Final Evidence Report: Executive Summary

Diabetes and Commercial Motor Vehicle Driver Safety

Presented to

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This report is comprised of research conducted to analyze the impact of Diabetes on Commercial Motor Vehicle Driver Safety. Federal Motor Carrier Safety Administration considers evidence, expert recommendations, and other data, however, all proposed changes to current standards and guidance (guidelines) will be subject to public-notice-and-comment and regulatory processes.

Policy Statement

This report was prepared by ECRI under subcontract to MANILA Consulting Group, Inc., which holds a prime contract with the Department of Transportation's Federal Motor Carrier Safety Administration. ECRI is an independent, nonprofit health services research agency and a Collaborating Center for Health Technology Assessment of the World Health Organization. ECRI has been designated an Evidence-based Practice Center (EPC) by the United States Agency for Healthcare Research and Quality. ECRI'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's research and experience are available through its publications, information systems, databases, technical assistance programs, laboratory services, seminars, and fellowships. The purpose of this evidence report is to provide information regarding the current state of knowledge on this topic. It is not intended as instruction for medical practice, or for making decisions regarding individual patients.

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Executive Summary

Purpose of Evidence Report

Of all occupations in the United States, workers in the trucking industry experience the third highest fatality rate, accounting for 12 percent of all worker deaths. About two thirds of fatally injured truck workers were involved in highway crashes. According to statistics from the U.S. Department of Transportation, there were 137,144 non-fatal crashes involving a large truck in 2005. Of these, 59,405 were crashes that resulted in an injury to at least one individual, for a total of 89,681 injuries. In 2004,[1] 4,862 large trucks were involved in fatal accidents for a total of 5,190 fatalities. The purpose of this evidence report is to examine the relationship between diabetes mellitus and the risk for a motor vehicle crash. In order to meet the aims of this evidence report we addressed four key questions. These four key questions are as follows:

Key Question 1: Are individuals with diabetes mellitus at increased risk for a motor vehicle crash when compared with comparable individuals who do not have diabetes?

Key Question 2: Is hypoglycemia an important risk factor for a motor vehicle crash among individuals with diabetes mellitus?

Key Question 3: What treatment-related factors are associated with an increased incidence of severe hypoglycemia among individuals with diabetes mellitus?

Key Question 4: How effective is hypoglycemia awareness training in preventing the consequences of hypoglycemia?

The effects of the chronic complications of diabetes mellitus on driving ability were beyond the scope of the present evidence report. However, it is the intent of the program under which this report was commissioned to address these complications in later proceedings.

Identification of Evidence Bases

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

A total of seven electronic databases (Medline, PubMed (pre Medline), EMBASE, PSYCH Info, CINAHL, TRIS, the Cochrane library) were searched (through May 28, 2006). In addition, we examined the reference lists of all obtained articles with the aim of identifying relevant articles not identified by our electronic searches. Hand searches of the “gray literature” were also performed. Admission of an article into an evidence base was determined by formal retrieval and inclusion criteria that were determined *a priori.*

[1] Fatality data for 2005 were not available at the time of writing.

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

The set of analytic techniques used in this evidence report was extensive. Random- and fixed-effects meta-analyses were used to pool data from different studies.(1-4) Differences in the findings of studies (heterogeneity) were identified using the Q-statistic and I^2.(5-7) Sensitivity analyses, aimed at testing the robustness of our findings, included the use of cumulative fixed- and random-effects meta-analysis.(8-10) The presence of publication bias was tested for using the "trim and fill" method.(11-13)

Presentation of Findings

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

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

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

Findings

<u>Key Question #1: Are individuals with diabetes mellitus at increased risk for a motor vehicle crash when compared with comparable individuals who do not have diabetes?</u>

General Answer to Key Question #1: <u>Yes (With Qualifications)</u>

Specific findings of our assessment of the evidence that addressed Key Question #1 are presented below:

1. **A paucity of data from studies that enrolled CMV drivers with diabetes precludes determination of whether CMV drivers with diabetes are at increased risk for a motor vehicle accident.**

   A single, moderate-quality case-control study evaluated crash risk among Canadian CMV drivers with diabetes as compared with comparable CMV drivers who did not have the disorder. While the results of this study are directly applicable to CMV drivers in the United States, it is not a high-quality study and its findings have not been replicated. Consequently, one cannot draw an evidence-based conclusion pertaining to the whether CMV drivers with diabetes are at an increased risk for a motor vehicle accident.

2. **As a group, drivers with diabetes are at an increased risk for a motor vehicle crash when compared with comparable drivers who do not have the disorder (Strength of Evidence: Weak). The magnitude of this increased risk is small but statistically significant (Risk Ratio=1.19; 95% CI: 1.08–1.31). In other words, the crash risk for an individual with diabetes is 1.19 times greater than a comparable individual who does not have the condition (Stability of Estimate of Risk Ratio: Weak).**

   Thirteen low- to moderate-quality case-control studies compared crash risk among drivers with diabetes (cases) and a comparable group of drivers who do not have the disorder (controls). Quantitative analysis of outcome data from these studies found that the outcome data were homogeneous. A fixed effects meta-analysis in which these data were pooled found than the risk for crash among drivers with diabetes was 1.19 (95% CI: 1.08–1.31) times greater that the risk for crash among drivers who do not have the disorder. A series of sensitivity analyses designed to test the stability of this estimate found this estimate to be robust.

   Despite the robustness of our findings, we have refrained from drawing a strong conclusion. This is because case-control studies are inherently susceptible to bias. Also, many of the studies included in the analysis were either poorly designed and/or conducted, or they were poorly reported. The most important potential source of bias to affect some of the studies in this evidence base was the failure to control for differences in exposure to risk (the amount of time driving) among the cases and controls. However, the fact that data extracted from the 13 studies were homogeneous suggests that failure to control for differences in exposure did not result in biased risk-ratio estimates. Also, a sensitivity analysis in which risk-ratio data were compared between two subgroups of studies (one subgroup composed of studies that controlled for exposure and the second subgroups consisting of studies that did not) found no evidence that failure to control for exposure resulted in a systematic over or underestimate of the observed risk ratio.

3. **Whether drivers with type 1 or type 2 diabetes are overrepresented in populations of drivers who have experienced a motor vehicle crash cannot be determined at this time.**
   Three moderate-quality case-control studies, all of which enrolled individuals older than age 65, compared the prevalence of drivers with diabetes among a cohort of drivers who had experienced a crash (cases) with the prevalence of drivers with diabetes among a cohort of drivers who had not experienced a crash (controls). Homogeneity testing found that the findings of the three included studies differed significantly. Because of the small size of the evidence base, we did not attempt to explain the inconsistency in the findings of the three studies. Consistent with the findings above, a random-effects meta-analysis found that drivers with diabetes do tend to be overrepresented among samples of drivers who have experienced a crash. However, this overrepresentation is not statistically significant (Odds Ratio=1.41; 95% CI: 0.86–2.29, P=0.1760). Consequently, we must conclude that at present, it is unclear whether drivers with diabetes are overrepresented among populations of drivers who have experienced a motor vehicle crash. More data are required before an evidence-based conclusion can be drawn about whether drivers with diabetes are overrepresented among populations of drivers who have crashed.

4. **Whether the subgroup of drivers with diabetes who are controlled by insulin is overrepresented in populations of drivers who have experienced a motor vehicle crash cannot be determined at this time.**

   All three of the case-control studies above attempted to determine whether drivers with diabetes treated using insulin are overrepresented among populations of drivers who have experienced a motor vehicle crash. These data were found to be homogeneous. Consequently, they were pooled using fixed-effects meta-analysis. As was the case in the previous analysis, the present analysis found that drivers with diabetes controlled using insulin tend to be overrepresented among samples of drivers who have experienced a crash. However, this overrepresentation is not statistically significant (Odds Ratio=1.35; 95% CI: 0.86–1.70, P=0.1695). Consequently, we conclude that at the present time, it is unclear whether drivers with diabetes are overrepresented among populations of drivers who have experienced a motor vehicle crash. More data are required before an evidence-based conclusion can be drawn about whether drivers with diabetes controlled by insulin are overrepresented among populations of drivers who have crashed.

Key Question #2: Is hypoglycemia an important risk factor for a motor vehicle crash among individuals with diabetes mellitus?

General Answer to Key Question #2: Yes (With Qualifications)

The findings of our assessment of the evidence addressing Key Question 2 are presented below. None of the included studies examined the effects of hypoglycemia on simulated driving ability and cognitive or psychomotor function in a group of CMV drivers with diabetes. Also, all of the included studies examined the effects of hypoglycemia in individuals with type 1 diabetes only. No individuals with type 2 diabetes were enrolled in any included study. Even if current interstate restrictions on CMV drivers with insulin-treated diabetes are lifted, non-insulin treated individuals with type 2 diabetes will still comprise the vast majority of CMV operators who have

the disorder. Consequently, the degree to which the findings of the included studies, particularly findings related to specific driving skills, can be generalized to CMV operators is unclear.

1. **Hypoglycemia has a significant deleterious effect on the driving ability of some individuals with type 1 diabetes (or IDDM) when measured using a driving simulator (Strength of Evidence: Moderate). Due to a paucity of data (only two studies), no attempt was made to determine a quantitative estimate of the relationship between the deterioration in driving competency and blood glucose levels.**

   Three small moderate-quality studies assessed the effects of induced hypoglycemia on simulated driving ability. No individuals with type 2 diabetes were enrolled in any included study. Consequently, the degree to which the findings of the included studies, particularly findings related to specific driving skills, can be generalized to CMV operators is unclear.

   All three studies found that driving ability was impaired during hypoglycemia across several variables. Despite agreement across studies that driving ability is impaired by hypoglycemia, there is little agreement as to exactly which aspects of driving ability are most vulnerable to hypoglycemia and at what levels of hypoglycemia these impairments begin to become manifest.

2. **Hypoglycemia has a significant deleterious effect on the cognitive and psychomotor function of individuals with type 1 (or IDDM) as measured by a number of different tests of cognitive function (Strength of Evidence: Moderate). Because no more than two studies used the same tests of cognitive or psychomotor function, no attempt was made to determine a quantitative estimate of the relationship between functional loss and blood glucose levels.**

   Ten small low- to moderate-quality studies assessed the effects of induced hypoglycemia on cognitive and psychomotor function. These 10 studies consistently demonstrated that moderate hypoglycemia (blood glucose levels of 2.5–3.0 mmol/L[45–54 mg/dl]) had an acute deleterious effect on the ability of some (but not all) individuals with insulin-dependent diabetes to perform a wide variety of cognitive and psychomotor tasks. At the present time no comparable data sets are available for individuals who do not require insulin to control their diabetes.

Key Question #3: What treatment-specific risk factors are associated with an increased incidence of severe hypoglycemia among individuals with diabetes mellitus?

General Answer to Key Question #3: Unclear

Known treatment-related risk factors for an increased incidence of severe hypoglycemia include lower HbA1c, the use of insulin, and intensified insulin treatment (multiple injections per day). The aim of this question was to determine the effect of specific treatment options (different types of insulin, different types of oral hypoglycemic agents, different treatment combinations) on the incidence of severe hypoglycemia among individuals with diabetes.

The most appropriate study designs for the evaluation of risk factors associated with a particular condition among representative populations while controlling for other known risk factors come

from epidemiology. Consequently, our searches focused on identifying epidemiological studies (case-control studies or cohort studies) that attempted to determine the relative risk for hypoglycemia that is associated with different treatment options, different treatment regimes, or different modes of treatment administration.

Most available information on the frequency of the occurrence of hypoglycemia among patients who undergo treatment for diabetes comes from efficacy and safety studies (usually randomized controlled trials). Although randomized controlled trials (RCTs) are often considered, "the gold standard cohort study," when used to assess treatment effectiveness and safety of a treatment, RCTs have a number of shortcomings, including the following:

- Safety and effectiveness trials tend to enroll carefully screened and selected patients who are not representative of the broader population.
- Safety and effectiveness trials use protocols that are not reflective of disease management in the broader population.
- Safety and effectiveness trials tend to be small and short-term, which precludes an accurate determination of the true incidence of hypoglycemia.

To ensure that any assessment of the available evidence addressing Key Question 3 was meaningful we developed restrictive retrieval and inclusion criteria designed to exclude studies that suffer from the shortcomings described above. As a consequence, several thousand articles were screened but not retrieved because they were either not generalizable to the broader population, they used protocols that were not reflective of how treatment would be used in clinical practice, or they were small or used a short follow-up time that precluded accurate estimation of the incidence of hypoglycemia.

Key Question #4: How effective is hypoglycemia awareness training in preventing the consequences of hypoglycemia?

General Answer to Key Question #4: Unclear

The findings of our analysis of the best available evidence pertaining to the effectiveness of Blood Glucose Awareness Training (BGAT) are presented below:

1. **BGAT improves the ability of individuals with type 1 diabetes to accurately estimate their blood glucose levels (Strength of Evidence: Moderate)**

   Qualitative assessment of the data from five-moderate quality studies consistently demonstrated that BGAT improves the ability of individuals with type 1 diabetes to accurately estimate their blood glucose levels.

2. **A paucity of consistent evidence precludes a determination from being made concerning whether BGAT is effective in reducing the incidence of severe hypoglycemia.**

   Simply because individuals who have undergone BGAT demonstrate improvements in their ability to accurately estimate their blood glucose levels does not necessarily mean that BGAT will lead to a reduction in the incidence of severe hypoglycemia. Consequently, we looked for direct evidence of a negative relationship between BGAT and the incidence of severe hypoglycemia. Two moderate-quality studies that enrolled

individuals with type 1 diabetes presented data on the incidence of severe hypoglycemia following exposure to BGAT. The results of these two small studies were inconsistent, with one study finding a benefit while the other study did not. The inconsistencies in the findings of the two studies cannot be explained. Given this, it remains unclear whether exposure to BGAT results in measurable reductions in the incidence of severe hypoglycemia among individuals with type 1 diabetes.

Conclusions

On the Findings of the Evidence Report

Direct evidence pertaining to diabetes and CMV driver safety was extremely scarce; only one such study (which addressed Key Question #1) was included in this evidence report. Consequently, we were obliged to turn to evidence from studies that assessed the relationship between diabetes and driver safety in the general population. On average, drivers in the general population differ from CMV drivers in that they are far less experienced. However, CMV drivers are exposed to far more risk than the average driver because that they are driving for longer periods of time over far greater distances in a large variety of traffic environments. Whether superior driving experience outweighs the risks associated with increased driving exposure is unclear; however, the fact that truck driving is considered to be a very dangerous occupation suggests that it does not.

Our assessment of the available evidence pertaining to crash risk found that the average driver with diabetes (type 1 or type 2) has a small but significant incremental increase in the risk for motor vehicle crash over and above that of a comparable individual who does not have the disorder (Risk Ratio=1.19, 95% CI; 1.08–1.31). In other words, the risk of an individual with diabetes being involved in a motor vehicle crash is approximately 1.19 times greater than that of a comparable individual who does not have the disorder.

One possible cause of the excess risk for a crash seen in individuals with diabetes is incapacitation due to hypoglycemia. Indeed there is ample anecdotal evidence in the literature (in the form of case reports) to suggest that some crashes experienced by individuals with diabetes can be attributed to hypoglycemia. To date no-well designed study has provided direct evidence supporting the contention that hypoglycemia is the major contributor to the increased risk for crash among individuals with diabetes. Indirect evidence, however, is reasonably plentiful. Our analysis of data from 13 independent studies consistently found that moderate-to-severe hypoglycemia has a deleterious effect on the driving ability, cognitive function, and psychomotor function of some individuals with type 1 diabetes. Due to a paucity of acceptable data, we were unable to determine the extent to which hypoglycemia affected these measures in individuals with type 2 diabetes.

Because there is a reasonably large body of literature showing that hypoglycemia occurs more often among individuals treated with insulin than among those treated by pharmacotherapy or diet alone, one would might reasonably expect that insulin-treated drivers are at a higher risk for a motor vehicle crash risk than non-insulin treated drivers. Surprisingly, a series of analyses designed to determine the excess risk associated with insulin treatment did not confirm this. One possible explanation for the finding that drivers with insulin-treated diabetes do not appear to be at a higher risk for a motor vehicle crash than drivers with non-insulin treated diabetes is that a process of self-selection occurs among individuals with insulin-treated diabetes whereby the

most severely affected individuals either restrict their driving or do not drive at all. As a consequence, crash risk estimates determined for drivers with insulin-treated diabetes are based on a subset of individuals with lower rates of hypoglycemia than would be seen if all individuals with insulin-treated diabetes drove.

Because there is evidence (albeit indirect) to suggest that hypoglycemia is a primary contributor to the excess crash risk observed among individuals with diabetes, a number of groups have attempted to develop programs that aim to diminish its incidence. One such program is BGAT. BGAT is a psychoeducational intervention program designed to assist individuals with type 1 diabetes in managing and maintaining tight diabetic control. The value of BGAT in managing and maintaining control in individuals with type 2 diabetes has not been assessed. Our analysis of studies of the effectiveness of BGAT found that the program was effective in improving the ability of individuals with type 1 diabetes to accurately estimate their blood glucose levels. However, currently available evidence has not consistently demonstrated that this improvement in blood glucose level estimation leads to measurable reductions in the incidence of severe hypoglycemia among individuals with type 1 diabetes.

On the Limitations of this Evidence Report

The findings of this evidence report cannot be viewed as definitive. Like all systematic reviews the soundness of the answers it provides is entirely dependent on the quality, quantity, consistency, robustness, and generalizability (to the specific target population of interest) of the available evidence. In this report, the best available evidence was of low- to moderate-methodologic quality. Also, because only one study was directly generalizable to CMV drivers, the generalizability of the findings of this evidence report to this specific population is unclear.

On the Need for Further Studies

The lack of data from CMV drivers is, to some degree, a consequence of the fact that individuals with insulin-treated diabetes have until recently been unable to obtain an interstate CMV drivers license. However, several states allow individuals to drive large trucks within state and individuals with non-insulin treated diabetes are not precluded from obtaining an interstate CMV driver's license. Consequently, populations of CMV drivers with diabetes do exist and crash risk studies need to be performed in these populations so that the risk of crash among CMV driver's can be determined more definitively.

The fact that non-insulin treated diabetes does not exclude an individual from obtaining a CMV license, the fact that individuals with non-insulin treated diabetes is common, and the fact that studies on motor vehicle crash risk associated with this type of diabetes are rare, suggest there is a general belief that non-insulin dependent diabetes is not a serious threat to road traffic safety. This belief is supported to some degree by the fact that the incidence of severe hypoglycemia is lower among individuals with non-insulin dependent diabetes. The findings of this evidence report, however, suggest that this belief may be misplaced. Our analyses of the available data suggest that the excess crash risk associated with insulin and non-insulin dependant diabetes is similar. Consequently, there is an urgent need for direct comparisons of crash risk data from reasonably well-matched individuals with non-insulin and insulin-dependent diabetes.

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