key Question 3 are presented in Table 36. Our assessment found that the median quality of the included studies was low. Six of the 21 included studies were graded as being of moderate quality. The remaining 15 studies were graded as low quality. Case-control studies generally did not control for important confounders and had deficiencies in assessment of exposure or outcome. Cohort studies were most often deficient in relying upon self-report of exposure and outcome. All of the surveys relied upon individual self-report of exposure and outcome, and these studies were also limited by generally poor reporting of the survey methodology.

Table 36. Quality of Studies for Key Question 3

Reference	Year	Quality Scale Used	Quality
Professional Drivers			
Sumer(134)	2003	ECRI Institure Quality Scale VI – Surveys	Low
Sullman et al.(137)	2002	ECRI Institure Quality Scale VI – Surveys	Low
Lajunen et al.(138)	2001	ECRI Institure Quality Scale VI – Surveys	Low
Other Drivers			
Gulliver and Begg(139)	2007	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Nabi et al.(140)	2007	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Verschuur and Hurts(141)	2007	ECRI Institure Quality Scale VI – Surveys	Low
Schwebel et al.(110)	2007	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Kontogiannis(142)	2006	ECRI Institure Quality Scale VI – Surveys	Low
Blows et al.(143)	2005	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Malta et al.(144)	2005	ECRI Institure Quality Scale VI – Surveys	Low
Nabi et al.(145)	2005	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Turner and McClure(146)	2004	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low
Karlsson et al.(109)	2003	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Wells-Parker et al.(101)	2002	ECRI Institure Quality Scale VI – Surveys	Low
Fong et al.(147)	2001	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low
Bell et al.(148)	2000	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Moderate
Alparslan et al.(149)	1999	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low
Deery and Fildes(150)	1999	ECRI Institure Quality Scale VI – Surveys	Low
Parker et al.(91)	1995	Revised Newcastle-Ottawa Quality Assessment Scale – Cohort Studies	Low
Rajalin(151)	1994	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Moderate
Mayer and Treat(152)	1977	Revised Newcastle-Ottawa Quality Assessment Scale – Case-Control Studies	Low

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the 21 studies that compose the evidence base for Key Question 3 are presented in Table 37.

The information presented in this table demonstrates that currently available data that is directly generalizable to CMV drivers is extremely limited, with only three studies that included distinct populations of CMV drivers (Sumer, Sullman et al., and Lajunen et al.). The remainder of the studies included private motor vehicle license holders, an unknown number of whom may have held commercial licenses.

The generalizability of the remaining 18 studies to CMV drivers is unclear. Exposure to risk is lower among noncommercial vehicle drivers because their driving exposure is lower than that of CMV drivers. Women tend to be overrepresented in studies of general driver populations. In this case, the number of females included in the studies of private motor vehicle license holders ranged from 0% to 67%, meaning that males may be underrepresented in these studies compared to the CMV driver population. The ages of the private motor vehicle license holders included in these studies appear to be within the range of typical CMV drivers. It is unclear whether the ethnicity of the private motor vehicle license holders included in these studies is representative of CMV drivers, due to lack of reporting.

Table 37. Individuals with Personality Disorders and/or Related Traits Enrolled in Studies That Address Key Question 3

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age	% Male	Ethnicity (%)	Comorbidity	
Professional Drivers									
Sumer(134)	2003	295	67	Individuals contacted via professional training seminar, private transportation companies, or at taxi waiting stations	Mean: 35.74 (SD: 9.80)	100	NR	Substance use	Yes
Sullman et al.(137)	2002	Crashed in past 3 years: 143 Not crashed in past 3 years: 235	378	Respondents to questionnaire	Average: 40.4	99.2	NR	NR	Yes
Lajunen et al.(138)	2001	273	67	Respondents to questionnaire	Mean: 36.7 (SD: 9.5)	100	NR	NR	Yes
Other Drivers									
Gulliver and Begg(139)	2007	1,037	NR	Cohort group of individuals born at Dunedin hospital between 1 April 1972 and 31 March 1973	18–26	51	NR	NR	Unclear
Nabi et al.(140)	2007	13,447	NR	GAZEL cohort (workers and recent retirees of a French national utility company)	48–68	NR	NR	NR	Unclear
Verschuur and Hurts(141)	2007	743	NR	Individuals randomly selected from "a large panel" and controls matched from the mobility statistics of the Dutch Ministry of Transportation	Cases: 18–34: 30.9% 35–54: 44.1% >55: 25%	50.1	NR	NR	Unclear
					Controls: 18–34: 27.9% 35–54: 43.5% >55: 28.6%	53.7			
Schwebel et al.(110)	2007	101	NR	Recruited from a database of research volunteers in Alabama	Mean age: 80.02	53	NR	NR	Unclear
Kontogiannis(142)	2006	714	NR	Respondents to questionnaires sent to companies throughout Greece	>29: 20.1% 29–34: 22.3% 35–40: 19.6% 41–46: 18.6% >46: 19.4%	67.7	NR	NR	Unclear

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age	% Male	Ethnicity (%)	Comorbidity	
Blows et al.(143)	2005	21,893	NR	Members of the New Zealand Blood Donors Health Survey	Cases: 16–24: 45.7% 25–39: 26.4% 40+: 27.9% Controls: 16–24: 36.6% 25–39: 24% 40+: 39.4%	Cases: 43.5 Controls: 46.4	NR	NR	Unclear
Malta et al.(144)	2005	Aggressive: 44 Nonaggressive: 44	NR	Volunteers from introductory psychology course at university	Mean age: 19.2	54.5	Aggressive drivers Minority: 15.9 Nonminority: 84.0 Nonaggressive drivers Minority: 25 Nonminority: 75	NR	Unclear
Nabi et al.(145)	2005	11,754	NR	GAZEL cohort (workers and recent retirees of a French national utility company)	39–54	NR	NR	NR	Unclear
Turner and McClure(146)	2004	Cases: 107 Controls: 870	NR	Cases: recruited from hospitals in Brisbane Australia Controls: recruited from random selection of 30 post codes Brisbane region who answered questionnaire	Cases: 17–24: 23.6% 25–29: 36.8% 40–60: 31.1% >60: 8.5% Controls: 17–24: 1.2% 25–29: 33.2% 40–60: 50.4% >60: 15.2%	Cases: 71 Controls: 71	NR	NR	Unclear
Karlsson et al.(109)	2003	8122	NR	Conscripts for military service in Sweden	Approx: 20	100	NR	Substance use	Unclear
Wells-Parker et al.(101)	2002	1382	NR	Telephone survey participants	Mean: 53.12 (SD: 16.85)	57.6	White: 77.7 African-American: 12 Hispanic: 4.6 Asian: 2.2 Native American: 0.5 No designation: 2.75	NR	Unclear
Fong et al.(147)	2001	146	NR	Volunteers recruited from patients at general practitioner's clinic	Mean: 37 (Range: 18–71)	37	NR	NR	Unclear
Bell et al.(148)	2000	99,981	NR	US Army personnel who completed Health Risk Appraisal surveys	18–20: 12% 21–25: 31% 26–30: 20% 31–35: 15% 36–40: 13% >41: 9%	88	Caucasian: 63 Non-Caucasian: 37	NR	Unclear

Study	Year	n =	CMV Drivers	Patient Selection	Characteristics of **Individuals** in Study				Generalizability to Target Population
					Age	% Male	Ethnicity (%)	Comorbidity	
Alparslan et al.(149)	1999	Case: 98 Control: 88	NR	NR	Case: 37.5 (Mean, SD: 9.3 Control: 35.9 (Mean; SD: 10.6)	Case: 100 Control: 93.1	NR	NR	Unclear
Deery and Fildes(150)	1999	198	NR	Participants solicited from driver licensing offices	16–19	55	NR	Substance use	Unclear
Parker et al.(91)	1995	1,373	NR	Responded to survey questionnaire	Mean: 41.5	50.3	NR	NR	Unclear
Rajalin(151)	1994	Cases: 615 Controls: 776	NR	Drivers involved in fatal crashes Drivers selected from driving license holders	Range: <25–64	Cases: >90 Controls: NR	NR	NR	Unclear
Mayer and Treat(152)	1977	Cases: 30 Controls: 30	NR	Volunteers from course at university	NR	43 43	NR	NR	Unclear

CMV: Commercial motor vehicles
NR: Not reported
SD: Standard deviation

Findings

The included studies examined reduction in driver safety (i.e., crashes) related to selected traits (i.e., hostility, aggression, impulsivity, sensation seeking) associated with personality disorders. They used approximately 24 separate testing instruments, including the following:

- ADHD/ODD: Attention Deficit Hyperactivity Disorder/Oppositional Defiant Disorder
- SCID I and II: Structural Clinical Interview for DMS-III-R
- DSP: Driver Stress Profile
- ZSSS: Zuckerman Sensation Seeking Scale

Quantitative analysis could not be performed because the outcomes and independent variables being examined were widely divergent, as evidenced by the fact that no single testing instrument out of 24 was used for more than 29% of all studies. Table 38 provides a summary of the results of each study. Following the table are separate summaries of the findings for CMV drivers and private motor vehicle drivers.

Table 38. Results of Included Studies on Traits Associated with Personality Disorders and Crash

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Professional Drivers								
Sumer(134)	2003	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Risky/aggressive driving behavior based on responses to testing instruments: Risk taking Physical aggression Verbal aggression Aberrant driving behaviors (errors and violations) Overtaking Speeding Psychological symptoms (anxiety, depression, hostility, psychoticism)	Yes	Crash	Yes	Significant correlations with crash (r^2): Aberrant driving behaviors: 0.25 Psychological symptoms: 0.24 *Statistical methodology: Factor analysis and a partial correlation matrix*
Sullman et al.(137)	2002	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Risky/aggressive driving behavior based on responses to testing instruments: Risk taking Verbal aggression Aberrant driving behaviors (errors and violations) Overtaking Speeding	Yes	Crash	Yes	Individuals who had experienced a crash in the 3 years previous to the study tended to have higher scores in the violations factor. (Pearson 0.202, p <0.001) Violations factor included 2 speeding violations, 1 tailgating violation, 1 reckless driving violation (going through a red light at an intersection), and 1 aggressive violation (racing away at traffic light to beat the driver adjacent Prediction OR† for violations factor: 1.505 (for each unit of change in violations factor score the odds of being involved in a crash increase by 1.5) *Statistical methodology: factor analysis and multivariate logistic regression*
Lajunen et al.(138)	2001	Survey	Drivers involved in >1 crash vs. drivers involved in no crashes or a single crash	Crash risk based on responses to testing instruments: Psychological symptoms (anxiety, depression, hostility, paranoia, and psychoticism)	No	Crash	Yes	Anxiety was positively related to crash involvement (OR 2.06) Paranoid ideation was negatively related to crash involvement (OR 0.62) *Statistical methodology: Multivariate logistic regression*

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Other Drivers								
Gulliver and Begg(139)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving based on responses to testing instruments: Speeding Sensation seeking Crash risk based on responses to testing instruments: Traditionalism Harm avoidance Aggression Alienation Stress reaction	Yes	Crash	Yes	Involvement in crash: Aggression: OR 2.09 (95% CI: 1.28 – 3.4) Alienation: OR 1.74 (95% CI: 1.00 – 3.08) Univariate logistic regression identifying personality predictors of persistent risky driving for males (low group as reference group): Aggression (medium): OR 5.14 (95% CI: 1.14 – 23.16) Aggression (high): OR 10.93 (95% CI :2.48 – 48.11) Multivariate logistic regression identifying personality predictors of crash involvement: Aggression (medium): OR 1.59 (95% CI: 0.99 – 2.56) (p = 0.06) Aggression (high): OR 1.78 (95% CI: 1.04 – 3.02) (p = 0.03) *Statistical methodology: Multivariate and univariate analyses*
Nabi et al.(140)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving based on responses to testing instruments: Speeding Violation of traffic law	Yes	Crash	Yes	Associations of risky driving behaviors and crashes: Speeding in built up area (km/h) (unadjusted rate ratios) 65–75 km/h: 1.29 (95% CI: 0.92 – 1.82) ≥75 km/h: 1.52 (95% CI: 0.94 – 2.45) Speeding on rural roads (km/h) (unadjusted rate ratios) 95–100 km/h: 1.26 (95% CI: 0.91 – 1.75) 105–110 km/h: 1.29 (95% CI: 0.90 – 1.85) ≥110 km/h: 1.29 (95% CI: 0.82 – 2.03) Speeding on highways (km/h) (unadjusted rate ratios) ≥155 km/h: 1.55 (95% CI: 1.02 – 2.36) Violations of a traffic law deemed improper (excluding speeding) (unadjusted rate ratios) Sometimes: 1.30 (95% CI: 1.01 – 1.59) ($p \leq 0.05$) Regularly: 2.62 (95% CI: 1.24 – 5.56)($p \leq 0.01$) Associations between attitudinal risk factors and behavioral predictors of crash (RRs) (attitudinal factor scores categorized according to centiles): (Behavioral predictor of crash) Maximum speed 90 km/h on rural roads (Attitudinal factor)

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
								Enforcement 25th – 75th 1.35 (95% CI: 1.22 – 1.50) ($p \leq 0.001$) ≥75th 2.09 (95% CI: 1.83 – 2.39) ($p \leq 0.001$) Speed limitations 25th – 75th 1.27 (95% CI: 1.14 – 1.41) ($p \leq 0.001$) ≥75th 1.80 (95% CI: 1.58 – 2.05) ($p \leq 0.001$) *Statistical methodology: Poisson regression models and principal component analysis with varimax rotation*
Verschuur and Hurts(141)	2007	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving and crash risk based on responses to testing instruments: Strategic decisions Attitudes Subjective/personal norms Perceived behavior control Psychological precursors (i.e., inattention, stress, temporary depression) Physical precursors Violations Inattention errors Dangerous errors	No	Crash	Yes	Crash involvement predicted by driving under unsafety-enhancing conditions as measured by: (all r^2) Psychological precursors (0.13)* Violations (0.08)* Inattention errors (0.02)* Dangerous errors (-0.05) (*significant at $p = 0.05$) Driving under unsafe conditions is predicted by psychological precursors as measured by: Physical precursors (0.25)* Attitudes approving of traffic violations (-0.29)* Strategic decisions (fewer made before starting a trip) (-0.12)* Driving under unsafe conditions is predicted by violations as measured by: Psychological precursors (0.20)* Attitudes approving of traffic violations (-0.32)* Subjective and personal norms approving of traffic violations (0.18)* Perceived behavioral control (feeling in control of behaviors provoking violations)(-0.04)* Strategic decisions (fewer made before starting a trip)(-0.18)* Driving under unsafe conditions is predicted by dangerous driving as measured by: Psychological precursors (0.06)* Attitudes approving of traffic violations (-0.21)* Perceived behavioral control (feeling in control of behaviors provoking violations)(0.09)* Physical precursors (0.19)* *Statistical methodology: Multivariate logistic regression*

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Schwebel et al.(110)	2007	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving, reckless driving, and crash risk based on responses to testing instruments: DBQ errors DBQ violations DBQ lapses Sensation seeking (thrill and adventure seeking; experience seeking; disinhibition; boredom susceptibility) Temperament (high intensity pleasure; inhibitory control; activation control; attentional control)	Yes	Crash	No	The overall model predicting crashes was not statistically significant and no individual predictors of interest emerged. The model predicting risky driving was not statistically significant. The model predicting reckless driving was significant on the second step of the logistic regression (F (6,82)=2.25, p <0.05). Two variables were significant predictors (p <0.05) of reckless driving on the second step: Male gender: beta = -0.23 Lower temperamental control: beta = -0.23 *Statistical methodology: Correlation matrix and stepwise linear regression*
Kontogiannis(142)	2006	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving and crash risk based on responses to testing instruments: DBI: aggression DBI: alertness DBI: dislike of driving DBI: confidence Aberrant driving behavior: Violations Errors Social disregard Negligence Speeding	No	Crash	Yes	Violations (R^2 = 0.35) and aggression (R^2 = 0.02) predicted crash rates (R^2 = 0.34). Aggression predicted crash rates indirectly, through violations (R^2 = 0.90). Violations variance was explained by age (-0.028), gender (-0.024), experience (0.18), mileage 0.18), and aggression (0.90) Speeding was predicted by gender and annual mileage. Speeding convictions were predicted by aggression and negatively related to dislike of driving. *Statistical methodology: Principle components analysis with varimax rotation*
Blows et al.(143)	2005	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving and crash risk based on variables: Racing for excitement Driving ≥20 km/h over speed limit Seatbelt use Drunk driving Driving unlicensed Traffic convictions within past 12 months	No	Crash	No	Individuals who reported frequently engaging in risky driving behaviors over the past 12 months were between 2 and 4 times more likely to have been injured while driving during the same time period compared to individuals who reported infrequently or never engaging in these behaviors. Risk levels were different by driver age. Unadjusted prevalence ratios (PR) for associations between risky driving behaviors, history of convictions, and driver injury (PR, 95% CI): Racing Once or twice: 1.4, 1.1 – 1.9 Several times/always: 1.4, 0.8 – 2.6

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
								Driving ≥20 km/h over speed limit Once or twice: 1.3, 0.9 – 1.7 Several times: 1.9, 1.4 – 2.6 Always: 4.5, 2.8 – 7.5 Traffic convictions One: 2.4, 1.7 – 3.3 Two: 3.6, 2.1 – 6.1 Three or more: 5.3, 2.9 – 9.7 *Statistical methodology: Multivariate prevalence ratios*
Malta et al.(144)	2005	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Aggressive driving, psychiatric diagnoses, and behavioral problems measured by: DSP SCI-II ADHD/ODD Interview IED Interview Personal/familial psychiatric and anger/aggression history interview	No	Crash	Yes	Aggressive drivers ranked significantly higher (Mann-Whitney U test) than nonaggressive drivers in: Number of serious crashes Number of moving violations Number of nonmoving violations Aggressive drivers had a significantly greater prevalence of Cluster B personality disorders (antisocial, borderline) with trends (p = 0.055) for a greater prevalence of Cluster A (paranoid) and Cluster C (avoidant) personality disorders *Statistical methodology: Chi square tests; Fisher's exact tests, Mann-Whitney tests*
Nabi et al.(145)	2005	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Aggressive/hostile personality traits and crash measured by Buss-Durkee Hostility Interview (aggression and hostility): Driving behavior and road safety questionnaire Speeding Drunk driving Cell phone use during driving	Yes	Crash	Yes	Aggression and hostility traits did not predict crashes in this group. There was a weak but statistically significant association between high irritability, high negativism, and crash after controlling for major confounding variables including gender, age, occupational category, driving mileage per year, alcohol consumption, maximum speed >±10 km/h above legal limits, risky use of cell phone, vehicle category, and scores of negative attitudes toward traffic regulation. *Statistical methodology: Chi square tests; univariate and multivariate negative binomial models*
Turner and McClure(146)	2004	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving and crash risk based on variables: Aggression Sensation-seeking Risk acceptance	No	Crash	Yes	Certain host factors increase the risk of motor vehicle crash. High risk acceptance and crashes: OR 8.6 (95% CI: 3.9 – 23.9) High driver aggression: OR 2.1 (95% CI: 1.03 – 4.2) *Statistical methodology: Chi squares and multivariate logistic regression*

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Karlsson et al. (109)	2003	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving and crash risk based on variables: Risky driving behaviors combined: Speeding Passing violations Tailgating Lane-usage violations Right of way violations Illegal turns Control signal violations Emotional control Psychiatric diagnosis	No	Crash	Yes	Unadjusted rates for individuals convicted of risky driving: Risky driving and crash: RR 2.8 (95% CI: 1.3 – 5.9) Psychosis diagnosis and risky driving: RR 14.6 (95% CI: 9.2 – 23.1) Adjusted for father's social class, divorced parents, truancy, runaway from home, criminality, low emotional control, risky use of alcohol, illicit drug use, smoking >10 cigarettes a day, sniffing of solvents: Risky driving and crash: RR 2.4 (95% CI: 1.0 – 5.5) Psychosis and risky driving: RR 6.3 (95% CI: 2.4 – 16.5) *Statistical methodology: Chi square tests; bivariate and multivariate Poisson regression analysis*
Wells-Parker et al.(101)	2002	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving, aggression, and crash risk based on following variables: Road rage scale score Speeding Angry/threatening driving Verbal aggression Moving violations Confrontational behavior	No	Crash	Yes	Angry/threatening driving score above the mean were more likely to be involved in a serious crash: OR 1.51 (95% CI: 1.17 – 1.94) 18.9% of confrontational individuals experienced a crash in the year preceding the study vs. 9% of nonconfrontational individuals. Subdivided by angry/threatening driving scores: Nonconfrontational respondents who scored above the mean had slightly more crashes (27.7%) than respondents who scored below the mean (21%). 57% of confrontational respondents scoring above the mean had a crash sometime in their driving experience, with 22% having had a crash in the previous year. *Statistical methodology: ANOVA; Multiple regression analysis including logistic regression; t-tests*
Fong et al.(147)	2001	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving, aggression, and crash risk based on following variables: Psychological morbidity Aggression	No	Crash	Yes	Respondents were separated into 4 groups: perpetrators (individuals who performed road-rage action), victims (victims of road rage who were not also perpetrators), mixed (individuals reporting road rage incidents both as victim and perpetrator), and control. There was no significant difference between the groups for personality disorder sum scores. Perpetrators scored significantly higher (82.7) than all other groups for aggression (controls 62.4; victims 64.4; mixed 65.0, $p = 0.035$) Subscore analysis found a significant difference at the 5% level for anger ($p = 0.037$) and physical aggression ($p = 0.038$). Perpetrators scored higher on verbal aggression and hostility subscores, but these differences were nonsignificant. *Statistical methodology: NR.*

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Bell et al.(148)	2000	Cohort	Drivers involved in crashes vs. drivers not involved in crashes	Risky driving, and crash risk based on following variables: Speeding Age Ethnicity Drinking Seat belt use	Yes	Crash	No	Unadjusted Cox model predictors of crash (Hazard Ratio or HR): Speeding >11 miles over limit: 1.52 (p <0.005) Multivariate model predictors of crash (HR): Significant Age <21: 4.9 (95% CI: 2.6 – 9.3) Age 21–25: 3.3 (95% CI: 1.8 – 6.2) Ethnicity (HR): Non-Caucasian: 1.8 (95% CI: 1.5 – 2.2) Drinking (HR): 7–14 drinks: 1.5 (95% CI: 1.1 – 2.1) >21 drinks: 1.8 (95% CI: 1.1 – 2.9) Seat belt use (HR): 0–50% of the time: 1.4 (95% CI: 1.1 – 1.9) Speeding was nonsignificant in the full model with trends in a direction suggesting it may still be an important risk factor. *Statistical methodology: Chi square tests; t-tests; Kaplan-Meier estimates of survival; log-rank tests; Cox proportional hazards model; multivariate regression*
Alparslan et al.(149)	1999	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	Crash risk based on the following variables: Personality disorders Avoidant Dependent Obsessive-compulsive Passive-aggressive Self-defeating Paranoid Schizotypal Schizoid Histrionic Narcissistic Borderline Antisocial	No	Crash	Yes	Findings suggest that drivers involved in a crash display asocial behaviors, difficulty in impulse control, alertness, and aggressive behaviors. The crash group had significantly higher scores in the following personality disorders compared to the control group (t values): Dependent (2.05, p <0.05) Passive-aggressive (2.11, p <0.05) Schizotypal (2.73, p <0.01) Histrionic (2.03, p <0.05) Borderline (2.51, p <0.05) Antisocial (2.09, p <0.05) *Statistical methodology: Chi square tests and t-tests*

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
Deery and Fildes(150)	1999	Survey	Drivers involved in crashes vs. drivers not involved in crashes	Crash risk based on the following variables: Assaultiveness Indirect hostility Verbal hostility Irritability Resentment Assertiveness Depression Emotional adjustment Locus of control Sensation seeking Competitive speed Aggression Perceived responsibility for crashes Driving inhibition	No	Crash	Yes	Individuals were separated into 5 different "clusters" or behavioral subtypes according to variable scores. Cluster 2 individuals (inhibited while driving, external locus of control, depressed, irritable, hostile, resentful) were more likely to experience a crash than individuals in the other clusters, with the exception of Cluster 5. Cluster 5 individuals (highest risk, with high levels of driving-related aggression, competitive speeding, driving to reduce tension, sensation seeking, and verbal hostility; depressed, resentful, irritable, hostile [indirect], and emotionally maladjusted) were more likely to experience a crash compared with other cluster individuals, except Cluster 2, in which there was no statistically significant difference between the two clusters. *Statistical methodology: Ward's cluster analysis with CCC output; Cluster analysis*
Parker et al.(91)	1995	Cohort	Drivers involved in crashes with violations vs. drivers involved in crashes with errors	Crash risk based on the following variables: Study 1 DBQ errors DBQ lapses DBQ violations Study 2 Speed	Yes	Crash	Yes	Study 1 DBQ violations were significantly correlated to (Rate Ratio, RR): Active crashes: 1.25 (p <0.001) Active loss-of-control crashes: 2.11 (p <0.01) Study 2 Speed was not correlated with any particular crash type after adjusting for demographic variables and decision-making thoroughness. *Statistical methodology: Multivariate logistic regression*
Rajalin(151)	1994	Case-control	Drivers involved in fatal crashes vs. drivers not involved in crashes	Risky driving and crash based on the following variables: Speeding Behavior offense Invalid license Alcohol use	Yes	Crash	No	Fatal crash drivers had more traffic offenses overall than controls (percentage): Traffic offenses — Fatal — Controls 0 — 52.1 — 73.7 1 — 24.9 — 17.7 2 — 11.4 — 5.7 3 — 5.4 — 2.3 4 or more — 6.2 — 0.6 x^2 = 66.71, df = 4, p <0.001 Running off the road crashes, intersection crashes, and head-on collisions made up 70% of all fatal crashes. • Running off the road crashes are frequently caused by excessive speed, loss of control, or driver error.

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
								• Intersection crashes are usually caused by attention or judgment errors. • Head-on collisions are frequently caused by bad weather and road surface conditions. In this population, drivers who ran off the road had committed the highest number of traffic offenses, or 1.91 times as many offenses as drivers involved in intersection crashes and 1.80 times as many offenses as drivers involved in head-on collisions. Individuals involved in fatal crashes were significantly more likely to commit all types of offenses compared to controls: Speeding: 1.84 (95% CI: 148 – 2.29) Driving behavior offenses: 3.72 (95% CI: 2.24 – 6.54) Driving without a license: 5.71 (95% CI: 2.86 – 12.99) Drunken driving: 2.20 (95% CI: 2.20 – 1.36) Total number of traffic offenses: 2.48 (95% CI: 2.11 – 2.92) *Statistical methodology: Log-linear modeling*
Perneger and Smith	1991	Case-control	Drivers involved in fatal two car crashes vs. drivers not involved in fatal 2-car crashes	Risky driving and crash based on the following variables: Substance use Invalid license (proxy for risky driving) No seatbelt use (proxy for risky driving behavior) Crash in the previous 12 months before the study	Yes	Crash	No	Fatal crashes were associated with the following (OR): No seat belt use: 2.31 (95% CI: 2.08 – 2.56) Prior crash within previous 12 months: 1.41 (95 % CI: 1.29 – 1.54) Invalid license: 3.02 (95% CI: 2.62 – 3.49) Substance use: 10.96 (95% CI: 9.45 – 12.72) Fatal crashes were not associated with: Speeding *Statistical methodology: Paired case-control analysis; conditional multiple logistic regression models*
Mayer and Treat(152)	1977	Case-control	Drivers involved in crashes vs. drivers not involved in crashes	Crash risk based on the following variables: Personal maladjustment Social maladjustment Impulsivity, including: Belligerence Risk-taking attitudes Unsafe attitudes Pro-competition attitudes Pro-speed attitudes	No	Crash	Yes	Seven tests discriminated best between the crash and no-crash groups: Citizenship Antisocial tendencies General psychopathology Number Comparison Negativism External control School socialization

Reference	Year	Study Design	Comparison	Driving/Behavior Measured*	Driving Exposure Controlled For?	Primary Outcome	Outcome Self-reported	Results
								The crash group scored higher (p <0.05) in the areas of: General psychopathology Negativism Antisocial tendencies Juvenile delinquency Impulsivity Risk taking *Statistical methodology: Not reported*

ADHD/ODD: Attention Deficit Hyperactivity Disorder/Oppositional Defiant Disorder
ANOVA: Analysis of variance
CI: Confidence interval
DBI: Driver Behavior Inventory
DBQ: Driver Behavior Questionnaire
IED: Intermittent Explosive Disorder
km/h: Kilometers per hour
OR: Odds ratio
RR: Risk ratio
SCI: Structural Clinical Interview

Professional Drivers

Summary

Our searches identified three direct risk crash studies with a total of 512 individuals who were commercial vehicle operators. It is unclear how similar the drivers in these studies are to CMV drivers because few characteristics of the drivers were reported; what can be ascertained is that there appears to be a comparable population of male drivers and that the age groups may also be comparable. The outcome of interest (crash) was self-reported; for this and other reasons, the quality assessments of all three studies was low.

Overall, the findings of the studies suggest that traits such as aggression, hostility, and impulsivity (distal determinants) influence driver behavior (proximal determinants) in such a way that driver safety practices may be reduced and the risk of a crash increased. The findings of the three studies included in the evidence base could not be combined in a meta-analysis due to a number of factors, including the use of a number of testing instruments that measured the same factors and the lack of a consistent definition of most of the factors. Two studies (Sumer and Sullman et al.) found that crash was related to higher violation scores, including aggressive violations. The authors noted that the crash risk model created for CMV drivers differed from the crash risk model for private drivers and suggested that investigations into CMV driver behavior should consider them a special and unique population. The third study (Lajunen et al.) found that crash was related to distinctive psychological symptoms, including anxiety (increased risk) and paranoid ideation (decreased risk).

Nonprofessional Drivers

Summary

Our searches identified 18 direct risk crash studies with a total of 164,027 individuals. It is unclear how similar the drivers in these studies are to CMV drivers because few characteristics of the drivers were reported. What can be ascertained is that there appears to be a higher percentage of female drivers (ranges 0% to 67%) compared to the CMV driver population and that the age groups in the study populations (range 18 to >60 years of age) would encompass individuals of similar age to those in the CMV driver population. None of these individuals were specifically identified as CMV drivers. The outcome of interest (crash) was self-reported in the majority of studies. For this and other reasons the quality assessments of 12 of the studies was low; the quality assessment of the six remaining studies was moderate.

Overall, the findings of the studies suggest that traits such as aggression, hostility, and impulsivity (distal determinants), and personality disorders (i.e., schizotypal, histrionic, borderline, antisocial, dependent, and passive-aggressive) influence driver behavior (proximal determinants) in such a way that driver safety practices may be reduced and the risk of a crash increased. The findings of the 18 studies included in the evidence base could not be combined in a meta-analysis for the same reasons cited in the summary of professional driver studies. Since many studies investigated the influence of multiple factors, studies will be counted in more than one category in this section.

Ten studies (Nabi et al. 2007, Schwebel et al., Blows et al., Turner and McClure, Bell et al., Karlsson et al., Deery and Fildes, Rajalin, Perneger and Smith, and Mayer and Treat) found that crash was related to risky driving, including behaviors such as speeding, sensation seeking, not using a seat belt while in a motor

vehicle, racing/competitive driving, and driving without an authorized license. Risky driving behaviors were related to negative attitudes about traffic safety and/or attitudes approving of the violation of traffic regulations, high risk acceptance, negative attitudes toward enforcement of traffic regulations, and temperamental control. Four studies noted that crash was directly related to violations, specifically violations related to aggression and risky driving behaviors (Verschuur and Hurts, Kontogiannis, Parker et al., and Rajalin). Nine studies noted that aggression (as a distal determinant) was related to an increase in crash risk (Gulliver and Begg, Kontogiannis, Malta et al., Turner and McClure, Wells-Parker et al., Fong et al., Alparslan et al., Deery and Fildes, and Mayer and Treat); one study noted that aggressive drivers were more likely to have a Cluster B personality disorder (antisocial, borderline, narcissistic, or histrionic) than nonaggressive drivers (Verschuur and Hurts); another study found that aggressive individuals had a higher lifetime prevalence rate for oppositional defiant disorder, attention-deficit hyperactivity disorder, intermittent explosive disorder and Cluster A and C personality disorders (Malta et al.). A different study, which found that aggression was related to crash, suggested that a tendency toward being angry and/or hostile may interact with current road situations to raise the risk of crash rather than the *a priori* assumption that aggression/hostility is directly related to crash. The last study found that crash risk was increased in relation to personality disorders including schizotypal (Cluster A), histrionic, borderline, and antisocial (Cluster B), and dependent (Cluster C) (Alparslan et al.). The last personality disorder listed by the authors, passive-aggressive, is no longer recognized in the DSM as a personality disorder.

Section Summary

- **The evidence suggests that individuals with traits associated with personality disorders are at an increased risk for a motor vehicle crash compared with comparable drivers who do not have traits associated with personality disorders. These traits include aggression, hostility, impulsivity, disregard for law (i.e., attitude toward traffic law violations), and various psychological symptoms. However, inconsistencies in the methodologies of the included studies preclude us from drawing an evidence-based conclusion pertaining to the strength of the relationship between traits associated with personality disorders and crash risk at this time.**

Our searches identified 21 direct crash risk studies with a total study population of 164,539 individuals, 512 of whom were CMV drivers. The quality assessment of 14 of the included studies was low; the quality assessment of the remaining 7 studies was moderate. Methodological limitations of these studies include the lack of uniformity in the definition of the traits, behaviors, and outcomes and the use of scales that may not have been age or gender appropriate. Since most of the studies did not include CMV drivers, the generalizability of the findings to the CMV driver population is unclear.

Because the studies used a number of different scales and methodologies to measure the traits and behaviors and the outcome measures could not be assumed to be uniform, we were precluded from combining them for quantitative analysis. Instead, we have provided a qualitative summary of the findings.

Overall, the studies suggest that traits such as aggression, hostility, impulsivity, disregard for laws (i.e., attitude toward traffic law violations), and various psychological symptoms are associated with an increase in crash risk. The same can be said of behaviors such as risky driving and violation of traffic laws. In turn, behaviors such as risky driving are associated with aggression, impulsivity, and psychological symptoms such as anxiety, depression, and psychosis. Violation of traffic laws is associated with risky driving and aggression. Table 39 provides a quick summary of the associations between factors and outcomes.

Table 39. Association between Factors and Outcomes for Key Question 3

	Aggression	Hostility	Impulsivity	Attitude toward traffic law violations	Psychological symptoms*	Behaviors	
						Risky driving	Violations of traffic laws
Crash	●	●	●	●	●	●	●
Risky driving	●	NA	●	●	●	—	●
Violations of traffic laws	●	NA	NA	NA	NA	●	—
Aggression	—	NA	NA	NA	●	●	●

● Factor has a negative impact on this outcome such that crash risk is increased.

*Psychological symptoms include anxiety, paranoid ideation, depression, psychosis, personality disorder, irritability, negativism, and antisocial tendencies.

NA: Not applicable. (This factor was not examined in relationship to the outcome of interest.).

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Appendix A: Search Summaries

Search Summary for Key Questions 1 through 3

The search strategies employed combinations of free text keywords as well as controlled vocabulary terms including the following concepts: accidents, mental disorders, mental disease, driving, and motor vehicle operation. The strategy below is presented in OVID syntax; the search was simultaneously conducted across EMBASE, MEDLINE, and PsycINFO. A parallel strategy was used to search the databases which the Cochrane Library comprises.

Psychiatric Disorders

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

Medical Subject Headings (MeSH), EMTREE, PsycINFO, and Keywords

Conventions:

OVID

$	=	truncation character (wildcard)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	Publication Type
[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	Text word

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Direct crash risk	Accident Accident prevention Accidents Accidents, occupational Accidents, traffic Highway safety Motor traffic accidents Occupational health Occupational safety Safety Traffic accident Traffic safety Transportation accidents	Accident$ Citation$ Collision$ Crash$ Ticket$ Wreck$
Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$
Unspecified mental disorders	Mental disease Mental disorders *Note: These terms were not exploded intentionally.*	

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement	# Identified	# Downloaded
1	Unspecified mental disorders	(Mental disorders or mental disease).de.		
2	Limit by population	1 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)		
3		2 and adult		
4		2 not 3		
5		1 not 4		
6	Limit by publication type	5 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)		
7	Accidents	6 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.		
8		6 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)		
9	Driving	6 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.		
10		6 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or motor$ or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.		
11		6 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.		
12	Combine sets	or/7-11	1,687	
13	Eliminate overlap	Remove duplicates from 12	1,529	
14	Limit by study type	13and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Followup studies/ or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham or mask)).mp. or latin square.mp. or (time adj series) or (case adj (study or studies) or ISRCTN$.mp. or ACTRN$.mp. or (NCT$ not nctc$)))	588	
		15 not 16	941	
		17 and (driving.ti. or driv$.hw.)	106	
				87

Total Identified	Total Downloaded	Total Retrieved	Total Included
71	**0**	**See Table at end of section.**	**See Table at end of section.**

Mood Disorders

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

Medical Subject Headings (MeSH), EMTREE, PsycINFO, and Keywords

Conventions:

OVID

$	=	truncation character (wildcard)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	Publication Type
[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	Text word

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Direct crash risk	Accident Accident prevention Accidents Accidents, occupational Accidents, traffic Highway safety Motor traffic accidents Occupational health Occupational safety Safety Traffic accident Traffic safety Transportation accidents	Accident$ Citation$ Collision$ Crash$ Ticket$ Wreck$
Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Mood disorders	Exp affective disorders/ Exp mania/ Exp mood disorder/ Exp mood disorders/	Affective disorder$ Bipolar BP BPD Cyclothymic Depressed Depression Depressive Dysthym$ Hypoman$ Mania Manic$ Melancholl$ Premenstrual dysphoric PMDD Mood disorder$ SAD.ti. Seasonal affective
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement
1	Mood disorders	Exp mood disorder/ or exp mood disorders/ or exp affective disorders/ or exp mania or ((mood or affective) adj disorder$)
2		Bipolar or bp or bpd or cyclothymic or depressed or depression or depressive or dysthym$ or hypoman$ or mania or manic$ or melancholl$ or premenstrual dysphoric or PMDD or seasonal affective or SAD.ti.
3	Combine sets	or/1-2
4	Limit by population	3 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)
5		4 and adult
6		4 not 5
7		4 not 6
8	Limit by publication type	7 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
9	Accidents	8 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.
10		8 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)
11	Driving	8 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.
12		8 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or motor$ or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.
13		8 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.
14	Combine sets	or/ 9-13
15	Limit by study type	14 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Followup studies/ or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham or mask)).mp. or latin square.mp. or (time adj series) or (case adj (study or studies) or ISRCTN$.mp. or ACTRN$.mp. or (NCT$ not nctc$)))
16		14 and (driving.ti. or driv$.hw.)
17	Combine sets	or/15-16
18	Eliminate overlap	Remove duplicates from 17

Total Identified	Total Downloaded	Total Retrieved	Total Included
2,587	**160**	**See Table at end of section.**	**See Table at end of section.**

Anxiety Disorders

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

Medical Subject Headings (MeSH), EMTREE, PsycINFO, and Keywords

Conventions:

OVID

$	=	truncation character (wildcard)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	Publication Type
[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	Text word

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Anxiety	Exp anxiety disorder/ Exp anxiety disorders/	Agoraphob$ GAD Generalized anxiety disorder$ Obsessive compulsive OCD Panic Phobia Phobic Post-traumatic PTSD Separation anxiety
Direct crash risk	Accident Accident prevention Accidents Accidents, occupational Accidents, traffic Highway safety Motor traffic accidents Occupational health Occupational safety Safety Traffic accident Traffic safety Transportation accidents	Accident$ Citation$ Collision$ Crash$ Ticket$ Wreck$
Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement
1	Anxiety disorders	(exp anxiety disorders or exp anxiety disorder)
2		(Agoraphob$ or (((obsessive adj compulsive) or panic or phobic or stress or generalized anxiety) adj2 disorder$))
3		((cardiac or separation or castration or death or generalized) adj anxiet$)
4		(OCD or GAD or PTSD or panic or post-traumatic or phobia$ or phobic).ti,ab.
5	Combine sets	or/1-4
6	Limit by population	5 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)
7		6 and adult
8		6 not 7
9		5 not 8
10	Limit by publication type	9 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
11	Accidents	10 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.
12		10 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)
13	Driving	10 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.
14		10 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or motor$ or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.
15		10 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.
16	Combine sets	or/ 11-15
17	Eliminate overlap	Remove duplicates from 16
18	Limit by study type	17 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Followup studies/ or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham or mask)).mp. or latin square.mp. or (time adj series) or (case adj (study or studies) or ISRCTN$.mp. or ACTRN$.mp. or (NCT$ not nctc$)))
19		17 not 18
20		19 and (driving.ti. or driv$.hw.)

Total Identified	Total Downloaded	Total Retrieved	Total Included
1,121	67	See Table at end of section.	See Table at end of section.

Psychotic Disorders

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

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.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	Publication Type
[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	Text word

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Direct crash risk	Accident Accident prevention Accidents Accidents, occupational Accidents, traffic Highway safety Motor traffic accidents Occupational health Occupational safety Safety Traffic accident Traffic safety Transportation accidents	Accident$ Citation$ Collision$ Crash$ Ticket$ Wreck$
Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$
Psychosis	Exp psychosis/ Exp schizophrenia and disorders with psychotic features/	Delusion$ Hallucin$ Psychos?s Psychotic Schizophren$

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement
1	Psychotic disorders	(Exp schizophrenia and disorders with psychotic features/ or exp psychosis/)
2		Psychos?s or Psychotic or Schizophren$
3	Combine sets	1 or 2
4	Limit by population	3 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)
5		4 and adult
6		4 not 5
7		3 not 6
8	Limit by publication type	7 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
9	Accidents	8 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.
10		8 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)
11	Driving	8 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.
12		8 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or motor$ or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.
13		8 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.
14	Combine sets	or/ 9-13 remove duplicates
15	Limit by study type	14 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Followup studies/ or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham or mask)).mp. or latin square.mp. or (time adj series) or (case adj (study or studies) or ISRCTN$.mp. or ACTRN$.mp. or (NCT$ not nctc$)))

Total Identified	Total Downloaded	Total Retrieved	Total Included
2,730	**263**	**See Table at end of section.**	**See Table at end of section.**

Total for all categories of psychiatric disorder included in Key Question 1

Total Identified	Total Downloaded	Total Retrieved	Total Included
10,217	**263**	**130**	**9**

Personality Disorders

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

Medical Subject Headings (MeSH), EMTREE, PsycINFO, and Keywords

Conventions:

OVID

$	=	truncation character (wildcard)
exp	=	"explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)
.de.	=	limit controlled vocabulary heading
.fs.	=	floating subheading
.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
.ti.	=	limit to title
.tw.	=	limit to title and abstract fields

PubMed

[mh]	=	MeSH heading
[majr]	=	MeSH heading designated as major topic
[pt]	=	Publication Type
[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
[sh]	=	MeSH subheading (qualifiers used in conjunction with MeSH headings)
[tiab]	=	keyword in title or abstract
[tw]	=	Text word

Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords
Direct crash risk	Accident Accident prevention Accidents Accidents, occupational Accidents, traffic Highway safety Motor traffic accidents Occupational health Occupational safety Safety Traffic accident Traffic safety Transportation accidents	Accident$ Citation$ Collision$ Crash$ Ticket$ Wreck$
Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$
Personality disorders	Antisocial personality disorder Borderline personality Borderline state Paranoid personality disorder Personality disorder Personality disorders *Note: The personality disorder and personality disorder terms were intentionally not exploded.*	Aggressive personality Antisocial personality Borderline personality Paranoid personality

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement
1	Personality disorders	(Personality disorder$ or antisocial personality disorder or Borderline personality disorder or Paranoid personality disorder or Borderline state).de.
2		(antisocial or borderline or paranoid or aggressive) adj3 personality
3	Combine sets	or/1-2
4	Limit by population	3 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)
5		4 and adult
6		4 not 5
7		4 not 6
8	Limit by publication type	7 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)
9	Accidents	8 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.
10		8 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)
11	Driving	8 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.
12		8 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or motor$ or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.
13		8 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.

Total Identified	Total Downloaded	Total Retrieved	Total Included
261	52	96	5

Psychotropic Medications

Electronic Database Searches

The following databases have been searched for relevant information.

Name	Date Limits	Platform/Provider
CINAHL (Cumulative Index to Nursing and Allied Health Literature)	1982 through January 28, 2008	OVID
The Cochrane Central Register of Controlled Trials (CENTRAL)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	through 2008, Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	through 2008, Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through January 28, 2008	OVID
Health Technology Assessment (HTA) Database	through 2008, Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through September 12, 2007	OVID
PreMEDLINE	Searched January 28, 2008	OVID
PsycINFO	through January 28, 2008	OVID
Transportation Research Information Service (TRIS)	Searched December 13, 2007	http://ntlsearch.bts.gov/tris/index.do
U.K. National Health Service Economic Evaluation Database (NHS EED)	through 2008, Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched December 13, 2007	http://www.ngc.gov

Medical Subject Headings (MeSH), EMTREE, PsycINFO, and Keywords

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.hw.	=	limit to heading word
.md.	=	type of methodology (PsycINFO)
.mp.	=	combined search fields (default if no fields are specified)
.pt.	=	publication Type
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PubMed

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[majr]	=	MeSH heading designated as major topic
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[sb]	=	Subset of PubMed database (PreMEDLINE, Systematic, OldMEDLINE)
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Topic-specific Search Terms

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Driving	Automobile driver examination Automobile driving Car driving Driv$.hw. Driver license Driving ability Driving behavior Drivers	Driver$ Driving[ti] Drive Highway Licens$
Motor vehicles	Automobiles Motor vehicle Motor vehicles	Bus Buses Car Cars Haul Long distance Lorry Lorries Motor$ Semi-trailer$ Truck$1 Vehicle$

CINAHL/EMBASE/MEDLINE/PsycINFO

English language, human

Set Number	Concept	Search Statement
1	Drug therapy	Exp *mental disorder/dt or exp *mental disorders/dt
2	Anticonvulsants & mood stabilizers	Exp antimanic agents/ or mood stabilizer.de.
3	Carbamazepine	Amizepin or Amizepine or Atretol or Biston or Calepsin or Carbamazepin or Carbamazepine or Carbategral or Carbatrol or Convuline or Epimax or Epitol or Equetro or Finlepsin or Lexin or Mazepine or Neurotol or Neurotop or Servimazepin or Sirtal or Tegral or Tegretal or Tegretol or Tegrital or Telesmin or Teril or Timonil
4	Lamotrigine	lamotrigine or lamictal or lamiktal or labileno or crisomet
5	Levetiracetam	etiracetam or etirazetam or keppra or levetiracetam
6	Lithium	Lithium or Camcolit or Candamide or Carbolith or Carbolitium or Cibalith or Contemnol or dilithium or Eskalith or Hypnorex or Limas or Linthane or Liskonium or Liskonum or Litarex or Lithane or Lithiumcarbonate or Lithobid or Lithocarb or Lithonate or Lithotabs or Maniprex or Mesin or Micalith or Neurolepsin or Plenur or Priadel or Quilonorm or Teralithe or Theralite or Theralithe
7	Oxcarbazepine	apydan or oxcarbazepine or oxocarbazepine or timox or trileptal
8	Topiramate	epitomax or topamax or topimax
9	Valproic acid	Apilepsin or Convulex or Depacon or Depakene or Depakin or Depakine or Deprakine or Dipropylacetate or Dipropylacetatic Acid or Diprosin or Epilim or Ergenyl or Everiden or Goilim or Labazene or Leptilan or Leptilanil or Mylproin or Myproic Acid or Orfiril or Orlept or Propymal or Valerin or Valparin or Valpro or Valproate or Valproic Acid or Vupral
10	MAOI inhibitors	exp monoamine oxidase inhibitors/ or monoamine oxidase inhibitor$ or MAO inhibitor$ or MAOI$ or RIMA
11		brofaromine OR isocarboxazide OR tranylcipromine OR moclobemide OR aurorix OR moclobamide OR phenelzine OR fenelzin OR nardil OR phenethylhydrazine
12	2nd generation antidepressants	exp antidepressive agents, second generation/ or exp serotonin uptake inhibitor/ or selective serotonin reuptake inhibitors or SSRI$ or norepinepherine reuptake inhibitor$
13		citalopram OR cytalopram OR escitalopram OR fluoxetine OR fluoxetin OR prozac OR sarafem OR fluvoxamine OR luvox OR paroxetine OR paxil OR seroxat OR sertraline OR Zoloft OR tetracyclic$ OR mianserin OR lerivon OR tolvon OR mirtazapine OR remeron OR zispin OR norset OR rexer OR trazodone OR molipaxin OR tradozone OR trittico OR bupropion OR amfebutamone OR quomen OR wellbutrin OR zyban OR zyntabac OR venlafaxine OR effexor OR efexor OR trevilor OR vandral OR dobupal
14		duloxetine OR cymbalta
15	Tricyclic antidepressants	exp Antidepressive agents, tricyclic/ or exp tricyclic antidepressant agent/ or (Tricyclic adj antidepressant$)
16		Amitriptyline OR amineurin OR amitrip OR amitrol OR anapsique OR "apo-amitriptyline" OR damilon OR domical OR elavil OR endep OR laroxyl OR lentizol OR novoprotect OR saroten OR sarotex OR syneudon OR triptafen OR tryptanol OR tryptine OR tryptizol OR clomipramine OR anafranil OR hydipen OR desipramine OR desmethylimipramine OR demethylimipramine OR pertofrane OR imipramine OR imidobenzyl OR imizin OR janimine OR melipramine OR norchlorimipramine OR pryleugan OR tofranil OR nortryptiline
17	Anti-anxiety & tranquilizers	Exp antianxiety agents/ or exp tranquilizer/ or exp tranquilizing drugs/ or (Anxiolytic or antipanic or serenic agent or tranquilizer$).ti,ab.

Set Number	Concept	Search Statement
18		Abecarnil or adatanserin or adinazolam or alnespirone or alpidem or Alprazolam or benactyzine or bentazepam or benzoctamine or bretazenil or bromazepam or busipirone or camazepam or cartazolate or chlordiazepoxide or chlormezanone or clobazam or clonazepam or clorazepate or clotiazepam or delorazepam or demoxepam or deramciclane or diazepam or doxepin or eglumetad or eltoprazine or emapunil or enciprazine or estazolam or etazolate or etizolam or fludiazepam or flunitrazepam or fluprazine or flurazepam or flutoprazepam or fluvoxamine or gepirone or geriforte or gidazepam or girisopam or halazepam or homofenazine or hydroxyzine or imidazenil or indorenate or ipspirone or isamoltane of kawain or ketazolam or lesopitron or limbitrol or loflazepate or lorazepam or mafoprazine or mebicar or medazepam or menrium or meprobamate or metaclazepam or mexazolam or midazolam or nabilone or nerisopam or niaprazine or nitrazepam or nitrazepine or norchlordiazepoxide or nordazepam or ocinaplon or ondansetrn or osemozotan or oxazafone or oxazepam or oxazolam or oxprenolol or pagoclone or panadiplon or pazinaclone or phenaglycodol or phenazepam or pinazepam or pipequaline or pivagabine or prazepam or propranolol or pritanserin or psyton or ricasetron or sunepitron or suriclone or talaglumetad or tandospirone or teflutixol or telazol or temazepam or tetrabenazine or tetrazepam or tracazolate or trancypromine or trazodone or triazolam or trimetozine or tuclazepam or umespirone or uxepam or zaleplon or zolazepam or zalospirone
19	Neuroleptics	Exp antipsychotic agents/ or exp neuroleptic agent/ or Neuroleptic or atypical antipsychotic$
20		Aceperone or acepromazine or aceprometazine or acetophenazine or alimemazine or azaperone or benperidol or blonaserin or brofoxine or bromospiperone or bromoperidol or butaclamol or butaperazine or carfenazine or carpipramine or centbutindole or chlorphenethazine or chlorpromazine or chlorprothixene or cinuperone or clocapramine or cloflumide or clofluperol or clopenthixol or clopipazan or clospipramine or clotiapine or clozapine or dimetotiazine or dixyrazine or dolestron or doperidol or droperidol or duperone or etazolate or etymemazine or farampator or fluanisone or flupenthixol or flupentixol or fluphenazine or fluspirilene or flutroline or gevetroline or haloperidol or isofloxythepin or isomolpan or lenperone or levomepromazine or loxapine or maroxepine or mazapertine or mepiprazole or mesoridazine or methiothepin or methopromazine or methotrimeprazine or metofenazate or molindone or neboglamine or noctran or norchlorpromazine or ondansetron or oxiperomide or oxypertine or oxyprothepine or pecazine penfluridol or perazine or periciazine or perphenazine or picobenzide or pimozide or piflutixol or pimethixene or pimozide or pipamperone or piperacetazine or pipotiazine or pirenperone or prochlorperazine or profenamine or promazine or prothipendyl or raclopride or remoxipride or reserpine or rimcazole or ritanserin or savoxepine or setoperone or spiperone or sulforidazine or sulpiride or tefludazine or tepirindole or thiopropazate or thioproperazine or thioridazine or thiothixene or tiapride or timiperone or tiotixene or tranylcypromine or triethylperazine or trifluoperazine or trifluperidol or trifulpromazine or umespirone or zetidoline or zoloperone or zuclopenthixol
21		Abilify or geodon or invega or risperdal or seroquel or zyprexa
22		Abaperidone or alentamol or amisulpride or amperozide or aripiprazole or asenapine or batelapine or bifeprunox or clozapine or emonapride or flumezapine or fluperlapine or iloperidone or lurasdione or melperone or norclozapine or ocaperidone or olanzapine or paliperidone or panamesine or pentiapine or perlapine or perospirone or quetiapine or remoxipride or rilapine or risperidone or sertindole or sulpiride or sultopride or tenilapine or tiapride or tiospirone or ziprasidone or zotepine
23	Combine sets	or/1-22 limit to english & human
24	Limit by population	23 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)
25		24 and adult
26		24 not 25
27		23 not 26
28	Limit by publication type	27 not ((letter or editorial or news or comment or case reports or note or conference paper).de. or (letter or editorial or news or comment or case reports).pt.)

Set Number	Concept	Search Statement
29	Accidents	28 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.
30		28 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)
31	Driving	28 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.
32		28 and (driver$ or driving$ or drive or licens$ or highway$ or car or cars or vehicle$ or semi-trailer$ or bus or buses or truck$1 or lorry or lorries or haul or (long adj distance)).ti.
33		28 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.
34		28 and simulator$
35	Combine sets	or/ 29-34
36	Limit by study type	35 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Followup studies/ or random$.hw. or random$.ti. or placebo$.mp. or ((singl$ or doubl$ or tripl$ or trebl$) and (dummy or blind or sham or mask)).mp. or latin square.mp. or (time adj series) or (case adj (study or studies) or ISRCTN$.mp. or ACTRN$.mp. or (NCT$ not nctc$)))
37		35 and (driving.ti. or driv$.hw.)
38	Combine sets	or/36-37

Total Identified	Total Downloaded	Total Retrieved	Total Included
1,950	**211**	**33**	**21**

Appendix B: Retrieval Criteria

Appendix B will list the retrieval criteria for each key question. An example of a small set of retrieval criteria is presented below.

Retrieval Criteria for Key Question 1

- Article must have been published in the English language.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash directly (risk for a fatal or nonfatal crash) associated with psychiatric disorders (specifically, psychotic disorder, mood disorder, anxiety disorder, or personality disorder).
- Article must describe a study that includes a comparison group comprising comparable subjects who do not have a psychiatric disorder.

Retrieval Criteria for Key Question 2

- Article must have been published in the English language.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash associated with pharmacotherapy for a psychiatric disorder (specifically, psychotic disorder, mood disorder, anxiety disorder, or personality disorder). If no such studies are available, studies that evaluated the risk for motor vehicle crash associated with psychotherapeutic agents in a general driver population will be included.
- Article must describe a study that includes a comparison group comprising comparable subjects who either do not have a psychiatric disorder or are not using psychotherapeutic agents.

Retrieval Criteria for Key Question 3

- Article must have been published in the English language.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash directly (risk for a fatal or nonfatal crash) associated with traits that are associated with personality disorders
- Article must describe a study that includes a comparison group comprising comparable subjects who do not have traits associated with a personality disorder.

Appendix C: Inclusion Criteria

Appendix C will lists the inclusion criteria for each of the three key questions addressed in this evidence report.

Inclusion Criteria for Key Question 1

- Article must have been published in the English language. Moher et al.(153) have demonstrated that exclusion of non-English language studies from meta-analyses has little impact on the conclusions drawn. Juni et al.(154) found that non-English studies typically were of lower methodological quality and that excluding them had little effect on effect-size estimates in the majority of meta-analyses they examined. Although we recognize that, in some situations, exclusion of non-English studies could lead to bias, we believe that the few instances in which this may occur do not justify the time and cost typically necessary for translation of studies to identify those of acceptable quality for inclusion in our reviews.(153,154)
- Article must be a full-length article. Abstracts and letters to the editor will not meet this inclusion criterion.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that enrolled subjects aged ≥18.
- Studies were limited to individuals with psychiatric disorders
- Article must describe a study that attempted to directly determine the risk for a motor vehicle crash (risk for a fatal or nonfatal crash) associated with psychiatric disorder (specifically, psychotic disorder, mood disorder, anxiety disorder, or personality disorder) using a direct measure of crash (no indirect measures, such as driving simulator data).
- Article must describe a study that includes a comparison group comprising comparable subjects who do not have a psychiatric disorder.
- Article must present motor vehicle crash risk data in a manner that will allow ECRI Institute to calculate (directly or through imputation) effect-size estimates and confidence intervals.
- If the same study is reported in multiple publications, the most complete publication will be the primary reference. Data will be extracted so as to avoid double-counting individuals.

Inclusion Criteria for Key Question 2

- Article must have been published in the English language.
- Article must be a full-length article. Abstracts and letters to the editor will not meet this inclusion criterion.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that enrolled subjects aged ≥18.

- Article must present motor vehicle crash risk data in a manner that will allow ECRI Institute to calculate (directly or through imputation) effect-size estimates and confidence intervals.
- If the same study is reported in multiple publications, the most complete publication will be the primary reference. Data will be extracted so as to avoid double-counting individuals.

Inclusion Criteria for Key Question 3

- Article must have been published in the English language.
- Article must be a full-length article. Abstracts and letters to the editor will not meet this inclusion criterion.
- Article must describe a study that enrolled 10 or more subjects.
- Article must describe a study that enrolled subjects aged ≥18.
- Article must measure association between unintentional crash and risky/aggressive driving behavior(s) (traits associated with personality disorders).
- Risky/aggressive driving behavior(s) must have been measured as an independent variable (specific scaled item or proxy indicator).
- Article must be a full-length article. Abstracts and letters to the editor will not meet this inclusion criterion.
- Article must present motor vehicle crash risk data in a manner that will allow ECRI Institute to calculate (directly or through imputation) effect-size estimates and confidence intervals.
- If the same study is reported in multiple publications, the most complete publication will be the primary reference. Data will be extracted so as to avoid double-counting individuals
- Article may present crash data that are documented or self-reported.[4]

[4] Arthur et al. (2001) concluded that self-reported data is not inferior to documented information and that the two may be used interchangeably.

Appendix D: Excluded Articles

Table D-1 Key Question 1

Reference	Year	Reason for Exclusion
Albert et al.(155)	1999	No crash data
Angst et al.(156)	1998	No crash data
Barnes et al.(157)	1997	Review
Godard et al.(158)	1990	Review
Berger et al.(159)	1975	Unrelated topic
Black et al.(160)	1985	Unrelated material
Black et al.(161)	1985	No crash data??
Blanchard et al.(162)	1995	No disorder of interest
Bolton et al.(163)	2006	Review
Brandaleone et al.(164)	1972	Review
Brown et al.(165)	1997	Data not usable
Butters et al.(166)	2006	Substance use disorder
Buttiglieri et al.(167)	1967	Unrelated material
C'de Baca et al.(168)	2004	Substance use (alcohol)
Cheetham et al.(169)	1974	Review
Costanzo et al.(170)	2002	Review
Cremona et al.(171)	1986	Review
Dagona et al.(172)	1996	Not available for review
Demers et al.(173)	1971	Cognitive/psychomotor study
Dersh et al.(6)	2007	Unrelated material
Dumais et al.(174)	2005	Data restricted to fatal accidents
Eelkema et al.(175)	1970	Unrelated material
Ehlers et al.(176)	2007	Cognitive/psychomotor study
Etminan et al.(177)	2004	May not have been psychiatric population
Frampton et al.(178)	2003	Unrelated material
Galindo Mendez(179)	1994	Review
Galovski et al.(180)	2006	Review
Galovski et al.(181)	2002	Unrelated topic
Galovski et al.(182)	2002	Disorder not of interest
Garrity et al.(135)	2001	Not crash related
Garvey et al.(183)	2003	Not crash related
Gau et al.(184)	2004	Unrelated material
Germain et al.(185)	2005	Simulated driving
Glozier et al.(186)	2002	Policy paper
Grabe et al.(187)	1998	Cognitive/psychomotor
Hanewinkel et al.(188)	1996	Cognitive/sychomotor
Hannerz et al.(189)	2000	Not crash related
Hannula et al.(190)	2006	Not crash related
Haslam et al.(191)	2005	Not crash related
Heikkila et al.(192)	2005	Not crash related
Hilakivi et al.(193)	1989	Reference
Hiroeh et al.(194)	2001	Crash not defined

Reference	Year	Reason for Exclusion
Honig et al.(195)	1999	Cognitive/psychomotor
Humphreys et al.(196)	1995	Reference
Issever et al.(197)	2002	Not crash related
Jin et al.(198)	1991	Unrelated material
Jin et al.(199)	1997	Not available
Johnstone et al.(200)	1991	Not crash related
Kastrup et al.(201)	1983	Substance use
Kastrup et al.(202)	1978	No comparison group
Kastrup et al.(203)	1977	Data not usable
Keene et al.(204)	2007	Not crash related
Kenyon et al.(205)	1970	Review
Lal et al.(206)	2001	Not psychiatric topic
Lapham et al.(207)	2006	Substance use
Lapham et al.(208)	2001	Substance use
Lauber et al.(209)	2000	Reference
Linnoila et al.(210)	1974	Cognitive/Psychomotor
Linnoila et al.(211)	1985	Review
Man-Son-Hing et al.(212)	2007	Not functional psychiatric disorder
Margolis et al.(213)	2002	Population not appropriate
Marottoli et al.(214)	1994	Combines crash data with moving violations
Mazer et al.(215)	2004	Review
McDowell et al.(216)	1996	Cognitive/psychomotor
McGorry et al.(217)	2006	Reference
McQuillen et al.(218)	2005	Reference
Metzner et al.(219)	1993	Review
Michaels et al.(220)	1991	Not psychiatric data
Morgan et al.(221)	1998	Reference
Mulligan et al.(222)	1978	Substance use
Murray et al.(223)	1984	Cognitive/psychomotor
Mykletun et al.(224)	2007	Unrelated material
Niveau et al.(225)	2001	Reference
Noyes et al.(226)	1985	Review
O'Hanlon et al.(227)	1993	Reference
Odell et al.(228)	2005	Reference
Orris et al.(229)	1997	No crash data
Palmer et al.(230)	2002	No crash data
Palmer et al.(231)	2007	Substance use
Parmentier et al.(232)	2005	Population not appropriate
Peele et al.(233)	2005	Reference
Penttila et al.(234)	1975	Cognitive/psychomotor
Perlick et al.(235)	2007	Reference
Petch et al.(236)	1996	Review
Pettis et al.(237)	1993	Reference
Phillips et al.(238)	1999	Substance use
Posel et al.(239)	1998	No crash data
Pristach et al.(240)	1991	Substance use
Ramadas et al.(241)	1975	No crash data

Reference	Year	Reason for Exclusion
Ramaekers et al.(242)	1997	Reference
Rasanen et al.(243)	1999	Substance use
Rasanen et al.(244)	2003	Unrelated material
Ratte et al.(245)	1997	No crash data
Ray et al.(246)	1993	No crash data
Rees et al.(247)	1967	No crash data
Reilly et al.(248)	2007	Reference
Ritsner et al.(249)	2007	Reference
Rosenberg et al.(250)	1972	Substance use
Rubinsztein et al.(251)	1995	Reference
San et al.(252)	2006	Reference
Saraswat et al.(253)	2006	Reference
Schmidt et al.(254)	1972	Insufficient data
Schneider et al.(255)	2001	Unrelated material
Seethalakshmi et al.(256)	2006	Postcrash psychiatric morbidity
Selzer et al.(257)	1969	Substance use
Shah et al.(258)	2006	Reference
Shlensky et al.(259)	1976	Reference
Signori et al.(260)	1974	Review
Silverstone et al.(261)	1988	Review
Smart et al.(262)	2003	No crash data
Smith et al.(263)	1983	Aviation
Stansfield et al.(264)	1996	No crash data
Steer et al.(265)	1984	Substance use
Steer et al.(266)	1982	Substance use
Steiner et al.(267)	1972	No crash data
Sullivan et al.(268)	1994	Reference
Tamrin et al.(5)	2007	No crash data
Thompson et al.(269)	1996	Reference
Tsuang et al.(270)	1985	Reference
Tsuang et al.(271)	1978	Substance use
Tuokko et al.(272)	2007	No crash data
Update from the Roads and Traffic Authority(273)	2000	Reference
Vaez et al.(274)	2007	No crash data
Wallace et al.(275)	1998	No crash data
Waller et al.(276)	1965	Unusable data
Warner et al.(277)	1996	Reference
Wise et al.(278)	2001	Reference
Williamson et al.(279)	2007	Substance use
Woodward et al.(280)	1999	Review
Yale et al.(281)	2003	Reference
Ysander et al.(282)	1970	Single individual with disorder of interest

Table D-2 Key Question 2

Reference	Year	Reason for Exclusion
Asoh et al.(283)	1993	No crash data; foreign language
Bandolier(284)	2005	Reference
Bech et al.(285)	1975	Simulated driving
Bech et al.(286)	1976	Simulated driving
Benzodiazepine Driving Collaborative Group(287)	1993	Unrelated study population
Berthelon et al.(288)	2003	Simulated driving
Betts et al.(289)	1972	Simulated driving
Betts et al.(290)	1988	Simulated driving
Biehl et al.(291)	1967	Reference
Blanke et al.(292)	1986	Reference
Bocca et al.(293)	1999	Simulated driving
Bulmash et al.(294)	2006	Cognitive/psychomotor
Bramness et al.(295)	2002	Substance use for control group
Bramness et al.(296)	2003	Substance use
Brunnauer et al.(70)	2006	Simulated driving
Brunnauer et al.(64)	2004	Cognitive/psychomotor
Campagne et al.(297)	2005	Reference
Carmen del Rio et al.(298)	2002	No control group
Clayton et al.(69)	1977	Simulated driving
Coleman et al.(299)	2004	No crash data
Crouch et al.(300)	1993	No diagnosis of interest
De Gier et al.(301)	1984	Reference
De Gier et al.(60)	1981	Simulated driving
Drummer et al.(302)	2003	Substance use
Elwood et al.(303)	1998	Reference
Emergency Medicine(304)	1998	Reference
Engeland et al.(305)	2007	Hypothetical situation
Freeman et al.(306)	1995	Cognitive/psychomotor
Galindo et al.(179)	1994	Reference
Gengo et al.(307)	1990	Driving simulator
Gerhard et al.(308)	1984	Cognitive/psychomotor
Grabe et al.(65)	1999	Cognitive/psychomotor
Gudgeon et al.(309)	1980	Simulated driving
Gull et al.(310)	2006	Review
Gurwitz et al.(311)	1999	Commentary
Hackett et al.(312)	2003	Reference
Harvard Health Letter(313)	1997	Reference
Hatcher et al.(314)	1990	Cognitive/psychomotor
Hebert et al.(315)	2007	Review
Hindmarch et al.(316)	1988	Simulated driving
Hindmarch et al.(317)	1983	Simulated driving
Hindmarch et al.(318)	1983	Simulated driving
Hindmarch et al.(319)	1980	Simulated driving
Hindmarch et al.(320)	1989	Simulated driving

Reference	Year	Reason for Exclusion
Hindmarch et al.(321)	1977	Simulated driving
Hindmarch et al.(322)	1988	Simulated driving
Hindmarch et al.(323)	1983	Simulated driving
Hindmarch et al.(324)	1988	Simulated driving
Hobi et al.(325)	1981	No crash data
Hobi et al.(326)	1982	No crash data
Hobi et al.(327)	1982	Reference
Javier et al.(328)	2002	Review
Job et al.(329)	1982	Review
Jones et al.(330)	2007	Review
Judd et al.(331)	1985	Cognitive/psychomotor
Kagerer et al.(332)	2003	Cognitive/psychomotor
Kieholz et al.(333)	1972	Reference
Kumar et al.(334)	2001	Review
Lam et al.(335)	2005	Not related to topic
Landauer et al.(336)	1981	Cognitive/psychomotor
Landauer et al.(337)	1969	Review
Laurell et al.(338)	1986	Simulated driving
Laurell et al.(339)	1991	Simulated driving
Leufkens et al.(340)	2007	Simulated driving
Lillsunde et al.(341)	1997	Review
Lin et al.(342)	2003	Substance use
Linnoila et al.(343)	1974	Simulated driving
Linnoila et al.(344)	1973	Simulated driving
Longo et al.(345)	2001	No diagnosis of interest
MacPherson et al.(346)	1984	Inclusion of alcohol
Mattila et al.(347)	1993	Inclusion of alcohol
Mercier-Guyon et al.(348)	1999	Simulated driving
Metzner et al.(219)	1993	Review
Mills et al.(349)	2001	Cognitive/psychomotor
Milner et al.(350)	1969	Substance use
Moser et al.(351)	1990	Cognitive/psychomotor
O'Hanlon et al.(61)	1995	Simulated driving
O'Hanlon et al.(352)	1982	Cognitive/psychomotor
O'Hanlon et al.(353)	1998	Simulated driving
O'Hanlon et al.(354)	1983	Substance use
Ogden et al.(355)	2004	Substance use
Oyefeso et al.(356)	2006	Insufficient crash data
Partinen et al.(357)	2003	Not psychiatric
Patat et al.(358)	1998	Review
Petch et al.(236)	1996	Review
Ramaekers et al.(359)	1992	Cognitive/psychomotor
Ramaekers et al.(68)	2003	Simulated driving
Ramaekers et al.(360)	1995	Simulated driving
Ramaekers et al.(361)	1994	Simulated driving

Reference	Year	Reason for Exclusion
Ramaekers et al.(362)	1992	Cognitive/psychomotor
Ramaekers et al.(363)	1998	Simulated driving
Richet et al.(364)	2004	Cognitive/psychomotor
Ridout et al.(365)	2003	Simulated driving
Ridout et al.(366)	2001	Simulated driving
Robbe et al.(367)	1991	Review
Robbe et al.(368)	1995	Simulated driving
Saario et al.(369)	1976	Psychomotor skills
Seppala et al.(370)	1976	Cognitive/psychomotor
Seymour et al.(371)	2000	Substance use
Seymour et al.(372)	1999	Unusable data
Siegel et al.(373)	1978	Review
Silveira et al.(374)	2002	Simulated driving
Silverstone et al.(261)	1988	Review
Soyka et al.(63)	2005	Review
Soyka et al.(66)	2005	Cognitive/psychomotor
Staner et al.(375)	2005	Not psychiatric
Stonier et al.(376)	1982	Cognitive/psychomotor
Tammelleo et al.(377)	1997	Reference
Thomas et al.(80)	1998	Review
Tornros et al.(378)	2001	Simulated driving
Van Laar et al.(62)	1992	Simulated driving
Van Laar et al.(59)	1998	Review
Van Laar et al.(379)	1995	Simulated driving
Vanakoski et al.(380)	2000	Simulated driving
Veldhuijzen et al.(381)	2002	Not a psychiatric population
Vermeeren et al.(382)	1995	Simulated driving
Vermeeren et al.(383)	2002	Inclusion of alcohol
Vermeeren et al.(384)	1998	Simulated driving
Verster et al.(385)	2002	Simulated driving
Verster et al.(386)	2002	Simulated driving
Vingillis et al.(387)	2002	Review
Volkerts et al.(388)	1992	Simulated driving
Volz et al.(389)	1995	Review; simulated driving
Wetherell et al.(390)	1979	Cognitive/psychomotor
Willumeit et al.(391)	1984	Simulated driving
Wingen et al.(392)	2006	Cognitive/psychomotor
Wilson et al.(393)	1981	Substance use included
Wilson et al.(394)	2002	Cognitive/Psychomotor
Wingen et al.(395)	2005	Simulated driving
Wylie et al.(67)	1993	Simulated driving

Table D-3 Key Question 3

Reference	Year	Reason for Exclusion
Benfield et al.(396)	2007	No crash data
Cheetham et al.(397)	1974	Review
Deffenbacher et al.(398)	2002	No crash data
Elander et al.(399)	1993	Reference
Filetti et al.(400)	2001	Reference
Galovski et al.(401)	2002	No control group
Iancu et al.(402)	1996	Review
Malt et al.(403)	1987	Review
McDonald et al.(404)	1996	Review
Meadows et al.(405)	1998	Not a psychiatric population
Repo-Tiihonen et al.(406)	2001	No crash data
Rodstein et al.(407)	1974	Review
Smith et al.(408)	1979	No crash data

Appendix E: Determining the Stability and Strength of a Body of Evidence

As stated in the main text, ECRI Institute evidence reports differ substantially from other systematic reviews in that we provide two types of conclusions: qualitative conclusions and quantitative conclusions. In order to reach these conclusions we use an algorithm developed by ECRI Institute to guide the conduct and interpretation of the analyses performed during the development of this evidence report.(20) The algorithm, which is presented in Figure E-2 through Figure E-5, formalizes the process of systematic review by breaking the process down into several discrete steps. At each step, rules are applied that determine the next step in the systematic review process and ultimately to the stability and strength-of-evidence ratings that are allocated to our conclusions. Because the application of the rules governing each step in the algorithm (henceforth called a decision point) guide the conduct of the systematic review process and how its findings are interpreted, much time and effort was spent in ensuring that the rules and underlying assumptions for each decision point were reasonable.

The algorithm comprises three distinct sections: a *General* section, a *Quantitative* section, and a *Qualitative* section. The system employs 14 decision points (Table 40). Four decision points are listed in the General section because they apply to both quantitative conclusions as well as qualitative conclusions. The other 10 apply specifically to either quantitative conclusions (Decision Points 5 through 9) or qualitative conclusions (Decision Points 10 through 14). The rest of this appendix defines these decision points and describes how we resolved them for this report. After these descriptions, the pathways for the full system appear in Figure E-2 through Figure E-5.

Note that we applied this system separately for each outcome of interest. This is because many aspects of the evidence (e.g., quality, consistency) can vary by outcome.

Table 40. Decision Points in the ECRI Institute System

Category	Decision Point
General	1) What is the quality of individual studies?
	2) What is the overall quality of evidence?
	3) Is a quantitative estimate potentially appropriate?
	4) Are data informative?
Quantitative	5) Are data quantitatively consistent (homogeneous)?
	6) Are findings stable (quantitatively robust)?
	7) Are there sufficient data to perform meta-regression?
	8) Does meta-regression explain heterogeneity?
	9) Is the meta-regression model robust?
Qualitative	10) Are data qualitatively robust?
	11) Is meta-analysis possible?
	12) Are data qualitatively consistent?
	13) Was at least one study a multicenter study?
	14) Is the magnitude of effect extremely large?

Decision Point 1: Acceptable Quality?

Decision Point 1 serves two purposes: (1) to assess the quality of each included study and; (2) to provide a means of excluding studies that are so prone to bias that their reported results cannot be considered useful. To aid in assessing the quality of each of the studies included in this evidence report, we used two study quality assessment instruments. The choice of which instrument to use was based on the design of the study used to address the key questions of interest. In this evidence report, we used the ECRI Institute Quality Scale III (for pre-/post-studies) and two revised versions of the Newcastle-Ottawa Quality Assessment Scale (one for case-control studies, one for cohort studies).(409) These instruments are presented in Appendix F. To assess the quality of an individual study, we computed a normalized score so that a perfect study received a score of 10, a study for which the answers to all items was "No" received a score of 0, and a study for which the answers to all questions was "NR" received a score of 5. Quality scores were converted to categories as shown in Table 8 (see Methods section of main document). The definitions for what constitutes low, moderate, or high quality evidence were determined *a priori* by a committee of four methodologists. Because the quality was determined separately for each outcome, a study that scored as high quality for one outcome might score as moderate or low quality for another outcome.

Decision Point 2: Determine Quality of Evidence Base

We classified the overall quality of each key question's specific evidence base into one of three distinct categories; high, moderate, or low quality. Decisions about the quality of each evidence base were based on data obtained using the quality assessment instruments described above using the criteria presented in Table E-1.

Table E-1. Criteria Used to Categorize Quality of Evidence Base

Category	Median NOQAS Score (case-control)	Median NOQAS Score (cohort)	Median EIQS VI Score (survey)
High Quality			
Moderate Quality	≥8.0	≥8.0	≥8.0
Low Quality	<8.0	<8.0	<8.0

EIQS VI: ECRI Institute Quality Scale VI
NOQAS: Newcastle-Ottawa Quality Assessment Scale

Decision Point 3: Is a Quantitative Analysis Potentially Appropriate?

The answer to Decision Point 3 depends upon the adequacy of reporting in available studies as well as the number of available studies. In order to permit a quantitative estimate of an effect size for a given outcome, the data for that outcome must be reported in at least three studies in a manner that allows the data to be pooled in a meta-analysis. If fewer than three studies are available, no quantitative estimate is usually appropriate, regardless of reporting. A quantitative estimate is not permitted when at least three studies are relevant to the general topic, but fewer than 75% of them reported the outcome or sufficient information for determination of the effect size and its dispersion, either by direct reporting from the trial or calculations based on reported information. If no quantitative estimate would be appropriate, then one moves directly to Decision Point 10 to determine whether the evidence supports a qualitative conclusion.

Decision Point 4: Are Data Informative?

When only a small number of patients are in an evidence base, statistical tests generally do not perform well. Under such circumstances, statistics cannot determine whether a true difference exists between treatments. This means that no clear conclusion can be drawn. For this decision point, we determined whether the precision of an evidence base was sufficient to permit a conclusion. Statistically significant results are informative because they mean that a treatment effect may exist. Statistically nonsignificant results are also potentially informative, but only if they exclude the possibility that a clinically significant treatment effect exists.

When a meta-analysis is performed, a key concern is the confidence interval around the random-effects summary statistic. If this interval is so wide that it is includes a clinically significant (or substantial) effect in one direction *and also an effect in the opposite direction*, then the evidence is inconclusive and therefore uninformative.(410)

Thus, when considering the summary effect size from a meta-analysis (or the effect size from a single study), there are three ways in which the effect can be "informative":

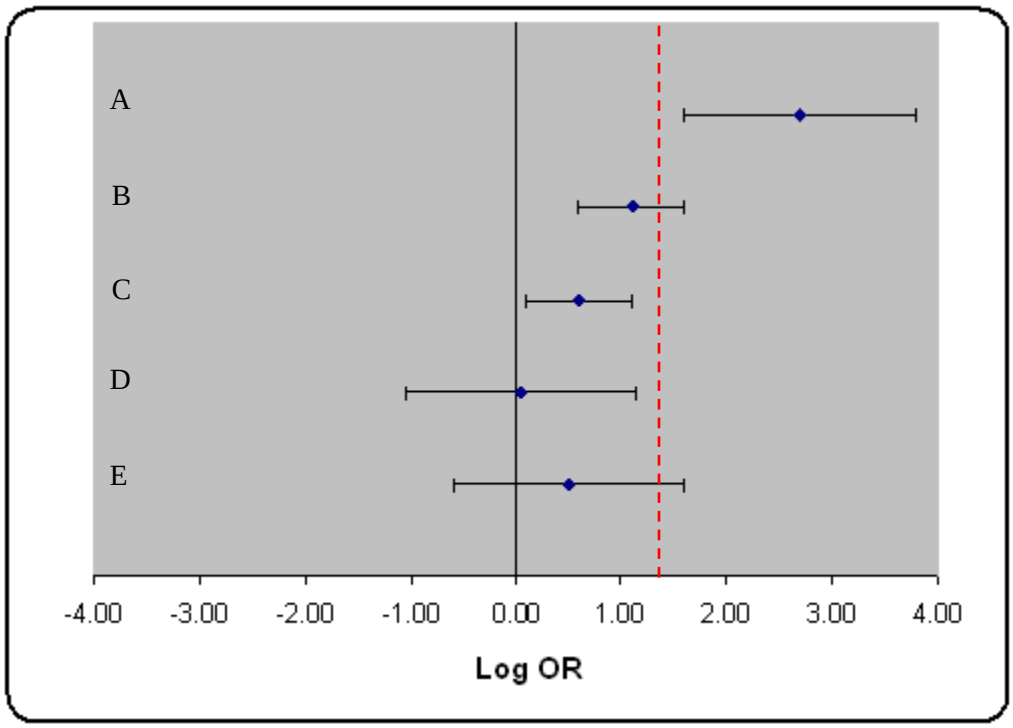
1. The effect size is statistically significantly different from zero. This would be indicated whenever the confidence interval does not overlap zero.

2. The confidence interval is narrow enough to exclude the possibility that a *clinically significant difference* exists.

3. The confidence interval is narrow enough to exclude the possibility that a *substantial difference* exists. This possibility is included to address situations when even a very small effect can be considered "clinically significant" (e.g., a difference in mortality rates), but the effect may not be "substantial."

Consider Figure E-1. Four of the findings in this figure are informative (A to D). Only finding E is noninformative.

Figure E-1. Informative Findings



The dashed line represents the threshold for a clinically significant difference.

Finding A shows that the treatment effect is statistically significant and clinically important. Finding B shows that the treatment effect is statistically significant, but it is unclear whether this treatment effect is clinically important. Finding C shows that the treatment effect is statistically significant, but that the treatment effect is too small to be considered clinically important. Finding D shows that it is unclear whether there is a statistically important treatment effect, but regardless, this treatment effect is not clinically important. Finding E shows that it is unclear whether there is a statistically important treatment effect, and it is also unclear whether the treatment effect is clinically important. This latter finding is thus noninformative.

Note that when the evidence base consists of one or two studies, and the only usable data from one study consists of a *p*-value that was calculated using the wrong statistical test, then the data cannot generally be considered "informative." If, however, the study reported sufficient information for one to perform the correct test, then informativeness can be determined.

Decision Point 5: Are Data Quantitatively Consistent (Homogeneous)?

This decision point was used only when the answer to Decision Point 3 was affirmative and a quantitative analysis was performed. Quantitative consistency refers to the extent to which the quantitative results of different studies are in agreement. The more consistent the evidence, the more precise a summary estimate of treatment effect derived from an evidence base will be. Quantitative consistency refers to consistency tested in a meta-analysis using a test of homogeneity. For this evidence report, we used Higgins and Thompson's I^2 statistic.(33) By convention, we considered an evidence base as being quantitatively consistent when I^2 <50%.

If the findings of the studies included were homogeneous (I^2 <50%), we obtained a summary effect size estimate by pooling the results of these studies using random-effects meta-analysis. If the findings were not homogeneous, we moved on to Decision Point 7 (exploration of heterogeneity, if ≥10 studies) or Decision Point 9 (qualitative analysis).

Decision Point 6: Are Findings Stable (Quantitatively Robust)?

If the findings of the random-effects meta-analysis were found to be homogeneous, we next assessed the stability of the summary effect-size estimate obtained. Stability refers to the likelihood that a summary effect estimate will be substantially altered by changing the underlying assumptions of the analysis. Analyses that are used to test the stability of an effect-size estimate are known as sensitivity analyses. Clearly, one's confidence in the validity of a treatment effect estimate will be greater if sensitivity analyses fail to significantly alter the summary estimate of treatment effect.

For this evidence report, we used three different sensitivity analyses. These sensitivity analyses are as follows:

1. *Removal of one study and repeat meta-analysis.* The purpose of this sensitivity analysis is to determine whether a meta-analysis result is driven by a particular trial. For example, a large trial may have a very strong impact on the results of a meta-analysis because of its high weighting.
2. *Publication bias test.* The publication bias test used in this evidence report was that of Duval and Tweedie.(47-49,411) Based on the degree of asymmetry in a funnel plot constructed from the findings of the included studies, this test(48,49) estimates the number of unpublished studies (and their effect sizes). After the addition of any "missing" data to the original meta-analysis, the overall effect size is estimated again. If evidence of publication bias was identified and the summary effect size estimate, adjusted for "missing" studies, differed from the pooled estimate of treatment effect determined by the original fixed-effects meta-analysis by >±5%, we determined that the findings of our original analysis are not robust and the effect-size estimate is not stable.
3. *Cumulative random-effects meta-analysis.* Cumulative meta-analysis provides a means by which one can evaluate the effect of the size of the evidence base (in terms of the number of individuals enrolled in the included studies and the number of included studies) on the stability of the calculated effect-size estimate. For this evidence report, we performed two different cumulative random-effects meta-analyses as follows:
    a. Studies were added cumulatively to a random-effects meta-analysis by date of publication/oldest study first.
    b. Studies were added cumulatively to a random-effects meta-analysis by date of publication/newest study first.

    In each instance, the pooled effect-size estimate was considered unstable if any of the last three studies to be added resulted in a change in the cumulative summary effect-size estimate of >±5%.

The prespecified tolerance levels for each of the potential effect-size estimates we could have utilized in this evidence report are presented in Table E-2.

Table E-2. Prespecified Tolerance Levels

Effect-size Estimate	Weighted Mean Difference	Standardized Mean Difference	% of Individuals	Rate Ratio	Odds Ratio
Tolerance	±5%	±0.1	±5	±0.05	±0.05

Decision Point 7: Are There Sufficient Data to Perform Meta-Regression?

We required a minimum of 10 studies before attempting meta-regression.

Decision Points 8 and 9: Exploration of Heterogeneity

We will always attempt to determine the source of heterogeneity when the evidence base consists of 10 or more studies using meta-regression. In preparing this evidence report, we did not encounter any situations in which we had a heterogeneous evidence base consisting of at least 10 studies. Consequently, Decision Points 8 and 9 are irrelevant to the present report, and we do not discuss them further.

Decision Point 10: Are Qualitative Findings Robust?

Decision Point 10 allows one to determine whether the qualitative findings of two or more studies can be overturned by sensitivity analysis. The same sensitivity analyses used to test quantitative robustness were used to test qualitative robustness. We considered our qualitative findings to be overturned only when the sensitivity analyses altered our qualitative conclusion (i.e., a statistically significant finding became nonsignificant as studies were added to the evidence base). Otherwise, we concluded that our qualitative findings were robust.

Decision Point 11: Is Meta-analysis Possible?

This Decision Point is used only when the evidence base for an outcome consists of two studies.

A meta-analysis is possible if each study reports an effect size and its standard error or if each study reports sufficient information for the reader to calculate these values. Note that meta-analysis is never appropriate if two studies have statistically significant effect sizes in opposite directions.

Decision Point 12: Are Data Qualitatively Consistent?

This Decision Point is used only when the evidence base for an outcome consists of two studies.

The purpose of this decision point is to determine whether the qualitative findings of an evidence base consisting of only two studies are the same. For example one might ask, "When compared to insulin injection, do all included studies find that inhaled insulin is a significant risk factor for a motor vehicle crash?"

Decision Point 13: Is at Least One Study a Multicenter Study?

Multicenter trials may increase the strength of a one or two-study evidence base because they demonstrate partial replication of findings; they have shown that different investigators at different centers can obtain similar results using the same protocol. We defined a multicenter trial as any trial that met the following two conditions: (1) 3 or more centers and (2) either at least 100 patients or at least 3 centers enrolled at least 20 patients per center.

Decision Point 14: Is Magnitude of Treatment Effect Large?

When considering the strength of evidence supporting a qualitative conclusion based on only one or two studies, magnitude of effect becomes very important. The more positive the findings, the more confident one can be that new evidence will not overturn one's qualitative conclusion.

The algorithm divides the magnitude of effect into two categories—large and not large. Determining the threshold above which the observed magnitude of effect can be considered to be "large" cannot usually be

determined *a priori*. In cases in which it is necessary to make judgments about whether an estimate of treatment effect is extremely large, the project director will present data from the two studies to a committee of three methodologists who will determine whether an effect-size estimate is "extremely large" using a modified Delphi technique.

Additional Consideration: Evidence from Indirect or Surrogate Outcomes

In certain instances when an evidence base includes only one or two studies with direct evidence (e.g., crash data), the strength of evidence may be increased by additional studies of indirect outcomes (e.g., driving simulator tests, visual function tests) that show findings consistent with the direct evidence study findings.

Figure E-2. General Section

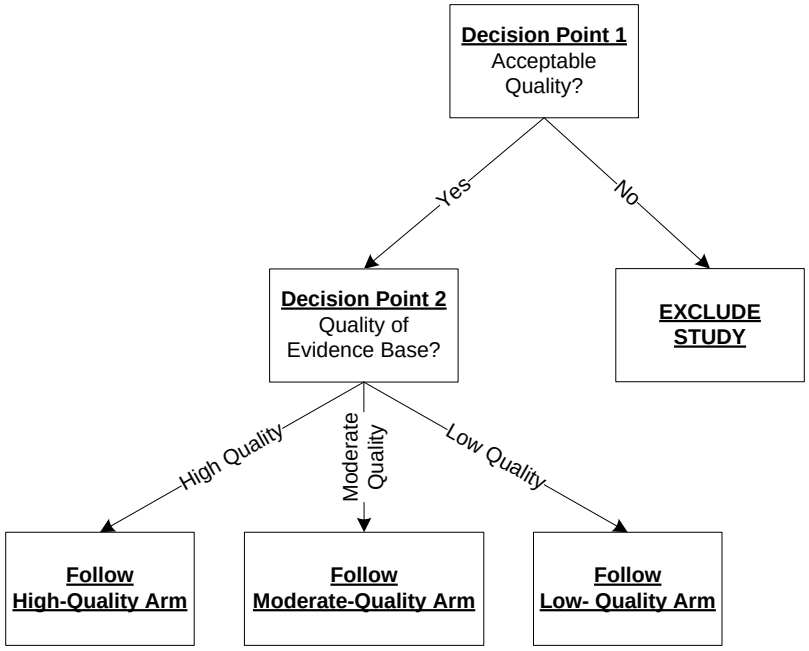


Figure E-3. High-quality Pathway

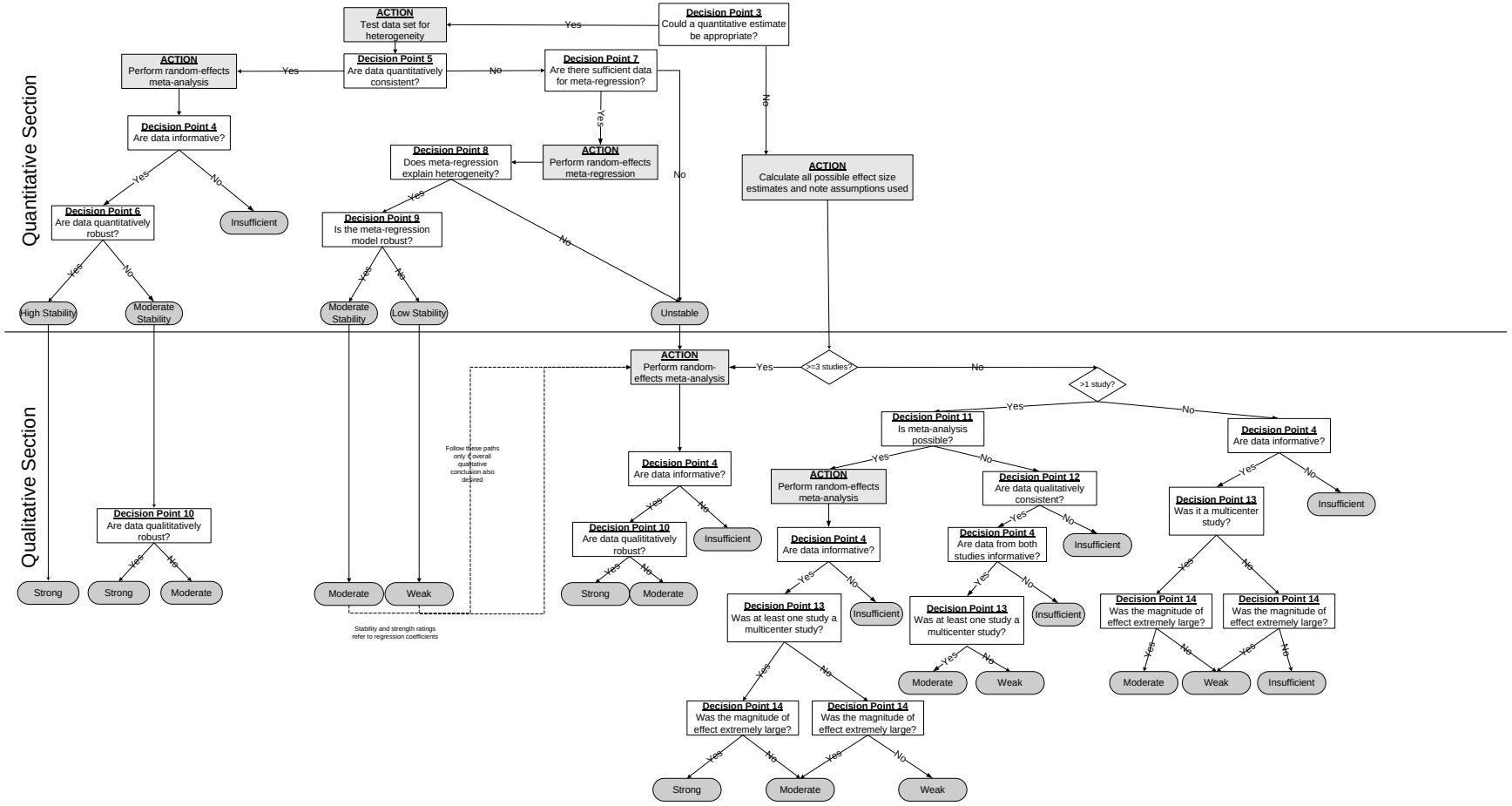


Figure E-4. Moderate-quality Pathway

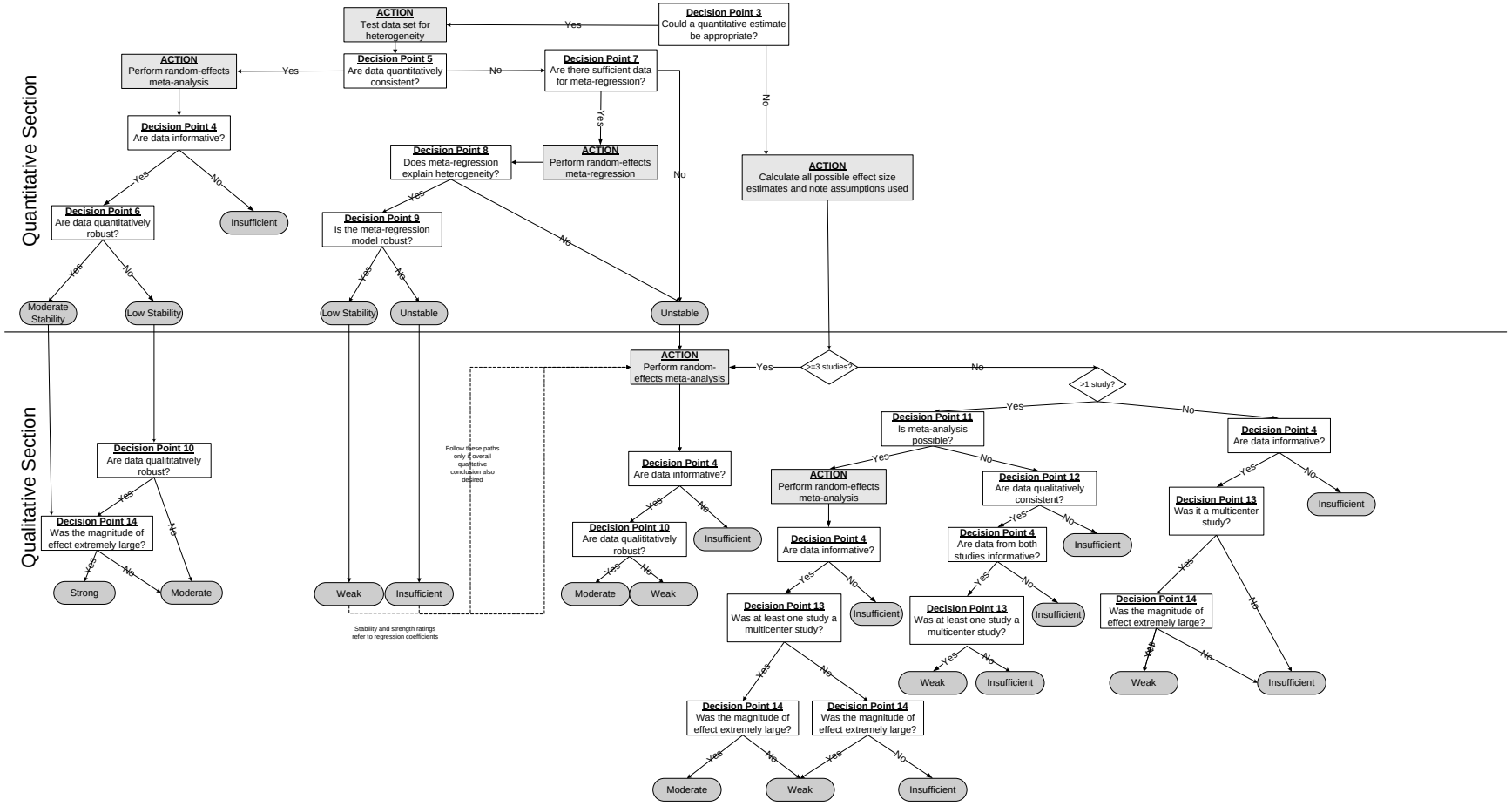
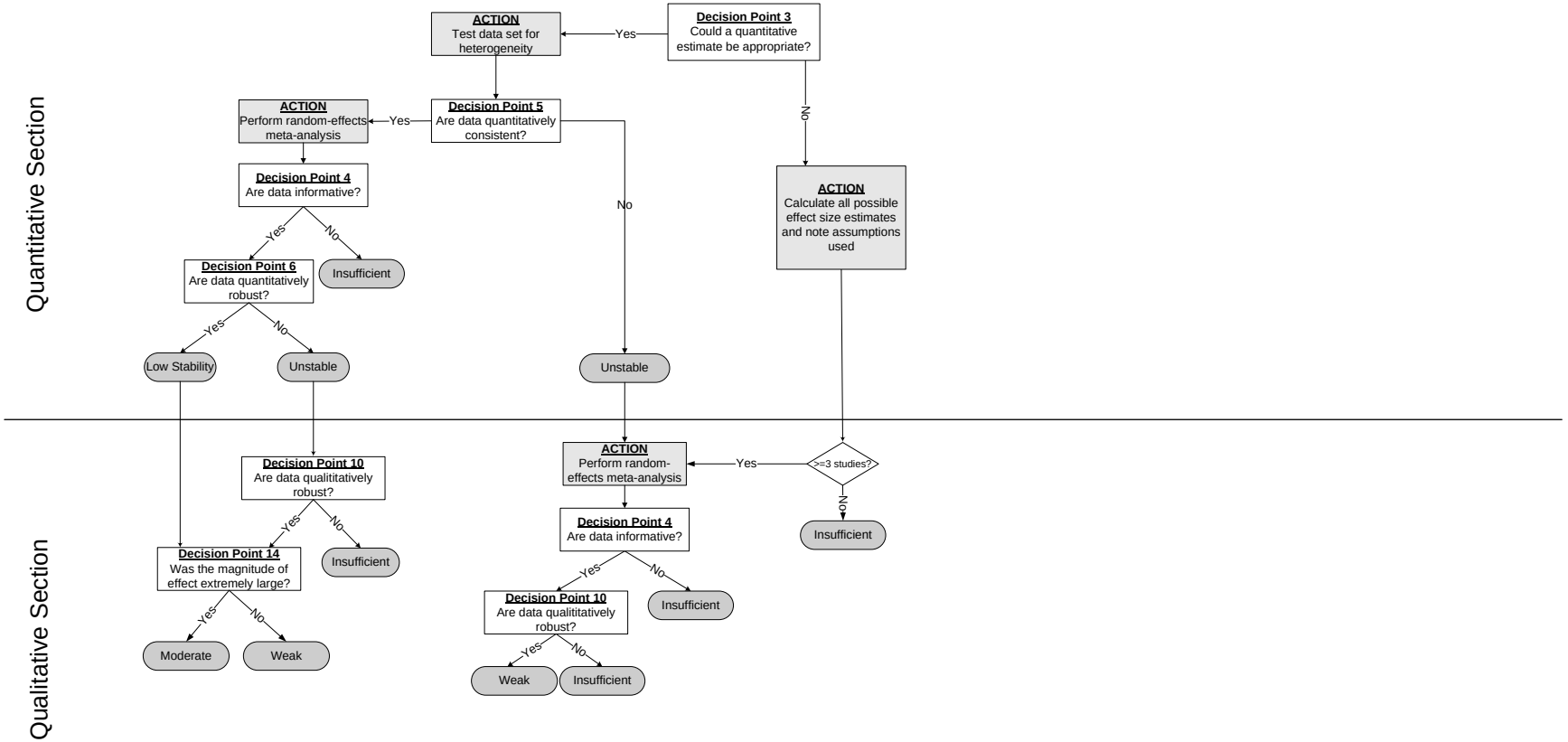


Figure E-5. Low-quality Pathway



Appendix F: Quality Assessment Instruments Used

Two different instruments were used to assess the quality of the studies included in the evidence bases for the key questions addressed in this evidence report; they are revised versions of the Newcastle-Ottawa Quality Assessment Scales for Cohort Studies and Case-Control Studies.(409)

Table F-1 Revised Newcastle-Ottawa Quality Assessment Scale for Cohort Studies

Question Number	Question
1	Is the exposed cohort representative of the average motor vehicle driver in the community?
2	Is the non-exposed cohort representative?
3	How was exposure determined? Secure record?
4	At the designated start of the study, were the controls free of the outcome of interest?
5	What is the comparability of the cohorts on the basis of design or analysis?
6	How was the outcome assessed?
7	Was follow-up adequate for outcome to occur?
8	Was the follow-up adequate for both exposed and nonexposed cohorts?
9	Was the funding free of financial interest?
10	Were the conclusions supported by the data?

Table F-2 Revised Newcastle-Ottawa Quality Assessment Scale for Case-Control Studies

The original Newcastle-Ottawa Quality Assessment Scale for Case-Control Studies consisted of 10 questions. We adapted the instrument to better capture some sources of bias that were not considered in the original 10-item scale.

Question Number	Question
1	Do the cases have independent validation?
2	Are the cases representative?
3	Are the controls derived from the community?
4	At the designated endpoint of the study, do the controls have the outcome of interest?
5	Does the study control for the most important confounder?
6	Does the study control for any additional confounders?
7	Was exposure/outcome ascertained through a secure record (e.g., surgical)?
8	Was the investigator who assessed exposure/outcome blinded to group patient assignment?
9	Was the same method of exposure/outcome ascertainment used for both groups?
10	Was the nonresponse rate of both groups the same?
11	Was the investigation time of the study the same for both groups?
12	Was the funding free of financial interest?
13	Were the conclusions supported by the data?

Table F-3 ECRI Institute Quality Scale VI: Surveys

Item	Question
1	Did all suitable individuals (or units) have the same chance to complete the survey?
2	If units were randomly sampled, did the study use appropriate randomization methods?
3	Was there concealment of the unit selection process?
4	Did the study have a survey response rate of ≥75% or were statistical adjustments made to minimize the effects or nonresponse bias?
5	Was the anonymity/confidentiality of responses ensured by the investigator and relayed to the participants?
6	Was the survey instrument used a validated survey for the population of interest?
7	Was the funding for the study derived from a source that would not benefit financially from results in a particular direction?
8	Were steps taken to ensure that all suitable participants could complete the survey?
9	For surveys attempting to gather factual information, were measures taken to ensure the responses were accurate?
10	Was respondent fatigue tested for or was the typical time to complete the survey reported and determined through pretesting to be acceptable to respondents?

Appendix G: Quality Score Tables

Key Question 1

Table G-1. Quality Assessment Table for Case-Control Studies

Reference	Year	Items													Quality Category
		1	2	3	4	5	6	7	8	9	10	11	12	13	
Koepsell et al.(56)	1994	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	Y	Moderate

N: No
NR: Not reported
Y: Yes

Table G-2. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Armstrong and Whitlock(51)	1980	Y	Y	N	N	N	N	Y	Y	NR	Y	Low
Buttiglieri and Guenette(52)	1967	S	Y	N	N	N	Y	Y	Y	NR	Y	Low
Crancer and Quiring(53)	1969	Y	Y	Y	N	N	Y	Y	Y	NR	Y	Low
Edlund et al.(54)	1989	Y	S	Y	N	N	N	Y	Y	NR	Y	Low
Foley et al.(55)	1995	Y	Y	Y	N	Y	Y	Y	Y	NR	Y	Low
Waller(58)	1965	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
Wear(57)	1985	N	Y	Y	N	N	Y	Y	Y	Y	Y	Low

N: No
NR: Not reported
S: Somewhat representative or partially validated
Y: Yes

Key Question 2

Table G-3. Quality Assessment Table for Case-Control Studies

Reference	Year	Items													Quality Category
		1	2	3	4	5	6	7	8	9	10	11	12	13	
Barbone et al.(71)	1998	Y	Y	Y	N	N	Y	Y	N	Y	Y	Y	N	Y	Low
Hemmelgarn et al.(72)	1997	Y	Y	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Y	Moderate
Honkanen et al.(73)	1980	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	Y	Y	Low
Leveille et al.(74)	1994	Y	N	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Moderate
McGwin et al.(75)	2000	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	Y	Moderate
Movig et al.(76)	2003	Y	Y	Y	Y	Y	Y	Y	N	Y	Y	Y	NR	Y	Moderate
Wadsworth et al.(79)	2005	N	Y	Y	Y	N	Y	N	N	Y	Y	Y	NR	Y	Low

N: No
NR: Not reported
Y: Yes

Table G-4. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Neutel(77)	1995	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Moderate
Ray et al.(78)	1992	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Moderate

NR: Not reported
Y: Yes

Table G-5. Quality Assessment Table for Surveys

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Wadsworth et al.(79)	2005	Y	NR	NR	N	NR	NR	Y	NR	NR	NR	Low

N: No
NR: Not reported
Y: Yes

Key Question 3

Table G-6. Quality Assessment Table for Case-Control Studies

Reference	Year	Items													Quality Category
		1	2	3	4	5	6	7	8	9	10	11	12	13	
Turner and McClure(146)	2004	Y	Y	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	Low
Fong et al.(147)	2001	N	Y	Y	Y	N	N	N	N	Y	Y	Y	NR	Y	Low
Alparslan et al.(149)	1999	N	Y	Y	Y	N	N	N	N	Y	Y	Y	NR	Y	Low
Rajalin(151)	1994	Y	Y	Y	Y	Y	N	Y	N	Y	Y	Y	NR	Y	Moderate
Mayer and Treat(152)	1977	N	Y	Y	Y	N	N	N	N	Y	Y	Y	NR	Y	Low

N: No
NR: Not reported
Y: Yes

Table G-7. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Gulliver and Begg(139)	2007	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Moderate
Nabi et al.(140)	2007	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Moderate
Schwebel et al.(110)	2007	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Moderate
Blows et al.(143)	2005	Y	Y	N	Y	N	N	Y	Y	Y	Y	Low
Nabi et al.(145)	2005	Y	Y	N	Y	Y	N	Y	Y	Y	Y	Moderate
Karlsson et al.(109)	2003	S	Y	N	Y	N	N	Y	Y	Y	Y	Low
Bell et al.(148)	2000	S	Y	Y	Y	Y	Y	Y	Y	Y	Y	Moderate
Parker et al.(91)	1995	Y	Y	N	Y	Y	N	N	Y	NR	Y	Low

N: No
NR: Not reported
S: Somewhat representative or partially validated
Y: Yes

Table G-8. Quality Assessment Table for Survey Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Sumer(134)	2003	Y	NR	NR	NR	NR	NR	Y	NR	NR	NR	Low
Sullman et al.(137)	2002	Y	NA	NA	N	NR	Y	NR	Y	N	NR	Low
Lajunen et al.(138)	2001	NR	NR	NR	NR	NR	NR	Y	NR	NR	NR	Low
Verschuur and Hurts(141)	2007	Y	NR	NR	NR	NR	Y	Y	NR	NR	NR	Low
Kontogiannis(142)	2006	Y	NR	NR	N	NR	Y	NR	NR	NR	N	Low
Malta et al.(144)	2005	Y	NA	NA	NR	NR	Y	NR	NR	NR	NR	Low
Wells-Parker et al.(101)	2002	Y	Y	NR	Y	NR	NR	NR	Y	NR	NR	Low
Deery and Fildes(150)	1999	NR	NA	NA	NR	NR	NR	Y	NR	NR	NR	Low

N: No
NA: Not applicable
NR: Not reported
Y: Yes

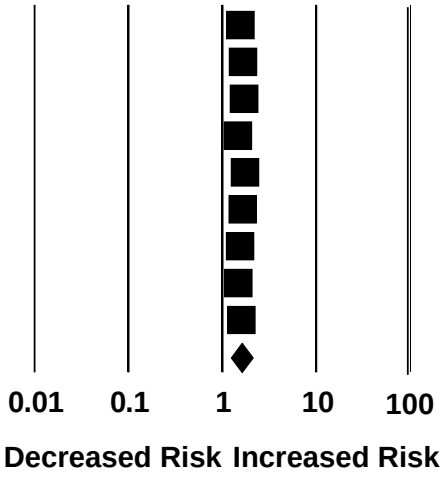
Appendix H: Additional Analyses

Sensitivity Analyses for Key Question 2

Subgroup Analysis, Key Question 2: Benzodiazepines and Crash Risk

Figure H-1. Random-effects Meta-analysis with One Study Removed

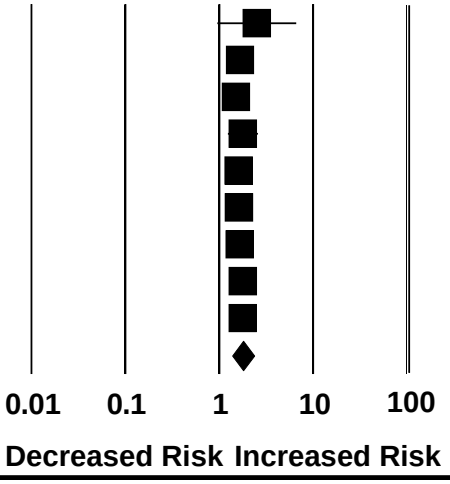
Study Name	Statistics with Study Removed				
	Point	Lower limit	Upper limit	Z-value	*p*-value
Honkanen	1.648	1.244	2.183	3.481	0.000
Ray	1.757	1.257	2.457	3.297	0.001
Leveille	1.803	1.339	2.428	3.885	0.000
Neutel	1.551	1.187	2.025	3.219	0.001
Hemmelgarn	1.844	1.314	2.587	3.542	0.000
Barbone	1.743	1.230	2.470	3.124	0.002
McGwin	1.636	1.252	2.138	3.602	0.000
Movig	1.565	1.222	2.004	3.547	0.000
Wadsworth	1.686	1.311	2.168	4.073	0.000
Summary	1.681	1.283	2.204	3.762	0.000



CI: Confidence interval

Figure 18. Cumulative Meta-analysis by Year of Publication

Study Name	Cumulative Statistics				
	Point	Lower limit	Upper limit	Z-value	*p*-value
Honkanen	2.378	0.891	6.353	1.729	0.084
Ray	1.578	1.160	2.145	2.910	0.004
Leveille	1.427	1.046	1.947	2.244	0.025
Neutel	1.686	1.153	2.466	2.694	0.007
Hemmelgarn	1.530	1.161	2.015	3.025	0.002
Barbone	1.534	1.239	1.899	3.924	0.000
McGwin	1.568	1.256	1.958	3.973	0.000
Movig	1.686	1.311	2.168	4.073	0.000
Wadsworth	1.681	1.283	2.204	3.762	0.000
Summary	1.681	1.283	2.204	3.762	0.000

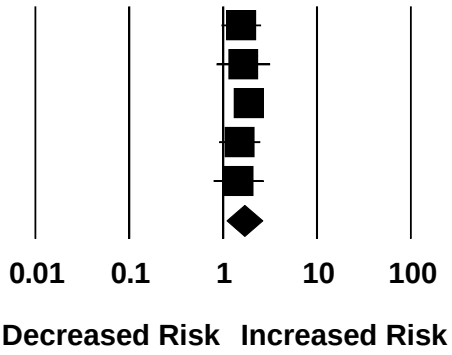


CI: Confidence interval

Subgroup Analysis, Key Question 2: Benzodiazepine Anxiolytics and Crash Risk

Figure 19. REMA with One Study Removed

Study Name	Statistics with Study Removed				
	Point	Lower limit	Upper limit	Z-value	*p*-value
Honkanen	1.558	0.945	2.571	1.737	0.082
Ray	1.643	0.839	3.216	1.449	0.147
Leveille	1.875	1.479	2.376	5.198	0.000
Neutel	1.502	0.896	2.519	1.544	0.123
Barbone	1.460	0.778	2.739	1.178	0.239
Summary	NC	1.072	2.576	2.271	0.023



CI: Confidence interval