

Original Investigation

Syncope and Motor Vehicle Crash Risk

A Danish Nationwide Study

Anna-Karin Numé, MD; Gunnar Gislason, MD, PhD; Christine B. Christiansen, MD, PhD; Deewa Zahir, MB; Mark A. Hlatky, MD; Christian Torp-Pedersen, MD, DSc; Martin H. Ruwald, MD, PhD

IMPORTANCE Syncope may have serious consequences for traffic safety. Current clinical guideline recommendations on driving following syncope are primarily based on expert consensus.

OBJECTIVE To identify whether there is excess risk of motor vehicle crashes among patients with syncope compared with the general population.

DESIGN, SETTING, AND PARTICIPANTS Danish nationwide cohort study from January 1, 2008, to December 31, 2012. Through individual-level linkage of nationwide administrative registers, all Danish residents 18 years or older were identified. Of 4 265 301 eligible Danish residents, we identified 41 039 individuals with a first-time diagnosis of syncope from emergency department or hospital.

MAIN OUTCOMES AND MEASURES Rate of motor vehicle crashes (including nonfatal and fatal crashes), based on multivariate Poisson regression models, using the total Danish population as reference.

RESULTS The 41 039 patients with syncope had a median age of 66 years (interquartile range [IQR], 47-78 years); 51.0% were women; and 34.8% had cardiovascular disease. Through a median follow-up of 2.0 years (IQR, 0.8-3.3 years), 1791 patients with syncope (4.4%) had a motor vehicle crash, 78.1% of which led to injury (n = 1398) and 0.3% to death (n = 6). The crude incidence rate of motor vehicle crashes was almost doubled among patients with syncope (20.6 per 1000 person-years; 95% CI, 19.7-21.6) compared with the general population (12.1; 95% CI, 12.0-12.1), with a rate ratio (RR) of 1.83 (95% CI, 1.74-1.91) after adjustment for age, sex, socioeconomic position, and relevant comorbidities and pharmacotherapy. Men had a relatively higher rate of motor vehicle crashes (RR, 1.91; 95% CI, 1.79-2.03) than women (RR, 1.74; 95% CI, 1.63-1.87). The excess risk of motor vehicle crashes persisted throughout the follow-up period. The 5-year crash risk following syncope was 8.2% (95% CI, 7.5%-8.8%) among the population aged 18 to 69 years compared with 5.1% (95% CI, 4.7%-5.4%) in the general population.

CONCLUSIONS AND RELEVANCE Prior hospitalization for syncope was associated with increased risk of motor vehicle crashes throughout the follow-up period. This study suggests that syncope should be considered as one of several factors in a broad assessment of fitness to drive.

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Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Anna-Karin Numé, MD, Department of Cardiology, Copenhagen University Gentofte Hospital, Kildegaardsvej 28, 8.3, Post 635, DK-2900 Hellerup, Denmark (annakarin.nume@gmail.com).

Syncope is characterized by a sudden loss of consciousness, although with spontaneous and complete recovery,¹ and could have serious consequences for public safety if it occurs in the driver of a motor vehicle. The lifetime cumulative incidence of syncope is 35%, and the cause usually differs in young and elderly individuals.¹⁻³ In addition, about one-third of patients with syncope will experience recurrent events within 3 years,^{1,4,5} so physicians face a difficult judgment about whether patients with syncope are fit to drive.⁶

Driver incapacity as a result of sudden medical illness appears to be an unusual cause of motor vehicle crashes, perhaps only 1% to 3%.⁷⁻⁹ Although overall crash rates have decreased, traffic crashes remain a leading cause of death and disability.¹⁰ Some studies have suggested that the incidence of syncope while driving is 2% to 10%,¹¹⁻¹⁵ but these studies were small, usually based on self-reported data among syncope subpopulations, and had limited information about follow-up crash risk. Consequently, current guideline recommendations on syncope and driving are mainly based on expert consensus, corresponding to level C evidence.^{1,16-19} According to the European Society of Cardiology,¹ reflex syncope should not lead to driving restrictions. In contrast, the guidelines suggest driving restrictions in case of recurrent syncope, substantial cardiovascular comorbidities, or “unexplained syncope,” unless definitive treatment can be ensured.¹ Recommendations from the Canadian Cardiovascular Society are similar.¹⁶

Motor vehicle travel in developed countries plays an essential part of daily living, so prohibiting an individual from driving could substantially impair their employment and quality of life.²⁰⁻²² We therefore conducted this study to provide objective, population-based evidence on the association of syncope with motor vehicle crashes. Our primary aim was to assess the risk of motor vehicle crashes among a nationwide cohort of patients with syncope. Our secondary aim was to examine the temporal relationship between syncope and subsequent motor vehicle crash risk.

Methods

Setting

This study was conducted from January 1, 2008, to December 31, 2012, in Denmark, where the health care is based on a tax-financed system that provides all inhabitants with equal access free of personal charge. The minimum age for obtaining driving permission is 18 years, and at age 70 years, all patients undergo mandatory driving license screening by their primary care physician.

Registers

In this nationwide study, we used a register-based follow-up design. At the time of birth or immigration, all individuals are given a unique and permanent civil registration number that enables individual-level linkage between nationwide administrative registers holding information on health care use.

Key Points

Question What is the association between prior syncope and motor vehicle crash risk?

Findings In this Danish nationwide cohort study of 41 039 patients with syncope, syncope was associated with a 2-fold increased risk of motor vehicle crashes compared with the general population. The elevated risk persisted throughout the follow-up period of 5 years.

Meaning The study suggests that patients with syncope are at increased risk of motor vehicle crashes, but as the absolute risk was relatively small, syncope should be considered as one of several factors in a broad assessment of fitness to drive rather than an absolute criterion.

Information about medical history and hospital contacts was retrieved from the Danish National Patient Register, which holds information about all hospitalizations since 1977.²³ At discharge, each hospitalization is coded with a primary diagnosis and, if appropriate, secondary diagnoses, based on the *International Classification of Diseases (ICD)*. Since 2008, the National Patient Register also holds information about hospitalizations due to motor vehicle crashes, coded according to the Nordic Medico-Statistical Committee's classification of External Causes of Injuries,^{24,25} which was used to identify all nonfatal crashes. We retrieved information about fatal crashes from the Cause of Death Register.²⁶ Medical history was broadened with information about dispensed prescriptions that has been consecutively registered according to the Anatomical Therapeutic Chemical classification system in the Danish Register of Medicinal Product Statistics.²⁷ Finally, average income in a 5-year period before inclusion was used as a proxy for socioeconomic status, as done previously.^{28,29} We obtained information on vital status, sex, date of birth, and migration from the National Population Register.³⁰

Study Population

The study population comprised all Danish residents between 2008 and 2012 who were at least 18 years old. We then identified a cohort including all patients discharged with a first-time primary diagnosis of syncope from hospital or emergency department (*International Classification of Diseases, Tenth Revision [ICD-10]* code R55.9). The discharge diagnosis of R55.9 has a positive predictive value of 95% and a sensitivity of 63%.³¹

Individuals were followed up until the first of the following occurrences: event of interest, emigration, death, or end of follow-up on December 31, 2012.

Comorbidity and Pharmacotherapy

We considered the following covariates as potential confounders based on current knowledge and literature: cardiovascular comorbidities, diabetes, cardiac pacemaker, implantable cardioverter-defibrillator, use of anxiolytic or antipsychotic drugs, and alcohol abuse,^{7,16,32-37} and we retrieved information from discharge, prescription, or surgical procedure codes (eTable 1 in the [Supplement](#)). Individuals were considered to have cardiovascular disease if they had a diagnosis code for

either ischemic heart disease, cardiac arrhythmia, heart failure, atrioventricular block, left bundle branch block, cerebral vascular disease, or peripheral vascular disease. We considered claimed prescriptions for anxiolytics or antipsychotics up to 180 days prior to inclusion as use of these agents. Recurrent syncope was defined as the second discharge diagnosis (emergency department or inpatient) of syncope.

Outcome

The primary outcome was the first motor vehicle crash that was either fatal or sufficiently severe to require evaluation in an emergency department or admission to a hospital. We included crashes that involved motorized vehicles (cars, motorcycles, and vans), for which sensitivities above 87% and positive predictive values above 92% previously have been found.²⁵ We considered a nonfatal crash within 30 days prior to a fatal crash as a fatal crash. In addition, we considered crashes documented 48 hours before or after the time of the syncope hospitalization to be related to the syncope event.

Statistical Analysis

We analyzed syncope in a time-dependent approach, so that individuals contributed to at-risk time in the general population until the date of a first-time hospitalization for syncope (syncope population). Baseline characteristics are therefore presented at time of inclusion for the general population and, correspondingly, at time of syncope hospitalization for the syncope population. Crude incidence rates were calculated as number of events per 1000 person-years at risk. We used multivariate Poisson regression analyses to examine incidence rate ratios (RRs) of motor vehicle crashes with 95% CIs following syncope compared with the general Danish population. We used the Lexis diagram to split the follow-up enabling continuous update of time-dependent covariates (ie, age, comorbidity, pharmacotherapy, and calendar year), and it included 3 time scales: calendar time, age, and follow-up. The Lexis diagram allows individuals to contribute to person-years to both unexposed and exposed groups by splitting each study individuals into several observations, one for each status defined by the time-dependent variable.

We constructed 2 Poisson models, both of which were adjusted for age, sex, calendar year, socioeconomic status, and the covariates listed in **Table 1**. In the first model, we included syncope as a time-dependent covariate to establish the RRs for subsequent motor vehicle crashes. In the second model, we further examined whether crash risk changed with time elapsed from syncope discharge by assessing risk at 1, 3, 6, and 12 months and every 12 months thereafter. To evaluate effect modification, relevant covariates, including age, sex, and cardiovascular disease, were selected a priori based on clinical relevance. Second, we examined the interactions by inclusion of interaction terms in the overall model using the likelihood ratio test, and if suitable, we presented the models stratified accordingly. A 2-sided $P < .05$ was considered statistically significant. All analyses were tested for validity in terms of constant RRs for each time period by performing the same analyses on a more frequent time scale.

Table 1. Characteristics of the Study Population

Characteristic	Study Population, No. (%)	
	Syncope (n = 41 039)	General Population (n = 4 224 262)
Age, median (IQR), y	66 (47-78)	45 (30-61)
Age group, y		
18-35	6838 (16.7)	1 442 515 (34.2)
36-69	18 962 (46.2)	2 227 465 (52.7)
≥70	15 239 (37.1)	554 282 (13.1)
Women	20 916 (51.0)	2 135 502 (50.5)
Men	20 123 (49.0)	2 088 760 (49.5)
Socioeconomic status (income), quartile		
<First	4776 (11.6)	843 504 (20.0)
First to third	30 467 (74.2)	2 520 885 (59.7)
>Third	5796 (14.1)	859 873 (20.3)
Cardiovascular disease	14 300 (34.8)	415 647 (9.8)
Ischemic heart disease	7137 (17.4)	190 891 (4.5)
Cardiac arrhythmias	5504 (13.4)	134 142 (3.2)
Cerebrovascular disease	4872 (11.9)	114 628 (2.7)
Heart failure	3251 (7.9)	62 806 (1.5)
Atrioventricular block and LBBB ^a	647 (1.6)	9898 (0.2)
Cardiac pacemaker	884 (2.2)	12 795 (0.3)
Implantable cardioverter-defibrillator	267 (0.7)	2385 (0.1)
Diabetes	4530 (11.0)	172 587 (4.1)
Alcohol abuse	2726 (6.6)	93 645 (2.2)
Anxiolytics	10 729 (26.1)	308 690 (7.3)
Antipsychotics	2807 (6.8)	78 274 (1.9)
Hospital admission type for syncope		
Inpatient	25 402 (61.9)	NA
Emergency department	15 637 (38.1)	NA
Follow-up, median (IQR), y	2.0 (2.5)	5.0 (0)

Abbreviations: IQR, interquartile range (quartile 1 to quartile 3); LBBB, left bundle branch block; NA, not applicable.

^a First-, second-, or third-degree atrioventricular block.

Additional analysis was performed with risk-set matching to construct cumulative incidence proportion curves to illustrate absolute motor vehicle crash risk following syncope. Thus the syncope population was included on date of syncope hospitalization and thereafter matched with 2 controls from the general population by age and sex. Cumulative incidence was assessed using a competing risk model to account for the competing risk of death from other causes than fatal crashes in the syncope population.³⁸ The matched population was used to calculate cumulative incidence only.

Finally, we undertook sensitivity analyses and investigated fatal crashes, hospital admission type for syncope, and the influence of recurrent syncope on motor vehicle crash risk following syncope.

Statistical analyses were performed using SAS software, version 9.4 (SAS Institute Inc) and R 3.2.2. (R Foundation for Statistical Computing).

Ethics

This study was approved by the Danish Data Protection Agency. In Denmark, ethical approval is not required for register-based studies.

Results

Between 2008 through 2012, we identified 4 265 301 Danish residents who were 18 years or older, of whom 41 039 had a first-time diagnosis of syncope from hospital or emergency department. Patients with syncope had a median age of 66 (interquartile range [IQR] 47-78) years; 51.0% were women; and 34.8% had cardiovascular disease (Table 1). During a median follow-up of 2.0 (IQR 0.8-3.3) years, a total of 1791 patients with syncope (4.4%) experienced a motor vehicle crash that required medical evaluation in an emergency department or hospital; 0.3% of these crashes were fatal, and 78.1% resulted in crash-related injury. These 1791 crashes were a minority (0.8%)

of the national total of 226 078, and the 6 fatalities were also a minority (0.8%) of the national total of 713 (Table 2). The average interval between syncope discharge and the occurrence of a crash was 315 (IQR 59-698) days.

The crude incidence rates of motor vehicle crashes per 1000 person-years were higher among the syncope population (20.6; 95% CI, 19.7-21.6) compared with the general population (12.1; 95% CI, 12.0-12.1). The crash rates were highest among the population aged 18 to 35 years and lowest among the population aged 70 years or older (Figure 1).

In multivariate analyses, which adjusted for age, sex, and calendar year, patients with syncope had a 2-fold higher RR of motor vehicle crashes compared with the general population (RR, 2.04; 95% CI, 1.95-2.14; $P < .001$). We found that men had relatively increased crash risk compared with women: RR, 1.91 (95% CI, 1.79-2.03) vs RR, 1.74 (95% CI, 1.63-1.87). The fully adjusted RRs of motor vehicle crash risk increased with age among men but decreased with age among women ($P < .001$ for the interaction) (Figure 1).

The excess risk of motor vehicle crashes among patients with syncope persisted throughout the follow-up of 5 years (Figure 2), with similar results in all age groups and regardless of recurrent syncope (eFigure 1 in the Supplement). Furthermore, the 5-year cumulative incidence for motor vehicle crashes remained significantly elevated among patients with syncope in a competing risk model that accounted for death from other causes, particularly in the population aged 18 to 69 years in which the risk was 8.2% (Figure 3).

Table 2. Motor Vehicle Crashes in Individuals With Syncope and in the General Population

Motor Vehicle Crash Characteristics	Study Population, No. (%)	
	Syncope (n = 41 039)	General Population (n = 4 224 262)
Total ^a	1791 (4.4)	224 287 (5.3)
Fatal	6 (0.3)	707 (0.3)
Nonfatal	1785 (99.7)	223 580 (99.7)
Crash-related injury		
Any	1398 (78.1)	193 194 (86.1)
Superficial ^b	974 (54.4)	140 924 (62.8)
Major ^c	424 (23.7)	52 270 (23.3)
Crash with syncope episode ^d	349 (19.5)	NA

Abbreviation: NA, not applicable.

^a Median follow-up was 2.0 years for the syncope population and 5.0 years for the general population.

^b Superficial injury defined as superficial lesion, wound, or sprain.

^c Major injury defined as fracture, traumatic amputation, crush lesion, internal lesion, or internal bleeding.

^d Motor vehicle crash in immediate relation to syncope.

Sensitivity and Subgroup Analyses

In subpopulations with and without cardiovascular disease, we found that the RRs of motor vehicle crashes were lower among patients with syncope who also had cardiovascular disease than those without cardiovascular disease (eFigure 2 in the Supplement). In addition, among a subgroup of patients with syncope with an implantable cardioverter-defibrillator, syncope was not significantly associated with motor vehicle crashes (eTable 2 in the Supplement). In contrast, we found that patients with recurrent syncope had a motor vehicle crash risk similar to patients with only a single hospitalization for syncope (eFigure 3 in the Supplement).

Figure 1. Motor Vehicle Crash Risk Following Syncope by Age and Sex

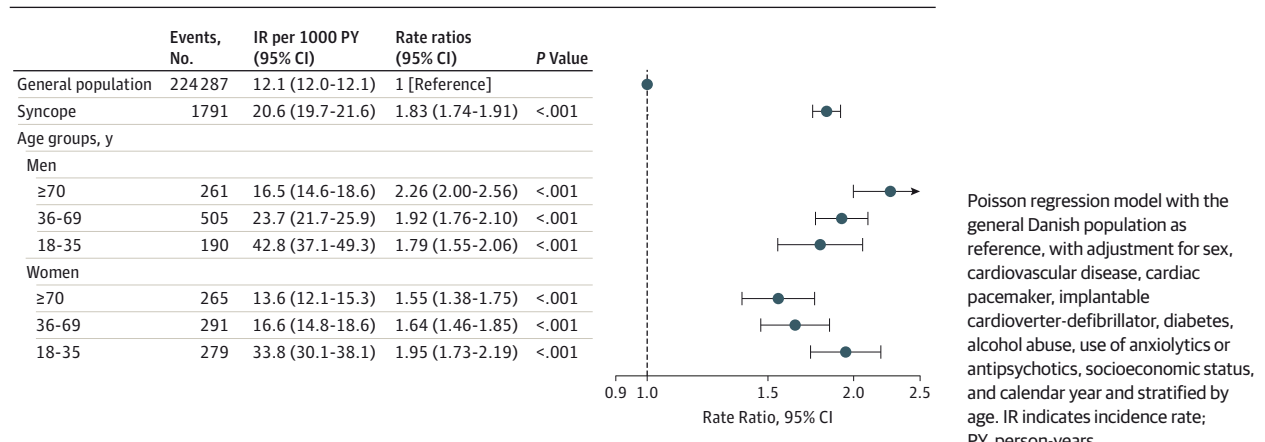
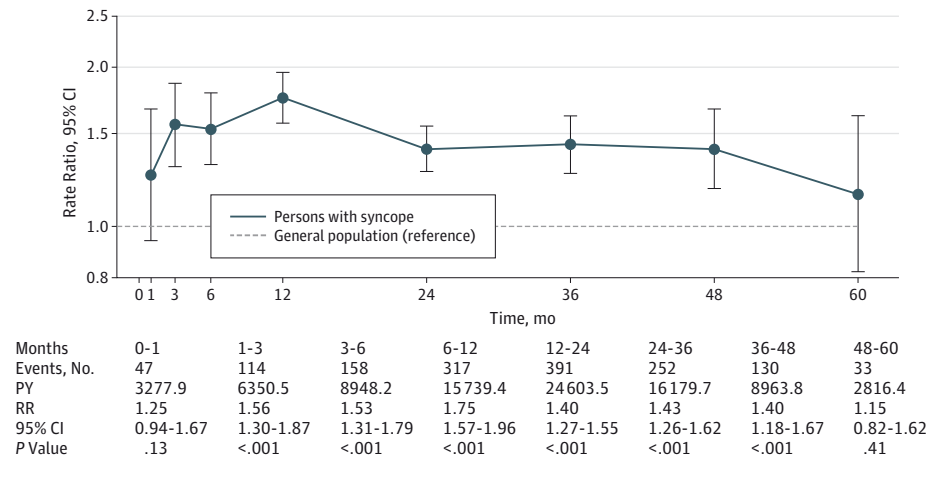
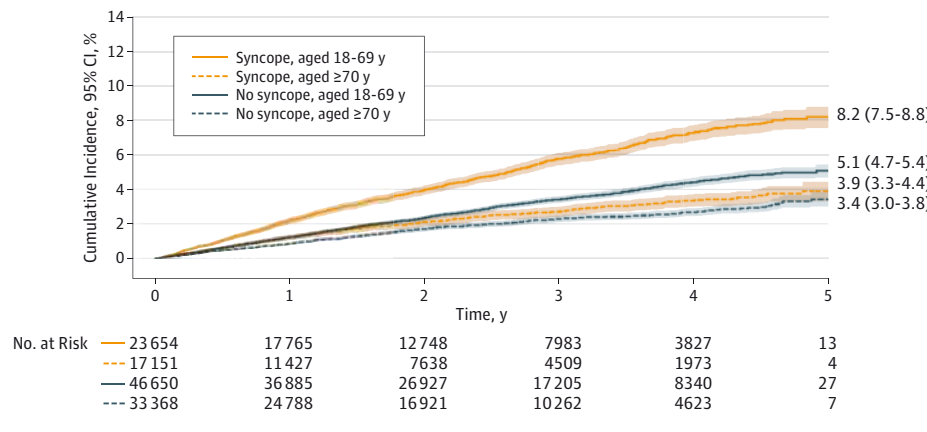


Figure 2. Time Elapsed From Syncope and Risk of Motor Vehicle Crashes



Poisson regression model with the general Danish population as reference, with adjustment for age, sex, socioeconomic status, calendar year, cardiac pacemaker, implantable cardioverter-defibrillator, cardiovascular disease, diabetes, alcohol abuse, and use of anxiolytics or antipsychotics. Crash events per person-year (PY) are reported for the syncope population. RR indicates rate ratio.

Figure 3. Elevated Cumulative Incidence for Motor Vehicle Crashes Following Syncope



Illustrated incidence is compared with an age- and sex-matched control population, accounting for competing risk of death from other causes.

The RRs of fatal crashes were similar to risk estimates for overall motor vehicle crashes, but the incidence rates were significantly lower (eFigure 4 in the Supplement). Patients with syncope who were discharged from emergency departments were younger, had less comorbidity (eTable 3 in the Supplement), and were associated with higher crash risk compared with inpatients (eFigure 5 in the Supplement).

Discussion

In this nationwide study of more than 4.2 million individuals, we found that first-time syncope was associated with a 2-fold increased risk of motor vehicle crashes that remained elevated throughout follow-up. Because to our knowledge, no previous large-scale study has investigated syncope and traffic safety, these data provide novel information for development of policies about syncope and driving.

We found that excess crash risk following syncope was consistent, although the degree of excess risk varied according to age, sex, and comorbidity. Our findings of higher crash rates among the younger age groups and men are in line with cur-

rent evidence: men drive more and are more likely to engage in risk-taking behavior such as speeding, failure to use seat belt, and driving while intoxicated.^{10,39-42} Medical screening as a condition for relicensing in the older drivers may lead to lower crash rates among the elderly population.⁴³ In addition, older persons are more likely to be severely injured or die in motor vehicle crashes because of increased fragility and be more likely to need hospital evaluation compared with younger persons.⁴⁴ Self-imposed behavioral restrictions, such as avoidance of driving in bad weather, at night, or during high-traffic periods, are common among older drivers and may lead to lower risk of motor vehicle crashes.^{45,46} Several studies suggest that women are more likely to self-regulate or cease their driving, which could explain the different trends by age for older men and women found in the current study.⁴⁵⁻⁴⁹

Only a small proportion of the patients with syncope in this study experienced a motor vehicle crash in immediate relation to index syncope. Acute illness is difficult to assess in motor vehicle crashes because it can be masked by severe injury, so we chose to analyze the relation of syncope with subsequent motor vehicle crashes in a time-to-event approach. Our finding of a 2.2% crash risk in the first year following syncope

is lower than 3.4% among participants in the AVID trial⁵⁰ (secondary prevention implantable cardioverter-defibrillator patients). In the MADIT-RIT trial⁵¹ (primary prevention implantable cardioverter-defibrillator patients), 3.1% of the study population had syncope while driving during 1.4 years of follow-up.

Another novel finding in the present study was that the motor vehicle crash risk following syncope remained elevated throughout the follow-up period. Several factors might contribute to this sustained risk. First, it is likely that syncope is a marker for a more severely sick population, with more cardiovascular and other comorbidities, who are receiving medical therapy that could influence risk of syncope as well as the motor vehicle crash risk.^{3,32,34-36} We hypothesized that cardiovascular disease would be associated with higher crash risk because it is likely to cause syncope with little or no warning and has been identified as an independent predictor of syncope while driving.¹¹ Our findings suggest, however, the opposite was true—namely, that presence of cardiovascular disease was associated with a relatively lower risk. A plausible explanation could be that more serious cases of cardiac syncope receive diagnoses of specific cardiac causes rather than the *ICD-10* diagnosis of syncope.³¹ It is also likely that these individuals were subject to driving restrictions imposed by the underlying cardiovascular conditions rather than the syncope per se.⁶ This would be in line with our findings from the syncope subpopulation with implantable cardioverter-defibrillators.³³

Information about syncope cause was unavailable in the current study. Several studies have identified reflex syncope (eg, vasovagal syncope caused by orthostatic stress) as the most common type of syncope while driving.^{11,14,15,52} Current guideline recommendations place no driving restrictions on patients with reflex syncope.^{1,16}

Recurrence rates for syncope are relatively high and remain high for several years.^{1,4,5} Although most guidelines recommend some form of abstinence from driving after recurrent syncope,^{1,16} we did not find a reduced crash risk among patients with recurrent syncope. However, it is possible that patients resumed driving whether or not they were advised by their physician not to do so.^{13,50,53} Also, as we defined recurrent syncope as a second hospital discharge of syncope, it is possible that recurrence occurred without subsequent hospitalization.

The main advantage of our study is the large cohort of patients with syncope with complete follow-up that enabled us to investigate relatively rare crash events accurately. This study also included data on fatal crashes.

The study has several potential limitations. First, it was based on observational data and therefore lacks clinical information on the cause of syncope, so risk estimates for individual causes remain unknown. However, the *ICD-10* code R55.9 is representative for the most common causes of syncope, and despite thorough investigation, the cause of the syn-

cope remains unexplained in 20% to 30% of cases.^{54,55} One-third of those hospitalized for syncope receive other more specific discharge diagnoses, such as ventricular arrhythmia, aortic valve stenosis, and atrioventricular block.³¹ In addition, only a smaller but probably selected proportion of individuals with syncope contact the emergency department or hospital,⁵⁶ but it is unknown in what direction this would influence crash risk.

Second, data regarding the circumstances of the traffic crash were unavailable, including use of alcohol or illicit drugs, use of seat belts, among other traffic conditions. We accounted for alcohol abuse⁵⁷ because it is a risk factor of crashes, but we acknowledge that use of alcohol and other substances in relation to the crash events were unmeasured in the present study and could have influenced crash risk particularly among the younger population.^{37,40-42}

Third, exposure to driving, driver status, and driving license were unavailable for the current study. In Denmark, 87% of the population 18 years or older have a driving license,³⁹ but the elderly population may self-regulate or cease driving, as might persons with other medical conditions with policies on driving.^{16,19,33} Private and commercial driving was not considered separately because this information was unavailable.^{1,16,19}

Fourth, information about crashes was obtained from hospitals' traffic crash registration; thus, it is possible that we have overestimated the proportion and severity of crash-related injuries. Conversely, it is likely that we have underestimated the rate and consequences of crashes because we did not include multiple events and had no data about minor crashes that did not require medical evaluation or led to evaluation in the offices of a general practitioner. Furthermore, we could not evaluate whether other individuals were also injured in the crash along with the patient with syncope, nor do we have any data on crashes that injured others, such as pedestrians, but did not injure the patient with syncope.

Conclusions

While much remains unknown about syncope and traffic safety, our findings suggest that patients with syncope are at increased risk of motor vehicle crashes compared with the general population. Since the absolute crash risk was relatively small, whether syncope should lead to restrictions on a patient's ability to drive is a difficult policy question that must balance multiple considerations. Syncope should be considered as one of several factors in a broad assessment of fitness to drive rather than an absolute criterion. We urge increased physician awareness about driving recommendations, accurate diagnosis, and appropriate treatment for patients with syncope to reduce motor vehicle crashes.

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Author Affiliations: Department of Cardiology, Copenhagen University Gentofte Hospital, Hellerup, Denmark (Numé, Gislason, Christiansen, Zahir, Ruwald); The National Institute of Public Health, University of Southern Denmark,

Copenhagen, Denmark (Gislason); The Danish Heart Foundation, Copenhagen, Denmark (Gislason); The Research House, Aalborg University Hospital, Aalborg, Denmark (Christiansen); Department of Health Research and Policy,

Stanford University School of Medicine, Stanford, California (Hlatky); Department of Medicine, Stanford University School of Medicine, Stanford, California (Hlatky); Institute of Health, Science and Technology, Aalborg University, Aalborg, Denmark (Torp-Pedersen).

Author Contributions: Drs Numé and Gislason had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Numé, Gislason, Zahir, Ruwald.

Acquisition, analysis, or interpretation of data:

Numé, Gislason, Christiansen, Hlatky, Torp-Pedersen, Ruwald.

Drafting of the manuscript: Numé.

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REFERENCES

- Moya A, Sutton R, Ammirati F, et al; Task Force for the Diagnosis and Management of Syncope; European Society of Cardiology (ESC); European Heart Rhythm Association (EHRA); Heart Failure Association (HFA); Heart Rhythm Society (HRS). Guidelines for the diagnosis and management of syncope (version 2009). *Eur Heart J*. 2009;30(21):2631-2671. doi:10.1093/eurheartj/ehp298.
- Ganzeboom KS, Mairuhu G, Reitsma JB, Linzer M, Wieling W, van Dijk N. Lifetime cumulative incidence of syncope in the general population: a study of 549 Dutch subjects aged 35-60 years. *J Cardiovasc Electrophysiol*. 2006;17(11):1172-1176. doi:10.1111/j.1540-8167.2006.00595.x.

- Ruwald MH, Hansen ML, Lamberts M, et al. The relation between age, sex, comorbidity, and pharmacotherapy and the risk of syncope: a Danish nationwide study. *Europace*. 2012;14(10):1506-1514. doi:10.1093/eurpace/eus154.
- Ruwald MH, Hansen ML, Lamberts M, et al. Comparison of incidence, predictors, and the impact of co-morbidity and polypharmacy on the risk of recurrent syncope in patients <85 versus ≥85 years of age. *Am J Cardiol*. 2013;112(10):1610-1615. doi:10.1016/j.amjcard.2013.07.041.
- Solbiati M, Casazza G, Dipaola F, et al. Syncope recurrence and mortality: a systematic review. *Europace*. 2015;17(2):300-308. doi:10.1093/eurpace/euu327.
- Costantino G, Sun BC, Barbic F, et al. Syncope clinical management in the emergency department: a consensus from the first international workshop on syncope risk stratification in the emergency department [published online August 4, 2015]. *Eur Heart J*. 2015. doi:10.1093/eurheartj/ehv378.
- Petch MC. Driving and heart disease. *Eur Heart J*. 1998;19(8):1165-1177.
- Herner B, Smedby B, Ysander L. Sudden illness as a cause of motor-vehicle accidents. *Br J Ind Med*. 1966;23(1):37-41.
- Norman LG. The health of bus drivers: a study in London transport. *Lancet*. 1958;2(7051):807-812.
- Peden M, Scurfield R, Sleet D, et al. *World Health Organization. World Report on Road Traffic Injury Prevention*. Geneva, Switzerland: World Health Organization; 2004.
- Sorajja D, Nesbitt GC, Hodge DO, et al. Syncope while driving: clinical characteristics, causes, and prognosis. *Circulation*. 2009;120(11):928-934. doi:10.1161/CIRCULATIONAHA.108.827626.
- Sheldon R, Koshman ML. Can patients with neuromediated syncope safely drive motor vehicles? *Am J Cardiol*. 1995;75(14):955-956.
- Maas R, Ventura R, Kretzschmar C, Aydin A, Schuchert A. Syncope, driving recommendations, and clinical reality: survey of patients. *BMJ*. 2003;326(7379):21.
- Li H, Weitzel M, Easley A, Barrington W, Windle J. Potential risk of vasovagal syncope for motor vehicle driving. *Am J Cardiol*. 2000;85(2):184-186.
- Folino AF, Migliore F, Porta A, Cerutti S, Illiceto S, Buja G. Syncope while driving: pathophysiological features and long-term follow-up. *Auton Neurosci*. 2012;166(1-2):60-65. doi:10.1016/j.autneu.2011.09.003.
- Simpson C, Ross D, Dorian P, et al. CCS Consensus Conference 2003: Assessment of the cardiac patient for fitness to drive and fly. *Can J Cardiol*. 2004;20(13):1313-1320.
- Epstein AE, Miles WM, Benditt DG, et al. Personal and public safety issues related to arrhythmias that may affect consciousness: implications for regulation and physician recommendations. A medical/scientific statement from the American Heart Association and the North American Society of Pacing and Electrophysiology. *Circulation*. 1996;94(5):1147-1166. doi:10.1161/01.CIR.94.5.1147.
- Sun BC, Costantino G, Barbic F, et al. Priorities for emergency department syncope research. *Ann*

Emerg Med. 2014;64(6):649-655.e2. doi:10.1016/j.annemergmed.2014.04.014.

- Epstein AE. *Cardiovascular Advisory Panel Guidelines for the Medical Examination of Commercial Motor Vehicle Drivers: Cardiac Arrhythmias, Pacemakers, Implantable Defibrillators*. Washington, DC: US Department of Transportation: Federal Motor Carrier Safety Administration; 2012.
- van Dijk N, Sprangers MA, Colman N, Boer KR, Wieling W, Linzer M. Clinical factors associated with quality of life in patients with transient loss of consciousness. *J Cardiovasc Electrophysiol*. 2006;17(9):998-1003. doi:10.1111/j.1540-8167.2006.00533.x.
- Linzer M, Pontinen M, Gold DT, Divine GW, Felder A, Brooks WB. Impairment of physical and psychosocial function in recurrent syncope. *J Clin Epidemiol*. 1991;44(10):1037-1043.
- Barbic F, Casazza G, Zamuner AR, et al. Driving and working with syncope. *Auton Neurosci*. 2014;184:46-52. doi:10.1016/j.autneu.2014.05.006.
- Lynge E, Sandegaard JL, Rebolj M. The Danish National Patient Register. *Scand J Public Health*. 2011;39(7)(suppl):30-33. doi:10.1177/1403494811401482.
- Nordic Medico-Statistical-Committee. *Nomesco Classification of External Causes of Injuries 4th revision*. Copenhagen: Nordic Medico-Statistical Committee; 2007.
- Laursen B, Nielsen JW, Frimodt-Møller B, Kejs AMT, Madsen M. *Quality of the Encoding of Accidents in the Danish National Patient Registry* [in Danish]. Copenhagen, Denmark: National Institute of Public Health; 2005.
- Helweg-Larsen K. The Danish Register of Causes of Death. *Scand J Public Health*. 2011;39(7)(suppl):26-29. doi:10.1177/1403494811399958.
- Gaist D, Sørensen HT, Hallas J. The Danish prescription registries. *Dan Med Bull*. 1997;44(4):445-448.
- Selmer C, Olesen JB, Hansen ML, et al. The spectrum of thyroid disease and risk of new onset atrial fibrillation: a large population cohort study. *BMJ*. 2012;345:e7895. doi:10.1136/bmj.e7895.
- Baadsgaard M, Quitzau J. Danish registers on personal income and transfer payments. *Scand J Public Health*. 2011;39(7)(suppl):103-105. doi:10.1177/1403494811405098.
- Pedersen CB. The Danish Civil Registration System. *Scand J Public Health*. 2011;39(7)(suppl):22-25. doi:10.1177/1403494810387965.
- Ruwald MH, Hansen ML, Lamberts M, et al. Accuracy of the ICD-10 discharge diagnosis for syncope. *Europace*. 2013;15(4):595-600. doi:10.1093/eurpace/eus359.
- Bänsch D, Brunn J, Castrucci M, et al. Syncope in patients with an implantable cardioverter-defibrillator: incidence, prediction and implications for driving restrictions. *J Am Coll Cardiol*. 1998;31(3):608-615.
- Vijgen J, Botto G, Camm J, et al; Task force members. Consensus statement of the European Heart Rhythm Association: updated recommendations for driving by patients with implantable cardioverter defibrillators. *Europace*. 2009;11(8):1097-1107. doi:10.1093/eurpace/eup112.
- Orriols L, Salmi L-R, Philip P, et al. The impact of medicinal drugs on traffic safety: a systematic

- review of epidemiological studies. *Pharmacoepidemiol Drug Saf.* 2009;18(8):647-658. doi:10.1002/pds.1763.
35. Brunnaer A, Laux G, Geiger E, Möller H-J. The impact of antipsychotics on psychomotor performance with regards to car driving skills. *J Clin Psychopharmacol.* 2004;24(2):155-160.
36. De Las Cuevas C, Ramallo Y, Sanz EJ. Psychomotor performance and fitness to drive: the influence of psychiatric disease and its pharmacological treatment. *Psychiatry Res.* 2010; 176(2-3):236-241. doi:10.1016/j.psychres.2009.02.013.
37. Mann RE, Macdonald S, Stoduto LG, Bondy S, Jonah B, Shaikh A. The effects of introducing or lowering legal per se blood alcohol limits for driving: an international review. *Accid Anal Prev.* 2001;33(5):569-583.
38. Andersen PK, Geskus RB, de Witte T, Putter H. Competing risks in epidemiology: possibilities and pitfalls. *Int J Epidemiol.* 2012;41(3):861-870. doi:10.1093/ije/dyr213.
39. Transportvaneundersoegelsen: Denmark Technical University. Car traffic in Denmark [in Danish]. 2013; updated July 9, 2015. <http://www.modelcenter.transport.dtu.dk/Transportvaneundersoegelsen/TU-udgivelser/Faktaark-om-biltransport-i-Danmark-2013>. Accessed January 25, 2016.
40. Mann RE, Stoduto G, Butters J, et al. Age group differences in collision risk. *J Safety Res.* 2010;41(5):445-449. doi:10.1016/j.jsr.2010.08.004.
41. Asbridge M, Hayden JA, Cartwright JL. Acute cannabis consumption and motor vehicle collision risk: systematic review of observational studies and meta-analysis. *BMJ.* 2012;344:e536.
42. Vingilis E, Wilk P. The effects of health status, distress, alcohol and medicinal drug use on subsequent motor vehicle injuries. *Accid Anal Prev.* 2008;40(6):1901-1907. doi:10.1016/j.aap.2008.06.020.
43. Grabowski DC, Campbell CM, Morrissey MA. Elderly licensure laws and motor vehicle fatalities. *JAMA.* 2004;291(23):2840-2846. doi:10.1001/jama.291.23.2840.
44. Li G, Braver ER, Chen L-H. Fragility versus excessive crash involvement as determinants of high death rates per vehicle-mile of travel among older drivers. *Accid Anal Prev.* 2003;35(2):227-235.
45. Betz ME, Lowenstein SR. Driving patterns of older adults: results from the Second Injury Control and Risk Survey. *J Am Geriatr Soc.* 2010;58(10):1931-1935. doi:10.1111/j.1532-5415.2010.03010.x.
46. Charlton JL, Oxley J, Fildes B, Oxley P, Newstead S. Self-regulatory behaviours of older drivers. *Annu Proc Assoc Adv Automot Med.* 2003; 47:181-194.
47. Sarkin AJ, Tally SR, Wooldridge JS, Choi K, Shieh M, Kaplan RM. Gender differences in adapting driving behavior to accommodate visual health limitations. *J Community Health.* 2013;38(6):1175-1181. doi:10.1007/s10900-013-9730-9.
48. Marie Dit Asse L, Fabrigoule C, Helmer C, Laumon B, Lafont S. Automobile driving in older adults: factors affecting driving restriction in men and women. *J Am Geriatr Soc.* 2014;62(11):2071-2078. doi:10.1111/jgs.13077.
49. Hakamies-Blomqvist L, Wahlström B. Why do older drivers give up driving? *Accid Anal Prev.* 1998; 30(3):305-312.
50. Akiyama T, Powell JL, Mitchell LB, Ehlert FA, Baessler C; Antiarrhythmics versus Implantable Defibrillators Investigators. Resumption of driving after life-threatening ventricular tachyarrhythmia. *N Engl J Med.* 2001;345(6):391-397. doi:10.1056/NEJM200108093450601.
51. Ruwald MH, Okumura K, Kimura T, et al. Syncope in high-risk cardiomyopathy patients with implantable defibrillators: frequency, risk factors, mechanisms, and association with mortality: results from the multicenter automatic defibrillator implantation trial-reduce inappropriate therapy (MADIT-RIT) study. *Circulation.* 2014;129(5):545-552. doi:10.1161/CIRCULATIONAHA.113.004196.
52. Blitzer ML, Saliba BC, Ghantous AE, Marieb MA, Schoenfeld MH. Causes of impaired consciousness while driving a motorized vehicle. *Am J Cardiol.* 2003;91(11):1373-1374.
53. MacMahon M, O'Neill D, Kenny RA. Syncope: driving advice is frequently overlooked. *Postgrad Med J.* 1996;72(851):561-563.
54. Soteriades ES, Evans JC, Larson MG, et al. Incidence and prognosis of syncope. *N Engl J Med.* 2002;347(12):878-885. doi:10.1056/NEJMoa012407.
55. Solano A, Menozzi C, Maggi R, et al. Incidence, diagnostic yield and safety of the implantable loop-recorder to detect the mechanism of syncope in patients with and without structural heart disease. *Eur Heart J.* 2004;25(13):1116-1119. doi:10.1016/j.ehj.2004.05.013.
56. Olde Nordkamp LRA, van Dijk N, Ganzeboom KS, et al. Syncope prevalence in the ED compared to general practice and population: a strong selection process. *Am J Emerg Med.* 2009;27(3):271-279. doi:10.1016/j.ajem.2008.02.022.
57. Staerk L, Lip GYH, Olesen JB, et al. Stroke and recurrent haemorrhage associated with antithrombotic treatment after gastrointestinal bleeding in patients with atrial fibrillation: nationwide cohort study. *BMJ.* 2015;351:h5876. doi:10.1136/bmj.h5876.

Invited Commentary

Syncope and the Risk of a Subsequent Motor Vehicle Crash

Donald A. Redelmeier, MD, FRCPC, MSHSR; Sheharyar Raza, HBSc

A 44-year-old man was driving northbound along Interstate I-81 in Pennsylvania under clear sunny skies in the mid-afternoon on Wednesday, November 25, 2015 (the day before the Thanksgiving holiday).¹ He fell unconscious, crossed a grassy median, and crashed into an oncoming tractor-trailer truck. He died instantly, as did his 12-year-old child passenger. This case is not unique and now becomes one more anonymized statistic among the 90 traffic fatalities that occur on an average day in the United States.² About a third involve drivers known to have an underlying medical illness such as a cardiac, neurologic, or psychiatric disorder.³ Almost all of these drivers visit a physician in the year before their motor vehicle crash.³

Numé et al⁴ in this issue provide a rigorous analysis of 41 039 adults diagnosed with syncope and followed for a median of 2 years. The primary outcome was a serious motor ve-

hicle crash, defined as an event sending a patient to the hospital (not necessarily admitted). The main findings suggest a doubling of risk relative to the population norm, equal to an absolute rate of about 1 serious motor vehicle crash per 50 patients with syncope annually. The increased risk extended for up to 5 years of follow-up and was particularly high for older men. The research is distinctive because syncope was based on International Classification of Diseases codes that excluded cases of third-degree heart block, epileptic convulsions, carotid sinus dysfunction, or orthostatic hypotension.

These findings are consistent with past research suggesting that syncope leads to a significant increase in the risk of a motor vehicle crash. A population-based study from Maryland (n = 7750) suggests that patients with syncope have about quadruple the crash risk of the population norm.⁵ A population-based study from Canada (n = 25 422) suggests that patients with syncope have about triple the crash risk of the population norm.⁶ A clinical trial from the United States (n = 559) sug-