Evidence Report

Cardiovascular Disease and Commercial Motor Vehicle Driver Safety

Presented to

Federal Motor Carrier Safety Administration

April 10, 2007

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This report is comprised of research conducted to analyze the impact of Cardiovascular Disease 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 prime Contract No. GS-10F-0177N/DTMC75-06-F-00039 with the Department of Transportation's Federal Motor Carrier Safety Administration (FMCSA). 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 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% of all worker deaths. About two-thirds of workers killed in the trucking industry are the consequence of highway crashes. According to statistics from the United States Department of Transportation, there were 4,932 fatal crashes involving a large truck in 2005 for a total of 5,212 fatalities. In addition, there were 137,144 nonfatal crashes; 59,405 of these were crashes that resulted in an injury to at least one individual (for a total of 89,681 injuries).

The purpose of this evidence report is to address several key questions posed by the Federal Motor Carrier Safety Administration (FMCSA). Each of these key questions was developed by FMCSA so that the questions' answers would provide information that would be useful in updating its current medical examination guidelines titled, "Cardiovascular Advisory Panel Guidelines for the Medical Examination of Commercial Motor Vehicle Drivers."(1) The six key questions addressed in this evidence report are as follows:

<u>Key Question 1:</u> Are individuals with cardiovascular disease (CVD) at an increased risk for a motor vehicle crash when compared to comparable individuals who do not have the disorder?

<u>Key Question 2:</u> What are the risk factors for rupture of an aortic (abdominal or thoracic) aneurysm?

<u>Key Question 3:</u> Is implantation of a pacemaker effective in preventing vasovagal syncope recurrence?

<u>Key Question 4:</u> What is the risk of sudden incapacitation or sudden death following implantation of an implantable cardioverter defibrillator (ICD)?

<u>Key Question 5:</u> What is the risk of sudden death or incapacitation in individuals with low left ventricular ejection fraction (LVEF) (<50%, <40%, <35%)?

<u>Key Question 6:</u> Is the relationship between LVEF and sudden death or incapacitation (if established) dependent on the underlying etiology of heart failure?

Identification of Evidence Bases

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

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

Grading the Strength of Evidence

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

Analytic Methods

The set of analytic techniques used in this evidence report was extensive. Random- and fixed-effects meta-analyses were used to pool data from different studies.(2-6) Differences in the studies' findings (heterogeneity) were identified using the Q-statistic and I^2.(7-9) Sensitivity analyses, aimed at testing the robustness of our findings, included the use of cumulative fixed- and random-effects meta-analysies.(10-12) The presence of publication bias was tested for using the "trim and fill" method.(13-15)

Presentation of Findings

In presenting our findings we made a clear distinction between qualitative and quantitative conclusions, and we assigned a separate strength-of-evidence rating to each conclusion format. The strength-of-evidence ratings assigned to these different types of conclusions is 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.
Acceptable	Although some evidence exists to support the qualitative conclusion, this evidence is tentative and perishable. There is a reasonable chance that new evidence will either overturn or strengthen our conclusions. ECRI recommends frequent monitoring of the relevant literature.
Unacceptable	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.

Evidence-based Conclusions

Key Question 1: Are individuals with CVD[1] at an increased risk for a motor vehicle crash when compared to comparable individuals who do not have the disorder?

A number of conclusions can be drawn from the findings of the analyses of the evidence pertaining to Key Question 1. These conclusions are presented below:

Drivers of Commercial Motor Vehicles (CMVs)

1. **A paucity of data from studies that enrolled CMV drivers with CVD precludes one from determining whether CMV drivers with the disorder are at an increased risk for a crash.**

[1] With an emphasis on crash risk associated with myocardial infarction, angina pectoris, coronary insufficiency and thrombosis

Two studies presented data directly relevant to the question of whether CVD has an impact on CMV driver safety.(16,17) Medgyesi et al.(16) (Quality Rating: Low) presented crash data for drivers with Class 1 through 4 licenses (comparable to U.S. CMV drivers) separately from Class 5 license holders (private motor vehicle drivers). However, we were precluded from calculating an estimate of the risk ratio for this study, because crash data for the controls with Class 1 though Class 4 licenses were not presented. Only crash data for the entire control group (Class 1 through Class 5) was presented, and this group was dominated by Class 4 license holders. Thus, useful evidence on the relationship between CVD and crash risk among CMV drivers is limited to the findings of just one study.

Dionne et al.(17) estimated the effects of different medical conditions on truck driver crash risk using data from a nested case-control study (Quality Rating: Moderate). These investigators did not find evidence supporting the contention that CMV drivers with CVD are at an increased risk for a crash. While these results are interesting, the study is not of high quality and its results have not been replicated. Consequently, an evidence-based conclusion pertaining to whether CMV drivers with CVD are at an increased risk for a motor vehicle crash is not drawn at this time.

Drivers of Non-CMVs

Because data from studies of CMV drivers with CVD are scarce, we deemed it worthwhile to examine relevant data from studies that investigated crash risk associated with CVD among more general driver populations. While the generalizability of the findings of these studies to CMV drivers may not be clear, such findings—do at the very least—provide the opportunity to draw evidence-based conclusions about the relationship between CVD and motor vehicle crash risk in general.

The findings of our analyses of crash data from these studies are summarized in Table 2.

Table 2. Summary of Findings

CVD	RR studies	Strength of Evidence Stability of SES	OR studies	Strength of Evidence Stability of SES
Any	Increased crash risk RR = 1.43 (95% CI: 1.11–1.84)	Strength of Evidence: Acceptable Stability of Estimate: Low	No evidence-based conclusion	Unacceptable
Hypertension	Increased crash risk RR = NP	Strength of Evidence: Acceptable Stability of Estimate: Unstable	No evidence-based conclusion	Unacceptable
Arrhythmia	No evidence-based conclusion	Unacceptable	No evidence-based conclusion	Unacceptable
Coronary Artery Disease	No evidence-based conclusion	Unacceptable	No evidence-based conclusion	Unacceptable

Other	No evidence-based conclusion	Unacceptable	No evidence-based conclusion	Unacceptable

CI Confidence interval.
NA Not applicable.
NP Not presented.
OR Odds ratio.
RR Rate ratio.
SES Summary effect size (summary estimate of RR).

The evidence-based conclusions that we draw from the findings summarized above are as follows:

1. **As a group, drivers with CVD are at an increased risk for a motor vehicle crash when compared with comparable drivers who do not have the disorder (Strength of Evidence: Acceptable).**

   - **The magnitude of this increased risk is small but statistically significant (RR = 1.45, 95% CI: 1.11–1.84). In other words, the crash risk for an individual with CVD is 1.43 times greater than for a comparable individual who does not have the condition (Stability of Estimate: Low).**

   Eight studies (Median Quality Rating: Low) reported data on the relative incidence of crash among individuals who have CVD (any type) and comparable individuals without the disorder. The findings of the eight studies were quantitatively consistent. Pooling of the data found that the crash rate ratio associated with CVD is 1.43 (95% CI: 1.11 to 1.84). Thus, if the underlying crash risk for a CMV driver is 0.08 crashes per person each year, the crash risk for a CMV driver with CVD will be approximately 0.11 crashes per person each year. Although a series of sensitivity analyses found this estimate to be robust, the strength of our conclusion must be tempered by the fact that the studies providing the data used to produce this estimate were of low methodologic quality. In addition, the fact that the crash data used in our analyses did not pertain to CMV drivers may further limit the value of our findings. The reason for this is because the generalizability of our findings to this population of drivers is unknown.

2. **Drivers with hypertension are at an increased risk for a motor vehicle crash when compared with comparable drivers who do not have the disorder (Strength of Evidence: Acceptable).**

   - **The magnitude of this increased risk cannot be determined at the present time.**

   Two included studies (Median Quality Rating: Low) reported on the difference in the incidence of a motor vehicle crash observed among individuals with hypertension and comparable individuals without the disorder. The findings of both studies suggest that individuals with hypertension are at an increased

risk for a motor vehicle crash when compared with individuals without the disorder. Because data from only two studies are available, however, we have not pooled their data using meta-analysis in order to obtain a summary estimate of the magnitude of this increased risk.

3. **A paucity of consistent data precludes one from drawing evidence-based conclusions as to whether individuals with coronary artery disease (CAD), arrhythmias, or other types of CVD are at increased risk for a motor vehicle crash.**

Key Question 2: What are the risk factors for rupture of an aortic (abdominal or thoracic) aneurysm?

Specific findings of our assessment of the evidence that addressed Key Question 2 are presented below:

1. **The most commonly observed risk factor for abdominal aortic aneurysm (AAA) is aneurysm size (Strength of Evidence: Moderate).**

   - **Due to the fact that there were a number of methodologic problems involving heterogeneity of the populations studied, biases, statistical power issues, and lack of standardization regarding aneurysm measurement and reporting, no attempt was made to construct a quantitative model describing the risk of rupture for an AAA.**

   Fourteen (Total N = 3,317) moderate-quality studies assessed the potential risk factors for rupture of an AAA. Of these 14 studies, 10 found that aneurysm size was the most important risk factor to be associated with AAA rupture. Other risk factors for AAA rupture that were identified included: chronic obstructive pulmonary disease (COPD) (k = 1 study), presence of hypertension (k = 2 studies), AAA expansion rate (k = 3 studies), smoking status (k = 1 study), aortic wall stress (k = 1 study), aortic tortuosity (k = 1 study), bronchiectasis (k = 1 study), aortic outpouching (k = 1 study), and female gender (k = 2 studies).

2. **The most commonly observed risk factor for thoracic aortic aneurysm (TAA) rupture is aneurysm size (Strength of Evidence: Acceptable).**

   - **Due to the fact that there were a number of methodologic problems involving heterogeneity of the populations studied, biases, statistical power issues, and lack of standardization regarding aneurysm measurement and reporting, we did not attempt to determine a quantitative model describing the risk of rupture for an aortic aneurysm or TAA.**

Seven (Total N = 3,908) low-quality studies assessed the potential risk factors for rupture of a TAA. All seven studies found that aneurysm size was the most important risk factor associated with aneurysm rupture. Other risk factors identified for TAA rupture included age, presence of uncharacteristic chronic pain, and COPD.

Key Question 3: Is implantation of a pacemaker effective in preventing vasovagal syncope recurrence?

Our assessment of the evidence that addressed Key Question 3 is presented below:

1. **The Best available evidence does not support the contention that permanent, implanted dual-chamber pacemakers are effective in reducing the recurrence of vasovagal syncope in individuals with high recurrence rates (Strength of Evidence: Moderate).**

   - **Because of inconsistencies in the findings of the studies that comprise the evidence base for Key Question 3, we refrain from providing a single estimate of treatment effect at this time.**

   Five moderate-to-high quality randomized controlled trials (RCTs) addressed Key Question 3. Outcomes assessed by all five studies included the proportion of individuals experiencing recurrent syncope, the time to recurrence, and adverse events.

   Analysis of these data found that the results of the high-quality (k = 2) and moderate-quality (k = 3) studies differed significantly. All three moderate-quality studies found that permanent dual-chamber pacemakers significantly reduce the number of recurrences of vasovagal syncope when compared to standard treatment. However, neither of the two high-quality studies found evidence to support the contention that permanent dual-chamber pacemakers offer an effective treatment option for individuals with recurrent syncope. The difference in findings may be attributed to a lack of blinding in the three moderate-quality studies in a group of individuals who are known to respond strongly to placebo.

Key Question 4: What is the risk of sudden incapacitation or sudden death following implantation of an ICD?

Specific findings of our assessment of the evidence that addressed Key Question 4 are presented below:

1. **Whether individuals with an ICD implant experience crash that can be directly attributed to CVD or the ICD implant itself cannot be determined at the present time.**

   Four of six included studies presented data on the number or frequency of crashes that occurred among individuals with an ICD. None of these studies compared crash rates occurring among individuals with an ICD to crash rates among individuals either without and active ICD or without CVD. Consequently, it is not possible to determine whether individuals with an ICD are at increased risk for a motor vehicle crash.

   Crashes reportedly occurred among individuals enrolled in only one of the four included studies. Eleven individuals enrolled in this study experienced at least one crash during follow-up. Of these, only one was reportedly the fault of the driver, and this crash was not the consequence of either CVD or an event associated with the implanted ICD. The fact that no crashes reportedly occurred in the remaining studies may be the combined consequence of the small size of these studies and their short follow-up times. In order to determine a reliable crash rate estimate among individuals with ICDs, studies with far larger sample sizes and longer follow-up times are needed.

2. **Whether individuals with an ICD implant experience sudden death or incapacitation during driving cannot be determined at the present time.**

   Three of six included studies reported on occurrence rates for syncope and sudden death among individuals with an ICD while they were driving. None of the individuals enrolled in these three studies experienced syncope or sudden-cardiac death (SCD) while driving. Because syncope and sudden death are rare events, the fact that no cases were observed in the three included studies cannot be considered as evidence that such events will not occur while driving. In order to determine reliable estimates of these rates among individuals with ICDs, studies with far larger sample sizes and longer follow-up times are needed.

3. **Some individuals with ICD will experience ICD discharge while they are driving (Strength of Evidence: Strong).**

   - **Quantitative assessment of the available data suggests that approximately 6.3% (95% CI: 4.7–8.4%) of individuals who drive with an ICD will experience an ICD discharge while driving (Stability of Estimate: Low).**

All six included studies reported on the occurrence of ICD discharge during driving. Five of these six studies reported that ICD discharge while driving did occur in some individuals. Despite the fact that follow-up times varied across studies, data on the proportion of individuals who experienced ICD discharge while driving were remarkably consistent. Pooling of these data found that the proportion of individuals with an ICD who experience at least one shock during driving (appropriate or inappropriate) was in the order of 6.3%. A series of sensitivity analyses found the findings of this analysis to be robust.

Key Question 5: What is the risk of sudden death or incapacitation in individuals with low LVEF (<50%, <40%, <35%)?

1. **Decreasing LVEF increases the risk of sudden death or incapacitation among individuals with CVD (Strength of Evidence: Moderate).**

   - **Due to the fact that no more than two studies used the same levels of LVEF stratification, no attempt was made to determine a quantitative estimate of the risk of sudden death or incapacitation in individuals with low LVEF.**

   Ten low-to-moderate quality studies assessed the risk of sudden death or incapacitation in individuals with low LVEF. Five of these studies used multiple levels of LVEF stratification. The remaining five studies used a single level of LVEF stratification. These 10 studies consistently demonstrated that decreasing LVEF increases the risk of sudden death or incapacitation in individuals with CVD. However, several studies have indicated that although LVEF is an important risk factor for sudden death or incapacitation, it is not the only risk factor. In order to better predict sudden death or incapacitation, one should consider other risk factors along with LVEF. For example, one study noted that rather than using particular risk markers, the use of a number of accumulated risk markers was a more powerful predictor for sudden death in patients with chronic heart failure.

Key Question 6: Is the relationship between LVEF and sudden death or incapacitation (if established) dependent on the underlying etiology of heart failure?

Due to a paucity of data, no conclusion pertaining to whether the relationship between sudden death or incapacitation and LVEF is drawn.

No studies met the inclusion criteria for this key question.

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