Expert Panel Commentary and Recommendations

Diabetes and Commercial Motor Vehicle Driver Safety

Presented to

Federal Motor Carrier Safety Administration

September 8, 2006

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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.

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Introduction

U.S. Secretary of Transportation Norman Y. Mineta announced on March 7, 2006, the five medical experts who will serve on the Federal Motor Carrier Safety Administration's (FMCSA) first Medical Review Board (MRB). Section 4116 of the Safe, Accountable, Flexible, Efficient Transportation Equity Act: A Legacy for Users (SAFETEA-LU, Public Law 109-59) requires the Secretary of Transportation, with the advice of the MRB and a Chief Medical Examiner, to "establish, review, and revise medical standards for operators of commercial motor vehicles (CMVs) that will ensure the physical condition of operators is adequate to enable them to operate the vehicles safely." The MRB will be charged initially with the review of all current Federal Motor Carrier Safety Regulation (FMCSR) medical standards (49 CFR 391.41), as well as proposing new science-based standards and guidelines to ensure that drivers operating CMVs in interstate commerce, as defined in CFR 390.5, are physically qualified to do so. The MRB will, in the future, be asked to provide guidance on the curriculum for the training of the approximately 400,000 state-licensed medical examiners who conduct the physical examinations that qualify the more than 7 million operators of CMVs.

To provide a mechanism to inform FMCSA and its MRB in their charge of establishing realistic and responsible medical standards, FMCSA developed a program that provides unbiased and science-based statements pertaining to issues of particular importance to CMV driver safety. This program consists of the development of a series of pertinent key questions to be addressed through a systematic review of the available scientific literature. The findings of this systematic review of the literature are summarized in an evidence report that is reviewed by a panel of carefully screened experts chosen for their expertise in a relevant clinical area and their freedom from scientific or financial conflicts of interest. Members of the present expert panel were identified by FMCSA. Having provided time for each member of the expert panel to review the evidence report, FMCSA then convened an expert panel proceeding. The purpose of this proceeding was to comment on the evidence report and propose recommendations for consideration by FMCSA and its MRB to change or add standards or guidance for commercial drivers' medical qualification.

In this light, FMCSA convened an expert panel proceeding to review an evidence report titled, "Diabetes and Commercial Motor Vehicle Driver Safety." This expert panel proceeding was held at the U.S. Department of Transportation, Washington, DC, August 8–10, 2006. The expert panel began with a discussion of the overall objectives of the proceedings, followed by a discussion of four key questions addressed by the evidence report and the methodology used to address these questions. The findings of the evidence report were presented to the expert panel and an open discussion of the results followed. Using the information presented and their knowledge of the issues that surround diabetes and CMV driver safety, the expert panel developed commentary for each key question. This commentary was presented orally to FMCSA on the final day of the conference. This commentary document formalizes the output of the diabetes expert panel proceeding.

Scope of Diabetes Proceedings

The scope of the expert panel conference was determined by the key questions addressed by the evidence report titled, "Diabetes and Commercial Motor Vehicle Driver Safety." This evidence report was developed by ECRI under a subcontract held with Manila Consulting Group. The four key questions addressed by the evidence report were developed by FMCSA. The charge of the expert panel was to review the evidence report and analyses and add further interpretation and insight to its findings. This was to be accomplished through the development of a commentary on each question. In addition, the panel was charged with developing consensus recommendations for consideration by FMCSA; including a presentation to the MRB, one of FMCSA's advisory groups.

Consensus was achieved using the nominal group technique. Each expert was asked to produce commentary independently on the findings for each key question addressed by the evidence report. Expert panel members were called on to present their commentary in rotating order. Each commentary from each panel member for each key question was then discussed until a single commentary developed.

When the expert panel noted gaps in the available evidence, recommendations for future studies were made. The expert panel requested that FMCSA provide it (and future expert panels) with access to information held in existing FMCSA administered databases and registries that are currently under development. The expert panel also recommended that several additional questions be addressed in a future evidence report. Finally, the expert panel members made recommendations on the appropriate evaluation of CMV license applicants with diabetes and the training of medical examiners and suggested a protocol for dealing with differences of opinion between medical examiners and personal physicians of applicants.

Key Questions Addressed

The four key questions addressed by the expert panel were 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?

In addressing this question we examined the relationship between hypoglycemia and the following direct and indirect outcome measures:

a) Simulated driving performance (indirect)

b) Driving-related cognitive and psychomotor performance (indirect)

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

Potential factors to be assessed in addressing this question included the following:

a) Mechanism of glycemic control (insulin, 1st generation[1] sulfonylureas, 2nd generation[2] sulfonylureas, meglitinides, and other hypoglycemic drugs used to control blood glucose levels)

[1] 1st generation sulfonylureas include: tolbutamide, acetohexamide, tolazamide, chloropropamide.

b) Route of insulin administration (inhaled, subcutaneous injection, pump)

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

Findings of Evidence Report and Commentary

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?

General answer to Key Question #1: *Yes (With Qualifications)*

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 one from determining whether CMV drivers with diabetes are at increased risk for a motor vehicle crash.**

   A single, moderate-quality nested case-control study(1) 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 whether CMV drivers with diabetes are at an increased risk for a motor vehicle crash.

   Expert Panel Comments

   The expert panel felt that the importance of the case study of Laberge-Nadeau et al.(1), should not be minimized, as it is the only study available that examines crash risk in CMV drivers with diabetes. They noted that the that this study found that there was no increase in crash risk with the singular exception of a small group of with diabetes who were not on insulin, who had no complications of the disorder, and who drove straight trucks. The panel commented that crash risk in such individuals should be examined in future epidemiologic studies of CMV drivers. The panel noted that the CMV drivers with diabetes who were on insulin did not appear to have an increase in risk of crash. They also noted that there was a relationship between exposure (miles driven) and crash risk, particularly in drivers of articulated trucks. The panel also recommended further study of the physical demands associated with the various types of trucks to explore possible reasons for these discrepancies.

The expert panel members commented that future publications from the Canadian registry of CMV truck drivers were expected and that they should be regularly reviewed for new information specific to diabetics.

[2] 2nd generation sulfonylureas include: glipizide, glyburide, glimepiride

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-moderate quality case-control studies(1-13) 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 that 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. Having said this, 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 subgroup 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.

Expert Panel Comments

The expert panel noted that the majority (12/13) of the studies included in the analysis described above enrolled a general population of drivers, not CMV drivers. They also noted that the studies were of low to moderate quality. Thus, while the available evidence does suggest that drivers with diabetes are more likely to crash than individuals without diabetes, the strength of this evidence is weak. The panel noted that the available evidence does not demonstrate a higher risk of crash for individuals with diabetes who are treated with insulin than for those treated with other therapies. The panel concluded that the estimate that drivers with diabetes are 1.19 times more likely to crash than are drivers without diabetes is not sufficiently high or strong to warrant prohibiting all drivers with diabetes from obtaining CMV licenses.

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,(14-16) which enrolled individuals over the age of 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 showed 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 the present time, it remains unclear whether drivers with insulin-treated diabetes are overrepresented among populations of drivers who have experienced a motor vehicle crash. More data are required before an evidence-based conclusion about whether drivers with diabetes are overrepresented among populations of drivers who have crashed.

Expert Panel Comments

The expert panel noted that the three included studies all enrolled a general population of elderly (aged ≥ 65 years) drivers, not CMV drivers. They also noted that the evidence is inconclusive on the question of whether drivers over the age of 65 with either type 1 or type 2 diabetes are overrepresented among drivers who have crashed.

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

   Three case-control studies(14-16) *attempted to determine whether drivers with diabetes treated with insulin are overrepresented among populations of drivers who have experienced a motor vehicle crash. Relevant outcome 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 remains 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 about whether drivers with diabetes treated with insulin are overrepresented among populations of drivers who have crashed.*

Expert Panel Comments

The expert panel noted that evidence is inconclusive on whether drivers (not CMV drivers) with diabetes treated with insulin are overrepresented among drivers who crash, and noted that only drivers over the age of 65 were included in the available studies. The panel noted that drivers over the age of 65 represented only 4 percent of all CMV crashes reported in the FMCSA database, and recommended that FMCSA determine the number of active CMV drivers over the age of 65.

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. No 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 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 Insulin Dependent Diabetes Mellitus (IDDM) when measured using a driving simulator (Strength of Evidence: Moderate). Due to a paucity of consistent data, 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(17-19) 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.

Expert Panel Comments

The expert panel noted that while the findings of three studies suggested a possible relationship between induced hypoglycemia and impairments of simulated driving performance in individuals with type 1 diabetes, it remains unclear whether this

predicts a relationship between hypoglycemia outside the laboratory setting and actual driving performance or crash risk. The panel strongly recommended further study of the ability of data from driving simulators to predict actual crash risk.

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). Due to the fact that 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.(19-28) These 10 studies consistently demonstrated that moderate hypoglycemia (blood glucose levels in the region 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-treated 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 treat their diabetes.

Expert Panel Comments

The expert panel commented that impairments in cognitive and psychomotor function are well-known sequelae of hypoglycemia. The panel noted, however, that there is marked inter-individual variation in the level of hypoglycemia likely to lead to these impairments. They noted that impairments were found in some but not all individuals included in the three included studies, and that impairments only occurred at very low blood glucose levels. The panel members noted that the vast majority of CMV drivers with diabetes have type 2 diabetes. They questioned the relevance of these data from individuals with type 1 diabetes to individuals with type 2 diabetes treated with insulin, as these latter individuals are far less likely to experience hypoglycemia of the severity found to produce impairment in the included studies. The panel recommended further study of the ability of various measures of impairment of cognitive and psychomotor function to predict actual crash risk.

The expert panel concluded that the overall question as to whether hypoglycemia causes an increase in crash risk in individuals with diabetes could not be answered. The panel also expressed the opinion that the requirement for CMV drivers to maintain blood glucose levels in the range of 100 mg/dL to 400 mg/dL could encourage poor control, and should be reexamined. While the panel members agreed that hypoglycemia (e.g., below 60 mg/dL) should generally be avoided, they stated that this can and should be achieved without producing significant hyperglycemia. The panel members recommended that a systematic review of strategies for reducing the risk of severe hypoglycemia in individuals with diabetes be performed.

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*

No studies were identified that met the inclusion criteria for this evidence report. Consequently, we have not answered Key Question 3.

Known treatment-related risk factors for an increased incidence of severe hypoglycemia include lower Hemoglobin A1c (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 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 efficacy and safety of a treatment, RCTs have a number of shortcomings that weaken their value when it comes to drawing conclusions about populations in the "real world." These weaknesses include the following:

- *Safety and effectiveness trials tend to enroll carefully screened and selected patients who are not representative of the broader population.*
- *Safety and efficacy 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.*

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

Expert Panel Comments

The expert panel members noted that evidence on risk of hypoglycemia taken from trials using older forms of insulin and oral hypoglycemic agents is not applicable to currently recommended management of diabetes. Panel members noted that several agents currently in use do not cause hypoglycemia when used alone. These agents include metformin, alpha-glucosidase inhibitors and thiazolidinediones. The panel recommended that a systematic review examining the risk of hypoglycemia during treatment with the following agents and insulin delivery systems be considered:

- Insulin analogs
  - Delivered by insulin pump
  - Delivered by multiple injections
- Newer (2^{nd} generation) sulfonylurea drugs
  - Glyburide
  - Glipizide
  - Glimepiride

The panel members emphasized, however, that hypoglycemia is not likely to be the only or even the most important risk factor for crash among individuals with diabetes.

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 (29-34) consistently demonstrated that BGAT improves the ability of individuals with type 1 diabetes to accurately estimate their blood glucose levels.

Expert Panel Comments

The expert panel noted that whether BGAT is more effective in improving estimation of blood glucose levels than other forms of education for individuals with type 1 diabetes is unclear.

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, ECRI 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.(29,31) 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.

Expert Panel Comments

The expert panel agreed with this assessment of current evidence. They commented that prevention of hypoglycemia in individuals with type 1 diabetes would likely have greater impact than would efforts to reduce hypoglycemia unawareness, as this condition occurs in a minority of individuals with type 1 diabetes. The panel members specifically noted that eliminating hypoglycemia for a period of time will restore an individual's awareness of hypoglycemia. Nonetheless, panel members emphasized that an individual with type 1 diabetes should not drive until hypoglycemia unawareness resolves. They recommended specific training for medical examiners on recognition of the phenomenon.

Conclusions

On the Findings of the Evidence Report

The average driver with diabetes (type 1 or type 2) has a small but statistically significant incremental increase in the risk for a motor vehicle crash.

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 by virtue of the fact 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 a 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. Because of a paucity of acceptable data, we were unable to determine the extent to which hypoglycemia affected these measures in individuals with type 2 diabetes.

No evidence was found to confirm that hypoglycemia is the reason for the excess risk associated with insulin treatment.

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 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.

Hypoglycemia awareness training improves accurate estimation of blood glucose levels in type 1 diabetics, but does not reduce incidents of severe hypoglycemia.

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 driver's license. However, several States allow individuals to drive large trucks within the 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 drivers 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, suggests that there is a general belief that non-insulin treated 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 treated 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-treated diabetes to be performed.

Commentary and Recommendations to FMCSA and its MRB from the Diabetes Expert Panel

Members of the Diabetes Expert Panel made the following commentary and recommendations:

> *In our opinion, with a risk estimate of 1.19 (1.08-1.36), the evidence is not sufficiently convincing to restrict all individuals with diabetes from driving, but whatever the risk, we do not believe that all people with diabetes have equal risk. If there is an increased risk of crash in diabetes, it does not appear to be due to insulin use. Thus, we have no evidence that eliminating the restriction on use of insulin would increase crash risk.*
>
> *We believe that hypoglycemia unawareness accounts for a very small percent of that possible risk. We believe that hypoglycemia* may *play a role in type 1 diabetes, but this population represents a very small (<5%) proportion of the potential diabetic CMV population as most drivers, even if on insulin, have type 2 diabetes. In the type 2 population, hypoglycemia is* not *likely to account for increased risk, and other comorbid conditions (e.g. cardiovascular disease) may play a bigger role. Although one can never make CMV driving 100% safe for anyone, current practices enable the examiner to identify those with increased risk (e.g. hypoglycemia unaware) and those with risk equivalent to the general population. Further study is needed to stratify the diabetic populations in terms*

of risk and on mechanisms to reduce hypoglycemia frequency and hypoglycemia unawareness in type 1 diabetes.

Members of the Diabetes Expert Panel made the following recommendations regarding the Certified Medical Examiner program:

We recommend creation of a CMV expert panel of endocrinologists to serve as a consultant resource to the certified medical examiners. These endocrinologists should receive additional training in CMV issues, including work environment and FMCSA regulations. We also recommend that medical examiner training include a diabetes module covering the following topics:

- Important questions to address in the medical history and medical record review from the treating physician
- How to review of glucose monitoring data (for insulin-treated individuals), with particular attention to evidence for severe (coma, seizure) hypoglycemia and hypoglycemia unawareness
- Physical examination of the individual with diabetes, including
    - Autonomic and peripheral neuropathy
    - Orthostatic hypotension
    - Vibratory and position sense
- Importance of other cardiovascular risk factors (per cardiovascular disease guidelines)

We recommend to FMCSA that evidence on physical examination of peripheral neuropathy with absent vibration sense should lead to a skill performance evaluation. We also recommend that if the primary examiner determines that the applicant should be excluded for any reason related to diabetes ,the applicant be referred to an endocrinologist for further evaluation prior to final determination. This could be the driver's treating endocrinologist. We recommend that differences of opinion between the primary medical examiner and the treating physician about diabetes exclusion be referred to the FMCSA expert endocrinologist, with a final decision on diabetes exclusion being the purview of the FMCSA endocrinologist.

The panel recommended that the following questions be addressed by FMCSA using Department of Transportation data on CMV drivers:

1. What is the age profile of active CMV drivers?

2. What was the crash incidence among drivers with diabetes treated with insulin who were included in previous exemption programs?

3. Is there a relationship between the type of commercial vehicle driven by an individual with diabetes and crash risk?

The panel recommended that the following question be addressed in future epidemiologic studies:

1. Are individuals with diabetes under 65 years of age and individuals with diabetes over 65 years of age overrepresented among those who experience a crash?

The panel recommended that the following questions be addressed in future assessments of diabetes and crash risk:

1. Is there evidence of the effect of hyperglycemia on crash risk, simulated driving performance or on cognitive and psychomotor function?
2. What is the evidence for the relative risk of hypoglycemia with the newer insulin analogs and newer sulfonylurea agents used in the current treatment of diabetes?
3. Which patient factors (not treatment-specific) predict higher risk of hypoglycemia in type 1 diabetes and in type 2 diabetes?

The panel recommended that the following question be addressed to better inform future assessments of conditions and treatments with respect to crash risk:

1. Does simulated driving performance predict crash risk?
2. Do commonly used measures of impairment of cognitive and psychomotor function predict crash risk?

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