increase of accidents as evidenced from risk models. As presented in Figure 1, host-characteristics associated with hypoglycemia including medical therapy are of critical importance. With alterations of treatment, potentially the hypoglycemic reactions could be recognized early and an accident averted either by stopping driving or reducing the frequency of hypoglycemic reactions with better therapeutic approaches.

In a recent review in Diabetes Care concerning driving and diabetes, a primary focus was on the frequency of severe hypoglycemic reactions(l). Table 1 presents the available data. We have also obtained information on the frequency of severe hypoglycemic reactions from the Epidemiology of Diabetes Complications (EDC) study, based in Pittsburgh, Pennsylvania. This is a prospective cohort study of over 600 individuals with IDDM. As part of this study, in-depth survey information was collected concerning hospitalizations for hypoglycemia and reported hypoglycemic reactions. In Pittsburgh, 52 individuals reported 61 hospitalizations for hypoglycemia in five years. During the five years, nine individuals reported two hospitalizations. The risk of hospitalizations for severe hypoglycemic reactions was thus .019/year.

Table 1

Incidence of Hypoglycemia in Insulin-Treated Diabetes

Studv	Severe Reactions/year	
	Type I	Type II
Diabetes Control & Complications Trial (53)		
Conventional Therapy	0.17	
Intensive Therapy	0.54	
Casparie and Elving(5)	0.115	0.045
Michigan Diabetes Research and Training Center (6)	1.7	1.3
Mulhauser, et al.(7)	0.19	
Orchard(8)	0.019	

Overall, our data from Pittsburgh represents a lower estimate of incidence for severe hypoglycemic reactions. The reasons for this are two-fold. The first is the definition of a severe reaction. This is defined as an individual needing to be hospitalized, in contrast to the other studies, thus reducing the estimate of the actual number of severe hypoglycemic reactions. However, our population is likely ***more*** reflective of the general population of insulin-dependent diabetic individuals as, unlike the other efforts, our population was not clinic-based. By definition, clinic patients attend clinics to receive care. Diabetic cases who do not have severe hypoglycemic reactions are less likely to attend diabetes clinics or participate in studies. Therefore, it is likely that the "true" estimate of the risk of severe hypoglycemic reactions would be between the respective figures of the clinic-based populations and our unselected population of IDDM cases.

Table 2 presents the risk factors for severe hypoglycemic reactions as identified in the literature. The strongest and most consistent determinant of risk is a history of previous hypoglycemic episodes. The relationship between the amount of insulin used per kilogram of body weight, age, and duration of diabetes are inconsistent in their relationship to risk Not unexpectedly, individuals who are insulin-dependent diabetic cases have an increased propensity for severe hypoglycemic reactions compared with those who are using insulin but could not be classified as insulin-dependent.

The blood-glucose related variables are suggestive of the concept that individuals whose blood-sugar profile is brought into the "normal" range have an apparently increased risk of hypoglycemic reactions, especially those individuals who have a history of severe hypoglycemic reactions(2). However, in unselected individuals where there is no concerted effort to bring the HbA levels into the normal range there does not appear to be a relationship between blood glucose control and risk of severe hypoglycemic reactions.

In Appendix A we review the current modes of therapy and control of diabetes for individuals taking insulin as requested in the contract. However, it is important to point out that, if anything, "tightening" control at least into the normal range likely increases risk for hypoglycemic reactions.

One aspect that has been neglected in previous discussions of hypoglycemic reactions in relationship to CMV driving is that of warning symptoms. A severe hypoglycemic reaction need not be dangerous for CMV driving if there are premonitory symptoms to which an individual can react and stop driving. A major concern, therefore, is unaware hypoglycemia; e.g., something that individuals cannot react to in order to avert an accident but not avert the severe hypoglycemic reaction. The only mention of the frequency where warning symptoms occur was from Bergada(11) where it was discovered that approximately 30 percent of the severe hypoglycemic reactions had warning signals.

The overall picture that emerges indicates that the primary determinant of a severe hypoglycemic reaction is a history of hypoglycemic reactions. Moreover, a history of hypoglycemic reactions appears to interact with attempts to achieve metabolic control. Therefore, those individuals having a history of hypoglycemic reactions and who are put into strict diabetes control designed to normalize their metabolic profile will be those individuals most likely to develop a hypoglycemic reaction.

The factor that potentially is most useful for regulation is a history of hypoglycemic reactions. It acts as a predictor of severe hypoglycemic reactions and can be readily identified. For example, of the 61 persons hospitalized in Pittsburgh, nine individuals had two episodes during this period of time. Excluding any person who was hospitalized for hypoglycemia during the previous five years from driving would have "prevented" 9/61 (15 percent) of the severe reactions.

Table 2

Risk Factors for Severe Hypoglycemic Reactions

	Goldstein 1981 (9)	Casparie 1985 (5)	Mulhauser 1985 (7)	DCCT 1987	McDonald 1987 (10)	Bergada 1989 (11)	Orchard 1990 (8)
Insulin Dose/kg	0	+		0		+	
Type of Diabetes (IDDM/NIDDM)		+					
Duration	0	0		+		0	
History of reactions	+	+	+	+		+	
Glucose Control (tight vs. loose)				+			
HbA_1 (low vs. high)	+	+	0	0		0	
Blood glucose				0			
SBGM (yes/no)							
Human vs. Pork							+
Male/Female						0	
Age (young vs. old)	0			0		0	
Exercise							

\+ association
0 no association

DISCUSSIONS AND CONCLUSIONS

Overall, the risk of severe hypoglycemic reactions among individuals with IDDM is between .019 to 1.7 per year, with the best estimate likely between .019 to .19, Of the severe hypoglycemic reactions, at least 30 percent would be associated with the identification of early warning signs that, if needed, would likely avert an accident but not necessarily the severe reaction.

The most potent risk factor for severe hypoglycemic reactions is a history of reactions. It is clear that the history of reactions is essential for use in regulation. Metabolic control appears to be a double-edge sword whereby achieving normal glycemia may delay the development of complications. However, very low HbA levels in the normal range are associated with an increase in hypoglycemic reactions. The locus of the increased risk appears to be individuals who have a history of hypoglycemic reactions.

There is little epidemiologic evidence to indicate that monitoring of blood glucose can prevent severe hypoglycemic reactions from occurring. It is likely that monitoring can make individuals more aware that they are entering into a hypoglycemic attack. The early awareness could avert accidents.

Screening for people who have a history of severe hypoglycemia, particularly those reactions with no prodromal symptoms, would provide the greatest benefit in regulation. Strict metabolic control designed to achieve normal glycemia may actually increase the risk of accidents. Blood glucose monitoring would likely reduce the risk of accidents, not necessarily through a reduction of the incidence of severe reactions, but rather through the increase in awareness of the early symptoms that an attack was forthcoming.

APPENDIX A

DIABETES CARE/TREATMENT

Diabetes is characterized by abnormally high concentrations of blood glucose. In the short term, if untreated, this can lead to ketoacidoses and death. In the long term, hypoglycemia is associated with a markedly increased risk of severe complications including retinopathy which may lead to blindness, nephropathy, neuropathy and macrovascular disease. These complications contribute to an eightfold to tenfold increased risk of death for individuals who have IDDM(13).

A primary goal of medical therapy for individuals who have IDDM is to achieve metabolic control. In the broadest sense, "perfect" metabolic control means a close approximation to glycemic levels that are seen in non-diabetic individuals. Treatment and insulin delivery systems have been established in an attempt to reduce, both acutely and chronically, the blood glucose levels with the hope that this will prevent or at least postpone the development of the severe consequences of diabetes.

A major difficulty for CMV driving is that these "intesnive" insulin treatment regimes have the side-effect of increasing the risk for hypoglycemia. A physician evaluating a CMV applicant, then, faces a decision regarding both the short-term and long-term impact of intensive insulin treatment. Data concerning the effect of medical therapy on blood glucose control and data concerning the relationship of various treatment approaches to the risk of hypoglycemia, as discussed in the body of the report, are weak. In general the greater the improvement of metabolic control, especially to the "normal range" of blood glucose levels the greater the risk for both mild and severe hypoglycemic reactions. There is little information describing the relationship between a modest degree of blood glucose control and the risk of hypoglycemic reactions.

The concept of achieving metabolic control is to approximate what occurs in the non-diabetic individual. With an increase in blood sugar resulting from eating, there is a rapid release of insulin from the pancreas. The increase is the result of "sensing" of the blood glucose concentrations and release of insulin in response to the glucose levels. This type of response occurs automatically, resulting in a short-term response to glucose and a lower overall metabolic profile of low blood glucose levels as the glucose is rapidly metabolized.

With insulin-dependent diabetes there is a breakdown of the system as insulin is not produced. The treatment systems have been designed to manually mimic the biologic system with manual blood glucose monitoring systems for acute fluctuations in blood-sugar levels, long-term assessments of control through glycosylated hemoglobin levels and more frequent insulin delivery systems through multiple injections per day and insulin pumps.

SHORT-TERM MONITORING OF BLOOD GLUCOSE

One of the most rapidly developing fields has been that of self-monitoring of blood glucose levels as discussed in a recent consensus statement by the American Diabetes Association (ADA)(14). The primary intended use of self-monitoring of blood glucose levels (SMBG) is to assist in the management and evaluation of patients with diabetes. In the ADA report, the advantages and disadvantages of SMBG are discussed and are overviewed here. The panel recommended the use of SMBG for individuals prone to hypoglycemia, specifically those who do not experience the usual warning symptoms. The SMBG will assist individuals in the early recognition of hypoglycemic events. It must be pointed out, however, that although clinically one would suspect that SMBG would be beneficial for greater awareness of potential hypoglycemic reactions, there are few data to indicate that there is an earlier awareness of hypoglycemic reactions for SMBG users, primarily because it has not been examined. According to biologic analyses, SMBG could be effective for reducing hypoglycemic reactions through early identification but there are few data to support this contention.

As concisely described in the position statement, with proper precautions, SMBG can provide a metabolic profile for an individual who has insulin-requiring diabetes. There is, however, the problem with the user variability such that more than 50 percent of the values are >20 percent out of range. Of concern for using the instruments to identify hypoglycemia, SMBG potentially is unreliable in the hypoglycemic range.

Since this report was published in 1986, companies have considerably improved the reliability of instruments while reducing the cost, making the instruments within range for most people who have diabetes. The instruments are readily adaptable for CMV drivers and should not impose any major barriers for use.

There is considerable evidence that SMBG is a very useful tool for improving diabetes control. However, there is very little evidence that in unselected populations of individuals those employing SMBG are in better control than those who do not. Thus, SMBG may be thought of as potentially being a necessary component to achieve glucose control, but not sufficient. For example, in the DCCT trial, were it not for continued and ongoing SMBG, it would not have been possible to achieve the major improvement in the control of blood sugar in the intensive therapy group (e.g., 2,3). However, just monitoring blood sugar without active intervention does not necessarily produce improvement in control (e.g., 15).

Perhaps the greatest usefulness of SMBG in the area of CMV driving is not necessarily to reduce the frequency of severe hypoglycemic reactions but rather to increase the awareness of the early warning symptoms that a hypoglycemic reaction is imminent. This is of particular concern for CMV driving, as with early identification drivers could avert an accident by merely stopping. Thus, although there is little evidence that SMBG can be used to “avert” severe hypoglycemic reactions, it is likely that it could be used to “avert” accidents as people become aware of the early warning symptoms and stop driving. It is estimated that 1,000,000 individuals who have diabetes are using the SMBG technology(14). There is no published information as to the number of CMV individuals who are using technology.

LONG-TERM MONITORING OF BLOOD GLUCOSE LEVELS

One of the major achievements in the area of blood glucose control has been the identification of glycosylated hemoglobin as a measure of long-term metabolic control The use of glycosylated hemoglobin has markedly altered the evaluation of the long-term control associated with diabetes. It has been shown to be an integrated measure of diabetes control which reflects a period of time prior to the sampling.

The concept is simple as the glycosylated hemoglobin reflects a number of electrophoretic components of hemoglobin that appear on etythrocytes. The most prevalent component is designated as hemoglobin A, which results from a reaction of glucose with the ammo group of the NH, terminal value of the two beta chains of the hemoglobin tetramer(16). The HbA reflects the blood glucose concentrations to which the etythrocytes have been exposed during their lifetime. There is strong relationship between HbA and the long-term glucose status of individuals(17). A primary goal of intensive therapy is the lowering of HbA levels which indicate an improvement in the control of diabetes. HbA measurements have demonstrated widespread utility and are a primary tool in therapy for people who require insulin. Appropriate monitoring of HbA levels can provide an active portrait of the long-term levels of glucose control.

As discussed previously, it appears that achieving HbA1 in the normal range may predispose individuals for hypoglycemic reactions, especially those with a history of reactions. As presented earlier, beyond the "normal" range, there does not appear to be a strong relationship between HbA and hypoglycemic reactions. HbA assays are readily available and easily applicable for any CMV physical examination. It should provide no obstacles to CMV drivers. Very low HbA with a history of severe hypoglycemic reactions should be contra-indicated for driving CMV.

INSULIN

During the last decade, there have been major changes to insulin and insulin-delivery systems in order to achieve a more physiologic approach to blood glucose control. One of the first advances was the development of DNA technology to produce a readily available quantity of human insulin(18). It was believed that human insulin would be less likely to produce insulin antibodies; however, this has not proven to be the case.

Most of Europe has gone almost exclusively to the use of human insulin. The use of human insulin in the United States has, however, lagged behind Europe, with only 18 percent of adults using human insulin in our area(12).

Recently, it has been suggested that human insulin is related to fatal hypoglycemic reactions as the result of reduced warning symptoms(19,20). However, this has been shown to be equivocal in subsequent reports. Dr. Orchard, from our group(12), has investigated the potential relationship between human insulin use and hypoglycemic reactions as part of the Epidemiology of Diabetes Complications (EDC) study. Overall, there was no increase in the number of severe hypoglycemic reactions in those using human insulin. However, there was evidence that mild hypoglycemic reactions were more prevalent in those individuals on human insulin. This occurred primarily among individuals with poor metabolic control.

Thus, human insulin might be associated with a slightly increased risk of mild hypoglycemic reactions. It is likely that in the next few years, greater numbers of insulin-using diabetic individuals will be on human insulin. It will be important to monitor this change and, once again, evaluate the data in relation to a history of hypoglycemic reactions. If CMV drivers are put on human insulin, there should be more frequent evaluation, especially in the initial changeover to human insulin.

INSULIN DELIVERY SYSTEMS

One rapidly changing therapy has been the introduction of multiple injections per day. Historically, most patients would receive a single injection of insulin per day. In the past five years most diabetologists have been recommending the use of multiple injections per day plus home blood glucose monitoring. From our work in Pittsburgh, an ever-increasing proportion are on multiple injections.

Biologically, this permits a more rapid response to raised blood glucose levels in an attempt to "normalize" blood glucose control. A combination of both monitoring blood glucose with multiple injections in addition to intensive supervision each day has clearly demonstrated reduced blood glucose levels, for example, in the DCCT trial(2). The relationship of insulin-delivery systems to hypoglycemic reactions, however, has not been effectively evaluated.

It is not clear whether multiple shots per day are beneficial or detrimental to the risk of CMV accidents. Decisions relating to the use of multiple shots per day should be made by the physician taking care of the diabetes. It is likely that most CMV drivers could go onto multiple shots per day, if needed.

INSULIN PUMPS

Open loop systems for providing a continuous supply of insulin were first developed and tested in the late 1970s (21,22). There was considerable hope for these systems to establish tight blood glucose control. However, during the past few years, interest in insulin pumps has waned as the existing pumps proved to be cumbersome for people to use. Moreover, there was an increased prevalence of complications associated with infection as well as an unfounded scare that hypoglycemic deaths were associated with their use. The other finding has been that equally effective diabetes control could be achieved through multiple injections per day. Open loop systems are still in the experimental stage.

Insulin pump systems cannot be recommended for CMV drivers to use. There is evidence that these systems are associated with a marked increase in risk for hypoglycemic reactions(23). Currently in the United States, few individuals are using insulin pumps. It is unlikely that many insulin-using diabetic patients, driving CMVs, will be on insulin pumps.

ARTIFICIAL PANCREAS

The ideal treatment would be the development of an insulin delivery system that would mimic the pancreas. This would include a sensor to determine the amount of glucose in circulation, with a corresponding response of insulin release. Despite intensive efforts in the development of reliable glucose sensors, a portable system is not available for mass use(22). Because of technical problems, it is unlikely that an artificial pancreas will be available during the next decade.

CONCLUSIONS ABOUT MEDICAL THERAPY

The overall conclusions related to therapy are that SMBG likely would have the greatest utility for the prevention of accidents for individuals driving CMVs. It is not clear that SMBG can prevent severe, or even mild, hypoglycemic reactions from occurring. However, SMBG likely can provide an early warning signal for the person to stop driving.

Very tight metabolic control can be achieved through multiple injections per day and SMBG. This is, however, associated with an increased risk of hypoglycemic reactions, especially for individuals who have a history of reactions.

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RISK ASSESSMENT

RISK ASSESSMENT

Currently, persons with insulin-treated diabetes are excluded from operating CMVs in interstate commerce. Job opportunities for individuals with diabetes have historically been restricted under the pretense that they (particularly those using insulin) are at higher risk for occupational accidents. This risk lies primarily in their susceptibility to hypoglycemia, although visual and cardiovascular impairment may also be limiting factors.

As the treatment procedures and technology available for diabetes care continue to improve, there is increasing pressure to begin to eliminate employment restrictions. However, due in part to present and/or previous restrictions, there is little reliable information available to consider whether persons with diabetes actually are at higher risk for accidents than those without diabetes.

BACKGROUND

Diabetes mellitus is a prevalent chronic health condition in the United States today. Based upon 1987 figures, an estimated 6.6 million individuals have been diagnosed with diabetes by a physician (NCHS 1988, NCHS 1989).

Diabetes is typically categorized into two distinct forms: Type I, insulin-dependent diabetes mellitus (IDDM), and Type II, noninsulin-dependent diabetes mellitus (NIDDM). Clear etiologic, clinical, and epidemiologic differences distinguish IDDM from NIDDM.

IDDM is diagnosed primarily prior to age 30, with a peak incidence of the disorder occurring during the adolescent years. Individuals with IDDM have substantial beta cell failure in the pancreas and are unable to produce insulin in any great quantity. All are dependent upon the daily administration of insulin by injection for their survival. IDDM cases comprise 5 to 10 percent of all cases of diabetes (NDDG 1985).

In contrast, NIDDM is most often diagnosed after age 55 and is common in the aged. Those with NIDDM suffer from impairment in the ability to recognize and utilize insulin, not in the ability to produce insulin. Treatment for NIDDM can be through the use of insulin or oral hypoglycemic drugs. A large number of affected individuals can rely solely upon diet restrictions to counteract the effects of the disease as well. Some individuals do not take any therapeutic measures to control their disease: 24 percent in one survey (Martin 1985). Persons with NIDDM make up the vast majority of all cases with diabetes.

The medical issue of most importance, regarding insulin-treated diabetes and motor vehicle operation, is the development of hypoglycemia while driving. If not treated promptly, hypoglycemia can lead to alteration in judgement and perception and loss of consciousness.

Several case reports (Christian 1972, Sturner 1983 and Cockram 1986) have shown that hypoglycemia occurring in truck drivers has resulted in accidents. Case reports do not consider what the pattern of accidents may be over a group of CMV operators. At present, there are no known published reports that describe the accident experience of diabetic drivers with regards to CMV operation. Risk assessment methods allow us to overcome the limited knowledge of actual experience and estimate the impact of a policy change. The purpose of this paper is to identify the conceptual framework and fundamental steps to be included in an assessment of the risks associated with allowing insulin-using diabetics to operate CMVs. The conceptual framework of this issue is presented first, followed by an outline of the steps involved in evaluating it. This general discussion gives way to an assessment of the risks associated with permitting insulin-using diabetics to operate CMVs.

CONCEPTUAL, FRAMEWORK

The strategy behind any evaluation of the role of insulin-treated diabetes mellitus (ITDM) in CMV road accidents concentrates, by necessity, around the contributions of medical factors in diabetes to crashes. Medical factors of importance with regards to ITDM are generally characterized by their acute and chronic elements. Acute factors include hypoglycemia and hyperglycemia, both of which are directly related to the control of blood glucose levels. Chronic medical factors include the complications of diabetes: retinopathy, nephropathy, cardiovascular disease, and autonomic neuropathy. Hypoglycemia is the central medical factor of concern with regard to road crashes among drivers with diabetes. The opportunity for sudden impairment from hypoglycemia-induced alteration of judgement or perception is, by definition, constantly present and may develop in a matter of minutes. Without recognition of the warning signs of hypoglycemia and sufficient time to react to them, an accident is a real possibility. Most insulin-dependent diabetics will experience hypoglycemia at some time in their lives.

The acute symptoms of hyperglycemia (in the form of ketoacidosis), in contrast, develop slowly over many hours or days and are clearly preventable with proper care. Similarly, the chronic complications of diabetes do not appear for a number of years in persons with IDDM. Driving regulations regarding visual fields and some aspects of cardiovascular disease already exist for the general population in a number of states.

Hypoglycemia

Hypoglycemia, characterized by low blood glucose levels, is generally caused by a relative excess of insulin and results from a mismatch of injected insulin and carbohydrate absorption. A number of factors, such as a missed meal, too much insulin injected, vigorous physical exercise, or stress can lead to its occurrence. Hypoglycemic symptoms commonly develop in most individuals when blood glucose levels drop to 35 to 50 mg/dl. They may also occur in other persons when drops of 100 mg/dl or more from very high blood glucose values are seen (FAA 1986).

A precipitous drop in blood glucose levels from any -ᶜ ᵗme forementioned factors would generally lead first to an activation of the sympathetic system and the telltale warning signs of pallor, sweating, and forceful heartbeat (Keen 1985). Without intervention to raise blood glucose levels at this point, cerebral symptoms (due to glucose deprivation of the central nervous system) would ensue and be marked by impairment in intellectual and physical performance. If still untreated, hypoglycemia can lead to loss of consciousness, coma, and convulsions.

This symptomatology is generally defined in the form of mild reactions and severe reactions. Mild reactions include those with the warning symptoms of pallor, sweating, and heart palpitations. Modest alterations of cognition and perception may also be present. Severe reactions are commonly defined as those requiring the assistance of another person to raise the blood glucose levels. Severe reactions may also be characterized by loss of consciousness and/or hospitalization.

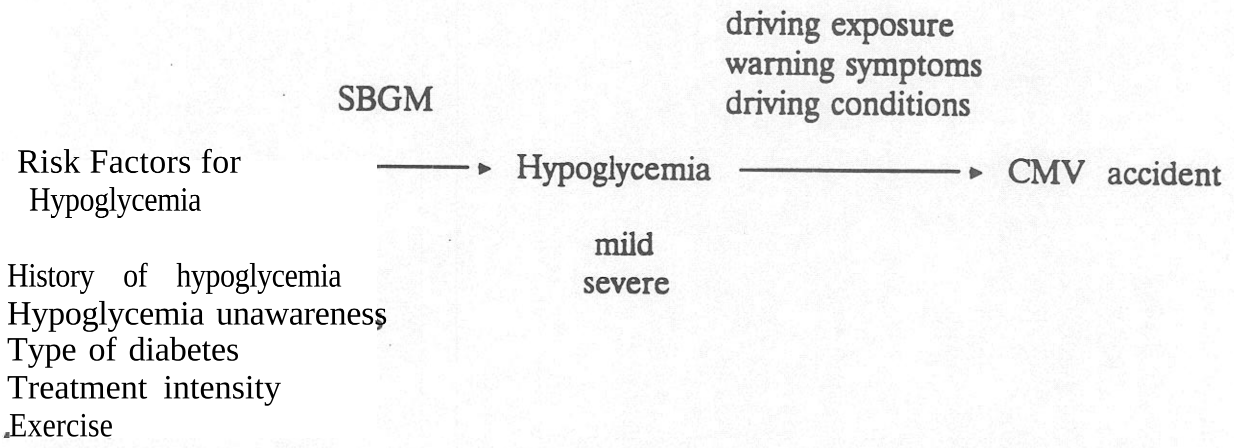
The presence of early warning signs to hypoglycemia (as indicated) generally serves as an indication that some form of intervention is required to raise blood glucose levels. In most of these early recognized cases, the consumption of food with a ready quantity of carbohydrate will be sufficient to eliminate the reaction. Warning symptoms may also allow sufficient time to pull the vehicle off the road if a reaction occurs while driving. Mild reactions may be a hazard if they occur during a critical phase of driving or in the presence of another safety problem (FAA 1986). Severe reactions are likely to be an extreme hazard if they occur while driving.

Some individuals suffer from a loss of the early warning symptoms to hypoglycemia, often due to the presence of autonomic neuropathy. This unawareness to hypoglycemia affects the individual's ability to intervene and results in an increased risk for severe reactions (Hepburn 1990). Hypoglycemia unawareness would suggest itself as a potential factor to consider in the licensing of CMV operation.

Model

In order to evaluate the potential role of hypoglycemia in CMV accidents, it is important to address not only the risk that hypoglycemia will lead to mishaps but also the risk factors behind who develops hypoglycemia and who does not. The identification of individuals at higher risk for hypoglycemia could be used to screen for persons who may be at higher risk for hypoglycemia-related accidents. The following diagram presents the model which underlies the current discussions.

In this model, priority is placed on identifying the risk factors for hypoglycemia and the elements that lead hypoglycemia, once it occurs, to result in a road accident. Mediating factors, denoted by points (a) and (b), influence the extent to which these model components lead ultimately to CMV accidents. This forms the basis of the conceptual framework to assess the risks of allowing ITDMs to operate CMV. A'detailed listing of the factors related to hypoglycemia and the risk for hypoglycemia-related accidents are shown in the following diagram.



As mentioned earlier, knowledge of the risk factors for hypoglycemia is important because it may be used to screen for individuals at increased risk for hypoglycemia-related accidents. By definition, all insulin-treated diabetics are at risk for hypoglycemia. However, a literature review finds that some persons are at higher risk than others.

A number of studies suggest that the strongest determinant of risk for severe hypoglycemia is a history of previous episodes (Goldstein 1981, Casparie 1985, Mulhauser 1985, DCCT 1987, and Bergada 1989). High risk for severe reactions has also been found among persons with hypoglycemia unawareness, or the lack of warning symptoms for hypoglycemia (Hepburn 1990).

Data from three studies also suggest that insulin-dependent diabetics have a higher frequency of hypoglycemia than insulin-treated Type II diabetics (Casparie 1985, Hiss 1986, and Klein personal communication). Intensive treatment of diabetes to achieve "tight" metabolic control has been indicated as a risk factor as well (DCCT 1987). Metabolic control appears to be a double-edged sword. While attaining physiologically normal blood glucose levels may delay the development of chronic diabetes complications, it appears to increase the risk for severe hypoglycemic reactions.

One potential mediating factor that may influence the development of hypoglycemia is the role of SBGM. The last decade has seen the evolution of highly efficient instruments for diabetes self-care. One of these instruments is the Blood Glucose Testing Monitor. With this monitor, individuals with diabetes are able to check their blood glucose levels at any time. It is argued that this advancement may be an important factor in allowing diabetic drivers to safely operate CMVs.

The importance of SBGM lies in its ability to help increase the diabetics' awareness of their blood glucose levels. By testing their blood glucose levels before starting off on a long drive, diabetic drivers may be more attentive to the potential for developing hypoglycemia during that drive. There is little evidence, however, to suggest that SBGM leads to a lower frequency of reactions.

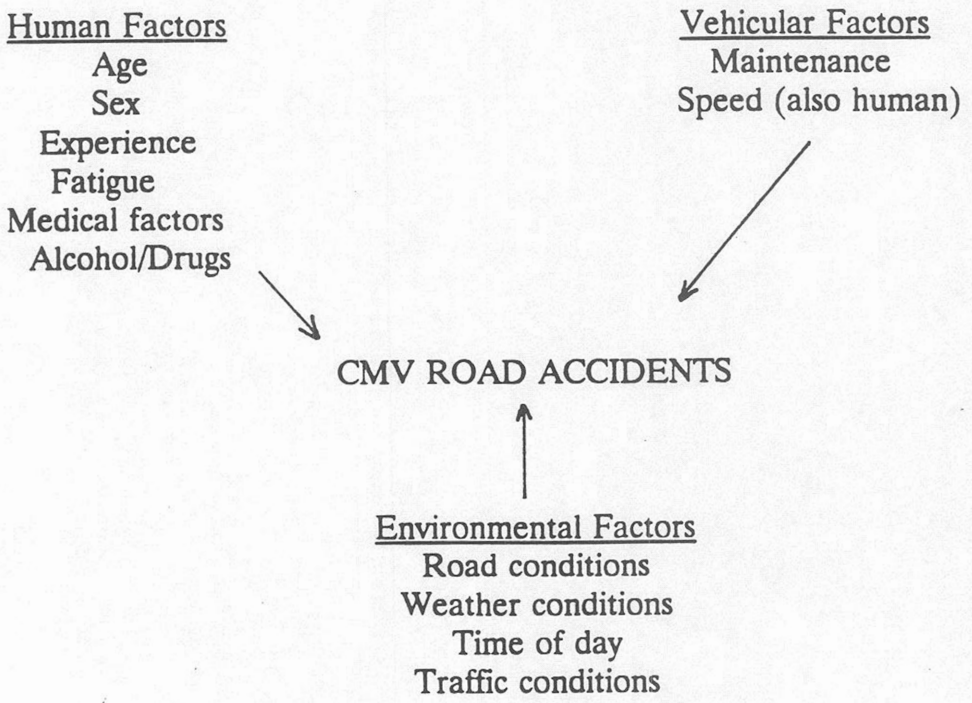
The elements that lead hypoglycemia, once it develops, to a road accident are quite diverse. As indicated earlier, it appears the risk for accident from a mild reaction is much lower than the risk related to a severe hypoglycemic reaction. There are no data available, however, to quantify this.

Recognition of the early warning signs of hypoglycemia may be equally as important to the prevention of accidents. Such recognition may allow the driver to park the motor vehicle and avoid an incident. This factor in the relationship of hypoglycemia to accidents has not been investigated previously. Driving conditions, on the other hand, may preclude the possibility of pulling the CMV to the side of the road (e.g., a restricted access highway with no pullover lane).

The role of driving exposure in hypoglycemia-related road crashes should merit consideration as well. An increased risk for such mishaps is likely to occur with higher levels of driving exposure (mileage driven). It is important to consider the influence of driving exposure in any evaluation of diabetes and CMV accidents.

To conclude, it is important to keep the evaluation of diabetes and accidents in perspective. The contribution of medical factors to road crashes is only one part of the puzzle that describes the accident risk of the diabetic driver. Other factors contribute to accidents as well. Haddon, Jr (1972) has elegantly categorized these as human factors, vehicular factors, and environmental factors. Figure 1 depicts the overall framework behind this discussion.

Figure 1: Risk factors for Motor Vehicle Accidents



While hypoglycemia may indeed result in CMV crashes, we should also consider the contribution of medical factors to road crashes in perspective to the contribution of the other risk factors for motor vehicle accidents.

Steps Towards Evaluating CMV Operation by ITDM Drivers

The steps towards evaluating the risks associated with allowing insulin-using diabetic drivers to operate CMV are outlined below.

I. Identify the Number of Drivers Expected to be Licensed
   a. Stratify by type of diabetes
   b. Disqualifying factors for diabetic drivers

II. Identify Frequency of Hypoglycemic Reactions
   a. Overall
   b. While driving

III. Evaluate Relationship of Hypoglycemia to CMV Road Accidents
   a. Accidents expected from mild reactions
   b. Accidents expected from severe reactions
   c. Accidents expected from hypoglycemia, overall

IV. Evaluate Role of Risk Factors for Hypoglycemia in Licensing Recommendations

V. Sensitivity Analysis

VI. Views of States Regarding Licensing of Insulin-Using CMV Ooerators

VII. Conclusions

RISK ANALYSIS

The purpose of this evaluation is to estimate the number of CMV accidents that might be expected if insulin-using diabetics were licensed to operate CMV in interstate commerce. The analysis follows the framework and outline presented earlier for discerning the role of diabetes in CMV road accidents. Considered first is the number of persons with diabetes using insulin who are expected to be licensed to operate CMVs. Next, an evaluation of the frequency of hypoglycemic episodes expected while driving is presented, followed by a look at the relationship between hypoglycemia and road accidents. Finally, a survey of the risk factors for hypoglycemia and their implications for regulation and accidents.

1. Number of Drivers Expected to Be Licensed

The number of insulin-treated diabetics expected to apply for licensure to drive CMV on an interstate level is presented below[1]. Estimates are based upon diabetes prevalence data available from two national surveys completed between 1976 and 1980 (NHANES II) and 1979 and 1981 (NHIS) respectively.

Method A: Prevalence data from NHANES II (Harris 1987)

Percent of population with diabetes by age:

20-44 MS	45-54 yrs	55-64 yrs
1.1	4.3	6.6

U.S. resident population by age, 1987 (NCHS 1990):

20-44 yrs	45-54 vrs	55-64 yrs
96,746,000	23,276,000	25019,000

Diabetes population by age:

20-44 yrs	45-54 yrs	55-64 yrs
1,064,206	1,000,868	1,453,254

1 Applicants between age 21 and 65. Data are presented as 20-64 years because of the age groups used in national surveys

The number of insulin users in the diabetes population was determined from NHANES II data on the percent of diabetics using insulin by age (Martin, 1985)

12-44 yrs	45-54 yrs	55-64 yrs
46 %	22 %	19 %

Insulin-using population by age:

20-44 yrs	45-54 yrs	55-64 yrs
489,535	220,191	276,118

Method B: Prevalence data from 1980 NHIS (Harris 1987)

Percent of population with diabetes by age:

20-44 yrs	45-54 yrs	55-64 yrs
1.0	4.3	6.8

Diabetes population by age, based upon US population, 1987:

20-44 yrs	45-54 yrs	55-64 yrs
967,460	1,000,868	1,497,292

The number of insulin users in the diabetes population by age:

20-44 yrs	45-54 yrs	55-64 yrs
445,032	220,191	284,485

Estimates of the total insulin-using population between 20 and 64 years of age from the two methods were fairly similar: 985,844 based upon the NHANES II prevalence data and 949,708 based upon the NHIS prevalence data. Taking the average of these figures, further analysis assumes that the insulin-using population at driving age is about 968,000 individuals.

IDDM and Insulin-Treated NIDDM. Of particular importance is the identification of the number of persons with IDDM and insulin-treated NIDDM in this 968,000 figure. A great deal of evidence suggests that these groups differ markedly, not only in their health characteristics but also in their health consequences.

Precise figures on the number of insulin-dependent Type I and insulin-treated Type II individuals are not known. It is possible to estimate what the breakdown might be, based upon the epidemiologic and natural history data available. This was done as follows: If one assumes that about 8 percent of all diabetic persons are IDDM, then it is likely that there are close to 528,000 (6.6 million x 0.08) insulin-dependent cases at all ages.

As discussed earlier, IDDM is diagnosed primarily during childhood and NIDDM is diagnosed much later in life. It is likely that almost all persons with diabetes under the age of 20 are insulin-dependent. Diabetes prevalence data (2 persons in 1000 under the age of 20 have diabetes, NCHS 1988) and the resident population under 20 years of age (71,524,000 . NCHS 1989) suggest that there are approximately 143,048 IDDM persons in this age range. By subtracting 143,048 from 528,000 we find almost 385,000 insulin-dependent individuals 20 years of age or older.

As an earlier analysis (FAA 1986) noted, life expectancy and insulin availability data suggest that the number of persons with true IDDM over age 65 is small. Mortality rates among persons with IDDM have been shown to be higher than those seen in the general population (Dorman 1984). Moreover, this high rate of mortality is prevalent at relatively young ages. Insulin has only been widely available for treatment purposes in the U.S. since the mid-1920s.

It is likely that the 385,000 figure is a good approximation to the number of IDDM subjects aged 20 to 64. Thus, persons with IDDM account for about 35 to 40 percent of the total insulin-using population between the ages of 20 and 64 (385,000/968,000).

Disqualifying and Discouragement Factors for Diabetic Drivers. There are many factors that are likely to affect the number of persons with diabetes who seek or qualify for CMV licensure. A review of the medical history of diabetes, as well as the social implications of diabetes, suggests that a fair proportion of individuals will not qualify or seek to drive CMVs. Health factors, including proliferative retinopathy, nephropathy, and macrovascular disease, may affect the medical qualifications to drive. An argument could be made over the role of a fourth complication: autonomic neuropathy.

Diabetic retinopathy is one of the leading causes of new cases of blindness among persons of working age in the United States (Klein 1985). Pathologically, diabetic retinopathy is characterized by changes in the blood vessels in the retina of the eye and is classified as nonproliferative or proliferative. Proliferative retinopathy is the more severe of the two and the condition most likely to affect driving capability (through the loss of visual acuity).

The development of retinopathy is strongly related to the duration of diabetes. Both frequency and severity of retinopathy increase with duration. Retinopathy, in some form, affects more than 90 percent of persons with IDDM of 15 years duration or longer (Klein 1985). Not surprisingly, proliferative retinopathy is more frequent in IDDM than in NIDDM.

Diabetic nephropathy accounts for nearly 25 percent of the new cases of End Stage Renal Disease in the United States (Herman 1985). The first sign of nephropathy commonly is the development of persistent proteinuria. End Stage Renal Disease follows some time afterwards (5 to 10 years). It is not clear if nephropathy is a disqualifying factor for motor vehicle operation. The difficulties of living with severe renal disease, though, are likely to prevent a large number of patients from applying by their own choice.

The prevalence of nephropathy is strongly related to the duration of diabetes. After fifteen years of living with IDDM, nearly one-third of the persons develop nephropathy (Herman 1985). Recent reports suggest that the risk decreases after this point in time. Again, the frequency of nephropathy is higher among IDDM patients than NIDDM patients.

Macrovascular disease in diabetics commonly includes conditions related to cardiovascular disease (myocardial infarction and stroke) and peripheral vascular disease (characterized in its most severe form by lower extremity amputation). From a driving viewpoint, the presence of cardiovascular disease may increase the risk for sudden collapse at the wheel. On the other hand, the loss of limbs due to amputation creates physical limitations in the capability to operate CMVs.

While many of the risk factors for cardiovascular disease (CVD) are the same in the diabetic and general population, the prevalence of CVD is nearly two times higher for diabetics than non-diabetics (Kannel 1979) and is seen at earlier ages. The excess risk of heart disease occurs in both IDDM and NIDDM patients and is not clearly related to duration of diabetes (Barrett-Connor 1985). Prevalence increases with age.

While amputation can be the most severe end result of peripheral vascular disease (PVD), Palumbo and Melton (1985) write that "as a rule, toe amputations can be related to infection, neuropathy, and/or occlusive arterial disease (PVD), but leg and thigh amputations are almost always due to occlusive arterial disease." Diabetes accounts for approximately 40 percent of the nontraumatic amputations in the U.S. (Palumbo 1985). Although amputations are more common among diabetics than non-diabetics, the prevalence of amputations does not appear to differ by type of diabetes.

Social factors, including discrimination and discouragement, may also affect the number of diabetic individuals who seek to drive. The impact of diabetes on employment opportunities has been well recognized in the past, but largely unquantified. Individuals with diabetes have been traditionally restricted from certain types of occupations where risk to the public or themselves was deemed to be high. As the legal barriers to employment have fallen in recent years, others have become evident. Foremost is the opportunity for blatant discrimination by employers towards diabetic applicants. More subtle is the persuasive powers of physicians and career advisors (family, friends, professionals, etc.) who discourage those with diabetes from even trying for certain forms of employment.

Expected Number of Drivers . To what extent are these health and social factors likely to affect the number of diabetic drivers applying for CMV licensure? The answer to this question is not entirely clear, but recent data from our survey of the licensing policies of all 50 states and selected foreign nations indicate that the number licensed will be substantially lower than the proportion seen in the general population.

The state of Michigan has permitted the intrastate licensure of insulin-treated diabetics with a special waiver program not unlike that proposed by the American Diabetes Association. From the time of initiation of the program in 1984, only 12 insulin-using individuals have been licensed to operate CMVs. Thls represents about 0.00023 percent of the 5,267,000 residents between 20 and 64 years of age.

The province of Quebec in Canada has allowed insulin-treated diabetics to apply for a CMV license since 1987. From that time, only 67 individuals have applied for, and obtained, a CMV license. This represents approximately 0.0018 percent of the 3,705,000 Quebec residents of driving age. The incidence of both IDDM and NIDDM in Quebec is similar to that for the United States.. Thus, it is likely that a similar proportion of diabetics might apply for CMV licensure in both locations.

The proportion of interstate CMV drivers in the general U.S. population, in contrast, is 3.8 percent., This figure was derived from the number of drivers licensed for interstate CMV operation, about 5.5 million (FHWA 1989), and the resident population of the U.S. between the ages of 20 and 64 years, 142,041,000 in 1987 (NCHS 1989).

Using the data from both Michigan and Quebec, it appears that the number of insulin-using diabetics who would be licensed in the U.S. after 3 to 6 years of eligibility would represent, on average, 0.001 percent of the resident population of driving age (142,041,000), or 1,420 drivers.

Assuming that the breakdown of the type of diabetes among the 1.420 drivers is similar to that seen before (35 percent IDDM, 65 percent insulin-treated NIDDM), the expected number of IDDM drivers would be about 500 and the number of NIDDM drivers would be approximately 920.

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2 population estimate: 9,240,000 multiplied by the percent of the population at driving age: @ 57%
3 population estimate: 6,500,000 multiplied by 57%