Draft Evidence Report

Traumatic Brain Injury and Commercial Motor Vehicle Driver Safety

(Comprehensive Review)

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 Panel (MEP). The MRB and MEP make recommendations on medical topics of concern to the FMCSA.

The FMCSA will consider all MRB and MEP recommendation; however, all proposed changes to current standards and guidelines will be subject to public notice and comment and relevant rulemaking 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 U.S. 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 on the current state of knowledge on this topic. It is not intended as instruction for medical practice or for making decisions about individual patients.

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Executive Summary

Purpose of Evidence Report

Of all occupations in the United States, workers in the trucking industry 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 (DOT), there were 4,584 fatal crashes involving a large truck in 2007 for a total of 4,808 fatalities. In addition, there were 139,587 nonfatal crashes; 56,487 of these were crashes that resulted in an injury to at least one individual (for a total of 83,908 injuries).

The purpose of this evidence report is to address several key questions posed by the Federal Motor Carrier Safety Administration (FMCSA). The FMCSA developed ach of these key questions so that the answers would provide information useful in updating its current medical examination guidelines. The four key questions addressed in this evidence report are:

Key Question 1: What is the impact of traumatic brain injury on crash risk/driving performance?

Key Question 2: What factors associated with traumatic brain injury are predictive of increased crash risk or poor driving performance?

Key Question 3: What is the impact of rehabilitation programs on crash risk/driving performance among individuals with a traumatic brain injury?

Key Question 4: What is the likelihood of a future seizure among individuals with a traumatic brain injury who did not experience a seizure at the time of the injury?

Identification of Evidence Bases

We identified separate evidence bases for each of the key questions addressed by this evidence report through a comprehensive search of the literature, an examination of abstracts of identified studies to determine which articles would be retrieved, and selection of the actual articles that would be included in each evidence base.

A total of six electronic databases (MEDLINE, PubMed [PreMEDLINE], EMBASE, TRIS, the Cochrane Library, and the National Guideline Clearinghouse™) were searched (through March 2009). In addition, we examined the reference lists of all obtained articles with the aim of identifying relevant articles not identified by our electronic searches. We also performed hand searches of the "gray literature." We determined whether to admit an article into an evidence base using formal retrieval and inclusion criteria 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 comprise the evidence base for each key question, but also the interplay between the quality, quantity, robustness, and consistency of the overall body of evidence.

Analytic Methods

We used an extensive set of analytic techniques in this evidence report. If appropriate, random-effects meta-analyses were used to pool data from different studies. Differences in the findings of studies (heterogeneity) were identified using I^2. Sensitivity analyses, aimed at testing the robustness of our findings, included the use of cumulative random-effects meta-analysis. The presence of publication bias was tested for using the "trim and fill" method when appropriate.

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 conclusions 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 in 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

Key Question 1: What is the impact of traumatic brain injury (TBI) on crash risk/driving performance?

The available evidence is insufficient to determine whether crash risk is elevated for drivers with TBI compared with uninjured controls. However, driving performance as measured by on-road driving tests and driving simulators was significantly impaired among individuals with TBI compared with uninjured controls. (Strength of Evidence: Moderate)

Direct Evidence—Crash Studies*: Five studies attempted to directly determine crash risk among drivers with TBI through evaluation of self-reported crashes or crashes recorded in a state licensing database. The median quality of the evidence base was moderate. Data from four of these studies were combined to determine an overall estimate of crash risk. The summary rate ratio was 1.32 (95% CI 0.77-2.25), a difference that trended toward slightly higher risk in the TBI group but did not reach statistical significance. The remaining study reported a statistically significant increase in the mean number of crashes/person among drivers with TBI compared with healthy controls. Given that the findings do not rule out either the possibility of an elevated risk for drivers with TBI or no difference in risk, the current evidence on crash risk among drivers with TBI remains inconclusive.*

Indirect Evidence—Studies of Driving Performance*: Four studies (median quality: moderate) assessed driving performance (on-road or simulated) of patients with TBI compared with healthy controls. Because none of these studies used the same measures of driving performance, we did not attempt to combine the findings in a meta-analysis. Two studies that evaluated simulated driving outcomes found statistically significant differences indicating decreased performance in at least one performance outcome for individuals with TBI compared with healthy controls. Similarly, two studies that evaluated on-road driving performance found statistically significant differences in overall test scores or scores on specific driving tasks that indicated decreased performance for individuals with TBI compared with healthy controls. Since neither study conducted actual driver licensing tests, the percentage of patients with TBI that would have been certified as fit to drive is unknown. Inclusion of individuals who may never recover enough ability to pass a driving test would lead to an underestimate of the average driving performance of individuals with TBI who are certified as fit to drive. Furthermore, the extent to which reduced performance on road tests or driving simulators affects crash risk remains unclear.*

Since the majority of studies did not report the percentage of commercial motor vehicle (CMV) drivers (if any) in their study population, the generalizability of these findings to CMV drivers is unknown.

Key Question 2: What factors associated with traumatic brain injury are predictive of increased crash risk or poor driving performance?

The available evidence is insufficient to determine whether any factors related to TBI can predict actual crash risk. However, current evidence suggests that cognitive function measured by certain

neuropsychological tests may predict the outcome of driving performance measured by a road test for patients with TBI. (Strength of Evidence: Moderate)

Direct Evidence—Crash Studies*: Five studies (median quality: moderate) attempted to determine whether certain variables were associated with risk of crash/driving offenses among patients with TBI. Two of these studies had possible overlap in their enrolled study populations, so these studies were generally analyzed as a single study. Evidence for an association between any TBI-related factor and risk of crash/driving offenses was mixed. One study provided evidence of a significant association between neuropsychological functioning and crash/driving incidents, while two other studies did not. However, none used the same set of neuropsychological function tests, and the severity of TBI among individuals in one of the negative studies differed substantially from the other study populations (mild versus moderate to severe). The conflicting evidence and low number of studies means that the evidence is currently insufficient to determine whether an association exists between any TBI-related factors and crash risk.*

Indirect Evidence—Studies of Driving Performance*: Seven studies (median quality: moderate) evaluated the association between various predictor variables and road test or closed-course driving outcomes. Several studies evaluated one or more neuropsychological tests; although there was overlap in some of the specific individual tests used, none of the studies evaluated the exact same set of tests. The only individual test that showed a significant association with road test outcome in more than one study was the Trail-making Test (two studies showed an association, while a third study did not). Several tests that were used in only a single study showed a significant association with road test outcomes. Therefore, while it is difficult to determine which specific tests have the best association with outcome, one can conclude that reduced cognitive function (as measured by neuropsychological tests as a group) seems to be associated with poor outcomes on a road test.*

Since the majority of studies did not report the percentage of CMV drivers (if any) in their study population, the generalizability of these findings to CMV drivers is unknown.

Prediction of driving test outcomes is not the same as prediction of crash risk. Patients who failed road tests would either not be allowed to drive or at least advised not to drive, depending on the laws of the particular state or country of residence. Thus, they would not be expected to be at risk for motor vehicle crash (unless they disregard laws or advice).

Key Question 3: What is the impact of rehabilitation programs on crash risk/driving performance among individuals with a traumatic brain injury?

The available evidence is insufficient to determine the impact of rehabilitation programs on crash risk or driving performance among individuals with TBI.

No studies provided direct evidence to address this question.

Indirect Evidence—Studies of Driving Performance*: One low-quality study compared the effectiveness of different rehabilitation strategies (structured exercises on an electric wheelchair vs. use of wheelchair with*

no structured exercises) for improving road test driving performance in patients with TBI. Although patients in the structured exercise group achieved significantly better mean scores on several road test measures (percent tracking, percent correct signs, composite score, and driver educator's score) compared with controls, the numerous quality deficiencies in this single small study preclude an evidence-based conclusion.

Key Question 4: What is the likelihood of a future seizure among individuals with a traumatic brain injury who did not experience a seizure at the time of the injury?

Individuals with TBI who have not experienced a seizure within the first week post-injury still have a significant likelihood of experiencing late seizure(s). Reported frequencies of late seizures in this population ranged from 1% to 25% during follow-up periods ranging from 1 to 11 years. (Strength of Evidence: Moderate)

The highest rate of late seizures (25%) was associated primarily with penetrating missile TBIs. (Strength of Evidence: Minimally Acceptable)

Among patients with closed TBIs, a diagnosis of severe TBI was associated with higher frequencies of first-time late seizures than diagnoses of mild or moderate TBI. (Strength of Evidence: Minimally Acceptable)

Among adults with moderate or severe TBI who develop late seizures, ≥50% experience their first late seizure within the first year after TBI. The rates fall substantially within the next two years and stabilize after the third year at roughly 2% to 4% (of the total patients who develop late seizures) per year out to 11 years. The pattern for mild TBI is less clear, but the rate of late seizure development does not appear much higher in the first year compared with subsequent years. (Strength of Evidence: Minimally Acceptable)

Our searches identified nine studies (median quality: moderate) that reported (or allowed independent calculation of) the frequency of patients whose first seizure was a late seizure (i.e., occurring after one week post-TBI). Owing to differences in several important factors among these studies, we did not attempt to combine the data from each study in a pooled analysis. Differences included severity of TBI, how severity was determined, length of follow up, whether children were analyzed with adults, whether patients with alcoholism were included, and whether prophylactic anti-seizure medication was used in the study.

The percentage of patients with a first-time late seizure ranged from 1% to 25%, most likely owing to one or more of the differences noted above. The study with the highest rate was the only study where most patients had penetrating missile TBIs; a comparison of missile and non-missile TBIs in this study found that the rate of late seizure development was much higher among patients with missile TBIs (32% versus 5%). The study with a 1% rate was unusual because all patients were classified as having severe TBI (other studies with similar patients reported rates close to 10%), but it was the only study where all patients were given prophylactic Phenobarbital for the entire 12-month follow up. This finding is not consistent with findings from controlled studies that did not find a preventive benefit of prophylactic anti-seizure

medication for late seizures. One study that analyzed seizure data separately based on severity of TBI found that first-time late seizures occurred more frequently among patients with severe TBI than among patients with mild or moderate TBI.

Two studies assessed the timing of late seizure development and found that first-time late seizures occurred most frequently in the first year following TBI. At least 50% of patients with moderate or severe TBI who developed late seizures experienced the first seizure within this time period (e.g., if the overall late seizure rate was 10%, then about 5% of the total patient group would develop late seizures within the first year after TBI). The percentage dropped substantially within the next two years and then stabilized at roughly 2–4% per year out to 11 years. The pattern for mild TBI is less clear, but the rate of late seizure development does not appear much higher in the first year compared with subsequent years.

Preface

Organization of Report

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

In the *Background* section, we provide general information about traumatic brain injury (TBI) and driving. Also included is information on current regulatory standards and guidelines from the FMCSA and three other government transportation safety agencies: the Federal Aviation Administration (FAA); the Federal Railroad Administration; and the Maritime Administration. In addition, we summarize equivalent information from other countries 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 synthesizing clinical study results.

The *Evidence Synthesis* section 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 *Evidence Synthesis* section closes with our evidence-based conclusions, which are based on our assessment of the available evidence.

Scope

Commercial driving is a hazardous occupation. The trucking industry has the third highest fatality rate of all occupations (12%) in the United States (http://www.bls.gov/iif/oshcfoiarchive.htm#2004charts). About two thirds of fatally injured truck workers were involved in highway crashes. According to the U.S. DOT, there were 139,587 nonfatal crashes involving a large truck in 2007. Of those, 56,487 crashes resulted in an injury to at least one individual, for a total of 83,908 injuries, and 4,584 of all crashes caused 4,808 fatalities (http://ai.volpe.dot.gov/CrashProfile/n_overview.asp). In 2007, the U.S. DOT *Brief Statistical Summary* reported a total of 802 motorists killed in large truck crashes, which amounted to a decrease of 0.4% compared with the statistics for 2006 (n = 805). The total number of motorists injured in large truck crashes was 23,000, which was identical to the 2006 statistics (http://www-nrd.nhtsa.dot.gov/Pubs/811017.PDF).

The purpose of this evidence report is to address several key questions posed by the FMCSA. The FMCSA carefully formulated each of these key questions so that each answer will provide it with the information necessary to update its current medical examination guidelines. The key questions addressed in this evidence report are:

Key Question 1: What is the impact of TBI on crash risk/driving performance?

Key Question 2: What factors associated with TBI are predictive of increased crash risk or poor driving performance?

Key Question 3: What is the impact of rehabilitation programs on crash risk/driving performance among individuals with TBI?

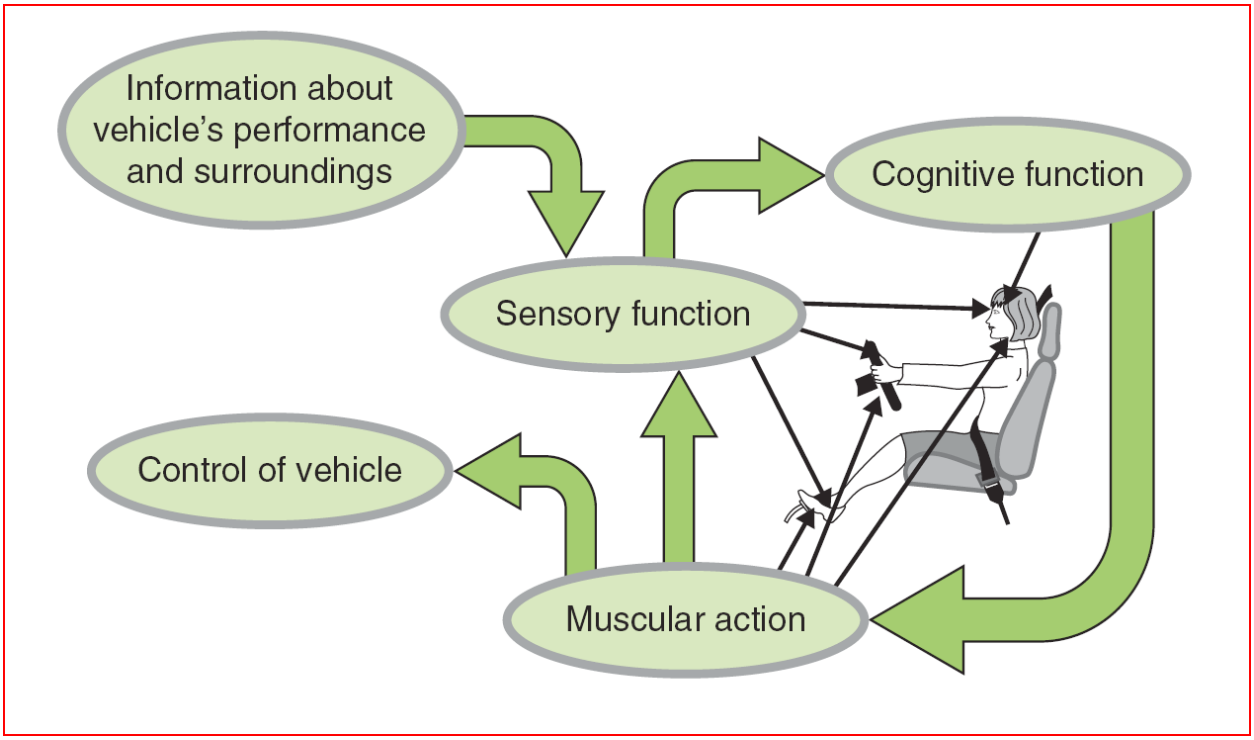
Key Question 4: What is the likelihood of a future seizure among individuals with TBI who did not experience a seizure at the time of the injury?

Background

Safe driving requires the driver to be able to maintain effective and reliable control of his or her vehicle; respond to the road, traffic, and other external clues; and follow the rules of the road. Commercial drivers consciously learn all these skills and demonstrate them as part of obtaining their commercial drivers license (CDL); the vast majority of people are able to achieve a satisfactory standard. Driving performance generally improves with experience, and driving ultimately becomes an over-learned skill that is subconsciously retained and can readily be used as required. Impairments caused by health problems can interfere with driving performance.

The purpose of this evidence report is to summarize the available data on the relationship between TBI and CMV driver performance/crash risk. 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 (Figure 1). Anything that interferes with any of these factors to a significant degree may impair driving ability.(1) TBI leads to neurological damage that potentially affects motor control, range of motion, cognitive abilities, and other functions that may affect driving performance.

Figure 1. The Driving Task



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

Traumatic Brain Injury

TBI is an acute injury to the brain caused by an external mechanical force. Immediately following a TBI, patients usually experience a diminished or altered state of consciousness. TBI may lead to permanent or temporary impairments of cognitive, physical, and psychosocial functions.

Underlying Mechanism of Traumatic Brain Injury

There are two major classes of traumatic head injury—open and closed. Open head injuries tend to produce more discrete or focal lesions, while closed head injuries are more likely to cause generalized or diffuse cerebral damage.(2) Features of both types of injuries, however, may be seen in the same individual, depending on the nature of the injury.

An open head injury results when the scalp and skull are penetrated by an object (e.g., bullet, shell fragment, rock). The primary damage in such injuries tends to be localized around the path of the penetrating object. Primary damage may also result from penetrating bone fragments in the case of skull fractures. With proper medical care, including surgical cleansing of the wound and debridement, other areas of the brain usually remain intact and unharmed, unless the force of the impact was severe enough to produce remote lesions.(2)

The mechanical forces present in closed head injury produce a complex mixture of focal and diffuse damage to the brain. Focal damage results from inward compression of the skull at the point of impact and rebound effects.(2) The forces in such blows may literally bounce the brain off the inside of the skull at the point of impact and at the opposite side. As brain surfaces are pushed against the inside of the skull, the brain sustains contusion or bruising. Because of the shape of the inner surface of the skull, focal injuries are most commonly seen in the frontal and temporal lobes. The consequences of these injuries typically manifest as changes in the regulation of behavior, affect, emotions, executive functions, memory and attention. Cerebral contusions are readily identifiable on computed tomography (CT) scans, but might take a day or two to become visible.(3)

Diffuse axonal injury (DAI) is associated with high levels of acceleration and deceleration (e.g., whiplash injuries in motor vehicle accidents). The resulting twisting movement of the head causes high-velocity rotation of the brain within the skull, putting strain on delicate nerve fibers and blood vessels.(4) This can cause stretching, tearing, and shearing of these microscopic structures, which almost always result in widespread diffuse brain dysfunction. The most consistent effect of diffuse brain injury is altered consciousness, which occurs from a disruption of the nerve fibers in the brainstem reticular formation. DAI is only visible on CT scan in the worst 5% to 10% of cases, and is most commonly seen as multiple subcortical lesions in and around the corpus callosum and deep white matter (axons).(3) Injury to axons is thought to result in reduced speed in processing and responding to information and in attention deficits. Concussion is considered a mild form of DAI.(5)

Trauma to the head, whether from open or closed injury, is associated with both primary and secondary or delayed complications. Primary complications are the direct result of the impact and lead to a variable

degree of irreversible damage to the neurological tissue. Following the initial blow to the head, a negative chain of events occurs that causes ongoing complications in the brain (secondary complications). Secondary complications may result from intracranial causes (mass lesions, brain swelling, intracranial pressure, seizures, vasospasm or infection) and/or extracranial causes (hypotension, hypoxia, hypoglycemia, anemia, and electrolyte abnormalities). These injuries eventually lead to cerebral ischemia, inflammation, oxidative stress, and neuronal death.(4) TBI has also been associated with development of seizures in some patients; this can occur not only at the time of injury but also within days, weeks, months, or even years post-injury.(6)

The Epidemiology of Traumatic Brain Injury

According to the Centers for Disease Control and Prevention (CDC), each year at least 1.4 million Americans sustain a TBI (adjusted annual incidence rate of 85.5 per 100,000 population). Since some patients with mild TBI may not go to a hospital, this is probably an underestimate of the true number of TBIs. Among those who experience TBI, 50,000 die, 230,000 are hospitalized, and 80,000 to 90,000 experience the onset of long-term disability.(7) The National Institutes of Health Consensus Development Panel on Rehabilitation of Persons with TBI estimated that 2.5-6.5 million Americans live with TBI-related disabilities.(5) While the risk of having TBI is substantial among all age groups, this risk is highest among adolescents, young adults, and persons older than 75 years. The risk of TBI among males is twice the risk among females.(8)

According to information from the National Center for Health Statistics (NCHS), the leading causes of TBI are:

- Falls (28%; the leading cause of TBI; highest rates among the elderly [≥75 years] and children ages 0 to 4 years)
- Motor vehicle crashes (20%; the leading cause of TBI resulting in hospitalization)
- Other accidents involving striking or being struck by objects (19%)
- Violence, especially suicidal behavior and assaults that involve firearms (11%; the leading cause of TBI-related death)

Classification/Diagnosis of Traumatic Brain Injury

The severity of TBI is typically evaluated by the findings on computed tomography (CT) and magnetic resonance imaging (MRI) scans, the length of coma, and the length of post-traumatic amnesia (PTA).(9,10) Degrees of severity are differentiated as follows:

- Moderate and severe TBI lesions include contusions, hemorrhages, and hematomas, which are rare in mild head injury.
- Scores on the Glasgow Coma Scale (GCS), which reflect level of arousal as determined by the patient's motor, verbal, and eye responses, are stratified as follows: mild brain injury corresponds to a GCS score of 13 to 15, moderate corresponds to a score of 9 to 12, and severe injury corresponds to a score of 3 to 8.(11)

- PTA is defined as the length of time from the point of injury until the individual has a continuous memory for ongoing events.(12) The PTA in mild head injury usually lasts for seconds or minutes, whereas in moderate to severe brain injuries, PTA can last for days and weeks. In severe head injuries, PTA typically lasts 7 or more days. The presence of PTA is judged by using the Galveston Orientation Amnesia Test (GOAT).(13) The GOAT evaluates the major spheres of orientation (i.e., time, place, and person) and provides an estimation of the interval both prior to and following injury for which the patient is unable to recall events. Evaluating PTA can be difficult with confused or aphasic patients.
- Length of loss of consciousness (or length of coma, LOC) is also sometimes used as a measure of brain injury severity.(10) LOC is the length of time the patient is non-responsive, with longer periods of time typically associated with more severe brain injury. LOC less than 30 minutes usually corresponds to mild TBI, LOC of 30 minutes to 6 hours corresponds to moderate TBI, and LOC longer than 6 hours corresponds to severe TBI.(8) An alternative time frame for classification that has been used in some studies is LOC from 30 minutes to 24 hours for moderate TBI and LOC longer than 24 hours for severe TBI.(14) LOC should be used with some caution, however, as patients are sometimes unaware of whether they had a period of LOC. Injuries may have been unwitnessed and patients may have regained consciousness by the time they are evaluated.(10)

Among imaging technologies, CT is the modality of choice for acute TBI assessment in emergency settings. CT is more sensitive than MRI in detecting fractures, and it provides better detection of contusions, edema, hematoma, hemorrhage, and other signs of focal brain damage. MRI is the preferred modality in non-emergency settings, such as follow-up monitoring exams, as it provides better imaging of degenerative changes over time. White matter damage, generalized cerebral atrophy, water and edema, and lesions associated with seizures are easily captured by MRI. Follow-up MRI scans are considered more predictive of long-term outcome post-TBI than day-of-injury CT scans.(15)

Treatments for Traumatic Brain Injury

Individuals who experience a TBI need numerous clinical services. The U.S. Department of Education's National Institute on Disability and Rehabilitation Research (NIDRR) supports a model system of care that provides a coordinated continuum of care from onset of injury to long-term follow up to ensure optimal community integration.(16) The model system of care has been adopted by a number of medical centers throughout the United States. The following Web site provides information about the model systems of care and the centers that have adopted this model: http://www.tbindsc.org/Centers/centers.asp.

Treatment of TBI can be classified in three stages: acute, subacute, and chronic. Acute treatment is performed to stabilize the patient immediately after TBI. Subacute treatment occurs after stabilization but during hospitalization—rehabilitation to return patients to the community or to admit them to a chronic care facility. Chronic treatment consists of continued rehabilitation to treat long-term impairments of functional abilities.(17)

Acute Treatment

According to the model system, the first priority for moderate-to-severe head-injured patients is complete and rapid physiologic resuscitation.(16) Signs of impending transtentorial herniation (unilateral posturing

and/or unilateral dilated pupil) or of rapid progressive neurological deterioration (without extracranial cause) indicate the presence of significant intracranial hypertension, and measures to control intracranial pressure (ICP) should be immediately instituted. A variety of interventions are used to control ICP, commonly in a stepwise manner. They include hyperventilation, osmotherapy (mannitol or hypertonic saline), cerebral spinal fluid drainage, barbiturates, and decompressive craniectomy. Other less well-studied interventions include hypothermia, normobaric hyperoxia, and hyperbaric oxygen therapy. Once a patient is stabilized, a CT scan is administered to determine the extent of damage to the brain and the need of further treatment.

Most patients with mild TBI do not require acute treatment other than a brief observation period and over-the-counter pain medication for headache. A subset of these patients may require subacute treatment. This is discussed in the next section.

Subacute Treatment

Once a patient has been medically stabilized, the NIDRR recommends that comprehensive rehabilitation services be provided by an interdisciplinary team of professionals that may include rehabilitation nurses, physical and occupational therapists, speech pathologists, neuropsychologists, social workers, and pharmacists. The specific services and composition of the professional staff should, according to the model systems, be based on the needs of the patient. Further, services may be provided in-patient or out-patient, depending on the severity of the patient's brain injury and the extent of other injuries.(16)

Within the context of a comprehensive model of care, services may include one or more of the following:

- Cognitive rehabilitation therapy (CRT): designed to alleviate acquired neurocognitive impairment and disability.
- Physical therapy: treatment to restore normal physical functioning.
- Therapeutic recreation: treatment that focuses on resuming leisure activities, and community or social skills.
- Occupational therapy: treatment that typically focuses on re-training patients on skills related to daily living tasks, such as dressing, feeding, cooking, and shopping.
- Speech and language therapy: treatment that encompasses re-learning verbal and non-verbal communication skills.
- Psychotherapy: treatment that targets emotional issues related to experiencing a TBI.
- Vocational therapy: treatment designed to help patients reach maximal levels of employment. Vocational therapy may involve re-training on tasks related to a specific job, job counseling, job placement, and/or making changes to patients' work environment that will help them in their ability to perform their job.
- Pharmacotherapy: medications used during rehabilitation may include stimulants (e.g., methylphenidate and amphetamines) to treat the lethargy, inattention, and distractibility associated with TBI.(18) Neuroleptics, beta-blockers, or anti-depressants may also be used to treat associated restlessness and agitation.

Subacute treatment is necessary for patients with moderate or severe TBI, but it may also be necessary for patients with mild TBI who develop post-concussion syndrome (PCS). PCS is characterized by a persistence of various combinations of the following symptoms: nausea, headache, memory loss, emesis, dizziness, blurred vision, diplopia, sleep disturbances, or emotional lability. PCS typically lasts for two to four months, but occasionally may persist for more than a year. In rare instances PCS may lead to permanent disability. Severe or persistent PCS is usually treated with a combination of pharmaceutical therapy, mental health services, social services, and occupational therapy.

Chronic Treatment

For patients with moderate to severe TBI or persistent PCS, disabilities may last a lifetime, and chronic treatment is usually necessary. The two major categories of chronic treatment include community-based rehabilitation for return to work or school, and treatment of long-term consequences of the injury. Chronic treatment is generally provided at outpatient facilities or in the home, and may involve any of the treatments listed under subacute treatment.(17)

The Burden of Traumatic Brain Injury

The injuries that result from TBI have both short- and long-term effects on individuals, their families, and society. The financial cost of these injuries can be enormous. The estimated cost of providing inpatient rehabilitation care and services for a person with severe TBI over an average lifetime ranges from $600,000 to $1,875,000.(19) These estimates, however, do not include the additional costs stemming from lost wages of survivors or of family members who remain home to provide care. The estimated total cost of TBI-related work loss and disability in the United States is roughly $20.6 billion.(20)

CMV Drivers and Traumatic Brain Injury

In this section of the evidence report we examine the potential interaction between TBI, CMV drivers, and ability to drive a CMV.

Are CMV drivers at an increased risk for occurrence of TBI?

A recent study in Denmark compared rates of various injuries among drivers working for road goods-transport contractors to the rates in the age-standardized general workforce. During 2000–2003, the rate of concussion among these drivers was significantly greater than the corresponding rate among the general workforce.(21) A concussion indicates the occurrence of at least a mild TBI. The rate of moderate or severe TBI among CMV drivers compared with the general population is unknown.

What are the physical demands associated with CMV operation that potentially limit the ability of an individual with TBI to operate a CMV safely?

The act of CMV driving places a number of demands on the human body: if a condition compromises the ability to perform the tasks required to safely operate a motor vehicle, the results may include crash, injury, or death. The interplay of functional abilities with the safe operation of a motor vehicle was

explored by Mazer et al. (2004), who noted that shifting gears, use of the emergency brake, and the ability to use the steering wheel in both directions was largely a product of sufficient ROM.(22)

A list of functional abilities required for motor vehicle operation, the component of the driving process they involve, and the proposed solutions for individuals with disabilities was created by Jones et al. as a way of assessing driver performance.(23) It was considered necessary to have satisfactory performance in two or more of these functional abilities in order to drive. These functional abilities, divided into primary and secondary areas of importance for each of the tasks required to operate a motor vehicle, are featured in Table 2.

Table 2. Tasks Required to Operate a Motor Vehicle

Primary Area of Function	Secondary Area of Function	Component of Driving Process	Proposed Solutions
Hand	Upper limb	Manipulate seat belt Manipulate key Use hand brake	Non-inertia reel. Extend stem of seat belt attachment. Modify seat belt clip. Build up key. Convert vertical lever for knock on/off action. Keep car in gear when parked. Use accelerator/clutch for hill start. Buy automatic transmission car.
Upper limb	Hand	Open and close door Adjust mirror Use gears	Keep door hinges and handles oiled. Modify buttons. Enlarge door handles. Ask other car drivers to reposition mirror. Increase length of gear stick. Modify hand piece. Buy automatic transmission car. Modify automatic gear stock to "push down" type.
Upper limb	Upper spine	Reach seat belt Steer/corner	Hook belt around seat lever. Prevent full recoil of seat belt. Steering wheel cover to increase bulk of wheel. "Threading" steering technique. Increase front tire pressure. Power steering.
Upper spine	Upper limb	Reverse	Undo seat belt when reversing. Install wide rear view mirror. Install near and off side mirrors. "Reversing" with mirrors.
Lower spine	Lower limb	Seat comfort and position	Extend seat runners. Alter seat back position. Wedge cushions. Lumbar cushion.
Lower limb	Lower spine	Exit and enter vehicle Use foot pedals	Enter buttocks rather than legs first. Extend seat runners. Pedal modification. Automatic transmission car.
Supratentorial		Be aware of traffic and pedestrians Have confidence	Practice with experienced driver in quiet streets. Limit driving to familiar streets. Take lessons with qualified driving instructor.
Pain and fatigue on long drives			Frequent stops on long trips. Judicious use of non-steroidal anti-inflammatory drugs (NSAIDs) and analgesics. Establish a relaxed driving position.

Adapted from Jones et al.(23)

Of the functions listed in the table, TBI may affect coordination of upper and lower limbs as well as supratentorial function. Incoordination of movements could affect steering ability and reaction time when braking. Changes in behavior, memory, and attention could affect a patient's awareness of traffic and pedestrians while driving.

Traumatic Brain Injury and Driving Regulations

Because of temporary or permanent impairments of cognitive, physical, and psychosocial functions, the potential exists for drivers with TBI to be at increased risk for a motor vehicle crash. To provide for public

safety, U.S. federal and state laws have been created that set physical standards for individuals with cognitive or physical impairment.

Current Medical Fitness Standards and Guidelines for CMV Drivers in the United States

Current Medical Fitness Standards

FMCSA Regulations, found in 49 Code of Federal Regulations (CFRs) 301 through 399, cover businesses that operate CMVs in interstate commerce. FMCSA regulations that pertain to fitness to drive a commercial vehicle are in 49 CFR 391 Subpart E. 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 standard for fitness to drive a CMV (49 CFR 391.41(b) subpart 5) states the following (note: we list only the physical qualifications that may be relevant to individuals with a TBI. For a complete list of qualifications see: http://www.fmcsa.dot.gov/rules-regulations/administration/fmcsr/fmcsrruletext.asp?section=391.41):

A person is physically qualified to drive a CMV if that person —

- Has no impairment of:
    - a hand or finger that interferes with prehension or power grasping; or
    - an arm, foot, or leg that interferes with the ability to perform normal tasks associated with operating a CMV; or any other significant limb defect or limitation that interferes with the ability to perform normal tasks associated with operating a CMV; or has been granted a skill performance evaluation (SPE) certificate pursuant to § 391.49.
- Has no established medical history or clinical diagnosis of rheumatic, arthritic, orthopedic, muscular, neuromuscular, or vascular disease that interferes with his/her ability to control and operate a CMV safely.
- 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.

49 CFR 349 Alternative Physical Qualification Standards for the Loss or Impairment of Limbs

49 CFR 349 states the following:

(a) A person who is not physically qualified to drive under § 391.41(b)(1) or (b)(2) and who is otherwise qualified to drive a commercial motor vehicle may drive a commercial motor vehicle, if the Division Administrator, FMCSA, has granted a Skill Performance Evaluation (SPE) Certificate to that person.

(b) *SPE certificate.* -- (b)(1) *Application.* A letter of application for an SPE certificate may be submitted jointly by the person (driver applicant) who seeks an SPE certificate and by the motor carrier that will employ the driver applicant, if the application is accepted.

(b)(2) *Application address.* The application must be addressed to the applicable field service center, FMCSA, for the State in which the co-applicant motor carrier's principal place of business is located. The address of each, and the States serviced, are listed in § 390.27 of this chapter.

(b)(3) *Exception.* A letter of application for an SPE certificate may be submitted unilaterally by a driver applicant. The application must be addressed to the field service center, FMCSA, for the State in which the driver has legal residence. The driver applicant must comply with all the requirements of paragraph (c) of this section except those in (c)(1)(i) and (iii). The driver applicant shall respond to the requirements of paragraphs (c)(2)(i) to (v) of this section, if the information is known.

(c) A letter of application for an SPE certificate shall contain:

(c)(1) Identification of the applicant(s):

(c)(1)(i) Name and complete address of the motor carrier coapplicant;

(c)(1)(ii) Name and complete address of the driver applicant;

(c)(1)(iii) The U.S. DOT Motor Carrier Identification Number, if known; and

(c)(1)(iv) A description of the driver applicant's limb impairment for which SPE certificate is requested.

(c)(2) Description of the type of operation the driver will be employed to perform:

(c)(2)(i) State(s) in which the driver will operate for the motor carrier coapplicant (if more than 10 States, designate general geographic area only);

(c)(2)(ii) Average period of time the driver will be driving and/or on duty, per day;

(c)(2)(iii) Type of commodities or cargo to be transported;

(c)(2)(iv) Type of driver operation (*i.e.,* sleeper team, relay, owner operator, etc.); and

(c)(2)(v) Number of years' experience operating the type of commercial motor vehicle(s) requested in the letter of application and total years of experience operating all types of commercial motor vehicles.

(c)(3) Description of the commercial motor vehicle(s) the driver applicant intends to drive:

(c)(3)(i) Truck, truck tractor, or bus make, model, and year (if known);

(c)(3)(ii) Drive train;

(A) Transmission type (automatic or manual -- if manual, designate number of forward speeds);

(B) Auxiliary transmission (if any) and number of forward speeds; and

(C) Rear axle (designate single speed, 2 speed, or 3 speed).

(c)(3)(iii) Type of brake system;

(c)(3)(iv) Steering, manual or power assisted;

(c)(3)(v) Description of type of trailer(s) (*i.e.,* van, flatbed, cargo tank, drop frame, lowboy, or pole);

(c)(3)(vi) Number of semitrailers or full trailers to be towed at one time;

(c)(3)(vii) For commercial motor vehicles designed to transport passengers, indicate the seating capacity of commercial motor vehicle; and

(c)(3)(viii) Description of any modification(s) made to the commercial motor vehicle for the driver applicant; attach photograph(s) where applicable.

(c)(4) Otherwise qualified:

(c)(4)(i) The coapplicant motor carrier must certify that the driver applicant is otherwise qualified under the regulations of this part;

(c)(4)(ii) In the case of a unilateral application, the driver applicant must certify that he/she is otherwise qualified under the regulations of this part.

(c)(5) Signature of applicant(s):

(c)(5)(i) Driver applicant's signature and date signed;

(c)(5)(ii) Motor carrier official's signature (if application has a coapplicant), title, and date signed. Depending upon the motor carrier's organizational structure (corporation, partnership, or proprietorship), the signer of the application shall be an officer, partner, or the proprietor.

(d) The letter of application for an SPE certificate shall be accompanied by:

(d)(1) A copy of the results of the medical examination performed pursuant to § 391.43;

(d)(2) A copy of the medical certificate completed pursuant to § 391.43(h);

(d)(3) A medical evaluation summary completed by either a board-qualified or board-certified physiatrist (doctor of physical medicine) or orthopedic surgeon. The coapplicant motor carrier or the driver applicant shall provide the physiatrist or orthopedic surgeon with a description of the job-related tasks the driver applicant will be required to perform;

(d)(3)(i) The medical evaluation summary for a driver applicant disqualified under § 391.41(b)(1) shall include:

(A) An assessment of the functional capabilities of the driver as they relate to the ability of the driver to perform normal tasks associated with operating a commercial motor vehicle; and

(B) A statement by the examiner that the applicant is capable of demonstrating precision prehension (*e.g.,* manipulating knobs and switches) and power grasp prehension (*e.g.,* holding and maneuvering the steering wheel) with each upper limb separately. This requirement does not apply to an individual who was granted a waiver, absent a prosthetic device, prior to the publication of this amendment.

(d)(3)(ii) The medical evaluation summary for a driver applicant disqualified under § 391.41(b)(2) shall include:

(A) An explanation as to how and why the impairment interferes with the ability of the applicant to perform normal tasks associated with operating a commercial motor vehicle;

(B) An assessment and medical opinion of whether the condition will likely remain medically stable over the lifetime of the driver applicant; and

(C) A statement by the examiner that the applicant is capable of demonstrating precision prehension (*e.g.,* manipulating knobs and switches) and power grasp prehension (*e.g.,* holding and maneuvering the steering wheel) with each upper limb separately. This requirement does not apply to an individual who was granted an SPE certificate absent an orthotic device prior to the publication of this amendment.

(d)(4) A description of the driver applicant's prosthetic or orthotic device worn, if any;

(d)(5) Road test:

(d)(5)(i) A copy of the driver applicant's road test, administered by the motor carrier coapplicant and the certificate issued pursuant to § 391.31(b) through (g); or

(d)(5)(ii) A unilateral applicant shall be responsible for having a road test administered by a motor carrier or a person who is competent to administer the test and evaluate its results.

(d)(6) Application for employment:

(d)(6)(i) A copy of the driver applicant's application for employment completed pursuant to § 391.21; or

(d)(6)(ii) A unilateral applicant shall be responsible for submitting a copy of the last commercial driving position's employment application he/she held. If not previously employed as a commercial driver, so state.

(d)(7) A copy of the driver applicant's SPE certificate of certain physical defects issued by the individual State(s), where applicable; and

(d)(8) A copy of the driver applicant's State Motor Vehicle Driving Record for the past 3 years from each State in which a motor vehicle driver's license or permit has been obtained.

(e) *Agreement.* A motor carrier that employs a driver with an SPE certificate agrees to:

(e)(1) File promptly (within 30 days of the involved incident) with the Medical Program Specialist, FMCSA service center, such documents and information as may be required about driving activities, accidents, arrests, license suspensions, revocations, or withdrawals, and convictions that involve the driver applicant. This applies whether the driver's SPE certificate is a unilateral one or has a coapplicant motor carrier;

(e)(1)(i) A motor carrier who is a coapplicant must file the required documents with the Medical Program Specialist, FMCSA, for the State in which the carrier's principal place of business is located; or

(e)(1)(ii) A motor carrier who employs a driver who has been issued a unilateral SPE certificate must file the required documents with the Medical Program Specialist, FMCSA service center, for the State in which the driver has legal residence.

(e)(2) Evaluate the driver with a road test using the trailer the motor carrier intends the driver to transport or, in lieu of, accept a certificate of a trailer road test from another motor carrier if the trailer type(s) is similar, or accept the trailer road test done during the Skill Performance Evaluation if it is a similar trailer type(s) to that of the prospective motor carrier. Job tasks, as stated in paragraph (e)(3) of this section, are not evaluated in the Skill Performance Evaluation;

(e)(3) Evaluate the driver for those nondriving safety related job tasks associated with whatever type of trailer(s) will be used and any other nondriving safety related or job related tasks unique to the operations of the employing motor carrier; and

(e)(4) Use the driver to operate the type of commercial motor vehicle defined in the SPE certificate only when the driver is in compliance with the conditions and limitations of the SPE certificate.

(f) The driver shall supply each employing motor carrier with a copy of the SPE certificate.

(g) The State Director, FMCSA, may require the driver applicant to demonstrate his or her ability to safely operate the commercial motor vehicle(s) the driver intends to drive to an agent of the State Director, FMCSA. The SPE certificate form will identify the power unit (bus, truck, truck tractor) for which the SPE certificate has been granted. The SPE certificate forms will also identify the trailer type used in the Skill Performance Evaluation; however, the SPE certificate is not limited to that specific trailer type. A driver may use the SPE certificate with other trailer types if a successful trailer road test is completed in

accordance with paragraph (e)(2) of this section. Job tasks, as stated in paragraph (e)(3) of this section, are not evaluated during the Skill Performance Evaluation.

(h) The State Director, FMCSA, may deny the application for SPE certificate or may grant it totally or in part and issue the SPE certificate subject to such terms, conditions, and limitations as deemed consistent with the public interest. The SPE certificate is valid for a period not to exceed 2 years from date of issue, and may be renewed 30 days prior to the expiration date.

(i) The SPE certificate renewal application shall be submitted to the Medical Program Specialist, FMCSA service center, for the State in which the driver has legal residence, if the SPE certificate was issued unilaterally. If the SPE certificate has a coapplicant, then the renewal application is submitted to the Medical Program Specialist, FMCSA field service center, for the State in which the coapplicant motor carrier's principal place of business is located. The SPE certificate renewal application shall contain the following:

(i)(1) Name and complete address of motor carrier currently employing the applicant;

(i)(2) Name and complete address of the driver;

(i)(3) Effective date of the current SPE certificate;

(i)(4) Expiration date of the current SPE certificate;

(i)(5) Total miles driven under the current SPE certificate;

(i)(6) Number of accidents incurred while driving under the current SPE certificate, including date of the accident(s), number of fatalities, number of injuries, and the estimated dollar amount of property damage;

(i)(7) A current medical examination report;

(i)(8) A medical evaluation summary pursuant to paragraph (d)(3) of this section, if an unstable medical condition exists. All handicapped conditions classified under § 391.41(b)(1) are considered unstable. Refer to paragraph (d)(3)(ii) of this section for the condition under § 391.41(b)(2) which may be considered medically stable.

(i)(9) A copy of driver's current State motor vehicle driving record for the period of time the current SPE certificate has been in effect;

(i)(10) Notification of any change in the type of tractor the driver will operate;

(i)(11) Driver's signature and date signed; and

(i)(12) Motor carrier coapplicant's signature and date signed.

(j)(1) Upon granting an SPE certificate, the State Director, FMCSA, will notify the driver applicant and co-applicant motor carrier (if applicable) by letter. The terms, conditions, and limitations of the SPE certificate will be set forth. A motor carrier shall maintain a copy of the SPE certificate in its driver qualification file. A

copy of the SPE certificate shall be retained in the motor carrier's file for a period of 3 years after the driver's employment is terminated. The driver applicant shall have the SPE certificate (or a legible copy) in his/her possession whenever on duty.

(j)(2) Upon successful completion of the skill performance evaluation, the State Director, FMCSA, for the State where the driver applicant has legal residence, must notify the driver by letter and enclose an SPE certificate substantially in the following form:Skill Performance Evaluation Certificate Name of Issuing Agency: Agency Address: Telephone Number: ( ) Issued Under 49 CFR 391.49, subchapter B of the Federal Motor Carrier Safety Regulations Driver's Name: Effective Date: SSN:DOB:Expiration Date:Address:Driver Disability:Check One:_New_Renewal Driver's License:_____ (State) (Number)

In accordance with 49 CFR 391.49, subchapter B of the Federal Motor Carrier Safety Regulations (FMCSRs), the driver application for a skill performance evaluation (SPE) certificate is hereby granted authorizing the above-named driver to operate in interstate or foreign commerce under the provisions set forth below. This certificate is granted for the period shown above, not to exceed 2 years, subject to periodic review as may be found necessary. This certificate may be renewed upon submission of a renewal application. Continuation of this certificate is dependent upon strict adherence by the above-named driver to the provisions set forth below and compliance with the FMCSRs. Any failure to comply with provisions herein may be cause for cancellation.

CONDITIONS: As a condition of this certificate, reports of all accidents, arrests, suspensions, revocations, withdrawals of driver licenses or permits, and convictions involving the above-named driver shall be reported in writing to the Issuing Agency by the EMPLOYING MOTOR CARRIER within 30 days after occurrence.

LIMITATIONS: 1. Vehicle Type (power unit):* 2. Vehicle modification(s): 3. Prosthetic or Orthotic device(s) (Required to be Worn While Driving):4. Additional Provision(s):

NOTICE: To all MOTOR CARRIERS employing a driver with an SPE certificate. This certificate is granted for the operation of the *power unit only.* It is the responsibility of the employing motor carrier to evaluate the driver with a road test using the trailer type(s) the motor carrier intends the driver to transport, or in lieu of, accept the trailer road test done during the SPE if it is a similar trailer type(s) to that of the prospective motor carrier. Also, it is the responsibility of the employing motor carrier to evaluate the driver for those non-driving safety-related job tasks associated with the type of trailer(s) utilized, as well as, any other non-driving safety-related or job-related tasks unique to the operations of the employing motor carrier.

The SPE of the above named driver was given by a Skill Performance Evaluation Program Specialist. It was successfully completed utilizing the above named power unit and _____(trailer, if applicable)

The tractor or truck had a _____ transmission.

Please read the *NOTICE* paragraph above. Name:Signature:Title:Date:

(k) The State Director, FMCSA, may revoke an SPE certificate after the person to whom it was issued is given notice of the proposed revocation and has been allowed a reasonable opportunity to appeal.

(l) Falsifying information in the letter of application, the renewal application, or falsifying information required by this section by either the applicant or motor carrier is prohibited.

[65 FR 25287, May 1, 2000, as amended at 65 FR 59380, Oct. 5, 2000; 67 FR 61824, Oct. 2, 2002]

More extensive information on this topic is available at the *Conference on Neurological Disorders and Commercial Drivers* at: http://www.fmcsa.dot.gov/

Medical Fitness Standards and Guidelines for Individuals Performing Transportation Safety in the United States

Current medical fitness standards and guidelines for individuals performing transportation safety in the United States are summarized in Table 3. Included in the table are pertinent rules and guidelines for pilots, railroad workers, and merchant mariners.

Table 3. Standards and Guidelines Pertaining to Individuals with Musculoskeletal Disorders: FAA, Railroad, and Merchant Marine

Condition	FAA* (all classes of airmen)	Railroad†	Merchant Marine‡
Traumatic Brain Injury	Aerospace Medical Dispositions Item 46. Neurologic A history or the presence of any neurological condition or disease that potentially may incapacitate an individual should be regarded as initially disqualifying. Issuance of a medical certificate to an applicant in such cases should be denied or deferred, pending further evaluation. A convalescence period following illness or injury may be advisable to permit adequate stabilization of an individual's condition and to reduce the risk of an adverse event. Applications from individuals with potentially disqualifying conditions should be forwarded to the AMCD. Processing such applications can be expedited by including hospital records, consultation reports, and appropriate laboratory and imaging studies, if available. Symptoms or disturbances that are secondary to the underlying condition and that may be acutely incapacitating include pain, weakness, vertigo or incoordination, seizures or a disturbance of consciousness, visual disturbance, or mental confusion. Chronic conditions may be incompatible with safety in aircraft operation because of long-term unpredictability, severe neurologic deficit, or psychological impairment. The following lists the most common conditions of aeromedical significance and course of action that should be taken by the examiner as defined by the protocol and disposition in the table. Medical certificates must not be issued to an applicant with medical conditions that require deferral, or for any condition not listed that may result in sudden or subtle incapacitation without consulting the AMCD or the RFS. Medical documentation must be	No specific standards or guidelines	Potentially disqualifying conditions listed in the Physical Evaluation Guidelines for Merchant Mariner's Documents and Licenses include any disease or constitutional defect that would result in gradual deterioration of performance of duties, sudden incapacitation, in some other way compromise shipboard safety—including required response in an emergency situation. Neurologic disorders that are potentially disqualifying include chronic organic/traumatic brain syndrome and any condition that seriously limits balance or coordination. Any convulsive disorder resulting in an altered state of consciousness regardless of control by medication requires further evaluation. Waivers may be considered where extenuating circumstances are such to warrant special consideration and it can be demonstrated that the applicant can perform safely the duties of the license or merchant mariner document. Requests for waivers will be submitted to the National Maritime Center (NMC-4C) by the REC for review and a final determination.

Condition	FAA* (all classes of airmen)	Railroad†	Merchant Marine‡
	submitted for any condition in order to support an issuance of an airman medical certificate. (Note: we are only listing conditions that may result from traumatic brain injury) **Item 46. Neurologic-Headaches** **Neurologic-Hydrocephalus and Shunts** **Disease/condition** Post-traumatic headache Hydrocephalus, secondary to a known injury or disease process; or normal pressure **Evaluation Data** Submit all pertinent medical records, current neurologic report, to include name and dosage of medication(s) and side effects **Disposition** Requires FAA decision **Item 46. Neurologic – Presence of any neurological condition or disease that potentially may incapacitate an individual** **Disease/condition** Head Trauma associated with: Epidural or Subdural Hematoma; Focal Neurologic Deficit; Depressed Skull Fracture; or Unconsciousness or disorientation of more than 1 hour following injury **Evaluation Data** Submit all pertinent medical records, current status report, to include pre-hospital and emergency department records, operative reports, neurosurgical evaluation, name and dosage of medication(s) and side effects **Disposition** Requires FAA decision **Item 46. Neurologic – Spasticity, Weakness, or Paralysis of the Extremities** **Disease/condition** Conditions that are stable and non-progressive may be considered for medical certification **Evaluation Data** Submit all pertinent medical records, current neurologic report, to include etiology, degree of involvement, period of stability, appropriate laboratory and imaging studies **Disposition** Requires FAA decision		

*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/item46/amd/

†Source of information for Federal Railroad Administration Guidelines: http://www.fra.dot.gov/us/content/1586

‡Source of information for Merchant Mariner Guidelines: http://www.uscg.mil/hq/cg5/nvic/pdf/1998/n2-98.pdf

AMCD: Aerospace Medical Certification Division
FAA: Federal Aviation Association
REC: Regional examination center
RFS: Regional flight surgeon

Regulatory Medical Fitness Standards for the United States and Selected Countries

The United States and other countries have established regulatory medical fitness standards for the protection and safety of the public interest, including licensed drivers. The medical standards are used to assess and determine the fitness of drivers operating CMVs. Likewise, TBI is defined (some countries use the term head injury), and the criteria for establishing these standards are constructed. Each country demonstrates its interpretation of TBI through definition and by determining the relevant population(s).

Regulatory standards and guidelines pertaining to TBI and CMV driving in several selected countries are presented in Table 4. We have included separate categories for certain sequelae or complications of TBI, such as cognitive impairments, intracranial hematoma, and post-traumatic seizure.

Table 4. Regulations and Guidelines Pertaining to Musculoskeletal Disorders and CMV Driving from Selected Countries

TBI or TBI-related Disorder	Australia	Canada	UK	New Zealand	Sweden
Reference source	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)	Determining medical fitness to operate motor vehicles. CMA (Canadian Medical Association) Driver's Guide 7th edition. (2006)	At-a-glance Guide to the current Medical Standards of Fitness to Drive (for Medical Practitioners) Issued by Drivers Medical Group. Driver and Vehicle Licensing Agency (DVLA), Swansea (September 2008)	Medical aspects of fitness to drive: A Guide for Medical Practitioners. Land Transport Safety Authority. (May 2002)	Swedish National Road Administration Statute Book (1999)
Traumatic brain injury or head injury	The criteria for an unconditional license are NOT met: • If the person has had head injury causing chronic functional disturbances. A conditional license may be granted by the Driver Licensing Authority, taking into account the opinion of an appropriate specialist, and the nature of the driving task, and subject to periodic review, taking into account factors including: • Medical assessment; • Neuropsychological testing; • Driver assessment (see also Cognitive Impairment); and • Other disabilities that may impair driving as per this publication.	**14.4.1 Immediate injury assessment** To drive safely, TBI survivors require insight into their disability, as well as • Adequate reaction times • Adequate ability to coordinate visual-motor function (for steering) • Adequate leg function for braking (or ability to use adaptive technology) • Adequate ability to divide attention to perform multiple simultaneous tasks • Enough responsibility to comply reliably with the rules of the road and to drive within any conditions set by the licensing authorities Knowledge about the effects of TBI, a careful history, information from family or other reliable informants and additional cognitive screening will help the physician make the best decisions. If cognitive or significant physical deficits are found, consider referral for rehabilitation assessment. If there were observations of the patient appearing confused immediately after the crash, even if only for a brief period, or if symptoms of concussion are evident, the patient should be advised not to drive until medically cleared to do so.	**Serious head injury** (compound depressed fracture requiring surgical treatment) or **significant head injury** (e.g. brain contusion without surgery) CMV drivers – Refusal or revocation of license. May be able to return to driving when the risk of seizure has fallen to no greater than 2% per annum, and with no debarring residual impairment likely to affect safe driving	**Minor head injury** A minor head injury should not impair driving ability for more than a few hours. An individual who sustains a minor head injury without loss of consciousness or any other complication should not drive for 3 hours. An individual who sustains a minor head injury but does lose consciousness should not drive for 24 hours and should have a medical assessment before returning to driving. An extension of the recommended periods that an individual should refrain from driving may be necessary if an individual exhibits loss of good judgment, decreased intellectual capacity, post-traumatic seizures, visual impairment or loss of motor skills. He or she should not be allowed to drive until cleared as fit to drive by a medical practitioner, having referred to the appropriate section of this guide. **Serious head injury** Serious head injuries, such as acute intracerebral hematoma requiring surgery or compound depressed fracture or dural tear or with more than 24 hours posttraumatic amnesia, present a number of problems with respect to driving safety.	**Acquired Brain Damage (including TBI)** A serious cognitive disturbance constitutes grounds for denial of possession. Disturbances in attention, judgment and memory, in visuospatial and psychomotor functions shall be taken into special consideration when making a medical assessment. The presence of emotional lability and increased fatigability shall also be taken into consideration. Regarding possession in Groups II and III, due consideration shall be given to the additional risks and dangers to traffic safety involved in such possession. **Reappraisal** Should occur at intervals considered suitable in each individual case.

TBI or TBI-related Disorder	Australia	Canada	UK	New Zealand	Sweden
		14.4.2 Long-term injury assessment The TBI survivor often has poor insight and awareness of the acquired deficits. The role of self-awareness of deficits is central in determining whether an individual with residual deficits may be able to drive safely. Collateral history is essential, as the TBI patient may lack insight. A history and physical are not enough to assess fitness to drive after TBI adequately when any signs of concussion or brain injury have been evident. Standard neurologic examination cannot always determine the presence or absence of cognitive dysfunction after TBI. In these cases, additional objective information is useful to support opinion. In addition to the standard visual acuity requirements, a minimal assessment should include visual field testing and cognitive screening (to assess memory, attention, reaction time, visual perception and visual-motor skills). **14.5 Functional impairment** The lack of consensus on measurement of cognitive indices continues to make this a problematic issue. If medical assessment alone is not sufficient to determine driving suitability, then further evaluation by medical specialists, neuropsychological testing or formal comprehensive driving assessment may give a more accurate evaluation and help to develop a better understanding of specific driving problems.		Serious head injuries carry a risk of post-traumatic epilepsy, which is much more common after penetrating (open) head injuries, particularly with dural penetration, injuries complicated by intradural (not subdural) hemorrhage and depressed fractures of the cranial vault. In addition, there may be associated post-injury cognitive and behavioral problems that may make it unsafe for an individual to drive, as well as post-traumatic physical disabilities that may make driving difficult or require vehicle modifications. It is imperative that all cases are fully and properly assessed before there is any suggestion of a return to driving. Most individuals with severe head injuries, including those with post concussion syndrome, should not drive within six months of the event, and a return to driving should be subject to medical practitioner assessment. **When driving should cease (CMV drivers)** Driving should cease for a period of 12 months minimum following severe head injuries, depending on the circumstances and the range of post-traumatic problems. The existence of post-traumatic epilepsy will require the application of the same rules as for tonic-clonic epilepsy. Generally the only exception to this would be the occurrence of immediate seizures (normally in the first 24 hours after injury), which are considered part of the acute process.	

TBI or TBI-related Disorder	Australia	Canada	UK	New Zealand	Sweden
				When driving may resume or may occur Most severe head injuries will result in the driver being considered unfit to drive. Individuals with severe head injuries should not drive for at least 12 months and there has been adequate evidence of a recovery sufficient to allow for safe driving relative to an individual's occupation. A specialist neurological assessment is required. In addition, an occupational therapist assessment is recommended.	
Intracranial hematoma			CMV drivers – refusal or revocation of license. Return to driving will depend on specialist assessment (risk of seizure must have fallen to no greater than 2% per annum) with no debarring residual impairment likely to affect safe driving.		
Cognitive impairments	The criteria for an unconditional license are NOT met: • If the person's dementia or cognitive impairment is confirmed A conditional license may be granted by the Driver Licensing Authority, taking into account the opinion of an appropriate specialist, and the nature of the driving task, and subject to periodic review after consideration of the following: • The cause of the condition and likely response to treatment; • Any appropriate neuropsychological tests; and • The results of a practical driving test. Intellectual Impairment (IQ <70) The criteria for an unconditional license are NOT met for intellectual impairment of such severity that it may affect driving safety.				

TBI or TBI-related Disorder	Australia	Canada	UK	New Zealand	Sweden
Post-traumatic seizure		A patient with a head injury may resume driving after a single post-traumatic seizure under certain conditions. **Commercial drivers**. A patient with a single post-traumatic seizure should not drive for at least 12 months and not until a complete neurological evaluation, including EEG with sleep recording and appropriate brain imaging, has been carried out.	Provoked seizures: for regular and possible commercial drivers or applicants, provoked or acute symptomatic seizures may be dealt with on an individual basis by DVLA if there is no previous seizure history. Provoked seizures include an immediate seizure (within seconds) at the time of a head injury, or seizure in the first week following a head injury, which is not associated with any damage on CT scanning, nor with posttraumatic amnesia of longer than 30 minutes.		
General	General Management Guidelines Dementia and other cognitive impairments. The person should not drive if there is significant impairment of memory, visuospatial skills, insight or judgment or if there are problematic hallucinations or delusions. Baseline and periodic review are required as most forms of cognitive impairment and dementia are progressive. Intellectual impairment. The severity of intellectual impairment should be judged individually and rely on appropriate professional advice, including neurological and neuropsychological advice. The Driver Licensing Authority will require a test by a driver assessor before considering the issue of a license or conditional license. Head Injury. A person who recovers from a loss of consciousness of less than 24 hours with no complications does not present any special risk. Similarly, immediate seizures that occur within 24 hours of a head injury are not considered to be epilepsy, but part of the acute process. Persons who have had minor head injuries should not drive immediately afterwards. The	Traumatic brain injury can cause symptoms that can lead to unsafe driving yet are difficult to detect (e.g., visual field defects). A careful history and physical examination, including an assessment of insight and judgment, are important. If a problem that may affect driving is suspected, then a comprehensive driver evaluation is the most practical method of determining fitness to drive. Where resources are available, assessment by a trained occupational therapist would be optimal. A motor vehicle licensing authority road test can be helpful in assessing functional capacity to drive. However, it cannot always be relied on to reveal the true extent of the disability, both because of the fluctuating nature of the symptoms and the examiner's inability to evaluate all potentially related physical and cognitive issues.	At age 70, the DVLA requires confirmation that no medical disability is present. After age 70, the maximum license period is 3 years, subject to a satisfactory completion of medical questions. Drivers have an obligation to declare medical conditions that may affect driving safety.		

TBI or TBI-related Disorder	Australia	Canada	UK	New Zealand	Sweden
	occurrence of persisting functional disturbances requires careful assessment to determine the driver's future license status, particularly for commercial vehicle drivers. This may include neuropsychological testing and practical driver assessment as well as referral to a neurologist.				

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, and the criteria used. The criteria include 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, etc., are documented in appendices.

Key Questions

This evidence report addresses four key questions. The FMCSA developed each question so that the answers would provide information useful in updating its current medical examination guidelines. The four key questions addressed in this evidence report are:

Key Question 1: What is the impact of traumatic brain injury on crash risk/driving performance?

Key Question 2: What factors associated with traumatic brain injury are predictive of increased crash risk or poor driving performance?

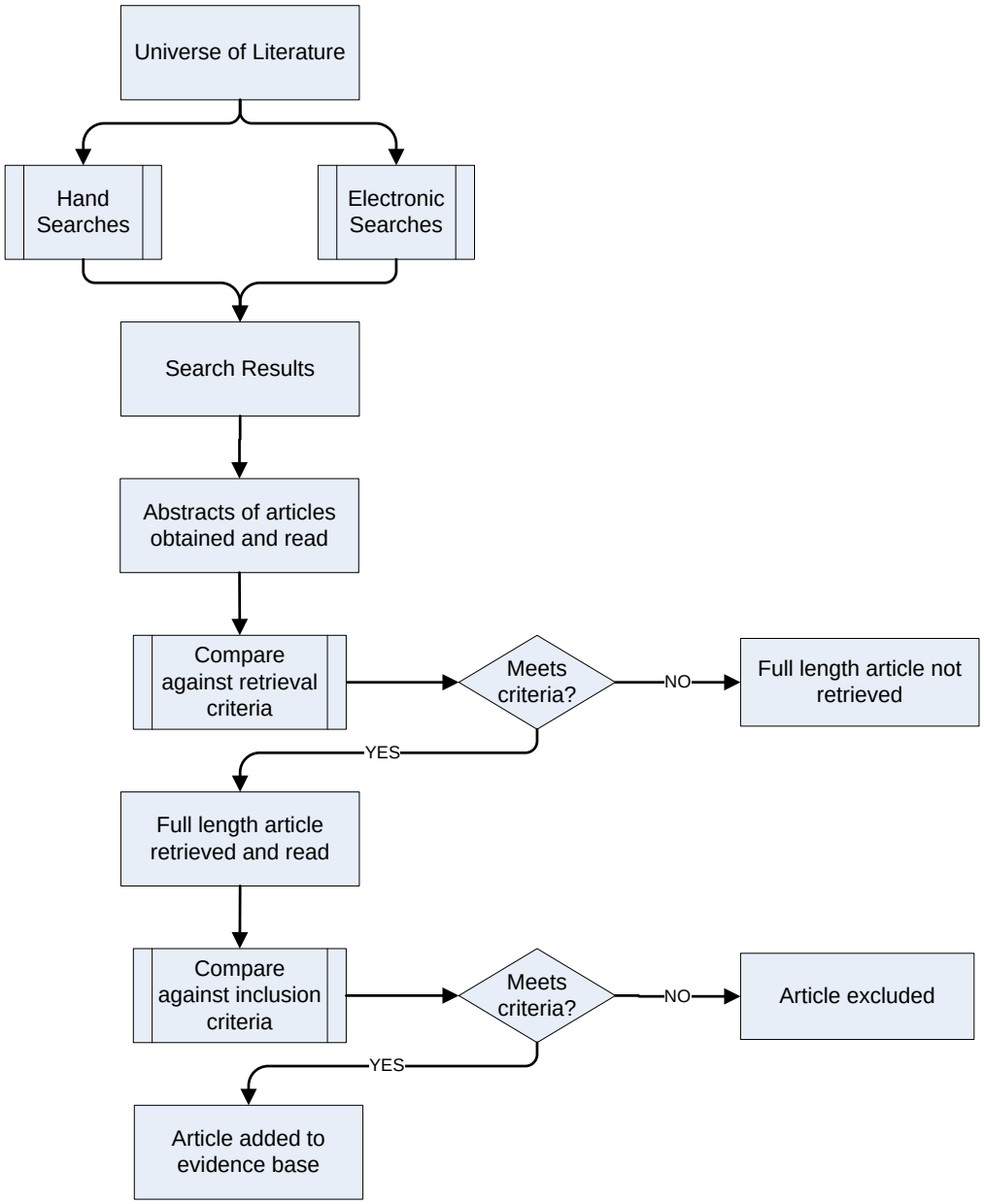
Key Question 3: What is the impact of rehabilitation programs on crash risk/driving performance among individuals with a traumatic brain injury?

Key Question 4: What is the likelihood of a future seizure among individuals with a traumatic brain injury who did not experience a seizure at the time of the injury?

Identification of Evidence Bases

The individual evidence bases for each of the four key questions addressed in this evidence report were identified using the multistage process captured by the algorithm presented in Figure 2. The first stage of this process consists of a comprehensive search of the literature. The second stage consists of the examination of abstracts of identified studies to determine which articles will be retrieved. The final stage consists of selection of the actual articles that will be included in the evidence base.

Figure 2. 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, which 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 5. A full description of these searches appears in Appendix A.

Table 5. Electronic Databases Searched

Name of Database	Date Limits	Platform/Provider
The Cochrane Central Register of Controlled Trials (CENTRAL)	Through 2009 Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2009 Issue 1	http://www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2009 Issue 1	http://www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2009 Issue 1	http://www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through March 20, 2009	OVID
Health Technology Assessment (HTA) Database	Through 2009 Issue 1	http://www.thecochranelibrary.com
MEDLINE	1950 through March 20, 2009	OVID
PubMed (PreMEDLINE)	Searched March 20, 2009	http://www.pubmed.gov
TRIS Online (Transportation Research Information Service Database)	Searched January 8, 2009	http://ntlsearch.bts.gov/tris/index.do
U.K. NHS Economic Evaluation Database (NHS EED)	Through 2009 Issue 1	http://www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched February 16, 2009	http://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—reports, studies, articles, and monographs produced by federal and local government agencies, private organizations, educational facilities, consulting firms, and corporations. These documents do not appear in 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 an article did not 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, are presented in Appendix D.

Evaluation of Quality and Strength of Evidence

Rather than focus on the quality of the individual studies that comprise 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.(24) Using this approach, which is described briefly in Appendix E, we took into account not only the quality of the individual studies that comprise the evidence base for each key question, but also 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., “Driving performance was significantly impaired among Individuals with TBI compared with uninjured controls”) and a quantitative conclusion (e.g., “When compared to individuals who do not have TBI, the risk ratio for a motor vehicle crash among individuals with TBI is X”). As shown in Table 6, we assigned a separate strength-of-evidence rating to each type of conclusion. Evidence underpinning a qualitative conclusion was rated according to its strength, and evidence underpinning a quantitative conclusion was rated according to the stability of the effect-size estimate that was calculated.

Table 6. 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 effecting 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. If appropriate, random- effects meta-analyses were used to pool data from different studies.(25-34) Important differences in the findings of different studies (heterogeneity) were identified using I^2.(30,35-40) Whenever appropriate, heterogeneity was explored using meta-regression techniques.(41-43) Sensitivity analyses, aimed at testing the robustness of our findings, were performed using cumulative random-effects meta-analyses.(44-50) When possible, the presence of publication bias was tested for using the "trim and fill" method.(51) Any meta-analyses in this evidence report were performed using Comprehensive Meta-Analysis software.(52-54)

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 (SMD). 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 7. 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.(55)

Table 7. 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 TBI who crashed; pt_{msd} = rate denominator (TBI group); b = number of individuals without TBI who crashed; $pt_{control}$ = rate denominator (control group)		
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 TBI who crashed; b = number of individuals without TBI who crashed; c = number of individuals with TBI who did not crash; d = number of individuals without TBI 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} = logrank expected number of events in treatment group; E_{ci} = logrank expected number of events in control group		

HR = Hazard ratio; OR = Odds ratio; RR = Rate ratio; SMD = Standardized mean difference; TBI = Traumatic brain injury; 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: What is the impact of traumatic brain injury on crash risk/driving performance?

Introduction

TBI is a concern to those responsible for road safety because of the potential cognitive, psychosocial, sensory, and motor impairments that can occur, particularly in cases of severe TBI. These impairments may contribute to an increased likelihood for a motor vehicle crash. Coupled with concerns about the impact of TBI on crash risk is the potential increase in the number of brain-injured persons who may, in the very near future, attempt to obtain a CMV license. This increase is conjectured based on the active recruitment by the trucking industry of veterans[1] from the ongoing conflicts in Iraq and Afghanistan,(57,58) a population with a higher prevalence of TBI than veterans of previous wars owing to the predominance of blast-related injuries and higher survival rates because of protective armor.(59,60) Furthermore, many cases of mild TBI may remain undiagnosed, particularly in cases of closed brain injury where soldiers have sustained more serious injuries concurrent with TBI.(61)

The active recruitment of military veterans by the trucking industry was initiated in response to a projected shortfall in the number of professional CMV drivers.(56,62) According to the American Trucking Association, the industry currently needs an additional 20,000 individuals to provide professional transportation; by 2014 the shortfall is expected to rise to 111,000 because of retirement, a lack of past recruitment, and increased demand.(63)

In this section we review the evidence pertaining to the crash risk and/or effect on driving ability associated with TBI. The purpose of this review is to determine whether TBI poses a risk to road safety inasmuch as it may affect the ability to perform the functions required to operate a CMV.

Identification of Evidence Base

To meet the aims of this section of the evidence report, we searched for trials that compared crash risk or driving ability among individuals who had sustained TBI and otherwise comparable individuals with no TBI. In addition, we looked for studies that compared the prevalence of TBI among cohorts of individuals who had or had not experienced a crash or among individuals who had or had not scored poorly on road tests, simulated driving, or functional tests.

[1] In testimony given before the Subcommittee on Economic Opportunity of the House Committee on Veterans Affairs (May 3, 2007) the President of the Truckload Carriers Association (TCA) North America asserted that the perceived skills military veterans brought to truck driver training made them particularly attractive to the transportation industry.(56)

The evidence-base identification pathway for Key Question 1 is summarized in Figure 3. Our searches[2] identified 968 articles that appeared relevant to this key question. Following application of the retrieval criteria for this question, 30 full-length articles were retrieved and read in full. Nine of the 30 retrieved articles were ultimately found to meet the inclusion criteria[3] for Key Question 1 (Table 8). Table D-1 of Appendix D lists the 21 articles that were retrieved, read in full, and then excluded.

Figure 3. Development of Evidence Base for Key Question 1

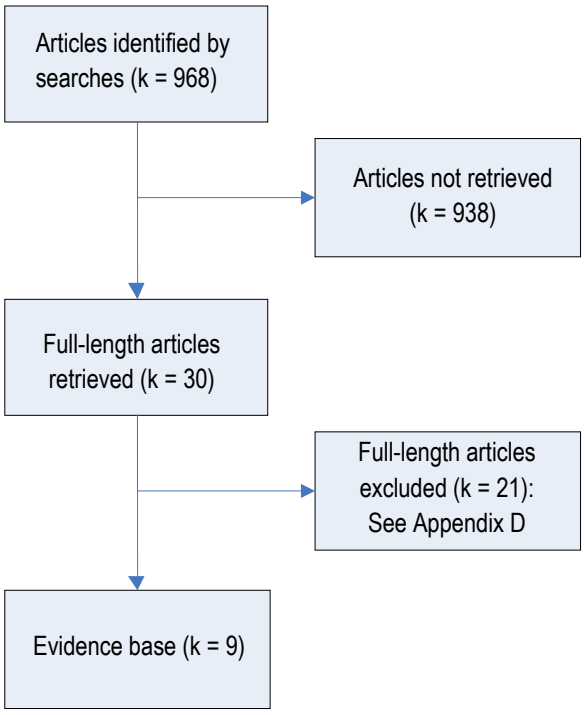


Table 8. Evidence Base for Key Question 1

Reference	Year	Study Location	Country
Studies that Evaluated Crash Data			
Schanke et al.(64)	2008	Nesoddtangen	Norway
Formisano et al.(65)	2005	Rome	Italy
Schneider and Gouvier(66)	2005	Baton Rouge, LA	USA
Schultheis et al.(67)	2002	West Orange and Newark, NJ	USA
Haselkorn et al.(68)	1998	Seattle, WA	USA
Studies that Evaluated Driving Performance (On-road or Simulation)			
Cyr et al.(69)	2008	Ottawa, Ontario	Canada
Lew et al.(70)	2005	Palo Alto, CA	USA
Korteling(71)	1990	Soesterberg	The Netherlands
Kewman et al.(72)	1985	Ann Arbor, MI	USA

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

Evidence Base

This subsection provides a brief description of the key attributes of the nine studies that comprise the evidence base for Key Question 1. Here we discuss applicable information on the quality of the included studies and the generalizability of each study's findings to CMV drivers. The key attributes of each included study are presented in Table 9. All studies used a cohort design that compared patients with TBI with a control (uninjured) population and assessed outcomes related to crash risk or driving performance.

Five retrospective studies measured the rate or risk of motor vehicle crash in the compared cohorts. Four of the five studies relied on self-report of crash, while the fifth study obtained crash records from a state licensing database. Information from databases is considered more reliable than information obtained from self-reporting. Only one study controlled for actual miles driven, which is an important potential confounder when comparing injured and uninjured cohorts (drivers with TBI may not drive as often or as far as healthy drivers). The other studies only controlled for the time period during which the crashes took place. However, all five studies controlled for age, which is another important potential confounder.

Four prospective studies measured on-road or simulated driving performance. Two studies evaluated simulator outcomes, one study evaluated on-road performance, and the remaining study evaluated both simulated and on-road performance. Only one of the studies reported controlling for miles driven, although this may be a less important factor for comparison of these indirect measures. Three of the studies controlled for age and gender, while the remaining study did not control for any potential confounding factors.

Table 9. Key Study Design Characteristics of Studies that Address Key Question 1

Reference	Year	Study Design	Objective	Comparison	Prospective or Retrospective?	Factors Controlled for?	Driving Exposure Controlled for?	Outcomes Relevant to KQ1	Definition of Crash	Outcome Self-reported?
TBI and Crash Risk										
Schanke et al.(64)	2008	Cohort	Follow-up of accident rate and driving patterns of patients 6-9 years after brain injury	TBI patients vs. population normative data (Norway)	Retrospective	Miles driven, age, gender	Yes	Crash	Motor vehicle accidents reported to police or insurance companies	Yes
Formisano et al.(65)	2005	Cohort	To investigate the road traffic accident rate in patients who have resumed driving after severe brain injury	TBI patients vs. expected crash rate for young males in Italy	Retrospective	Age, gender, years of driving exposure	Partly (crashes that occurred during 5 years, but miles driven not controlled for)	Crash	Unclear	Yes
Schneider and Gouvier(66)	2005	Cohort	To examine the utility of the Useful Field of Vision (UFOV) in predicting accidents among individuals with mild TBI and noninjured controls	TBI patients vs. uninjured controls	Retrospective	Age, gender, race	Partly (crashes that occurred in both groups during a 2-year period)	Crash	NR	Yes
Schultheis et al.(67)	2002	Cohort	To examine objective and subjective measures of driving behaviors in the last 5 years for individuals with TBI and healthy controls	TBI patients vs. uninjured controls	Retrospective	Age, education, years of driving experience	Partly (accidents that occurred in both groups during a 5-year period)	Crash	Reported accidents (reported to police or insurance companies) Unreported accidents (not reported to police or insurance companies)	Yes
Haselkorn et al.(68)	1998	Cohort	To determine whether individuals with TBI or stroke have an increased risk of subsequent motor vehicle crash or moving violation	TBI patients vs. matched nonhospitalized controls	Retrospective	Age, gender, zip code	Partly (accidents that occurred in both groups during a 2-year period from the same reference date)	Crash	Motor vehicle crashes reported in database	No, records from Washington state Department of Licensing (DOL)

Reference	Year	Study Design	Objective	Comparison	Prospective or Retrospective?	Factors Controlled for?	Driving Exposure Controlled for?	Outcomes Relevant to KQ1	Definition of Crash	Outcome Self-reported?
TBI and Driving Performance (on-road test or simulation)										
Cyr et al.(69)	2008	Cohort	To examine the role of impaired divided attention and speed of processing in TBI drivers in high-crash-risk simulated road events	TBI drivers vs. uninjured controls	Prospective	Age, gender	NR	Simulator crashes	NA	No
Lew et al.(70)	2005	Cohort	To evaluate whether driving simulator and road test evaluations can predict long-term driving performance in patients with moderate to severe TBI	TBI patients vs. uninjured controls	Prospective	Age and gender were similar but not perfectly matched	NR	Driving simulator outcomes	NA	No
Korteling(71)	1990	Cohort	To identify variables that may be sensitive to the effects of brain damage or aging and to determine how reaction time (RT) tasks relate to driving performance	TBI patients vs. uninjured controls	Prospective	Age, gender, educational level, and kilometers driven over a 3-year period	Yes	Simulated and on-road driving tasks	NA	No
Kewman et al.(72)	1985	Cohort	To test whether a training program composed of a set of visuomotor and attentional tasks would generalize to a complex functional skill (automobile driving)	TBI patients vs. uninjured controls	Prospective	None	No	On-road driving performance	NA	No

NA: Not applicable
NR: Not reported
TBI: Traumatic brain injury

Quality of Evidence Base

The findings of our assessment of the quality of the studies that comprise the evidence base for Key Question 1 are summarized in Table 10. Complete details of our quality assessment can be found in Table G-1 presented in Appendix G. Our assessment found that the median quality of the included studies that directly assessed crash risk was moderate (two low-quality studies and three moderate-quality studies). The median quality of the four studies that measured driving performance was also moderate (three studies were moderate quality; one was low quality). Although observational studies may statistically adjust for known confounding factors, only random allocation can control for unknown confounding; however, random allocation is not possible in this study design. Therefore, the quality rating of cohort studies can never be high. Low-quality scores were mostly caused by a lack of independent or blind outcome assessment plus retrospective study design and/or failure to control for factors that might affect study outcomes.

Table 10. Quality of the Studies that Assess Key Question 1

Reference	Year	Quality Scale Used	Quality
TBI and Crash Risk			
Schanke et al.(64)	2008	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Formisano et al.(65)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low
Schneider and Gouvier(66)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low
Schultheis et al.(67)	2002	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Haselkorn et al.(68)	1998	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
TBI and Driving Performance (On-road Test or Simulation)			
Cyr et al.(69)	2008	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Lew et al.(70)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Korteling(71)	1990	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Kewman et al.(72)	1985	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the nine studies that comprise the evidence base for Key Question 1 are presented in Table 11. As noted in the table, direct evidence pertaining to the effect of TBI 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. Therefore, the generalizability of our findings 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. Average age of patients in these studies ranged from 22 to 45; most therefore had a somewhat younger patient population on average than is typical of the CMV driver population. The percentage of males ranged from 40% to 100%, with the majority of studies reporting percentages of 65% to 89%. This means that women are somewhat overrepresented in most of these studies compared with the CMV driver population.

Factors that could potentially lead to differences among individual study results are the severity of TBI among the enrolled patients, and to a lesser extent, the methods used to classify severity. Three of the five crash studies did not report the severity of TBI; of the remaining two, one enrolled only patients with severe TBI and the other enrolled only patients with mild TBI. The studies of on-road or simulated driving performance showed more consistency among their study populations, with three of four studies enrolling a mixed population of patients with moderate or severe TBI. The fourth study enrolled only patients with severe TBI. Of the studies that reported methods of severity classification, two used LOC, one used GCS score, one used GCS score plus LOC, and one used length of post-traumatic amnesia.

Table 11. Characteristics of Patients with TBI Enrolled in Studies that Address Key Question 1

Reference	Year	Number of Individuals with TBI	Severity of TBI	Method of classifying severity	Number Driving vs. Number Not Driving	Age Distribution	% Male	% CMV Drivers	Driving Exposure	Ethnicity
TBI and Crash Risk										
Schanke et al.(64)	2008	28	NR	NR	28 driving	Mean (SD): 45.8 (14.8)	89	NR	81.5% drove daily, 14.8% weekly, 3.7% "seldom"	NR
Formisano et al.(65)	2005	90	Severe	GCS score and LOC ≥48 hours	29 driving 61 not driving	Drivers: 28.4 (9.6)	83	NR	NR	NR
Schneider and Gouvier(66)	2005	40	Mild (90%) Moderate (10%)	Length of post-traumatic amnesia	40 driving	22 (4.1)	40	0	NR	Caucasian: 85% African-American: 12.5% Hispanic: 2.5%
Schultheis et al.(67)	2002	47	NR	NR	40 driving 7 not driving	39.2 (19.5)	72.3	NR	69% drove ≥5 days/week 31% drove <5 days/week	NR
Haselkorn et al.(68)	1998	896	NR	NR	NR	Range: 16 to >70	69.1	NR	NR	NR
TBI and Driving Performance (On-road Test or Simulation)										
Cyr et al.(69)	2008	17	Moderate (n = 2) or Severe (n = 15)	GCS score	17 driving	39.5 (11.0)	64.7	NR	NR	NR
Lew et al.(70)	2005	11	Moderate or severe	NR	11 driving	29 (12) Range: 18 to 58	82	NR	NR	NR
Korteling(71)	1990	30	Moderate or severe	LOC	NR	30 (range 21 to 43)	100	NR	NR	NR
Kewman et al.(72)	1985	24	Severe	LOC	No individuals with TBI driving	Mean: 24.2	NR	NR	NR	NR

GCS: Glasgow Coma Scale
LOC: Length of coma
NR: Not reported
SD: Standard deviation
SEM: Standard error of the mean

Findings

Our searches identified nine studies that attempted to determine whether individuals with TBI are at an increased risk for a motor vehicle crash. The findings of these studies are presented below.

Direct Evidence —Crash Studies

Five studies attempted to directly determine crash risk among drivers with TBI through evaluation of self-reported crashes or crashes recorded in a state licensing database. Table 12 summarizes the individual study findings.

The studies by Schanke et al. and Formisano et al. reported crash rates among their enrolled patients with TBI compared with expected number of crashes based on normative population data for the countries in which the studies were conducted (Norway and Italy). Both studies reported that the difference between observed and expected rates was statistically significant.(64,65) This was based on calculation of cumulative probabilities assuming a Poisson distribution. However, because there is uncertainty in the degree of error for the expected number of crashes, we calculated rate ratios and used a more conservative method (logarithmic transformation) for calculating 95% confidence intervals. This conservative method resulted in p-values that did not quite reach statistical significance. Since the findings of these studies depend on the statistical assumptions of the analysis, this means that at best the data suggest a non-robust trend toward increased crash risk among individuals with TBI. The study by Schanke et al. was the only study of the five that evaluated crash risk to adjust for kilometers driven, which is possibly the most important potential confounding variable.

Two studies (Schultheis et al. and Haselkorn et al.) reported number of crashes among individuals with TBI vs. healthy controls and calculated odds ratios for these numbers. Both studies found no significant difference between-group difference in crash risk, with odds ratios close to 1.0.(67,68) We independently calculated rate ratios to allow us to combine the data from all four studies that reported the number of events.

The remaining study by Schneider and Gouvier reported a statistically significant increase in the mean number of crashes per person among individuals with TBI compared with healthy controls.(66) Since the authors did not report measures of dispersion for the means, we could not perform an independent calculation to confirm the statistical significance of the finding.

We combined the data from the four studies that allowed calculation of rate ratios (Figure 4). A test for heterogeneity found that although there were some differences between study results (I^2 = 44.9%), they were below the threshold that we considered substantial. We therefore conducted a random effects meta-analysis to determine whether crash rates were significantly elevated among patients with TBI and if so, by what margin compared with general population or uninjured controls. Although the summary rate ratio was 1.32 (95% CI: 0.77-2.25, p = 0.31), suggesting a trend toward slightly higher risk associated with TBI, the difference between groups was not statistically significant. Since this finding does not rule out the possibility of an elevated crash risk for drivers with TBI, the results of this analysis are inconclusive.

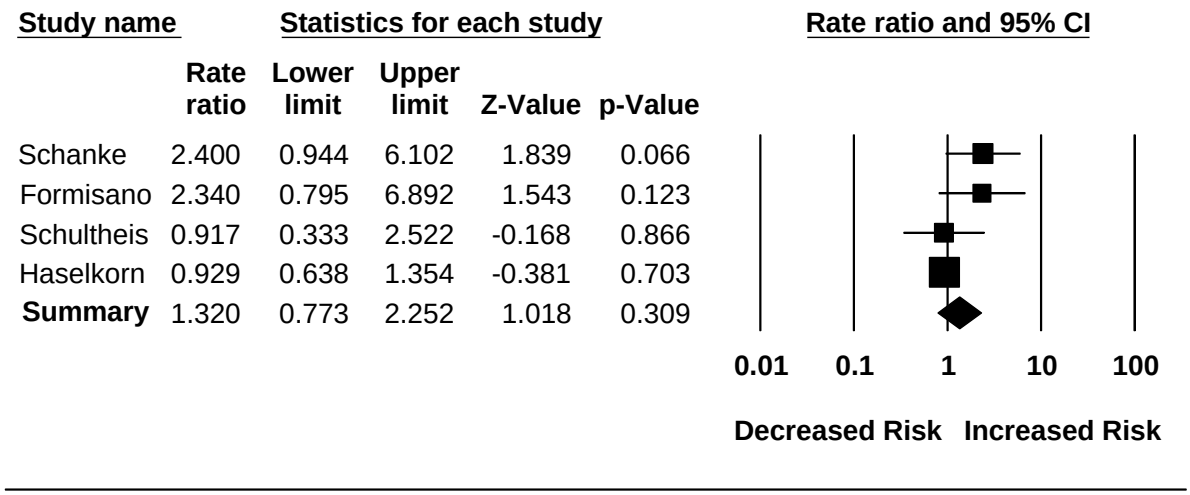
Table 12. Results of Studies Comparing Crash Risk of Individuals with TBI and Healthy Controls

Reference	Year	Severity of TBI	Results	Effect Size	p-value
Schanke et al.(64)	2008	NR	Crash rate TBI: 15.0/million km driven Expected: 6.25/million km driven	Rate ratio = 2.40 (95% CI: 0.94-6.10)*	0.07*[a]
Formisano et al.(65)	2005	Severe	Crash rate TBI: 11/29 Expected: 4.7/29	Rate ratio = 2.34 (95% CI: 0.80-6.89)*	0.12*[a]
Schneider and Gouvier(66)	2005	Mild (90%) Moderate (10%)	Mean number of crashes/person TBI: 0.60 Control: 0.33	Difference in means: 0.27* (cannot calculate confidence intervals)	<0.05
Schultheis et al.(67)	2002	NR	Number of individuals with one or more reported crashes TBI: 10/40 Control: 6/22	Rate ratio = 0.92 (0.64-2.52)*	0.87*
Haselkorn et al.(68)	1998	NR	Number of individuals with reported crash TBI: 41/896 Control: 80/1625	Rate ratio = 0.93 (0.64-1.35)*	0.70*

* Calculated by ECRI Institute.
*[a]Schanke et al. and Formisano et al. both reported that the difference between groups was statistically significant; our own statistical analysis used more conservative assumptions that led to non-statistically significant p-values for the between-group comparisons.

NR: Not reported
OR: Odds ratio

Figure 4. Meta-analysis of Crash Rate Ratios—TBI vs. Control



Indirect Evidence—Studies of Driving Performance (On-road or Simulated)

Four studies assessed driving performance (on-road or simulated) of patients with TBI compared with healthy controls. Table 13 summarizes the individual study results. Because none of these studies used the same measures of driving performance, we did not attempt to combine the findings in a meta-analysis. Instead, the results of each individual study are analyzed separately.

Two studies evaluated simulated driving outcomes; all of the enrollees with TBI had driving licenses. Both studies found statistically significant differences in at least one performance outcome between individuals with TBI and healthy controls.(69,70) These differences, including increases in simulated crashes and violations and fewer hits on divided attention tasks, indicated poorer performance among individuals with TBI.

Two studies evaluated on-road driving performance.(71,72) One study performed an actual road test measuring specific driving tasks which contributed to an overall score.(72) Percent tracking, percent turning, percent correct signs, composite score, and driver educator's score were all significantly lower among individuals with TBI compared with healthy controls; major errors were significantly higher among individuals with TBI. Another study evaluated specific driving tasks involved in platoon car following (when two or more vehicles closely follow one another).(71) This study found that brake reaction time (given minor or major task loads) and delay time were significantly longer for individuals with TBI, while speed reproduction was significantly lower compared with healthy controls.

Since neither study performed actual driving exams that patients would need to pass to get a driving license, the percentage of patients with TBI that would have been certified as fit to drive is unknown. Some of these individuals might never recover enough functional ability to pass a driving exam, in which case they would not be at risk for motor vehicle crash. Thus, it is possible that these studies may underestimate the average driving ability of the individuals with TBI who may someday be judged fit to drive.

Table 13. Results of Studies Comparing Driving Performance of Individuals with TBI and Healthy Controls

Reference	Year	Severity of TBI	Results			
Cyr et al.(69)	2008	Moderate (n = 2) or severe (n = 15)	**Simulator Outcomes**	**TBI**	**Control**	**p-value**
			Simulator crashes (mean ± SD)	0.26 ±0.19	0.14 ±0.16	0.049
			Reaction time to the dual task (mean ± SD)	2.30 ±0.73	1.89 ±0.34	NS
			Accuracy was also not statistically significant between groups.			
Lew et al.(70)	2005	Moderate or severe	**Simulator Outcomes**	**TBI**	**Control**	**p-value**
			Simulator driving violations (median and IQR):	28 (19-48)	5.5 (2-11)	<0.05
			Divided attention task (median and IQR):			
			Hits (% of targets)	27% (9-45%)	64% (45-86%)	<0.05
			Reaction time (seconds)	3.0 (2.6-3.2)	2.5 (1.8-3.1)	NS
			% patients who passed the simulator trial	45	100	0.002*
			TBI patients performed significantly more poorly on two global measures of simulator performance: the Simulator Performance Index (p <0.001) and the Driving Performance Inventory (p <0.001).			
Korteling(71)	1990	Moderate or severe	**Platoon Car Following Task**	**TBI**	**Control**	**p-value**
			Brake reaction time (milliseconds):			
			Minor task load	784	592	<0.005
			Major task load	906	649	<0.005
			Delay time (milliseconds)	1,370	980	<0.05
			Speed reproduction was lower for TBI patients than control individuals (p <0.01).			
Kewman et al.(72)	1985	Severe	**On-road driving test scores (mean and SD)**	**TBI (post training)**	**Control**	**p-value***
			% tracking	0.89 (0.12)	0.99 (0.02)	0.006
			% turning	0.55 (0.28)	0.87 (0.12)	<0.0001
			% correct signs	0.43 (0.34)	0.86 (0.10)	<0.0001
			Major errors	6.86 (7.56)	0.27 (0.47)	0.004
			Composite score	1.87 (0.63)	2.72 (0.17)	<0.0001

Reference	Year	Severity of TBI	Results			
			Driver Educator's score	3.42 (1.28)	5.00 (0.00)	<0.0001

*Calculated by ECRI Institute.

IQR: Interquartile range
NS: Not statistically significant

Section Summary

The available evidence is insufficient to determine whether crash risk is elevated for drivers with TBI compared with **uninjured controls. However, driving performance as measured by on-road driving tests and driving simulators was significantly impaired among individuals with TBI compared** with **uninjured controls. (Strength of Evidence: Moderate)**

Direct Evidence—Crash Studies*: Five studies attempted to directly determine crash risk among drivers with TBI through evaluation of self-reported crashes or crashes recorded in a state licensing database. The median quality of the evidence base was moderate. Data from four of these studies was combined to determine an overall estimate of crash risk. The summary rate ratio was 1.32 (95% CI 0.77-2.25), a difference that trended toward slightly higher risk in the TBI group but did not reach statistical significance. The remaining study reported a statistically significant increase in the mean number of crashes/person among drivers with TBI compared with healthy controls. Given that the findings do not rule out either the possibility of an elevated risk for drivers with TBI or no difference in risk, the current evidence concerning crash risk among drivers with TBI remains inconclusive.*

Indirect Evidence—Studies of Driving Performance*: Four studies (median quality: moderate) assessed driving performance (on-road or simulated) of patients with TBI compared with healthy controls. Because none of these studies used the same measures of driving performance, we did not attempt to combine the findings in a meta-analysis. Two studies that evaluated simulated driving outcomes found statistically significant differences indicating decreased performance in at least one performance outcome for individuals with TBI compared to healthy controls. Similarly, two studies that evaluated on-road driving performance found statistically significant differences in overall test scores or scores on specific driving tasks that indicated decreased performance for individuals with TBI compared with healthy controls. Since neither study conducted actual driver licensing tests, the percentage of patients with TBI that would have been certified as fit to drive is unknown. Inclusion of individuals who may never recover enough ability to pass a driving test would lead to an underestimate of the average driving performance of individuals with TBI who are certified as fit to drive. Furthermore, the extent to which reduced performance on road tests or driving simulators affects crash risk remains unclear.*

Since the majority of studies did not report the percentage of CMV drivers (if any) in their study population, the generalizability of these findings to CMV drivers is unknown.

Key Question 2: What factors associated with traumatic brain injury are predictive of increased crash risk or poor driving performance?

Introduction

As noted in the Background, TBI can lead to various temporary or permanent cognitive, psychosocial, sensory, and motor impairments, any of which could potentially impair driving ability and increase crash risk. Because these characteristics are difficult to measure objectively, they are most commonly measured by a variety of neuropsychological and functional tests. Thus far, no consensus exists as to which test or combination of tests is the best measure of the types of impairments associated with TBI. However, studies that use neuropsychological tests to measure impairments and also collect crash data or evaluate driving performance may provide evidence that certain impairments are more likely to increase crash risk or decrease driving performance. In addition, other factors related to severity of TBI (such as coma duration or length of posttraumatic amnesia) could potentially be associated with driving performance or crash risk.

Identification of Evidence Base

To address Key Question 2, we searched for trials that evaluated the potential association between one or more predictor variables and crash risk or driving performance among individuals with TBI.

The evidence base identification pathway for Key Question 2 is summarized in Figure 5. Our searches (Appendix A) identified a total of 968 articles that appeared relevant to this key question. Following application of a set of retrieval criteria (Appendix B), 26 full-length articles were retrieved and read in full. Of these 26 retrieved articles, 12 were found to meet the inclusion criteria for Key Question 2 (Appendix C). Table 14 lists these 12 included studies. Table D-2 of Appendix D lists the 14 articles that were retrieved but then excluded from inclusion in the evidence base for Key Question 2, and it provides the reason for their exclusion.

Figure 5. Development of Evidence Base for Key Question 2

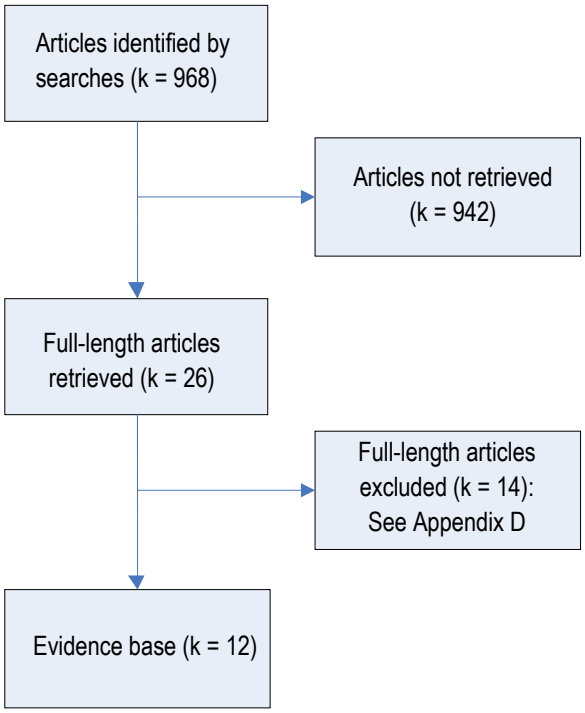


Table 14. Evidence Base for Key Question 2

Reference	Year	Study Location	Country
Studies of factors associated with crash/driving offenses			
Rapport et al.(73)	2008	Detroit, MI	USA
Formisano et al.(65)	2005	Rome	Italy
Pietrapiana et al.(74)	2005	Turin	Italy
Schneider and Gouvier(66)	2005	Baton Rouge, LA	USA
Coleman et al.(75)	2002	Detroit, MI	USA
Studies of factors associated with road test outcomes			
Bouillon et al.(76)	2006	Laval, Quebec	Canada
Novack et al.(77)	2006	Birmingham, AL	USA
Radford et al.(78)	2004	Nottingham	UK
Strypstein et al.(79)	2001	Brussels	Belgium
Korteling and Kaptein(80)	1996	Soesterberg	The Netherlands
Brooke et al.(81)	1992	Boston, MA	USA
Gouvier et al.(82)	1989	Baton Rouge, LA	USA

Evidence Base

This subsection provides a brief description of the key attributes of the 12 studies that comprise the evidence base for Key Question 2. Here we discuss pertinent information on the quality of the included studies and the generalizability of each study's findings to drivers of commercial vehicles. Key characteristics of the 12 included studies that address Key Question 2 are presented in Table 15.

Five retrospective cohort studies evaluated the potential relationship between one or more predictor variables and the occurrence of motor vehicle crash and driving offenses among patients with TBI. Four of the five studies relied on self-reporting of crash and the remaining study used Dept. of Motor Vehicle records. Only one study included amount of driving among factors evaluated for association with risk of crash/driving offenses. One other study included age among the variables tested. Since these are known potential confounding factors, ideally studies should control for these factors when testing the association of other variables with crash/driving offenses.

Seven cohort studies (five prospective, two retrospective) evaluated the potential association between various predictor variables and outcome of on-road driving tests or closed-course driving tests. Only one study included driving experience as one of the factors evaluated, while three studies included age. Most of the studies only evaluated outcomes of neuropsychological tests to determine whether any of the tests was a predictor of driving performance.

Table 15. Key Study Design Characteristics of Studies that Address Key Question 2

Reference	Year	Study Design	Objective	Comparison	Prospective or Retrospective?	Factors Evaluated for Association with Outcomes	Outcomes Relevant to KQ2	Definition of Crash	Outcomes Self-reported?
Studies of Factors Associated with Crash/Driving Offenses									
Rapport et al.(73)	2008	Cohort	To examine resumption of driving after TBI and its relation to community integration	Drivers with TBI who experienced driving incidents vs. drivers with TBI with no incidents	Retrospective	Years post-injury, amount of driving, neuropsychological functioning, self-rating of driving ability	Crash, traffic tickets, near-miss accidents	NR	Yes
Formisano et al.(65)	2005	Cohort	To investigate the road traffic accident rate in patients who have resumed driving after severe brain injury	TBI with moderate disability vs. TBI with good recovery	Retrospective	Glasgow outcome scale (GOS) scores	Crash	Unclear	Yes
Pietrapiana et al.(74)	2005	Cohort	To explore the possibility of predicting post-injury fitness to safe driving in patients with severe TBI	TBI with subsequent car accidents/ traffic violations vs. TBI without car accidents/ traffic violations	Retrospective	Age at interview, age at TBI, year post-injury, education, age at license achievement, years of driving pre-TBI, accidents and violations pre-TBI, Glasgow Coma Scale (GCS) scores, length of coma (LOC) duration, functional independence measure (FIM) and functional assessment measure (FAM), visual search test (VST), Wechsler Adult Intelligence Scale-Revised, symbol-digit subtest (WAIS-R SDS), pre-TBI risky personality index, and pre-TBI risky driving style index	Crash or traffic violation	NR	Yes
Schneider and Gouvier(66)	2005	Cohort	To examine the utility of the UFOV in predicting accidents among individuals with mild TBI and noninjured controls	TBI patients vs. noninjured controls	Retrospective	UFOV, Trails A and B, Digit Symbol, Symbol Search, Processing Speed, Symbol Digit Modalities Test (SDMT)	Crash	NR	Yes
Coleman et al.(75)	2002	Cohort	To examine predictors of driving status and fitness to drive after TBI	TBI with subsequent crash/ traffic convictions vs. TBI without crash/ traffic convictions	Retrospective	Years post-injury, pre-injury driving record, Disability Rating Scale (DRS) score at discharge, neuropsychological composite score, and Patient Competency Rating Scale (PCRS) scores (patient and significant other)	Crash or traffic conviction	Not defined, but included all crashes reported to the Dept. of Motor Vehicles	No
Studies of Factors Associated with Road Test Outcomes									
Bouillon et al.(76)	2006	Cohort	To compare Cognitive Behavioral Driver's Inventory (CBDI) scores for drivers who passed or failed a driving evaluation and identify factors associated with outcome of road test	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Retrospective	Age, gender, comprehension, expression, and time since diagnosis, CBDI score (includes WAIS-R, Picture Completion and Digit Symbol subtests; Trail-making Test Parts A and B; brake reaction test, and examination of visual fields), Motor-Free Visual Perception Test (MFVPT) score, Bell's Test score	On-road test outcome (pass/fail)	NA	No

Reference	Year	Study Design	Objective	Comparison	Prospective or Retrospective?	Factors Evaluated for Association with Outcomes	Outcomes Relevant to KQ2	Definition of Crash	Outcomes Self-reported?
Novack et al.(77)	2006	Cohort	To investigate the relationship between performance on the UFOV test and driving performance following TBI	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Prospective	Age, Trail-making Test (Parts A and B), brake reaction time, Useful Field of View (UFOV) test scores	On-road test outcome (global rating score)	NA	No
Radford et al.(78)	2004	Cohort	To determine whether the Stroke Drivers Screening Assessment (SDSA) could be used either alone or in conjunction with other cognitive tests to predict driving fitness in people with TBI	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Prospective	SDSA tests, Paced Auditory Serial Addition Tasks (PASAT), Adult Memory and Information Processing Battery (AMIPB)	On-road test outcome (pass/fail)	NA	No
Strypstein et al.(79)	2001	Cohort	To determine which neuropsychological tests have the most predictive accuracy for fitness to drive among patients with TBI	Patients with TBI declared fit to drive vs. patients with TBI declared unfit to drive	Retrospective	Neuropsychological test scores (Rey, UFOV, visual field, neglect, incompatibility, visual scanning, divided attention, and flexibility)	Fitness to drive decision (fit/unfit)	NA	No
Korteling and Kaptein(80)	1996	Cohort	To evaluate and develop simple tools to assess the driving fitness of brain-damaged patients	Patients with TBI declared fit to drive vs. patients with TBI declared unfit to drive	Prospective	Age, coma duration, driving experience, additional lessons, perceptual speed (PS), symbol-digit substitution (SDS), time estimation (TE), tracking reaction (TR)	Driving fitness (fit/unfit)	NA	No
Brooke et al.(81)	1992	Cohort	To examine the relationship between tests of cognitive function and tests of driving performance for patients with TBI	Patients with TBI declared safe to drive vs. patients with TBI declared unsafe to drive	Prospective	Trail-making Test, Tactual Performance Test, Wechsler Memory Scale, WAIS-R	Driving fitness (safe/unsafe)	NA	No
Gouvier et al.(82)	1989	Cohort	To identify which psychometric and performance measures were useful in predicting driving performance among disabled individuals	Patients with TBI who passed a closed-course road test vs. patients with TBI who failed a closed course road test	Prospective	WAIS, MFVPT, Baylor Adult Visual Perceptual Assessment, Trail-making Test (parts A and B), Symbol-Digit Modalities Test, Driver Performance Test (DPT), computerized tasks of visual reaction time (REACT) and visual searching efficiency (SEARCH), Tracking Simulator performance	Closed-course driving test (pass/fail)	NA	No

NA: Not applicable
NR: Not reported

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 16. Complete details of our quality assessment can be found in Table G-2 presented in Appendix G. Our assessment found that the median quality of the included studies was moderate for both the group of studies that evaluated factors associated with crash/driving offenses and the group of studies that evaluated factors associated with road test outcomes. Four studies were graded as low quality. These studies scored low because they failed to adjust for potential confounding factors that might influence any observed associations and a lack of independent or blind outcome assessment in combination with either retrospective design or lack of description of the derivation of the cohort.

Table 16. Quality of Studies for Key Question 2

Reference	Year	Quality Scale Used	Quality
Studies of Factors Associated with Crash/Driving Offenses			
Rapport et al.(73)	2008	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Formisano et al.(65)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low
Pietrapiana et al.(74)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Schneider and Gouvier(66)	2005	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low
Coleman et al.(75)	2002	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Studies of Factors Associated with Road Test Outcomes			
Bouillon et al.(76)	2006	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Novack et al.(77)	2006	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Radford et al.(78)	2004	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Strypstein et al.(79)	2001	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low
Korteling and Kaptein(80)	1996	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Brooke et al.(81)	1992	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Gouvier et al.(82)	1989	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the 12 studies that comprise the evidence base for Key Question 2 are presented in Table 17. The generalizability of the findings of these studies to CMV drivers is unclear. All of the studies included private motor vehicle license holders, an unknown number of whom may have held commercial driver licenses. The percentage of males included in these studies ranged from 40% to 90.7%, which is lower than the percentage of males in the CMV population. The average ages of the individuals included in these studies are somewhat younger (range of average ages: 22 to 42 years) than the average age in the CMV driver population. It is unclear whether the ethnicity of the individuals included in these studies is representative of CMV drivers owing to lack of reporting in most of the studies.

Severity of TBI and methods for classifying severity were reported in all of the crash studies but only one of the road test studies. There was variation in severity of TBI in different study populations, but most studies used GCS score to classify severity.

Table 17. Characteristics of Patients with TBI Enrolled in Studies that Address Key Question 2

Reference	Year	Number of Individuals with TBI	Severity of TBI	Method of Classifying Severity	Number Driving vs. Number Not Driving	Age Distribution	% Male	% CMV Drivers	Driving Exposure	Ethnicity
Studies of Factors Associated with Crash/Driving Offenses										
Rapport et al.(73)	2008	261	Mild (21.1%) Moderate or severe (76.9%)	GCS score	116 driving 145 not driving	Drivers: 42 (14)	78.4	NR	NR	NR
Formisano et al.(65)	2005	90	Severe	GCS score and LOC ≥48 hours	29 driving 61 not driving	Drivers: 28.4 (9.6)	83	NR	NR	NR
Pietrapiana et al.(74)	2005	66	Severe	GCS score	31 driving 35 not driving	Drivers: 33.5 (10.3)	81.8	NR	NR	NR
Schneider and Gouvier(66)	2005	40	Mild (90%) Moderate (10%)	Length of post-traumatic amnesia	40 driving	22 (4.1)	40	0	NR	Caucasian: 85% African American: 12.5% Hispanic: 2.5%
Coleman et al.(75)	2002	71	Moderate or severe	GCS score	33 driving 38 not driving	Drivers: 38.8 (12.5)	80.3	NR	NR	African American: 64.8% Caucasian: 28.2% Hispanic: 2.8% Mixed race: 4.2%
Studies of Factors Associated with Road Test Outcomes										
Bouillon et al.(76)	2006	58	NR	NR	NR	NR	NR	NR	NR	NR
Novack et al.(77)	2006	60	Severe (72%) Moderate (18%)	GCS score	60 driving	33 (range 16-68)	63.3	NR	NR	Caucasian: 90% African American: 10%
Radford et al.(78)	2004	52	NR	NR	NR	39.1 (12.8)	84.6	NR	NR	NR
Strypstein et al.(79)	2001	54	NR	NR	NR (75.9% had a driver license)	30.5	90.7	NR	NR	NR
Korteling and Kaptein(80)	1996	38	NR, but most appear to be severe	NR	NR, but all had licenses and were considered able to resume driving with remedial teaching if necessary	29.8 (10.9)	86.8	NR	NR	NR
Brooke et al.(81)	1992	13	NR	NR	NR	Within the range 18-65	NR	NR	NR	NR
Gouvier et al.(82)	1989	10	NR, but most appear to be severe	NR	NR	29.3 (range 18-48)	70	NR	NR	NR

GCS: Glasgow Coma Scale
LOC: Length of coma
NR: Not reported

Findings

The 12 studies that addressed Key Question 2 were divided into two groups: those that evaluated the potential association between various predictor variables and crash risk/driving offenses among patients with TBI, and those that evaluated the potential association between various predictor variables and driving performance among patients with TBI. The findings from each of these study groups are analyzed separately below. The best statistical methods that studies can use to identify significant predictors of outcome include either multiple regression models or discriminant function analysis. These techniques are superior to simple univariate comparisons because they statistically adjust for the effects of other variables in the model; thus, the identified correlations represent the true association of the predictor variable and the outcome.

Direct Evidence—Crash/Driving Offenses Studies

Five studies attempted to determine whether certain variables were associated with risk of crash/driving offenses among patients with TBI. Four studies used multiple regression models to identify statistically significant predictor variables, while one study simply compared the proportion of patients who crashed and did not crash among patients with different Glasgow outcome scale (GOS) scores (moderate disability vs. good recovery).

The possibility exists that two of the studies (Rapport et al. and Coleman et al.) had an overlapping patient population.(73,75) The same authors were involved in both studies, and both included patients from the Southeastern Michigan Brain Injury System database. However, there were differences in some of the predictor variables evaluated in each study and in the methods used to obtain data on driving incidents (crashes plus violations). Rapport et al. collected outcome data from a patient survey (self-report), while Coleman et al. obtained similar data from the Department of Motor Vehicles. Because of these differences, we report the data separately for each study, but in the analysis we consider these studies to be partially duplicative because of the high potential for overlap in the patient population. For predictor variables that were used in both studies, we consider these as one study.

Two studies with regression models identified years post-injury as a significant predictor of crash/driving incidents (Rapport et al. and Coleman et al. were considered together as one study because both used this predictor). Events increased with increasing years post-injury. This would likely be true for healthy drivers as well, since the number of accidents for most driving populations increases with increasing driving exposure. Thus, it is not a unique predictor for patients with TBI. Two studies had conflicting findings regarding pre-injury driving record; Pietrapiana et al. found it was a significant predictor variable while Coleman et al. found no significant association with post-TBI driving incidents. Like years post-injury, however, pre-injury driving record is a factor unrelated to TBI.

Neuropsychological functioning is a factor that is directly related to TBI, assuming that patients do not have a comorbid condition which could also affect cognitive functioning. The studies by Rapport et al. and Coleman et al. identified neuropsychological functioning and self-rating of driving ability as significant predictor variables. Again, for purposes of analysis, these are considered to represent a single study. In contrast, the studies by Pietrapiana et al. and Schneider and Gouvier did not find an association

between several neuropsychological test scores and crash risk. However, these studies did not use all of the same neuropsychological tests. Also, Schneider and Gouvier differed from other studies in that most of the patients had mild TBI (in other studies, the majority of patients had moderate to severe TBI).

The study with the model that best explained variance was Pietrapiana et al.; the authors found that a model combining years post-injury, pre-TBI accidents and violations, pre-TBI risky personality index, and pre-TBI risky-driving-style index explained 72.5% of the variance. Note that none of these factors is directly related to TBI. The best models in the studies by Rapport et al. and Coleman et al. (which are in some ways the same study) explained only 30% to 34% of the variance; these models included years post-injury, neuropsychological functioning, and self-rating of driving ability. Formisano et al. found a non-significant association between GOS score (a broad descriptive measure of disability) and crash, and the lack of multivariable analysis to control for other predictor variables increases the uncertainty of the findings.

Table 18. Factors Associated with Crash/Driving Offenses among Patients with TBI

Reference	Year	Comparison	Factors Evaluated for Association with Outcomes	Results
Rapport et al.(73)	2008	Drivers with TBI who experienced driving incidents vs. drivers with TBI with no incidents	Years post-injury, amount of driving, neuropsychological functioning (composite score derived from average performance on the Symbol Digit Modalities Test, Judgment of Line Orientation-Short Form, Wechsler Adult Intelligence Scale [WAIS] letter-number sequencing, Stroop test, California Verbal Learning Test-II, Trail-Making Tests, and Digit Vigilance Test), self-rating of driving ability	Variables that best predicted driving incidents in multiple regression model. **Variables** — **r^2** — **p-value** *Model 1* Years post-injury — 0.05 — 0.038 *Model 2* Years post-injury — 0.34 — <0.001 Amount driving Neuropsychological functioning Self-rating of driving ability Significant interaction effects between predictors: Neuropsychological composite by amount of driving: p = 0.032 Neuropsychological composite by self-rating of current ability: p = 0.006 Model 2 explained 34% of the variance.

Reference	Year	Comparison	Factors Evaluated for Association with Outcomes	Results
Pietrapiana et al.(74)	2005	TBI with subsequent car crashes/ traffic violations vs. TBI without car crashes/ traffic violations	Age at interview, age at TBI, years post-injury, education, age at license achievement, years of driving pre-TBI, accidents and violations pre-TBI, Glasgow coma scale (GCS) scores, length of coma (LOC) duration, functional independence measure (FIM) and functional assessment measure (FAM), visual search test (VST), Wechsler Adult Intelligence Scale-Revised, symbol-digit subtest (WAIS-R SDS), pre-TBI risky-personality index, and pre-TBI risky driving style index	Variables that best predicted outcome (post-TBI accidents and violations) in multiple regression model. **Variables** **r^2** **p-value** *Model 1* Years post-injury 0.210 0.01 *Model 2* Years post-injury 0.667 <0.001 Pre-TBI crashes and violations *Model 3* Years post-injury 0.692 <0.001 Pre-TBI accidents and violation Pre-TBI risky personality index *Model 4* Years post-injury 0.725 <0.001 Pre-TBI crashes and violations Pre-TBI risky personality index Pre-TBI risky-driving-style index Model 4 explained 72.5% of the variance.
Schneider and Gouvier(66)	2005	TBI with subsequent car accidents vs. TBI without car accidents	Useful Field of View (UFOV), Trails A and B, Digit Symbol, Symbol Search, Processing Speed, Symbol Digit Modalities Test (SDMT)	Multiple regression (stepwise method) showed that neither the UFOV nor any of the neuropsychological tests were significant predictors of crash group status
Coleman et al.(75)	2002	TBI with subsequent crash/ traffic convictions vs. TBI without crash/ traffic convictions	Years post-injury, pre-injury driving record, Disability Rating Scale (DRS) score at discharge, neuropsychological composite score (derived from WAIS-III letter-number sequencing test, WAIS-III matrix reasoning test, and Colored Trails Test), and Patient Competency Rating Scale (PCRS) scores (patient and significant other)	Variables that best predicted outcome (post-TBI driving incidents) in multiple regression model. **Variables** **r^2** **p-value** *Model 1* Years post-injury 0.11 0.012 *Model 2* Years post-injury 0.19 0.003 DRS at discharge *Model 3* Years post-injury 0.27 0.001 DRS at discharge Neuropsychological composite *Model 4* Years post-injury 0.30 0.003 DRS at discharge Neuropsychological composite Sig other-patient drives safely Patient-patient drives safely Model 4 explained 30% of the variance.
Formisano et al.(65)	2005	TBI with moderate disability vs. TBI with good recovery	Glasgow outcome scale (GOS) scores	No regression performed in this study. GOS score Traffic Accidents Yes No GOS4 (moderate disability) 2 10 GOS5 (Good recovery) 9 8 Fisher exact test for difference: p = 0.064

Indirect Evidence—Studies of Driving Performance

Seven studies evaluated the association between various predictor variables and road test or closed-course driving outcomes. Six studies used multiple regression models to identify statistically significant predictor variables, while one study performed univariate testing of the association between potential predictor variables and driving performance.

Three studies included patient characteristics such as age, gender, coma duration, and driving experience among the examined predictor variables.(76,77,80) Only one of three studies that evaluated age found it to be a significant predictor variable for driving performance.(77) The only study that evaluated coma duration and driving experience found that these two variables were significantly associated with driving performance in a best-fit multiple regression model.(80)

All studies evaluated one or more neuropsychological tests as potential predictor variables. Two of three studies that included the Trail-making Test (TMT) Parts A and B found a significant association between Part B of the test or the sum of rated scores from the TMT and driving performance.(77,81) However, one of these studies did not conduct multiple regression to adjust for the effect of other variables.(81) The Useful Field of View (UFOV) test was evaluated in two studies;(77,79) one of these studies found a significant association between the UFOV subtest 2 and driving performance.(77) Two studies that evaluated the Motor-free Visual Perception Test found no significant relationship between test scores and driving performance.(76,82)

One study found a significant association between the Cognitive Behavioral Driver's Inventory (CBDI) score and driving performance.(76) However, this finding is complicated by the fact that the CBDI included several other tests that most other studies evaluated separately, including the TMT, the Wechsler Adult Intelligence Scale-Revised (WAIS-R), the brake reaction test, and examination of visual fields. Whether the observed association between CBDI and driving performance is because of one or more of these subtests within the CBDI remains unclear.

A few neuropsychological tests were found to be significantly associated with driving performance in a single study, but no other study included these tests. This was true for the Stroke Drivers Screening Assessment (SDSA) and the Adult Memory and Information Processing Battery (AMIPB),(78) visual field testing and visual scanning,(79) perceptual speed testing and tracking reaction,(80) the Symbol-Digit Modalities Test and the Driver Performance test (DPT),(82) and the Tactual Performance Test (TPT).(81)

Overall, these studies suggest that poorer scores on neuropsychological tests may be associated with likelihood of failure on road tests for patients with TBI, although there was not much consistency across studies as to which neuropsychological tests were used.

Table 19. Factors Associated with Road Test Outcome among Patients with TBI

Reference	Year	Comparison	Factors Evaluated for Association with Outcomes	Results
Bouillon et al.(76)	2006	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Age, gender, comprehension, expression, time since diagnosis, Cognitive Behavioral Driver's Inventory (CBDI) score (includes visual reaction differential response, visual discrimination differential response II, visual scanning III, WAIS-R Picture Completion and Digit Symbol subtests; Trail-making Test Parts A and B; brake reaction test, and examination of visual fields), Motor-Free Visual Perception Test (MFVPT) score, Bell's Test score	Variables that best predicted outcome of road test in multiple regression model. **Variable** **β** **p-value** **Odds Ratio** CBDI score -0.24 0.02 0.79 (0.64-0.96)
Novack et al.(77)	2006	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Age, Trail-making Test (Parts A and B), brake reaction time, UFOV test scores	Variables that best predicted outcome of global evaluation in multiple regression model. **Variables** **R^2** **p-value** Age 0.50 <0.01 Trails B 0.29 <0.05 UFOV subtest 2 -0.32 <0.05 Variables that best predicted outcome of observer-rated driving assessment scale (DAS) in multiple regression model. **Variables** **R^2** **p-value** Age 0.40 <0.01 UFOV subtest 2 -0.35 <0.05
Radford et al.(78)	2004	Patients with TBI who passed an on-road test vs. patients with TBI who failed an on-road test	Stroke Drivers Screening Assessment (SDSA) tests, Paced Auditory Serial Addition Tasks (PASAT), Adult Memory and Information Processing Battery (AMIPB)	Variables found to predict outcome of road test in discriminant function analysis. Equations: PASS (SDSA Dot cancellation time in seconds x 0.095) + (SDSA Dot cancellation errors x 0.148) + (SDSA Directions x 0.162) + (SDSA Compass x 0.224) + (SDSA Road sign recognition x 2.745) + (Stroop Color word score x 0.274) + (AMIPB Information Processing Task B Adjusted score x 0.181) + 50.221 (Constant). FAIL (SDSA Dot cancellation time in seconds x 0.095) + (SDSA Dot cancellation errors x 0.171) - (SDSA Directions x 0.074) + (SDSA Compass x 0.293) + (SDSA Road sign recognition x 2.379) + (Stroop Colour word score x 0.248) + (AMIPB Information Processing Task B Adjusted score x 0.139) + 48.937 (Constant). These formulas correctly classified outcomes in 87% of cases (95% of those who passed and 64% of those who failed).
Strypstein et al.(79)	2001	Patients with TBI declared fit to drive vs. patients with TBI declared unfit to drive	Neuropsychological test scores (Rey, UFOV, visual field, neglect, incompatibility, visual scanning, divided attention, and flexibility)	Variables that best predicted fitness to drive in multiple regression model. **Variable** **β** **p-value** Visual field 0.518 0.011 Scanning 0.0004 0.033

Reference	Year	Comparison	Factors Evaluated for Association with Outcomes	Results
Korteling and Kaptein(80)	1996	Patients with TBI declared fit to drive vs. patients with TBI declared unfit to drive	Age, coma duration, driving experience, additional lessons, perceptual speed (PS), symbol-digit substitution (SDS), time estimation (TE), tracking reaction (TR)	Variables that best predicted outcome of fitness-to-drive evaluation in multiple regression model. **Variables** **R^2** **p-value** *Model* PS TR-reaction time Driving experience Coma duration 0.353 <0.05 The model accounted for 35.3% of the variability in rated driving performance. The model correctly classified outcomes in 71% of cases (80% of those who passed and 54% of those who failed).
Gouvier et al.(82)	1989	Patients with TBI who passed a closed-course road test vs. patients with TBI who failed a closed course road test	WAIS, MFVPT, Baylor Adult Visual Perceptual Assessment, Trail-making Test (parts A and B), Symbol-Digit Modalities Test (SDMT), Driver Performance Test (DPT), computerized tasks of visual reaction time (REACT) and visual searching efficiency (SEARCH), Tracking Simulator performance	Multiple regression model that best explains outcomes: Full-sized vehicle test outcome = 13.262 + 0.419 SDMT (oral) + 0.368 DPT (R^2 = 0.79, p <0.001) This model explained 79% of the variance in driving scores.
Brooke et al.(81)	1992	Patients with TBI declared safe to drive vs. patients with TBI declared unsafe to drive	Trail-making Test (TMT), Tactual Performance Test (TPT), Wechsler Memory Scale, WAIS-R	No multiple regression conducted in study. A significant relationship was found between sum of rated scores from the TMT and TPT and the global pass/fail rating from the driving test (Spearman correlation = 0.44).

WAIS-R: Wechsler Adult Intelligence Scale-Revised

Note that prediction of driving test outcomes is not the same as prediction of crash risk. Patients who failed road tests would either not be allowed to drive or at least advised not to drive, depending on the laws of the particular state or country of residence. Thus, they would not be expected to be at risk for motor vehicle crash (unless they disregard laws or advice). Simulated driving tests are even further removed from the assessment of crash risk. The extent to which simulated driving performance is related to performance on road tests has not been evaluated in this patient population.

Section Summary

The available evidence is insufficient to determine whether any factors related to TBI can predict actual crash risk. However, current evidence suggests that cognitive function measured by certain neuropsychological tests may predict the outcome of driving performance measured by a road test for patients with TBI. (Strength of Evidence: Moderate)

Direct Evidence—Crash Studies*: Five studies (median quality: moderate) attempted to determine whether certain variables were associated with risk of crash/driving offenses among patients with TBI. Two of these studies had possible overlap in their enrolled study populations, so these studies were generally analyzed as a single study. Evidence for an association between any TBI-related factor and risk*

of crash/driving offenses was mixed. One study provided evidence of a significant association between neuropsychological functioning and crash/driving incidents while two other studies did not. However, none of the studies used the same set of neuropsychological function tests, and the severity of TBI among individuals in one of the negative studies differed substantially from the other study populations (mild versus moderate to severe). The conflicting evidence and low number of studies means that the evidence is currently insufficient to determine whether an association exists between any TBI-related factors and crash risk.

***Indirect Evidence – Studies of Driving Performance**: Seven studies (median quality: moderate) evaluated the association between various predictor variables and road test or closed-course driving outcomes. Several studies evaluated one or more neuropsychological tests; although there was overlap in some of the specific individual tests used, none of the studies evaluated the exact same set of tests. The only individual test that showed a significant association with road test outcome in more than one study was the Trail-making Test (two studies showed an association while a third study did not). Several tests that were used in only a single study showed a significant association with road test outcomes. Therefore, while it is difficult to determine which specific tests have the best association with outcome, one can conclude that reduced cognitive function (as measured by neuropsychological tests as a group) seems to be associated with poor outcomes on a road test.*

Since the majority of studies did not report the percentage of CMV drivers (if any) in their study population, the generalizability of these findings to CMV drivers is unknown.

Note that prediction of driving test outcomes is not the same as prediction of crash risk. Patients who failed road tests would either not be allowed to drive or at least advised not to drive, depending on the laws of the particular state or country of residence. Thus, they would not be expected to be at risk for motor vehicle crash (unless they disregard laws or advice).

Key Question 3: What is the impact of rehabilitation programs on crash risk/driving performance among individuals with a traumatic brain injury?

Introduction

Following medical stabilization after the initial injury, patients with moderate to severe TBI (and mild TBI associated with post-concussion syndrome) will generally receive some type of rehabilitation therapy. The NIDRR recommends that comprehensive rehabilitation services be delivered by an interdisciplinary team of professionals that may include rehabilitation nurses, physical and occupational therapists, speech pathologists, neuropsychologists, social workers, and pharmacists. The services provided may include CRT, physical therapy, therapeutic recreation, occupational therapy, speech and language therapy, psychotherapy, vocational therapy, and pharmacotherapy (for more information on these specific therapies, see the Background section of this report). Many individuals with TBI will require chronic rehabilitative treatment owing to lifetime persistence of disabilities. However, no consensus exists as to what types, combinations, or intensity of rehabilitative services produces the best outcomes for these patients.

Identification of Evidence Base

To address this question, we searched for studies that compared the effectiveness of different types of rehabilitation therapy for reducing crash risk or improving driving performance among individuals with TBI.

The evidence identification pathway for Key Question 3 is presented in Figure 6. Our searches identified a total of 249 articles that appeared relevant to Key Question 3. Four articles were retrieved and read in full. Of these, one was found to meet the inclusion criteria for this question. This study is listed in Table 20. Details of the three retrieved articles that did not meet our inclusion criteria are presented in Table D-3 of Appendix D, along with the reasons for their exclusion.

Figure 6. Development of Evidence Base for Key Question 3

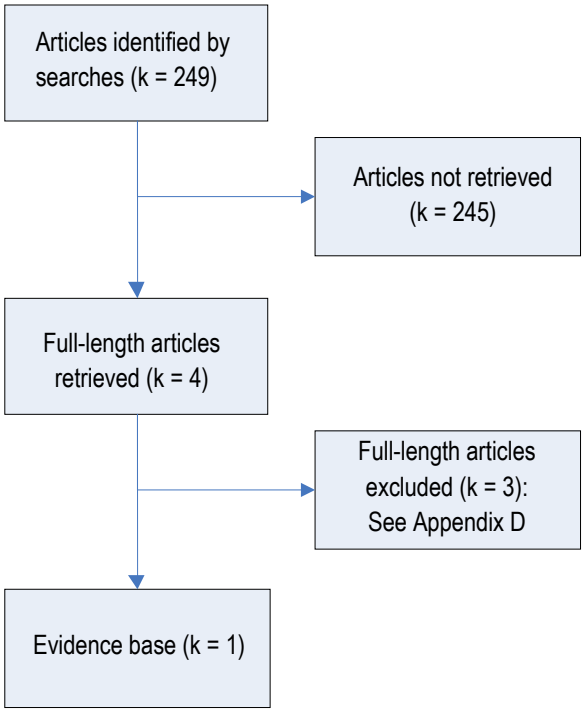


Table 20. Evidence Base

Primary Reference	Year	Study Location	Country
Studies that evaluated driving performance (on-road or simulation)			
Kewman et al.(72)	1985	Ann Arbor, MI	USA

Evidence Base

The key attributes of the single included study are summarized in Table 21. This was a prospective cohort study that compared on-road driving performance between two groups of TBI patients: those with full motorized vehicle training and those without full motorized vehicle training. The study did not control for any potential confounding variables such as driving exposure or age.(72)

Table 21. Key Study Design Characteristics of Studies that Address Key Question 3

Reference	Year	Study Design	Objective	Comparison	Prospective or Retrospective?	Factors Controlled For?	Driving Exposure Controlled For?	Outcomes Relevant to KQ1	Definition of Crash	Outcome Self-reported?
Rehabilitation for TBI and Driving Performance (on-road test or simulation)										
Kewman et al.(72)	1985	Cohort	To test whether a training program composed of a set of visuomotor and attentional tasks would generalize to a complex functional skill (automobile driving)	TBI patients with full motorized vehicle training vs. TBI patients without full motorized vehicle training	Prospective	None	No	On-road driving performance	NA	No

NA: Not applicable

Quality of the Evidence Base

The results of our analysis of the quality of the sole included study for Key Question 3 are presented in Table 22 and Table G-2 (Appendix G). This study scored as low quality. It had numerous flaws, including lack of independent or blind outcome assessment, failure to control for factors that might affect study outcomes, no description of how TBI diagnosis was made, and no description of the derivation of the cohorts.

Table 22. Quality of Included Studies

Reference	Year	Quality Scale Used	Quality
Rehabilitation for TBI and Driving Performance (on-road test or simulation)			
Kewman et al.(72)	1985	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low

Generalizability of Evidence Base to Target Population

The characteristics of the individuals enrolled in this study are summarized in Table 23. The generalizability of the findings of this study to CMV drivers is unclear. The mean age of study enrollees was substantially younger than the average age of the CMV driver population. The study did not report information concerning the percentage of males, driving exposure, or ethnicity.

Table 23. Characteristics of Patients with TBI Enrolled in Studies that Address Key Question 3

Reference	Year	Number of Individuals with TBI	Severity of TBI	Method of classifying severity	Number Driving vs. Number not Driving	Age Distribution	% Male	% CMV Drivers	Driving Exposure	Ethnicity
Rehabilitation for TBI and Driving Performance (On-road Test or Simulation)										
Kewman et al.(72)	1985	24	Severe	LOC	NR	Mean: 24.2	NR	NR	NR	NR

LOC: Length of coma
NR: Not reported

Findings

Indirect Evidence—Studies of Driving Performance (Road Test or Simulated Driving)

The lone study that met the inclusion criteria for this question compared the on-road driving performance of patients with severe TBI who had received structured training on a small electric vehicle (wheelchair) to the performance of patients with severe TBI who were allowed to operate the vehicle but did not participate in structured exercises. The structured training consisted of eight two-hour driving sessions where the subjects were trained on seven driving related exercises: a straightaway, an S-curve, a figure eight, a serpentine, a serpentine with special visual monitoring designed as a divided-attention task, a serpentine with special auditory monitoring designed as a divided-attention task, and a serpentine with both the visual and auditory monitoring tasks combined.

The retraining and post training scores for the on-road driving test are summarized in Table 24. No statistically significant differences were observed in the pretraining scores for the two groups of patients. However, the authors found statistically significant differences between groups on the post training scores for percent tracking, percent correct signs, composite score, and the driver educator's score. All of these differences were caused by better mean scores in the experimental group compared with the control group, suggesting that the structured training might be beneficial for patients with TBI. However, given the numerous quality deficiencies in this single small study, no evidence-based conclusion is possible.

Table 24. Mean Scores of Patients with TBI on Components of the On-road Driving Test

Reference	Year	Driving Measure	1 Week Pretraining			Post-training		
			TBI Experimental Group (n = 13) mean (SD)	TBI Control Group (n = 11) mean (SD)	p-value[a] of Difference	TBI Experimental Group (n = 13) mean (SD)	TBI Control Group (n = 11) mean (SD	p-value[a] of Difference
Kewman et al.(72)	1985	% tracking	0.65 (0.21)	0.62 (0.16)	NS	0.89 (0.12)	0.58 (0.12)	p <0.001
		% turning	0.41 (0.25)	0.48 (0.19)	NS	0.55 (0.28)	0.40 (0.21)	NS
		% correct signs	0.15 (0.25)	0.11 (0.13)	NS	0.43 (0.34)	0.18 (0.20)	p <0.05
		Major errors	13.86 (12.94)	11.55 (6.35)	NS	6.86 (7.56)	10.55 (4.39)	NC
		Composite score	1.21 (0.55)	1.21 (0.29)	NS	1.87 (0.63)	1.16 (0.35)	p <0.01
		Driver Educator's score	2.63 (1.25)	2.18 (0.68)	NS	3.42 (1.28)	2.05 (0.99)	p <0.02

[a] p-values reported by the authors based on nonparametric analysis using the Mann-Whitney U test
NC: Not calculated, because data were not collected on this variable for 6 subjects in the experimental group
NS: Not statistically significant

Section Summary

The available evidence is insufficient to determine the effect of rehabilitation programs on crash risk or driving performance among individuals with TBI.

No studies provided direct evidence to address this question.

***Indirect Evidence – Studies of Driving Performance**: One low-quality study compared the effectiveness of different rehabilitation strategies (structured exercises on an electric wheelchair vs. use of wheelchair*

with no structured exercises) for improving road test driving performance in patients with TBI. Although patients in the structured exercise group achieved significantly better mean scores on several road test measures (percent tracking, percent correct signs, composite score, and driver educator's score) compared with controls, the numerous quality deficiencies in this single small study preclude an evidence-based conclusion.

Key Question 4: What is the likelihood of a future seizure among individuals with a traumatic brain injury who did not experience a seizure at the time of the injury?

Introduction

Numerous studies have documented that at some time following TBI, a subset of patients will experience a seizure or repeated seizures that are somehow related to the trauma. These have generally been classified into two groups: early seizures (usually defined as occurring within the first seven days following TBI), and late seizures (usually defined as occurring after the first seven days following TBI).(6) Immediate seizures that occur within hours of TBI are sometimes considered a separate subset of early seizures.(83) Early seizures are considered to be provoked (acute reactions to the trauma), while late seizures are considered unprovoked; two or more unprovoked late seizures are classified as posttraumatic epilepsy.(83,84)

The percentage of patients with TBI who develop seizures may be influenced by the type of TBI. Evidence from studies of TBI during various wars, including World Wars I and II, Korea, and Vietnam, suggest that patients who sustain a dural tear/penetration are at higher risk for seizure than patients with closed head injuries. The frequency of seizure development in patients with dural penetration ranged from 36% to 50%, while for patients without dural penetration the rates of seizure ranged from 6% to 23%.(85) Despite improvements in treatment of head wounds in later conflicts, as well as the novel prophylactic use of anticonvulsant drugs in Vietnam, the overall rate of posttraumatic epilepsy was relatively constant from World War I through World War II, Korea and Vietnam, ranging from 30% to 34%.(86) This suggests a multifactorial genetic predisposition to development of seizures following head trauma in certain individuals.(85)

Since TBIs sustained by civilians are mostly closed head injuries, the rates of seizure development tend to be lower than those observed in military conflicts. Posttraumatic epilepsy rates have ranged from about 2% to 14% in larger studies (with 500 or more patients) of civilian populations.(6,87,88) Differences in rates among different studies may reflect variation in the average severity of TBI in the different sample groups; some studies included a majority of patients with mild or moderate TBIs, while others included a majority of patients with severe TBIs. Some studies that have analyzed seizure development based on TBI severity have found that patients with severe TBIs are more likely to develop seizures than patients with mild or moderate TBIs.(14,87) Another factor that may create heterogeneity among study findings is that different studies may use different methods to classify severity of TBI. Furthermore, studies with longer patient follow up will tend to report higher rates of posttraumatic

seizure development, because some patients may not experience their first seizure until many years following TBI.

Although there is evidence suggesting that early seizures may increase a patient's likelihood of developing late seizures,(88,89) the latter also occur in patients who have not experienced an early seizure. The purpose of this key question is to determine the percentage of patients with TBI who have not experienced early seizures yet go on to develop late seizures within weeks, months, or years following TBI.

Identification of Evidence Base

We searched for trials that reported the number of patients whose first seizure was a late seizure divided by the total number of patients who did not experience early seizures. Studies did not have to report the actual percentage as long as they provided enough information to allow independent calculation of the percentage. This usually required that a study report the number of patients who had early seizures as well as the number of patients with late seizures who had early seizures. The total number of patients with early seizures is then subtracted, and the remaining patients with late seizures are divided by the overall number of patients who did not experience early seizures to determine the relevant percentage.

The evidence base identification pathway for Key Question 4 is summarized in Figure 5. Our searches (Appendix A) identified a total of 3,768 articles that appeared relevant to this key question. Following application of a set of retrieval criteria (Appendix B), 48 full-length articles were retrieved and read in full. Of these 48 retrieved articles, 9 were found to meet the inclusion criteria for Key Question 4 (Appendix C). Table 14 lists these 9 included studies. Table D-2 of Appendix D lists the 39 articles that were retrieved but then excluded from inclusion in the evidence base for Key Question 4, and it provides the reason for their exclusion.

Figure 7. Development of Evidence Base for Key Question 4

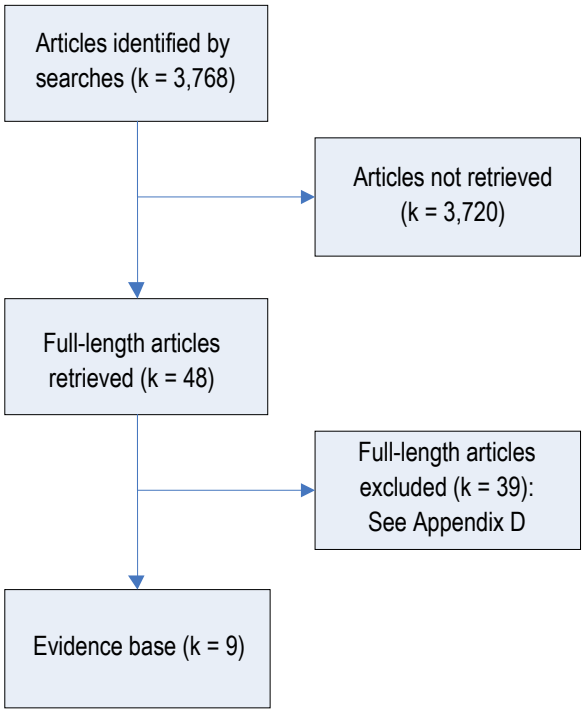


Table 25. Evidence Base for Key Question 4

Reference	Year	Study Location	Country
Diaz-Arrastia et al.(90)	2003	Dallas, TX	USA
Englander et al.(88)	2003	Four trauma centers in CA, CO, MI, and VA	USA
Annegers et al.(14,87)	1998, 1980	Olmsted County, MN	USA
Murri et al.(91)	1992	Pisa	Italy
Heikkinen et al.(92)	1990	Oulu	Finland
McQueen et al.(93)	1983	Edinburgh and Newcastle	UK
Wohns and Wyler(94)	1979	Seattle, WA	USA
Jennett(95)	1975	Oxford, Glasgow, Rotterdam	UK and the Netherlands
Weiss and Caveness(96), Evans(97)	1972, 1963	Bethesda, MD	USA

Evidence Base

This subsection provides a brief description of the key attributes of the nine studies that comprise the evidence base for Key Question 4. Here we discuss pertinent information on 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 4 are presented in Table 15.

All the studies but one were single-arm cohort studies; five were prospectively conducted, and three were retrospective analyses of previously-collected data. The remaining study was technically a

randomized controlled trial (RCT), but for the purpose of addressing this question, both arms were combined into a single prospective cohort. Most studies did not report whether seizures were self-reported, but it is likely that many were self-reported in all studies, because many occurred outside of a hospital setting. Only two studies reported that seizure reports were assessed by neurologists blinded to patients' identity and/or characteristics.

Table 26. Key Study Design Characteristics of Studies that Address Key Question 4

Reference	Year	Study Design	Objective	Prospective or Retrospective?	Seizures Self-reported?	Seizure reports assessed by neurologists blinded to patient identity/characteristics?
Diaz-Arrastia et al.(90)	2003	Cohort	To determine whether inheritance of APOE ε4 is associated with increased risk of developing late post-traumatic seizures	Prospective	Yes	Yes
Englander et al.(88)	2003	Cohort	To ascertain the natural history and to stratify risks for the development of late posttraumatic seizures in individuals with moderate to severe TBI	Prospective	Yes	Yes
Annegers et al.(14,87)	1998 1980	Cohort	To identify the characteristics of TBI that are associated with the development of seizures; To determine the magnitude and duration of the risk of posttraumatic seizures	Retrospective	Unclear. Medical records were used, but may have been based on reporting of seizures by patients rather than EEG scan.	NR
Murri et al.(91)	1992	Cohort	None stated; describes one group's experience with Phenobarbital used for prophylaxis of late posttraumatic seizures	Prospective	NR	NR
Heikkinen et al.(92)	1990	Cohort	To determine the factors pertinent to the development of posttraumatic epilepsy	Prospective	NR	NR
McQueen et al.(93)	1983	RCT, but treated as single cohort	To determine the effectiveness of phenytoin in preventing epilepsy in patients who had suffered a serious head injury	Prospective	NR	NR
Wohns and Wyler(94)	1979	Cohort	None stated; describes use of prophylactic phenytoin to prevent posttraumatic epilepsy in patients with severe TBI	Retrospective	NR	NR
Jennett(95)	1975	Cohort	To perform an analysis of the occurrence of epilepsy in a series of patients admitted to a single hospital for non-missile head injury	Prospective	NR	NR
Weiss and Caveness(96), Evans(97)	1972 1963	Cohort	To determine prognostic indicators of posttraumatic epilepsy	Retrospective	Yes	NR

NR: Not reported

Quality of Evidence Base

The results of our assessment of the overall quality of the evidence base for Key Question 4 are presented in Table 16. Complete details of our quality assessment can be found in Table G-4 presented

in Appendix G. The median quality of the included studies was moderate. Only one study was graded as low quality owing to a lack of independent or blind outcome assessment, retrospective study design, and selection criteria that are not typical for the broader population of patients with TBI.

Table 27. Quality of Studies for Key Question 4

Reference	Year	Quality Scale Used	Quality
Diaz-Arrastia et al.(90)	2003	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Englander et al.(88)	2003	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Annegers et al.(14,87)	1998, 1980	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Murri et al.(91)	1992	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Heikkinen et al.(92)	1990	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
McQueen et al.(93)	1983	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Wohns and Wyler(94)	1979	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Jennett(95)	1975	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Moderate
Weiss and Caveness(96), Evans(97)	1972, 1963	Newcastle-Ottawa Quality Assessment Scale for Cohort Studies	Low

Generalizability of Evidence to Target Population

Important characteristics of the individuals represented in the nine studies that comprise the evidence base for Key Question 4 are presented in Table 17. Since this question does not involve driving-related outcomes, the generalizability of the findings of these studies specifically to individuals with commercial driver licenses is less of an issue. For example, there is no known characteristic specific to CMV drivers that should lead to a different likelihood of developing seizures following TBI compared with an age- and gender-matched population.

However, factors such as age and gender may be relevant inasmuch as they potentially could have a role in the likelihood of developing seizures following TBI. Thus, studies where the age and gender makeup is similar to that of the CMV driver population may be more generalizable to that population, although this is by no means certain. Aside from one military study that included 100% males, the percentage of females included in the studies ranged from 18% to 25.5%, which is higher than the percentage of females in the CMV driver population. The ages of the private motor vehicle license holders included in these studies are within the typical range of CMV drivers, except for three studies that included children as well as adults. Since initial seizures can occur during adulthood in patients who experienced TBI during childhood, we did not exclude studies that included children as long as the majority of patients were adults at the time of TBI. It is unclear whether the ethnicity of the private motor vehicle license holders included in these studies is representative of CMV drivers, owing to lack of reporting.

Table 28. Characteristics of Patients with TBI Enrolled in Studies that Address Key Question 4

Reference	Year	Number of Individuals with TBI	Severity of TBI	Method of Classifying Severity	Age Distribution	% Male	Ethnicity
Diaz-Arrastia et al.(90)	2003	106	Moderate or severe	CT scan findings	38.8 (19.4)	82	Caucasian: 67% African American: 9.4% Hispanic: 17.9%

Reference	Year	Number of Individuals with TBI	Severity of TBI	Method of Classifying Severity	Age Distribution	% Male	Ethnicity
							Other: 4.8%
Englander et al.(88)	2003	647	Moderate or severe	GCS score or CT scan findings	Range: 16 to >50	77	Caucasian: 43% African American: 25% Hispanic: 16% Asian: 4% Other: 12%
Annegers et al.(14,87)	1998, 1980	4,541 (includes children [38%] and adults [62%])	Mild (60.7%), Moderate (32%), Severe (7.2%)	LOC or length of post-traumatic amnesia	2,815 patients were age 15 or older	NR	NR
Murri et al.(91)	1992	293 (includes children [30%] and adults [70%])	Severe	CT scan findings or LOC	Range: 11 to 64	76	NR
Heikkinen et al.(92)	1990	55	Mild, moderate or severe	GCS score	42.8 (range 17 to 76)	74.5	NR
McQueen et al.(93)	1983	164 (includes 43 children)	Severe	Imaging findings or length of post-traumatic amnesia	Range 5 to 65	79	NR
Wohns and Wyler(94)	1979	62	Severe	NR	29 (19)	75.8	NR
Jennett(95)	1975	1,106 (783 adults)	Mild, moderate or severe	Length of post-traumatic amnesia and imaging findings	<5 to >65	NR	NR
Weiss and Caveness(96), Evans(97)	1972, 1963	356 (1972 study), 370 (1963 study)	NR; all war injuries, 56% missile, 44% nonmissile	NR	Range: 25 to 50	100	NR

GCS: Glasgow Coma Scale
LOC: Length of coma
NR: Not reported

Findings

The results of studies that allowed calculation of the percentage of patients with TBI whose first seizure was a late seizure (occurring >7 days following TBI) appear in Table 29. Most of these studies did not directly report the relevant percentages, but presented enough data to allow independent calculation of these percentages. For studies that included both children and adults, we performed separate calculations for the adults when possible (i.e., if the studies reported separate data for children and adults).

We did not attempt to combine the data from each study in a meta-analysis due to differences in several important factors among the studies in this evidence base. These differences include severity of TBI, how severity was determined, length of follow up, whether children were analyzed with adults, and whether prophylactic anti-seizure medication was used in the study. Also, some studies included patients with alcoholism while others did not; alcohol withdrawal may lead to seizures that are unrelated to TBI. Each of these factors may have an effect on the percentage of patients whose first seizure was a late seizure. However, there were too few studies and insufficiently detailed reporting to adequately explore the potential impact of these differences on study results using meta-regression.

The percentage of patients with a first-time late seizure varied considerably among these studies, ranging from 1% to 25.2%; this variability is most likely caused by one or more of the differences noted above. The study by Murri et al. reported the lowest percentage (1% of patients at 12 months). Although this is one of only two studies that included only patients with severe TBI, it was the only study that reported treating all patients with prophylactic Phenobarbital (an anti-seizure medication) prior to seizure development. The drug was administered during the entire 12-month follow-up period to all patients whether or not they had a seizure.(91) However, controlled studies of prophylactic anti-seizure drugs have not noted a consistent preventive effect in late seizures.(6,83,98) The three other studies that separately reported late seizure rates associated with severe TBI found rates ranging from 9.7% to 10%. The study with the highest percentage of first-time late seizures (25.2%) was the only study of a military population (Korean war veterans) and the only study where the majority of TBIs were missile-related.(96) Separate analysis of missile and nonmissile TBIs revealed that the rate was much higher among patients with missile injuries (31.7%) than among patients with non-missile injuries (5.2%).(97) This finding is supported by the high rates of late seizures reported in other wars where the majority of injuries were missile-related.(86) Penetrating brain injuries appear to increase the probability of late seizure development above that observed for closed (non-penetrating) brain injuries.

Of the eight studies that reported the severity of TBI in their study populations, three included a mixture of patients with mild, moderate, and severe TBI, two included a mixture of patients with moderate or severe TBI, and three included only patients with severe TBI. The remaining study was the military study where the majority of patients had missile-related penetrating TBIs. Although this study did not report the severity level, one can presume that the majority of TBIs would likely be classed as severe. Of the studies that included patients with different severity levels, only one study (Annegers et al.) reported the seizure data separately based on TBI severity. This study found that patients with severe TBI were much more likely to experience first-time late seizures than patients with mild or moderate TBI.(14)

Table 29. Percentage of Patients with Late Seizures Who Did Not Have an Early Seizure

Reference	Year	Number with TBI (Number Without Early Seizure)	Severity of TBI	Length of Follow up	Likelihood of Late Seizure Among Patients Who Did Not Have an Early Seizure
Diaz-Arrastia et al.(90)	2003	106 (99)	Moderate or severe	6 months	17/99 = 17.2%*
Englander et al.(88)	2003	647 (626)	Moderate or severe	24 months or until a first confirmed seizure event >7 days after TBI	61/626 Cumulative probability (Kaplan-Meier) = 13.1%
Annegers et al.(14,87)	1998	4,541 (4,424) (includes children [38%] and adults [62%])	Mild (60.7%), Moderate (32%), Severe (7.2%)	A minimum of 11 years or until first unprovoked seizure or death	85/4424 = 1.9%*
	1980	1,616 adults (1,587) 1,132 children (1,103)	Mild (63.6%), Moderate (28%), Severe (8.4%)	NR	Adults / Adults + Children Mild TBI: 8/1,024 = 0.8% / 12/1,634 = 0.7% Moderate TBI: 5/441 = 1.1% / 14/893 = 1.6% Severe TBI: 13/122 = 10.7% / 16/163 = 9.8% Total: 26/1,587 = 1.6%* / 42/2,690 = 1.6%*
Murri et al.(91)	1992	293 (287) (includes children [30%] and adults [70%])	Severe	12 months	3/287 = 1.0%* (all patients had prophylaxis with Phenobarbital)
Heikkinen et al.(92)	1990	55 (45)	Mild, moderate, or severe	Mean: 5.7 years (range 4.5-6.8 years)	5/45 = 11.1%*
McQueen et al.(93)	1983	164 (includes 43 children)	Severe	24 months	15/155 = 9.7%*
Wohns and Wyler(94)	1979	62 (only 50 with useful data)	Severe	Up to 24 months	5/50 = 10% (all treated with phenytoin)
Jennett(95)	1975	1106 total (868) 783 adults (663)	Mild, moderate, or severe	NR	Adults / Adults + Children 22/663 = 3.3% / 29/868 = 3.3%
Weiss and Caveness(96), Evans(97)	1972	356 (330)	NR; all war injuries, 56% missile, 44% nonmissile	8-11 years	83/330 = 25.2%*
	1963	370 (343)	NR, 59.7% missile, 40.3% nonmissile	2-10 years	Missile TBI: 66/208 = 31.7%* Nonmissile TBI: 7/135 = 5.2%*

*Calculated by ECRI Institute

NR: Not reported

The time of onset of first late seizure is also of interest. If the chances of late seizure development diminish after a certain period of time, then driver safety would be increased after that time. Two studies provided a time course of initiation of late seizures among patients who did not experience early seizures (Table 30). Annegers et al. and Weiss and Caveness both found that the majority of first late seizures occur within the first year following TBI.(14,96) Annegers et al. further analyzed the findings by TBI severity and found that this held true only for patients with moderate to severe TBI; patients with mild TBI had a relatively low proportion of late seizure development within the first year. Because they did not break down the data for each year after the first year, we cannot determine whether the development of seizures was constant over the next four years in the mild TBI group. Although actual percentages were not reported, Annegers et al. stated that the incidence of first seizures for the total group 5 or more years after head trauma was not greater than expected in the general population.(14)

Weiss and Caveness analyzed seizure development for each single year out to 11 years. They found that seizure development diminished substantially in the second year, even further in the third year, and thereafter remained at a relatively low level with a few minor fluctuations. However, even patients who were seizure free for 10 years still had a small chance of developing a late seizure.(96)

Although these two studies were the only studies that allowed separate determination of time of onset for those patients who did not have early seizures, another study that did not separate out such patients showed a similar pattern of late seizure development. Jennett et al. analyzed time of onset for 481 patients with late seizures (some may have had early seizures also). They found that 56% of these patients developed their first late seizures within the first year post-TBI, 13% in the second year, 8% in the third year, and thereafter the rate was relatively constant at 2-4% out to 10 years.(95) Other studies have shown a similar pattern.(6)

Table 30. Time of Onset of First Seizure (Late) after TBI

Reference	Year	Total Patients with First-Time Seizures (Late)	Time of Onset of First Seizure (Late) and Number or Percent of Patients with First Seizure in Each Time Period										
Annegers et al.(14)	1980	Adults only Mild 0.8% Moderate 1.1% Severe 10.7%	**<1 year** 0.1% 1.0% 7.7%	**1-5 years** 0.7%* 0.6%* 5.6%*				**>5 years** NR					
		All patients Mild 0.7% Moderate 1.6% Severe 9.8%	 0.1% 0.7% 7.1%	 0.5%* 0.9%* 4.5%*				NR					
Weiss and Caveness (96)	1972	83	**≤1 year** 45	**1-2 years** 15	**2-3 years** 6	**3-4 years** 3	**4-5 years** 1	**5-6 years** 4	**6-7 years** 1	**7-8 years** 6	**8-9 years** 1	**9-10 years** 0	**10-11 years** 1

*Expected percentages if all patients had been followed for 5 years

NR: Not reported

Section Summary

Individuals with TBI who have not experienced a seizure within the first week post-injury still have a significant likelihood of experiencing late seizure(s). Reported frequencies of late seizures in this population ranged from 1% to 25% during follow-up periods ranging from 1 to 11 years. (Strength of Evidence: Moderate)

The highest rate of late seizures (25%) was associated primarily with penetrating missile TBIs. (Strength of Evidence: Minimally Acceptable)

Among patients with closed TBIs, a diagnosis of severe TBI was associated with higher frequencies of first-time late seizures than diagnoses of mild or moderate TBI. (Strength of Evidence: Minimally Acceptable)

Among adults with moderate or severe TBI who develop late seizures, ≥50% experience their first late seizure within the first year after TBI. The rates fall substantially within the next two years and stabilize after the third year at roughly 2% to 4% (of the total patients who develop late seizures) per year out to 11 years. The pattern for mild TBI is less clear, but the rate of late seizure development does not appear much higher in the first year compared with subsequent years. (Strength of Evidence: Minimally Acceptable)

Our searches identified nine studies (median quality: moderate) that reported (or allowed independent calculation of) the frequency of patients whose first seizure was a late seizure (i.e., occurring after one week post-TBI). owing to differences in several important factors among these studies, we did not attempt to combine the data from each study in a pooled analysis. Differences included severity of TBI, how severity was determined, length of follow up, whether children were analyzed with adults, whether patients with alcoholism were included, and whether prophylactic anti-seizure medication was used in the study.

The percentage of patients with a first-time late seizure ranged from 1% to 25%, most likely owing to one or more of the differences noted above. The study with the highest rate was the only study where most patients had penetrating missile TBIs. A comparison of missile and non-missile TBIs in this study found that the rate of late seizure development was much higher among patients with missile TBIs (32% vs. 5%). The study with a 1% rate was unusual because all patients were classified as having severe TBI (other studies with similar patients reported rates close to 10%), but it was the only study where all patients were given prophylactic Phenobarbital for the entire 12-month follow up. This finding is not consistent with findings from controlled studies that did not find a preventive benefit of prophylactic anti-seizure medication for late seizures. One study that analyzed seizure data separately based on severity of TBI found that first-time late seizures occurred more frequently among patients with severe TBI than among patients with mild or moderate TBI.

Two studies assessed the timing of late seizure development and found that first-time late seizures occurred most frequently in the first year following TBI. At least 50% of patients with moderate or severe TBI who developed late seizures experienced the first seizure within this time period (e.g., if the overall late seizure rate was 10%, then about 5% of the total patient group would develop late seizures within the first year after TBI). The percentage dropped substantially within the next two years and then stabilized at roughly 2% to 4% per year out to 11 years. The pattern for mild TBI is less clear, but the rate of late seizure development does not appear much higher in the first year compared with subsequent years.

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Appendix A: Search Summaries

Search Summary for Key Questions 1 through 4

The search strategies used combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the following concepts. 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 comprising the Cochrane Library.

Electronic Database Searches

The following databases have been searched for relevant information:

Name of Database	Date Limits	Platform/Provider
The Cochrane Central Register of Controlled Trials (CENTRAL)	Through 2009 Issue 1	www.thecochranelibrary.com
The Cochrane Database of Methodology Reviews (Methodology Reviews)	Through 2009 Issue 1	www.thecochranelibrary.com
The Cochrane Database of Systematic Reviews (Cochrane Reviews)	Through 2009 Issue 1	www.thecochranelibrary.com
Database of Abstracts of Reviews of Effects (DARE)	Through 2009 Issue 1	www.thecochranelibrary.com
EMBASE (Excerpta Medica)	1980 through March 20, 2009	OVID
Health Technology Assessment (HTA) Database	Through 2009 Issue 1	www.thecochranelibrary.com
MEDLINE	1950 through March 20, 2009	OVID
PubMed (PreMEDLINE)	Searched March 20, 2009	www.pubmed.gov
TRIS Online (Transportation Research Information Service Database)	Searched January 8, 2009	http://ntlsearch.bts.gov/tris/index.do
U.K. NHS Economic Evaluation Database (NHS EED)	Through 2009 Issue 1	www.thecochranelibrary.com
U.S. National Guideline Clearinghouse™ (NGC)	Searched February 16, 2009	www.ngc.gov

Hand Searches of Journal and Nonjournal Literature

Journals and supplements maintained in ECRI Institute's collections were routinely reviewed. We also screened nonjournal publications and conference proceedings from professional organizations, private agencies, and government agencies. Other mechanisms used to retrieve additional relevant information included review of bibliographies/reference lists from peer-reviewed and 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. These documents do not appear in the peer-reviewed journal literature).

Search Strategies

The search strategies employed combinations of freetext keywords as well as controlled vocabulary terms including (but not limited to) the concepts. Presented in the strategy below in OVID syntax; the search was simultaneously conducted across EMBASE and MEDLINE. A parallel strategy was used to search the databases comprising the Cochrane Library.

MeSH, EMTREE, 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

.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$

Concept	Controlled Vocabulary	Keywords
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$1 Vehicle$
Rehabilitation	Cognitive rehabilitation Cues Learning strategies Memory training Neuropsychological rehabilitation exp Rehabilitation/	Cognitive rehab$ Cognitive remediat$ Cognitive train$ Compensatory rehab$ Compensatory remediat$ Compensatory train$ Memory rehab$ Memory remediat$ Memory train$ Neuropsych$ rehab$ Neuropsych$ remediat$ Neuropsych$ train$ Rehab$ Restorative rehab$ Restorative remediat$ Restorative train$
Risk	Proportional hazard model Proportional hazard models exp Risk/	Risk$
Seizures	exp Epilepsy/ exp Seizures/	Convuls$ Epilep$ Fits Seizure$
Traumatic brain injury	exp Acquired brain injury/ exp Brain injury/ exp Brain injuries/ exp Traumatic brain injury/	Acquired brain injury Traumatic brain injury ABI TBI

Key Questions 1 and 2

CINAHL/EMBASE/MEDLINE

Set Number	Concept	Search Statement	Number Identified
1	Traumatic brain injury	Exp traumatic brain injury/ or exp brain injury/ or exp brain injuries/ or exp acquired brain injury/	51,320
2		((post or trauma$ or acquir$) adj2 brain injur$) or (tbi or abi).ti.	15,872
3	Combine sets	1 or 2	53,180
4	Limit by publication type	3 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.)	43,203
5	Limit by population	4 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)	13,340
6		5 and adult	7,606
7		5 not 6	5,734
8		4 not 7	37,469
9	accidents	8 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.	1,198
10		8 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)	1,360
11	Driving	8 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.	187
12		8 and (driver$ 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$1 or lorry or lorries or haul or (long adj distance)).ti.	682
13		8 and (Automobile driver examination or Licensure or Driver license or Safety or Traffic safety or Highway safety or Occupational safety or Occupational Health or Occupational disease).de.	237
14	Combine sets	or/9-13	2,267
15	Limit by study type	14 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or crossover studies or crossover procedure or double-blind procedure or single-blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Follow up studies/ or random$.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$)))	
16	Eliminate overlap	Remove duplicates from 15	1,095
17	Risk	16 and (Exp risk/ or risk$.ti. or proportional hazard models.de. or proportional hazards model.de.)	968

Key Question 3

CINAHL/EMBASE/MEDLINE

Set Number	Concept	Search Statement	Number Identified
1	Traumatic brain injury	Exp traumatic brain injury/ or exp brain injury/ or exp brain injuries/ or exp acquired brain injury/	51,320
2		((post or trauma$ or acquir$) adj2 brain injur$) or (tbi or abi).ti.	15,872
3	Combine sets	1 or 2	53,180
4	Limit by publication type	3 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.)	43,203
5	Limit by population	4 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)	13,340
6		5 and adult	7,606
7		5 not 6	5,734
8		4 not 7	37,469
9	Rehabilitation	8 and (Exp rehabilitation/ or rehab$.ti,ab,sh. or rh.fs.)	6,762
10		8 and (cognitive rehabilitation or neuropsychological rehabilitation or memory training or learning strategies or cues).de.	122
11		8 and ((Cognitive$ or neuropsych$ or memory or compensatory or restorative) adj2 (remediat$ or rehab$ or train$))	671
12	Combine sets	or/9-11	6,836
13	Limit by study type	12 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Follow up studies/ or random$.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$)))	3,608
14	accidents	13 and (accident or accidents or accidents, traffic or traffic accident or motor traffic accidents or accidents, occupational or accident prevention or occupational accident or transportation accidents).de.	133
15		13 and ((accident$ and (motor or traffic)) or collision$ or crash$ or wreck$ or citation$ or ticket$)	162
16	Driving	13 and (Automobiles or Motor vehicles or Motor vehicle or Automobile driving or Car driving or Driving ability or Driving behavior or Drivers).de.	40
17		13 and (driver$ 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.	99
18		13 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.	21
19	Combine sets	or/9-13	286
20	Eliminate overlap	Remove duplicates from14	249

Key Question 4

CINAHL/EMBASE/MEDLINE

Set Number	Concept	Search Statement	Number Identified
1	Traumatic brain injury	Exp traumatic brain injury/ or exp brain injury/ or exp brain injuries/ or exp acquired brain injury/	51,320
2		((post or trauma$ or acquir$) adj2 brain injur$) or (tbi or abi).ti.	15,872
3	Combine sets	1 or 2	53,180
4	Limit by publication type	3 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.)	43,203
5	Limit by population	4 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)	13,340
6		5 and adult	7,606
7		5 not 6	5,734
8		4 not 7	37,469
9	Seizures	Exp epilepsy/ or exp seizures/ or (seizure$ or epilep$ or convuls$ or fits).ti.	13,0951
10		(Post-traumatic seizure or PTS or (late adj2 seizure$) or delayed onset)	9,244
11	Combine sets	9 or 10	139,699
12	Combine sets	8 and 11	2,490
13	Risk	12 and (Exp risk/ or risk$.ti,ab. or proportional hazard models.de. or proportional hazards model.de.)	448
14		12 and (unprovoked or first or solitary).ti.	32
15	epidemiology	11 and ep.fs.	9,735
16		8 and 15	193
17	Limit by population	15 and (exp child/ or adolescent.de. or child$ or pediatr$ or paediatr$ or juvenile$ or adolescen$ or teen$ or youth$)	5,120
18		17 and adult	2,516
19		17 not 18	2,604
20		15 not 19	7,131
21	Limit by study type	20 and ((Randomized controlled trials or random allocation or double-blind method or single-blind method or placebos or cross-over studies or crossover procedure or double blind procedure or single blind procedure or placebos or latin square design or crossover design or double-blind studies or single-blind studies or triple-blind studies or random assignment or exp controlled study/ or exp clinical trial/ or exp comparative study/ or cohort analysis or follow-up studies.de. or intermethod comparison or parallel design or control group or prospective study or retrospective study or case control study or major clinical study).de. or Case control studies/ or Cohort/ or Longitudinal studies/ or Evaluation studies/ or Follow-up studies/ or Prospective studies/ or Retrospective studies/ or Case control study/ or Cohort analysis/ or Longitudinal study/ or Follow up/ or Cohort analysis/ or Follow up studies/ or random$.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$)))	3,687 Studies including epidemiology of seizures in adults
22	Combine sets	13 or 14 or 21	4,113
23	Eliminate overlap	Remove duplicates from	3,768

Project Statistics (KQ1-KQ4)

Total Identified	Total Downloaded	Total Retrieved	Total Included
4,985	472	149	27

Appendix B: Retrieval Criteria

Appendix B lists the retrieval criteria for each key question. An example of a small set of retrieval criteria are presented below.

Retrieval Criteria for Key Question 1

- Article must have been published in the English language.
- Article must have enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash associated with TBI directly (crash data) or indirectly (road test, simulated driving, driver-related functional tasks).
- Article must describe a study that includes a comparison group composed of comparable subjects without TBI.

Retrieval Criteria for Key Question 2

- Article must have been published in the English language.
- Article must have enrolled 10 or more subjects.
- Article must describe a study that attempted to evaluate the association between predictor variables and the risk for a motor vehicle crash associated with TBI directly or indirectly (road test, simulated driving, driver-related functional tasks).

Retrieval Criteria for Key Question 3

- Article must have been published in the English language.
- Article must have enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash associated with TBI directly (crash data) or indirectly (road test, simulated driving, driver-related functional tasks) among patients receiving some type of rehabilitation therapy.
- Article must describe a study that includes a comparison group composed of comparable subjects without these disorders.

Retrieval Criteria for Key Question 4

- Article must have been published in the English language.
- Article must have enrolled 10 or more subjects.
- Article must describe a study that attempted to determine the likelihood of developing a first-time late seizure among individuals with TBI.

Appendix C: Inclusion Criteria

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

Inclusion Criteria for Key Question 1

- 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 have enrolled 10 or more subjects per group.
- Article must have enrolled subjects aged ≥18 years.
- Studies must include individuals with TBI.
- Article must describe a study that includes a comparison group composed of comparable subjects without TBI.
- Article must present data in a manner that will allow ECRI Institute to calculate (directly or through imputation) effect-size estimates and CIs.
- 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 have enrolled 10 or more subjects.
- Article must have enrolled subjects aged ≥18 years.
- Studies must include individuals with TBI.
- Article must describe a study that attempted to evaluate the association between predictor variables and the risk for a motor vehicle crash associated with TBI directly or indirectly (road test, simulated driving, driver-related functional tasks).
- Article must present data in a manner that will allow ECRI Institute to calculate (directly or through imputation) effect-size estimates and CIs.
- 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 have enrolled 10 or more subjects.
- Article must have enrolled subjects aged ≥18 years.
- Article must describe a study that attempted to determine the risk for a motor vehicle crash associated with TBI directly (crash data) or indirectly (road test, simulated driving, driver-related functional tasks) among patients receiving some type of rehabilitation therapy.
- Article must describe a study that includes a comparison group composed of comparable subjects with TBI who received either no rehabilitation therapy or a different type or intensity of rehabilitation therapy. Alternatively, the control group could include individuals without TBI.

Inclusion Criteria for Key Question 4

- 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.
- Studies must include individuals with TBI.
- Article must have enrolled 10 or more subjects.
- Article must have enrolled a majority of subjects aged ≥18 years.
- Article must describe a study that attempted to determine the likelihood of developing a first-time late seizure among individuals with TBI who did not experience an early seizure (within one week after TBI). Alternatively, the data must be presented in a manner that allows independent calculation of the relevant percentages by ECRI Institute. Studies that did not separate out patients who had early seizures or early plus late seizures from patients who had first-time late seizures were excluded.
- 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.

Appendix D: Excluded Articles

Table D-1. Key Question 1

Reference	Year	Reason for Exclusion
Schultheis et al.(99)	2007	No relevant outcomes
Rapport et al.(100)	2006	No relevant outcomes
Leon-Carrion et al.(101)	2005	No relevant outcomes
Patomella et al.(102)	2004	No relevant outcomes, mostly stroke patients
Stern et al.(103)	2004	No patients with TBI
Wikman et al.(104)	2004	Mostly stroke patients, only 2 patients had TBI
Fisk et al.(105)	2002	No relevant outcomes
Huchler et al.(106)	2002	Data from TBI patients mixed with stroke and tumor patients
Formisano et al.(107)	2001	Duplicates data from included study(65)
Lundqvist and Ronnberg(108)	2001	No relevant outcomes, no control group
Martelli and Mazzucchi(109)	2001	No relevant outcomes
Novack et al.(110)	2000	No relevant outcomes
Fisk et al.(111)	1998	No control group
Haikonen et al.(112)	1998	Most patients had stroke, only 3 patients had TBI
Laaperi et al.(113)	1997	Combines patients with several disabilities/disorders in their data analysis
Haaland et al.(114)	1994	No relevant outcomes
Katz et al.(115)	1990	Combined analysis of patients with TBI and stroke
Van Zomeren et al.(116)	1988	<10 patients/group
Stokx and Gaillard(117)	1986	<10 patients/group for driving task outcomes
Sivak et al.(118)	1981	Combined analysis of patients with TBI, stroke and cerebral palsy
Bowers and Marshall(119)	1980	No relevant outcomes

Table D-2. Key Question 2

Reference	Year	Reason for Exclusion
Lundqvist et al.(120)	2008	Combined data analysis of patients with TBI and subarachnoidal hemorrhage
Lundqvist and Alinder(121)	2007	Most brain injuries were non-traumatic
Klonoff et al.(122)	2006	No relevant outcomes
McKenna et al.(123)	2004	Combined data analysis of patients with TBI, stroke, and dementia
Kreutzer et al.(124)	2003	No relevant outcomes
Schultheis et al.(125)	2003	No relevant outcomes
Formisano et al.(107)	2001	Duplicates data from included study(65)
Hawley(126)	2001	No relevant outcomes
Lundqvist(127)	2001	Combined data analysis of patients with TBI and subarachnoidal hemorrhage
Galski et al.(128)	1993	Combined data analysis of patients with TBI and stroke
Fox et al.(129)	1992	Combined data analysis of patients with TBI, stroke, and other disorders
Galski et al.(130)	1992	Combined data analysis of patients with TBI and stroke
Galski et al.(131)	1990	Combined data analysis of patients with TBI and stroke
Priddy et al.(132)	1990	Combined data analysis of patients with TBI, stroke, and other disorders

Table D-3. Key Question 3

Reference	Year	Reason for Exclusion
Salazar et al.(133)	2000	No relevant outcomes
Sivak et al.(134)	1984	No relevant outcomes, <10 patients
Sivak et al.(135)	1982	Not a full article, <10 patients

Table D-4. Key Question 4

Reference	Year	Reason for Exclusion
Skandsen et al.(136)	2008	Doesn't report whether any patients had early seizures
Ryan et al.(137)	2006	Study does not separate data for early and late seizures
Watson et al.(138)	2004	Study does not report percent of patients whose first seizure was a late seizure
Mazzini et al.(139)	2003	Unclear whether study only reported number of patients with >1 late seizure
Temkin(140)	2003	Study does not report percent of patients whose first seizure was a late seizure
Singer(141)	2001	Study does not separate data for early and late seizures
Aarabi et al.(142)	2000	Study does not separate data for early and late seizures
Annegers and Coan(87)	2000	Duplicate publication of included study(87)
Angeleri et al.(143)	1999	Study does not report percent of patients whose first seizure was a late seizure
Asikainen et al.(144)	1999	Study does not report percent of patients whose first seizure was a late seizure
Timkin et al.(145)	1999	Study does not report percent of patients whose first seizure was a late seizure
Marcikic et al.(146)	1998	Study does not separate data for early and late seizures
Haltiner et al.(147)	1997	Study does not report percent of patients whose first seizure was a late seizure

Reference	Year	Reason for Exclusion
Haltiner et al.(148)	1996	Study does not report percent of patients whose first seizure was a late seizure
Salazar et al.(149)	1995	Study does not separate data for early and late seizures
Bontke et al.(150)	1993	Study does not follow patients beyond inpatient rehabilitation period
Manaka(151)	1992	Study does not report percent of patients whose first seizure was a late seizure
De Santis et al.(152)	1992	Study does not report total percentage of patients with late seizures
Da Silva et al.(153)	1990	Study does not report percent of patients whose first seizure was a late seizure
Temkin et al.(154)	1990	Study does not report percent of patients whose first seizure was a late seizure
Wroblewski et al.(155)	1990	Study does not address question – evaluates seizures associated with antidepressant use
Guidice and Berchou(156)	1987	Study does not report percent of patients whose first seizure was a late seizure
Weiss et al.(157)	1986	Study does not report percent of patients whose first seizure was a late seizure
Salazar et al.(158)	1985	Study does not separate data for early and late seizures
Weiss et al.(159)	1983	Study does not report percent of patients whose first seizure was a late seizure
Young et al.(160)	1983	Study only reports data concerning early seizures
Young et al.(161)	1983	Study does not report percent of patients whose first seizure was a late seizure
Servit and Musil(162)	1981	Study does not separate data for early and late seizures
Zajac et al.(163)	1980	Unclear whether any patients had early seizures
Lewin et al.(164)	1979	Study does not report percent of patients whose first seizure was a late seizure
Penry et al.(165)	1979	Meeting abstract
Young et al.(166)	1979	Study does not report percent of patients whose first seizure was a late seizure
Jennett(167)	1973	Study duplicates data presented in included reference(95)
Jennett et al.(168)	1973	Study does not report percent of patients whose first seizure was a late seizure
Nuutila and Huusko(169)	1972	Study does not report what percent of patients (if any) had early seizures among those who had late seizures
Courjon(170)	1970	Study evaluated only TBI patients who developed post-traumatic epilepsy
Paillas et al.(171)	1970	Study does not report percent of patients whose first seizure was a late seizure
Miller and Jennett(172)	1968	No relevant outcome
Russell(173)	1968	Study does not report percent of patients whose first seizure was a late seizure

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

As stated in the main text, ECRI evidence reports differ substantially from other systematic reviews in that we provide two types of conclusion—qualitative conclusions and quantitative conclusions. In order to reach these conclusions we use an algorithm developed by ECRI to guide the conduct and interpretation of the analyses performed during the development of this evidence report.(24) 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 is composed of three distinct sections: a *General* section, a *Quantitative* section, and a *Qualitative* section. The system uses 14 decision points (Table 31). Four of them 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 5-9) or qualitative conclusions (Decision Points 10-14). 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 (quality, consistency, etc.) can vary by outcome.

Table 31. Decision Points in the ECRI 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; 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 two revised versions of the Newcastle-Ottawa Quality Assessment Scale (one for case-control studies, one for cohort studies).(174) 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" was 5. Quality scores were converted to categories as shown in Table 6 (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 (cohort)
High Quality	
Moderate Quality	≥8.0
Low Quality	<8.0

NOQAS: Newcastle-Ottawa quality assessment scale

Decision Point 3: Is a Quantitative Analysis Potentially Appropriate?

The answer to Decision Point 3 depends on 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 less than three studies are available, no quantitative estimate is usually appropriate, regardless of reporting. Another situation that does not permit a quantitative estimate is when at least three studies are relevant to the general topic, but fewer than 75% of them reported the outcome and as well as 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 there are only a small number of patients 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 non-significant results are also potentially informative, but only if they exclude the possibility that a clinically significant treatment effect exists.

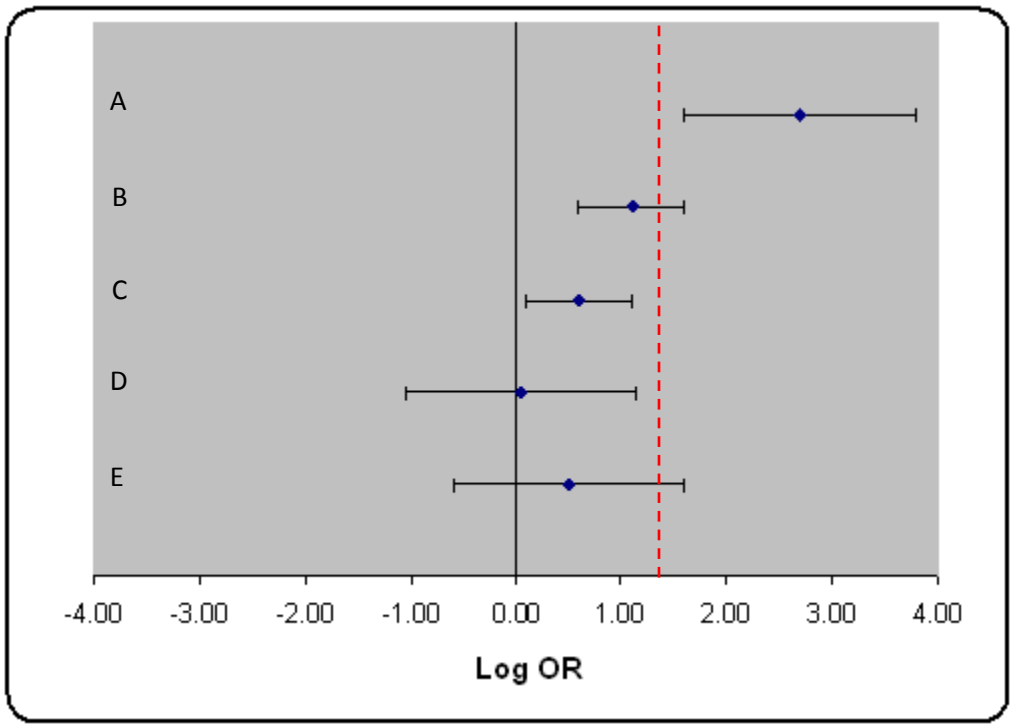
When a meta-analysis is performed, a key concern is the confidence interval around the random-effects summary statistic. If this interval is so wide that it includes a clinically significant (or substantial) effect in one direction *and also an effect in the opposite direction*, then the evidence is inconclusive, and therefore uninformative.(175)

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 0. This would be indicated whenever the confidence interval does not overlap 0.
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 non-informative.

Figure E-1. Informative Findings



Dashed Line = 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 non-informative.

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.(37) 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 (REMA). 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.

We use three different sensitivity analyses. These sensitivity analyses are:

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.* If a meta-analysis has 10 or more studies, we perform a test to determine the likelihood of publication bias. The publication bias test used in this evidence report was that of Duval and Tweedie.(51-54) Based on the degree of asymmetry in a funnel plot constructed from the findings of the included studies, this test(53,54)estimates the number of unpublished studies (and their effect sizes). After 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 random-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. We typically perform two different cumulative random-effects meta-analyses:
    a. Studies are added cumulatively to a random-effects meta-analysis by date of publication-oldest study first.
    b. Studies are added cumulatively to a random-effects meta-analysis by date—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 effect of >±5%.

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

Table E-2. Prespecified Tolerance Levels

Effect size Estimate	WMD	SMD	% of Individuals	RR	OR
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 where we had a heterogeneous evidence base consisting of at least 10 studies. Consequently, Decision Points 8 and 9 are irrelevant to this 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 non-significant 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 with drug-

free controls, do all included studies find that cannabis abuse 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 centers and 2) either ≥100 patients or at least 3 centers enrolled ≥20 patients/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 where 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

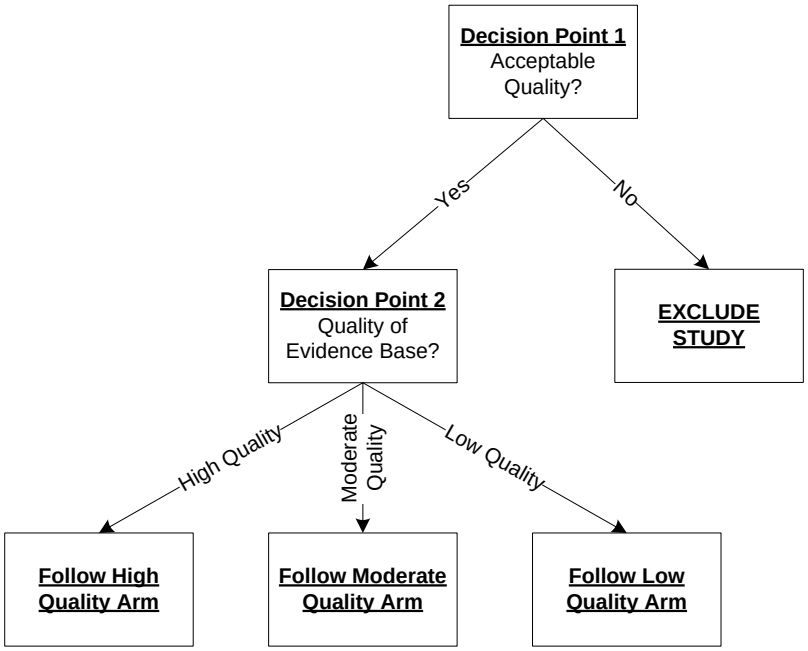


Figure E-3. High Quality Pathway

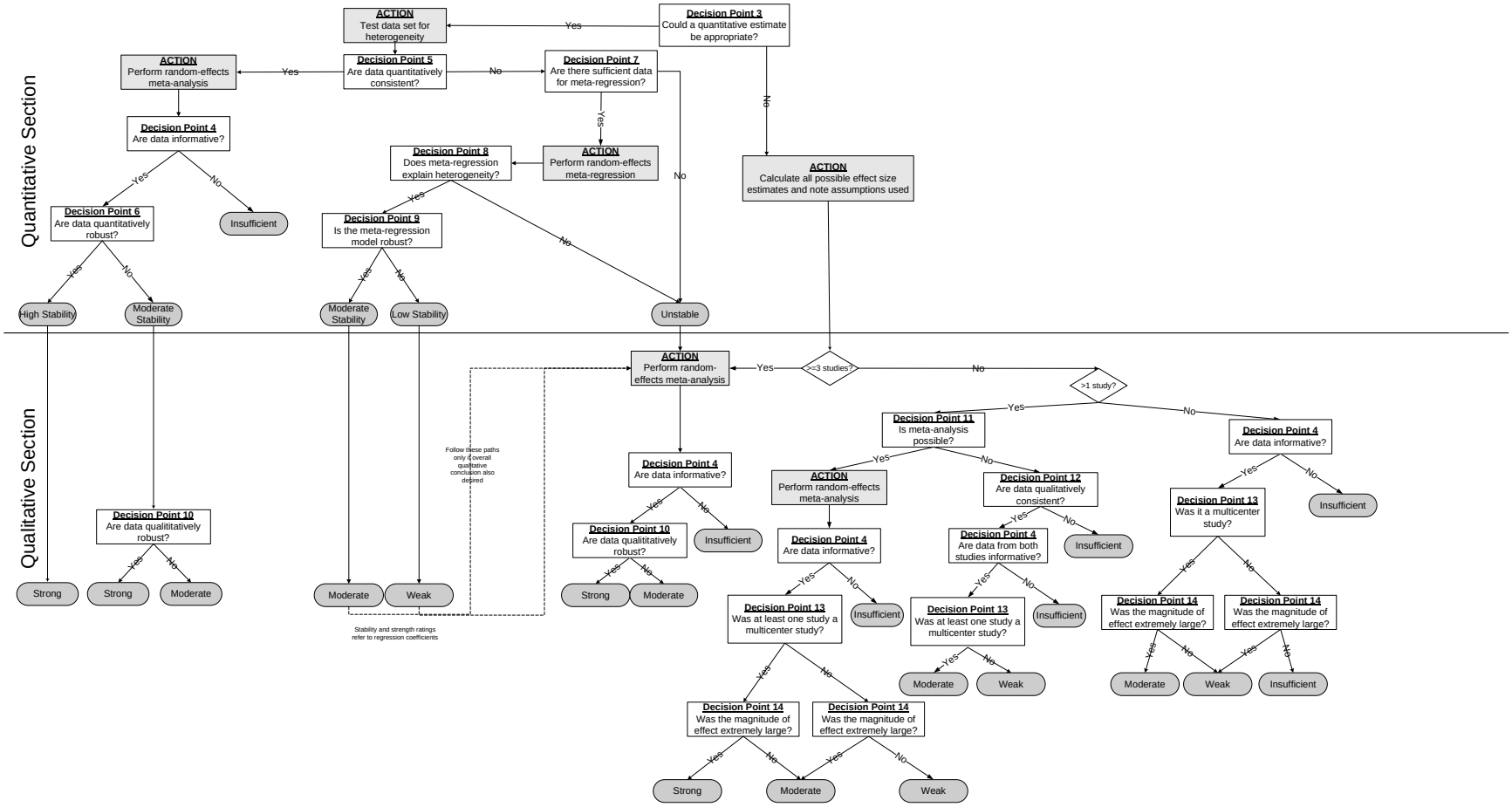


Figure E-4. Moderate Quality Pathway

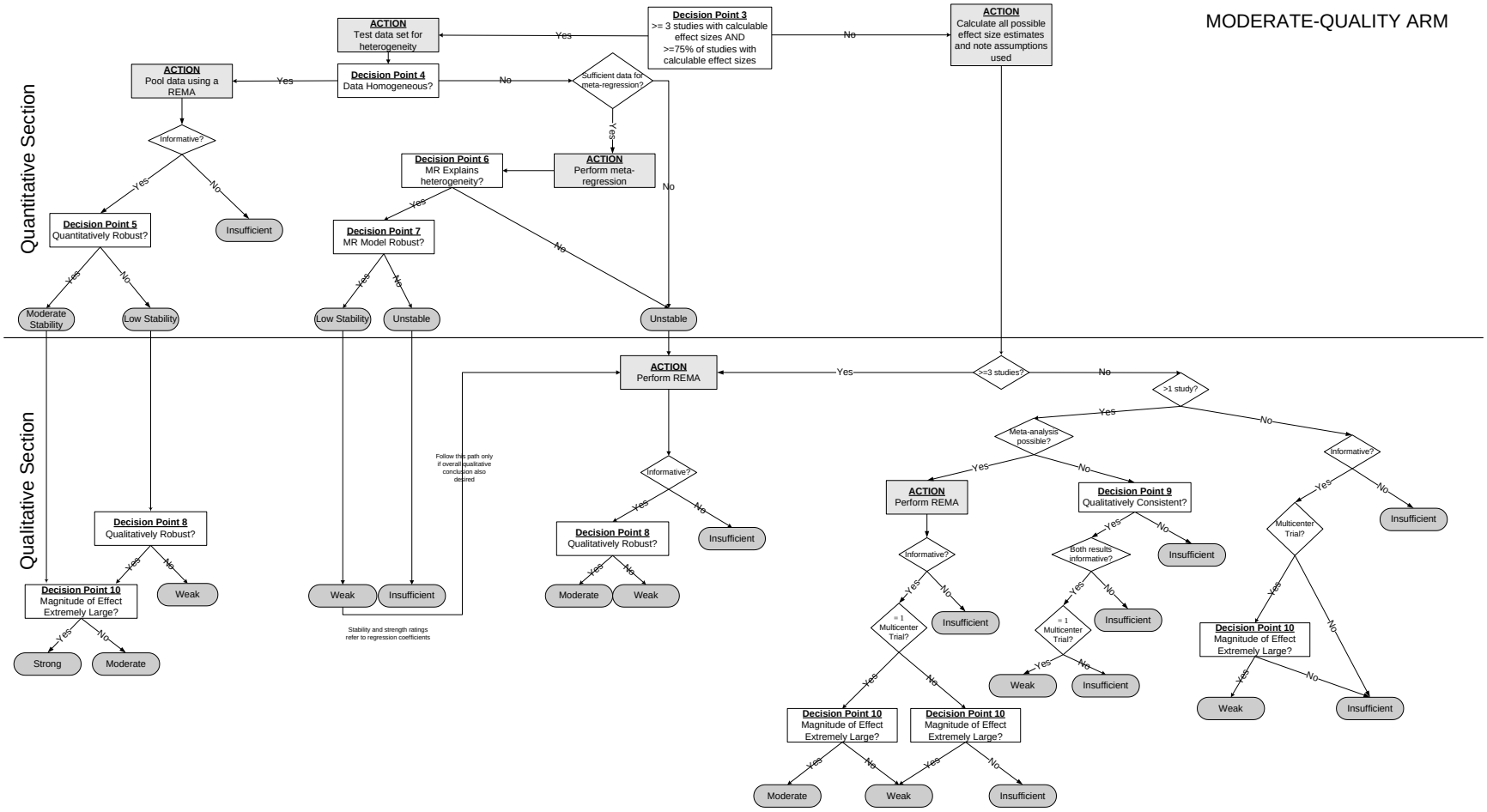
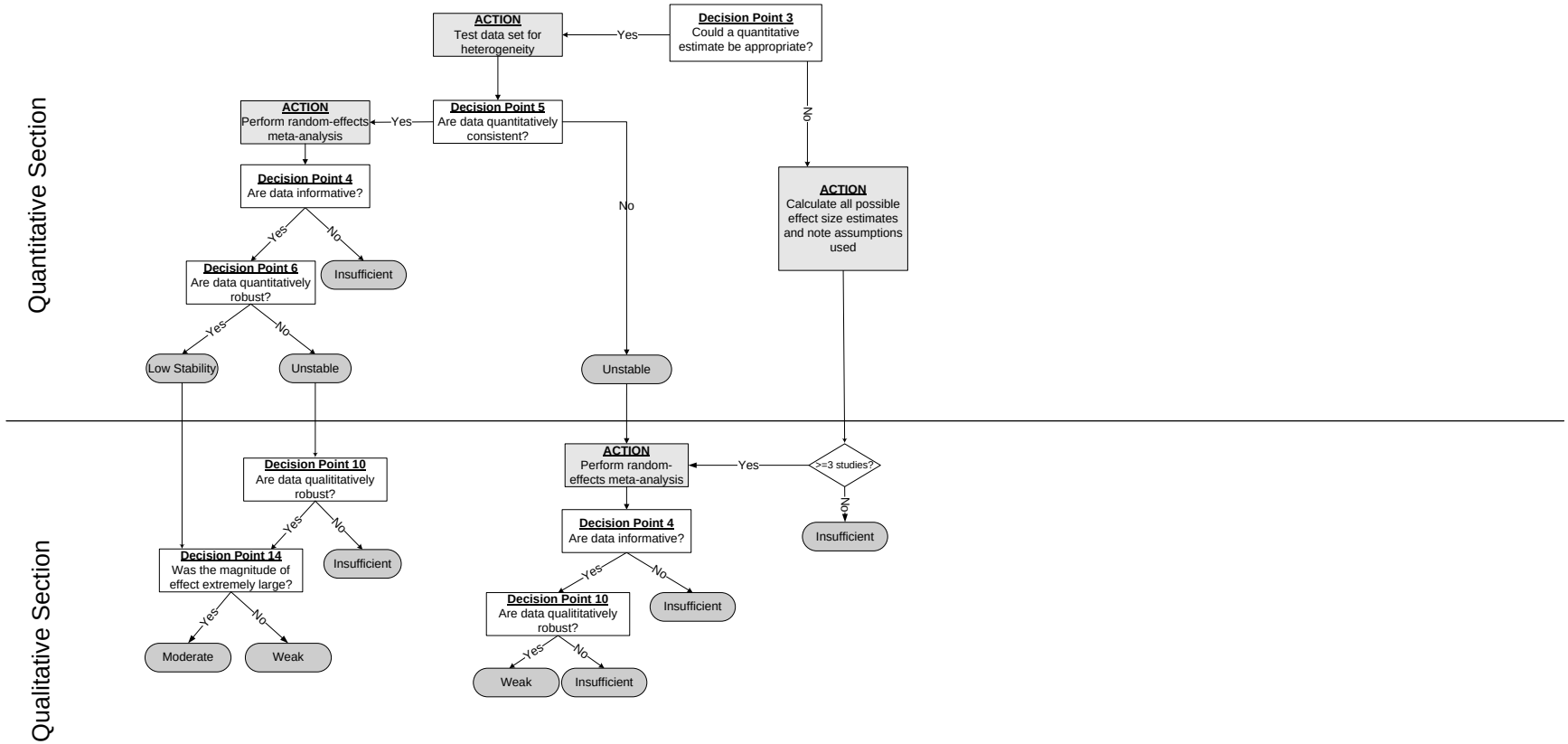


Figure E-5. Low Quality Pathway



Appendix F: Quality Assessment Instruments Used

Since the evidence base for all four key questions consisted of controlled or uncontrolled cohort studies, study quality was assessed using a revised version of the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies.(174)

Revised Newcastle-Ottawa Quality Assessment Scale for Cohort Studies

Question #	Question
1	Are the exposed cohorts representative of the average motor vehicle driver in the community?
2	Are the non-exposed cohorts 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 non-exposed cohorts?
9	Was the funding free of financial interest?
10	Were the conclusions supported by the data

Appendix G: Quality Score Tables

Key Question 1

Table G-1. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
TBI and Crash Risk												
Schanke et al.(64)	2008	Y	Y	Y	N	Y	N	Y	Y	NR	Y	Moderate
Formisano et al.(65)	2005	Y	S	Y	N	Y	N	Y	Y	NR	Y	Low
Schneider and Gouvier(66)	2005	Y	Y	S	N	Y	N	Y	Y	NR	Y	Low
Schultheis et al.(67)	2002	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Moderate
Haselkorn et al.(68)	1998	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	Moderate
TBI and Driving Performance (on-road test or simulation)												
Cyr et al.(69)	2008	Y	Y	Y	Y	Y	N	Y	Y	NR	Y	Moderate
Lew et al.(70)	2005	Y	Y	Y	Y	Y	N	Y	Y	NR	Y	Moderate
Korteling(71)	1990	Y	Y	Y	Y	Y	N	Y	Y	NR	Y	Moderate
Kewman et al.(72)	1985	N	N	N	Y	N	N	Y	Y	Y	Y	Low

Key Question 2

Table G-2. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Studies of Factors Associated with Crash/Driving Offenses												
Rapport et al.(73)	2008	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Moderate
Formisano et al.(65)	2005	Y	Y	Y	N	N	N	Y	Y	NR	Y	Low
Pietrapiana et al.(74)	2005	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Moderate
Coleman et al.(75)	2002	Y	Y	Y	N	N	Y	Y	Y	Y	Y	Moderate
Studies of Factors Associated with Road Test Outcomes												
Bouillon et al.(76)	2006	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Moderate
Novack et al.(77)	2006	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Moderate
Radford et al.(78)	2004	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Moderate
Strypstein et al.(79)	2001	Y	Y	Y	N	N	N	Y	Y	NR	Y	Low
Korteling and Kaptein(80)	1996	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	Moderate
Brooke et al.(81)	1992	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Moderate
Gouvier et al.(82)	1989	N	N	Y	Y	N	N	Y	Y	Y	Y	Low

Key Question 3

Table G-3. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Kewman et al.(72)	1985	N	N	N	Y	N	N	Y	Y	Y	Y	Low

Key Question 4

Table G-4. Quality Assessment Table for Cohort Studies

Reference	Year	Items										Quality Category
		1	2	3	4	5	6	7	8	9	10	
Diaz-Arrastia et al.(90)	2003	S	S	Y	Y	Y	Y	Y	Y	Y	Y	Moderate
Englander et al.(88)	2003	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Moderate
Annegers et al.(14,87)	1998, 1980	Y	Y	Y	N	Y	N	Y	Y	NR	Y	Moderate
Murri et al.(91)	1992	S	S	Y	Y	Y	N	Y	Y	NR	Y	Moderate
Heikkinen et al.(92)	1990	Y	Y	Y	Y	Y	N	Y	Y	NR	Y	Moderate
McQueen et al.(93)	1983	Y	Y	Y	Y	Y	N	Y	Y	N	Y	Moderate
Wohns and Wyler(94)	1979	Y	Y	Y	N	Y	N	Y	Y	Y	Y	Moderate
Jennett(95)	1975	Y	Y	Y	Y	Y	N	Y	Y	NR	Y	Moderate
Weiss and Caveness(96), Evans(97)	1972, 1963	S	S	Y	N	Y	N	Y	Y	NR	Y	Low