

■ Review article

The role of acute medical conditions, drugs and alcohol in motor vehicles accidents: a narrative review

Azam Saei^{1,2}, Ali Rahmani^{3*}, Abbas Ebadi⁴, Hamid Reza Khankeh⁵

(Received: 16 Dec 2016; Accepted: 15 Mar 2017)

Abstract

Background and Purpose: Clinicians and other health care providers should consider association of acute medical conditions and motor vehicle collision. This study was performed to determine the role of acute medical conditions, drugs, and alcohol in motor vehicle accidents.

Methods: This study was a narrative review performed during 2006 to 2016 through searching electronic databases (PubMed, Ovid Medline, EMBASE, Transport Research International Documentation [TRID], Scopus, and Global Health). The following keywords were applied: “acute medical conditions”, “driver”, “drugs”, “alcohol”, “motor vehicle accident”, and “collision”. Relevant articles were selected after evaluation and full text articles were assessed.

Results: In this study, among the 35279 retrieved articles, 20 were selected. The articles were divided into three main categories of impaired driving due to acute medical conditions, impaired driving caused by medications, and alcohol-impaired driving.

Conclusion: Results of studies indicated that medicines and acute medical conditions render the driver at significant risk of accidents. Therefore, clinicians should be aware of this problem, educate their patients, and/or consider safer alternatives for some medications. Medical evaluation forms are necessary in support of licensing decisions for medically at-risk drivers. In addition, screening programs should be implemented for high-risk drivers to minimize unsafe driving due to acute medical conditions.

Keywords: Acute medical conditions, Alcohol, Collision, Driving, Drugs, Motor vehicle crash, Road traffic accidents

Introduction

Globally, road traffic accidents (RTAs) are responsible for a considerable fraction of morbidities and cause mortality more than any disease (1). RTAs pose a global health burden, especially in low- and middle-income countries where more than 90% of deaths occur (2). Traffic accident deaths remain a global public health problem. Approximately 1.2 million people die of RTAs annually, which equates to nearly 3500 people every day. RTAs are a major cause of death and health problems in Iran (3).

The World Health Organization (WHO) statistics indicate that Iran has one of the highest rates of morbidity and mortality from traffic accidents, such that the rate of traffic accidents in Iran is fifteen times higher than developed countries (4). RTAs are one of the current challenges that societies face, which impose heavy psychological and financial costs (5).

It has been estimated that in 90–95% of all traffic accidents, human factors are the main cause or a

¹ Department of Health, Rescue and Treatment of Iran Police, Tehran, Iran

² Trauma Research Center, Faculty of Nursing, Baqiyatallah University of Medical Sciences, Tehran, Iran

^{3,*} Corresponding author: Trauma Research Center, Faculty of Nursing, Baqiyatallah University of Medical Sciences, Tehran, Iran.
Email: rahmani4143@gmail.com

⁴ Behavioral Sciences Research Center, Department of Medical Surgery, Faculty of Nursing, Baqiyatallah University of Medical Sciences, Tehran, Iran

⁵ Division of Social Medicine, Department of Public Health Sciences, Karolinska Institutet, Norrbacka, Stockholm, Sweden

determining factor. Human factors include physical, psychological, social, and cultural aspects (6). Driving is a highly complex activity involving a wide range of cognitive, perceptual, and motor activities that take place in a complex and dynamic manner (7). The need for effective preventive strategies for high-risk drivers should be addressed (8).

While an extensive body of literature exists on how chronic illnesses can impair driving ability (9), there is a scarcity of studies on the risk of individual disease categories for RTAs (10). Awareness regarding medical conditions that affect functional abilities (e.g., sensory, motor, or cognitive functioning) is of great importance. Medical conditions can significantly affect drivers' performance and promote the risk for accidents and casualties (11). According to some studies, several physical factors and illnesses contribute to traffic accidents, namely advanced age (12, 13), use of medications (13), fatigue, drowsiness (14), obesity (15), as well as chronic conditions such as apnea (16) and depression (17). On the other hand, stress and immobility predispose drivers to diabetes mellitus and cardiovascular diseases (18, 19) and accelerate their mortality rate, and thereby, affect the incidence of traffic accidents (20). Besides, addictive substances, alcoholic drinks, and medications are known to impair drivers' performance and the rate of traffic accidents (21). To prevent trauma from RTAs, physicians warn patients on the risks of potentially driver-impairing medications, and acute medical conditions are known as a risk factor for RTAs (22, 23).

The association between acute medical conditions and motor vehicle collision should to be considered by clinicians and other health care providers. Due to the limited number of review studies in this regard, evidence in this regard should be evaluated and highlighted (24). The primary goal of this study was to review studies on the role of acute medical conditions, drugs, and alcohol on motor vehicles accidents.

Materials and Methods

This narrative review was performed through

searching electronic databases (PubMed, Ovid Medline, EMBASE, Transport Research International Documentation [TRID], Scopus, and Global Health) using the following keywords: "motor vehicle crash", "traffic accident", "driving", "acute medical conditions", "drugs", and "alcohol". We also manually searched references of the relevant articles and used the PubMed function "Search all related". This study aimed to review the literature in order to investigate the role of acute medical conditions, drugs, and alcohol in motor vehicle accidents. The search terms for each database were defined according to the research questions and several peer-review discussions. The syntax of keywords was employed based on the number of non-replicated (NNR) indices (as carried out in the initial search of studies using the databases listed above in cooperation with AR as the supervisor). Titles and abstracts were independently screened for inclusion in the narrative review and discrepancies between the researchers were resolved by discussion. After screening, the full text articles were coded and the obtained data was classified; consequently, content analysis was performed.

Inclusion and exclusion criteria

We included observational analytical studies and those on acute medical conditions, drugs, alcohol, road traffic accidents, and driving, published in review journals and accident analysis and prevention texts. The language was limited to English. Only papers published after January 2006-2016 were considered. The population included all drivers of any gender and age group. Studies not associated with acute medical conditions, road traffic accidents, drugs, and alcohol were excluded.

Results

According to Figure 1, our search yielded 35279 articles, of which 20 studies met the inclusion criteria. The findings were divided into three categories. In the current study, acute medical conditions, as well as drug- and alcohol-related driving impairment were the main three causes of RTAs. Results from the British alcohol- and drug-use survey indicated that alcohol and drugs can

be detected in the body fluids of 1.4-27.5% of all drivers killed in driving accidents and 5-15.7% of all drivers injured in RTAs (25). According to the National Motor Vehicle Crash Causation Survey, the main causes of medical emergencies in drivers of all ages were seizure (35%), blackout (29%), diabetic reaction/hyperglycemia/hypoglycemia (20%), myocardial infarction (11%), and cardiovascular accident (3%) (26). These main categories were noted in the literature and approved by many experts.

Acute medical conditions and driving impairment

The rate of mortality due to medical conditions are globally on the rise. Six studies pointed out the role of acute medical conditions motor vehicle crashes (22,

23, 26-29). In practice, different types of diseases and medication classes affect fitness to drive. A wide range of medical-pharmacotherapy conditions could impair the ability to drive to some extent, furthermore, untreated medical conditions could pose higher risk than consumption of appropriate medications. However, some evidence regarding accident-risk of various medical conditions may lack, therefore, to decide on which group of patients are unsafe to is difficult for decision-makers (10). However, diseases and complications that may affect driving performance of a driver can be very dangerous. There are two basic types of conditions and co-morbidities that a person can develop while driving a car: diseases that may cause sudden,

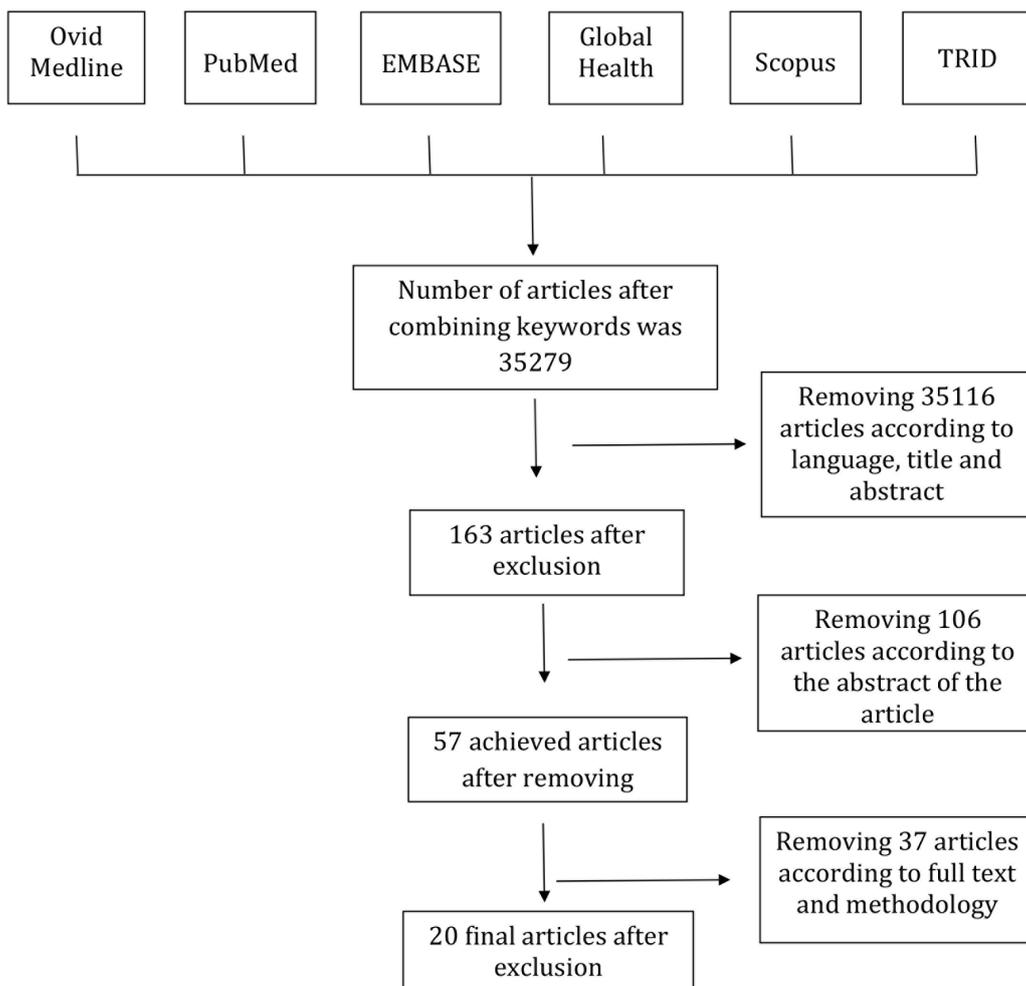


Figure 1. Process of selecting articles of the study

Table 1. Acute medical conditions leading to traffic accidents

1. Diseases that may cause sudden, unexpected death of the driver while driving	2. Diseases and symptoms that may affect the driving performance of a driver
1. Cardiovascular diseases	<ol style="list-style-type: none"> 1. Acute coronary syndrome 2. Myocardial infarction 3. Aortic aneurysm rupture 4. Aortic dissection 5. Cardiomyopathy 6. Myocarditis 7. Pacemaker malfunction 8. Deep vein thrombosis or pulmonary embolism 9. High-grade cardiac conduction abnormalities (Mobitz II or higher, bifascicular block, or alternating AV block) 10. Cardiac arrhythmia (atrial or ventricular in origin)
2. Neurological diseases	<ol style="list-style-type: none"> 1. Rupture of cerebral aneurysm 2. Hypertensive brain hemorrhage 3. Brain infarction 4. Transient ischemic attack or cerebrovascular accident 5. Severe head injury or brain surgery
3. Pulmonary diseases	<ol style="list-style-type: none"> 1. Pulmonary thromboembolism 2. Bronchial asthma 3. Acute chronic obstructive pulmonary disease (COPD) exacerbation
4. Digestive tract diseases	1. Rupture of esophageal varices
5. Others	<ol style="list-style-type: none"> 1. Diabetic ketoacidosis (>800 mg/dL) 2. Hypoglycaemia (<80 mg/dL) 3. Attacks of dizziness or vertigo 4. Seizure 5. Active cancer

unexpected death of the driver and those that may affect driving performance of the driver. A sudden, unexpected death is one in which a healthy individual unexpectedly develops an endogenous disease and dies within 24 h of initial onset (27). Table 1 shows acute medical conditions leading to traffic accidents.

Drug-related driving impairment

Driving is an important activity, and seven studies have pinpointed the role of drug consumption in driving (30-36). Medications can improve or stabilize many medical conditions, which may also enhance the ability to drive. The risk-to-advantage ratio must be evaluated for each patient before prescribing any medications (37). Unfortunately, some specific classes of commonly prescribed drugs are associated with driving impairment as measured by road performance, driving simulation, and motor vehicle crashes. The fact that a high percentage of people (15%) use medications to treat depression, anxiety, and insomnia indicates that this group of

drivers is at risk of RTAs due to consuming these psychotropic medications. Therefore, the effect of medications on driving should be considered while prescribing a medication regimen (37). In addition, high level of pain may influence cognition and psychomotor function, because poorly managed pain is found to compete with attentional resources or affect other aspects of cognitive functioning (38).

Driving is known as a complex task, in which individuals are required to integrate psychomotor and cognitive skills, visual-spatial abilities, decision-making, divided attention, motor skills, and behavioral and emotional control (37). Medications may have some effects on the visual, cognitive, and/or motor abilities needed for safe driving. Human factors can determine transition between stages of driver information processing (DIP) model, namely perception, decision, and reaction. This model shows that ability to drive is contingent upon our eyes, brain, and musculoskeletal system to work in harmony (21). Ophthalmic medications also cause blurred vision or dizziness; some medications may cause tremor,

Table 2. Driver-impairing medications

Some driver-impairing medications	Application	Such as
1. Psychotropic medications 1. Barbiturate 2. Benzodiazepine (BZDs) 3. Non-BZD hypnotics 4. Tricyclic antidepressants (TCAs) 5. Selective serotonin reuptake inhibitors (SSRIs) 6. Second generation /related antidepressants	Anxiety, seizure, insomnia sleep disorders Major depressive disorder Neuropathic pain, certain anxieties, and menopausal symptoms Depression, anxiety disorders Antidepressant	Phenobarbital, amobarbital, secobarbital alprazolam , lorazepam, midazolam zolpidem, zaleplon, eszopiclone Nortriptyline, desipramine, doxepin Fluoxetine, citalopram, escitalopram, sertraline Venlafaxine, duloxetine trazodone, nefazodone
2. Analgesics 1. Opioid analgesics 2. Nonsteroidal anti-inflammatory drugs (NSAIDs)	Analgesia, sedation Pain, inflammation, fever	Ibuprofen, naproxen, indomethacin
3. Centrally active medications 1. Antiepileptic drugs (AEDs) 2. Antipsychotics 3. Antiparkinsonian agents 4. Skeletal muscle relaxants (SMRs)	Anticonvulsants Antipsychotics Parkinson's disease Skeletal muscle disorders	Carbamazepine, phenytoin, valproate Olanzapine, quetiapine, clozapine Levodopa, amantadine, carbidopa Meprobamate, baclofen cyclobenzaprine, dantrolene
4. Others 1. Antihistamines 2. Intestinal and antiemetic agents 3. Hypoglycemic agents	Histamine release Treatment of emesis intestinal spasticity, and abdominal cramping Diabetes	Diphenhydramine, doxylamine, loratadine and fexofenadine Belladonna alkaloids such as scopolamine, atropine, and hyoscyamine Dicyclomine and glycopyrrolate insulin

impaired coordination, or myopathy, and others can impact the central nervous system (CNS) by causing sedation, confusion, or dizziness (34).

Some medications are characterized to have the potential to impair driving performance. Twenty-five classes of medications were proposed to be associated with at least a 40% higher crash risk in the LeRoy and Morse study, which is perhaps the most cited reference regarding driver impairing medications (39). Our findings reflected that odds ratio (OR) of RTAs increases with consumption of driver impairing medications. Some of these drugs included barbiturate, benzodiazepine (BZD), non-benzodiazepine, hypnotics, tricyclic antidepressants (TCAs), narcotics, opioids, hypoglycemics, anticholinergics, non-steroidal anti-inflammatory drugs (NSAIDs), antihistamine, antipsychotics, antidepressants, selective serotonin reuptake inhibitors (SSRIs), second generation/related antidepressants, anxiolytics, antiepileptic drugs, antiparkinsonian drugs, skeletal muscle relaxants, antiplatelet drugs, antithrombotic agents, antihypertensives, and antidepressants (37). Table 2 presents driver-impairing medications.

Alcohol-related driving impairment

In the majority of accidents where the drivers were considered responsible, drivers were under the influence of alcohol or drugs alone or in combination

(37). Some studies pointed out the role of alcohol in RTAs (32-34, 40). Findings indicated that alcohol is still one of the most dangerous psychoactive substances ever used by drivers, and the greatest risk for traffic accidents was associated with high blood alcohol concentrations or concomitant use of alcohol, recreational drugs, and medications (34). Most of seriously injured or killed drivers who are tested positive for alcohol consumption. The legal blood alcohol content is 0.5 g/l, and blood alcohol content of 1.2 g/l is classified as severe intoxication (32). One study indicated that heavy alcohol consumption contributes to one-thirds of motor vehicle collisions. Among all, 42% of cases had used alcohol and/or drugs. In single vehicle crashes, 66% of all drivers younger than 30 years of age were driving under the influence (8).

High levels of alcohol consumption can pose an exponential risk of most diseases, thus if very heavy drinking occasions were eliminated, the number of deaths and risk of disease would be minimized over-proportionally. Consumption of alcohol is lethal for all living creatures and humans are no exception. With the lowest blood alcohol content, concentration and alertness diminish (31). Although the definition of ‘moderate alcohol use’ varies from one patient to another, usually no more than one alcoholic beverage (14 grams) should be ingested

per day by females, while two for males (36). Patients consuming more than the suggested amount of alcohol may present with depressive symptoms. When plasma level of alcohol increases, alcohol crosses the blood-brain barrier and affects the central nervous system (41). Alcohol consumption raises the risk of overdose with benzodiazepines, triggers decline in psychomotor function, respiration, and alertness. It also causes hypoglycemia induced by sulfonyleureas and bisguanides, orthostasis by sympatholytic agents, and drowsiness by skeletal muscle relaxants (37).

A person's breath alcohol concentration is equivalent to nearly 1/2000th of his or her blood alcohol content (35). Even with low blood and breath alcohol content, impaired function occurs; thus, in some governments, these individuals are not allowed to drive (41). In a normal traffic accident, investigators can determine whether the driver is under the influence of alcohol as long as they can measure the person's breath or blood alcohol content at the time the accident occurs. Findings revealed that alcohol in blood stains evaporates so fast and becomes undetectable in just a few hours (34). To determine whether an individual intoxicated while driving, it is important to collect blood stains as quickly as possible after the accident and keep the samples in airtight containers. It is also found that as stimulants remain stable in blood stains for a prolonged period, investigators can examine blood stains to make a definitive judgment on whether the individual was under the influence at the time of accident (34).

Discussion

According to several studies, a wide spectrum of factors impair the ability to operate a vehicle. These main factors are optical field loss (28, 42), cardiovascular diseases (43), diabetes mellitus (18, 19), and drug use (13). For example, heart disease and arrhythmia, which account for the majority of sudden, unexpected deaths, can develop while an individual is driving. Valvular heart disease is a known risk factor for the development of syncope and arrhythmia (43). Although heart disease can

indeed kill a driver, most drivers who suddenly experience heart failure are still capable of moving their shoulder and parking their car when symptoms first begin to appear; pedestrian and passenger deaths resulting from the sudden onset of heart failure in a driver are thus rare (22). More importantly, the physiologic stress of RTAs may provoke underlying coronary artery disease, causing myocardial ischemia or acute myocardial ischemia preceding a collision.

Therefore, the odds ratio for the prevalence of acute medical conditions among drivers may serve as an estimate of the relationship between occupancy status and risk of acute medical problems. Conditions such as epilepsy and diabetes mellitus, which can cause loss of consciousness or loss of body control, are important with regards to traffic safety (44). One in ten drivers presents with at least one acute medical illness, and careful history taking and examination can identify these drivers (8).

Although some medications can help with operating a motor vehicle safely, they can exacerbate the medical condition. The risk-to-benefit ratio must be evaluated for each patient before the medication is prescribed. When the expected benefits outweigh risks of use, medications need to be prescribed in a clear, comprehensible, and individualized manner. The lowest effective dose should be given, so that therapeutic effect is produced while decreasing adverse outcomes on driving (21).

Not surprisingly, medications reducing an individual's ability to operate a vehicle are classified as potentially driver impairing (PDI). There is low agreement on what should be labeled a PDI, or if there is sufficient evidence to suggest that clinicians modify their prescribing behaviors toward any specific occupation (37). Health care professionals should urge against alcohol while driving or in combination with centrally acting agents because it can exacerbate the PDI effects of certain medications. Psychotropic agents and those with CNS side effects are associated with different measures of impaired driving performance. To determine whether accidents are a result of medication use or acute medical conditions is a difficult task.

Regardless, clinicians should be aware of the increased risk of impaired driving in specific populations and classes of medications when prescribing these agents, educate their patients, and/or consider safer alternatives (37). In 2010, a large registry-based study in the USA demonstrated increased risk of unsafe driving in female drivers aged 25 to 55 years and male drivers aged 25 to 65 years involved in fatal traffic accidents due to consumption of opioids (29). A study performed in Norway showed that the risk of involvement in a traffic accident was markedly increased in users of natural opium alkaloids, benzodiazepine tranquillizers, and benzodiazepine hypnotics (30). The driver impairing drugs should be taken as prescribed by physician; in so doing, the mortality rates will be lowered (38).

According to a WHO survey, alcohol is associated with over 130 disease categories. A study revealed that approximately 33% of road traffic injuries in men and 11% in women are as a result of alcohol-related crashes while driving. For pedestrians, 40% of men and 17% of women dying of road traffic injuries are estimated to be as a result of alcohol consumption, while for male and female cyclists, these rates are 20% and 18%, respectively. The risk differs by age and sex (higher among younger males) (32, 34). A study showed a significantly increased risk of RTAs due to driving while intoxicated (40). Patients should be encouraged to avoid or limit alcohol intake, especially when they are expected to drive. Physicians have a responsibility to advise patients on the dangers of ethanol.

The previous studies suffer from several limitations. First, data was collected through a self-report technique, in which participants may forget or be unwilling to share certain information. Future studies should investigate the effects of acute medical conditions, drugs, and alcohol on driving as the primary research question, and use a study design that offers low risk of bias, such as a randomized, controlled trial with blinded outcome assessors, and take into consideration the most relevant confounders. Second, some eligible reports may have been missed due to language. Most of the studies included in this review were performed

in developed countries. Therefore, the results may not be generalizable to low- and middle- income countries where traffic regulations and driving practices may be different. Third, most of the studies did not describe the acute conditions well enough for the reader to understand the role of acute medical conditions, drugs, and alcohol in crashes. This resulted in some challenges and ambiguities in extracting data.

In summary, the available evidence suggests that alcohol consumption, drugs, and acute medical conditions increase the risk of accidents, and acute medical conditions remains to be one of the leading causes of mortality in many countries. Thus, clinicians and nurses should be able to use this information for the management of drivers with acute medical conditions and those at risk of driving under the influence.

Conclusion

To have a driver's license is valuable and drivers do not want to lose it. Thus, drivers must be characterized by their electronic health records. All individuals should visit a physician in case of acute conditions and their high-risk drugs should be recorded electronically. All those who wish to drive must have electronic health records for monitoring their medical qualification in addition to biographies and related examinations and questionnaires. Studies suggest that patients at ages 60 and older, and those with a history of cerebrovascular disease, valvular heart disease, diabetes mellitus, and consumption of driving impairing drugs should become an integral part of trauma assessment. In addition, more studies from low- and middle-income countries, where the majority of road traffic deaths occur, are needed.

Conflicts of interest

None declared.

Authors' contributions

A. Saei contributed with study conception, data collection, and drafting the manuscript. A. Rahmani

and A. Ebadi supervised the study design and helped with conducting this study. HR. Khankeh was the study advisor. All the authors critically evaluated the paper and provided the final draft.

Acknowledgements

We wish to thank Tehran Traffic Police Research Center for their financial support and Deputy of Trauma Research Center of Baqiyatallah University of Medical Sciences, Tehran, Iran, for their cooperation with this study.

References

1. Elvik R. Why some road safety problems are more difficult to solve than others. *Accid Anal Prev* 2010; 42(4):1089-96.
2. Kumar GA, Dilip TR, Dandona L, Dandona R. Burden of out-of-pocket expenditure for road traffic injuries in urban India. *BMC Health Serv Res* 2012; 12(1):285.
3. Ardalan A, Masoomi GR, Goya MM, Sarvar MR, Haddadi M, Miadfar J, et al. Road traffic injuries: a challenge for Iran's health system. *Iran J Public Health* 2009; 38(1):98-101.
4. Moafian G, Aghabeigi MR, Heydari ST, Hoseinzadeh A, Lankarani KB, Sarikhani Y. An epidemiologic survey of road traffic accidents in Iran: analysis of driver-related factors. *Chin J Traumatol* 2013; 16(3):140-4.
5. World Health Organization. Global status report on road safety 2013: supporting a decade of action. Geneva: World Health Organization; 2013.
6. Karacasu M, Er A. An analysis on distribution of traffic faults in accidents, based on driver's age and gender: eskisehir case. *Proc Soc Behav Sci* 2011; 20:776-85.
7. Shappell SA, Wiegmann DA. Human factors investigation and analysis of accidents and incidents. In: Siegel JA, Saukko PJ, editors. *Encyclopedia of forensic sciences*. Waltham: Academic Press; 2013. P. 440-9.
8. Redelmeier DA, Tien HC. Medical interventions to reduce motor vehicle collisions. *CMAJ* 2014; 186(2):118-24.
9. Marshall SC. The role of reduced fitness to drive due to medical impairments in explaining crashes involving older drivers. *Traffic Inj Prev* 2008; 9(4):291-8.
10. Vaa T. Impairments, diseases, age and their relative risks of accident involvement: Results from meta-analysis. Oslo, Norway: Institute of Transport Economics; 2005.
11. Sagberg F. Driver health and crash involvement: a case-control study. *Accid Anal Prev* 2006; 38(1):28-34.
12. Borowsky A, Shinar D, Oron-Gilad T. Age, skill, and hazard perception in driving. *Accid Anal Prev* 2010; 42(4):1240-9.
13. Clarke DD, Ward P, Bartle C, Truman W. Older drivers' road traffic crashes in the UK. *Accid Anal Prev* 2010; 42(4):1018-24.
14. Jayatilleke AU, Nakahara S, Dharmaratne SD, Jayatilleke AC, Poudel KC, Jimba M. Working conditions of bus drivers in the private sector and bus crashes in Kandy district, Sri Lanka: a case-control study. *Inj Prev* 2009; 15(2):80-6.
15. Anderson JE, Govada M, Steffen TK, Thorne CP, Varvarigou V, Kales SN, et al. Obesity is associated with the future risk of heavy truck crashes among newly recruited commercial drivers. *Accid Anal Prev* 2012; 49:378-84.
16. Rodenstein D. Sleep apnea: traffic and occupational accidents—individual risks, socioeconomic and legal implications. *Respiration* 2009; 78(3):241-8.
17. Hilton MF, Staddon Z, Sheridan J, Whiteford HA. The impact of mental health symptoms on heavy goods vehicle drivers' performance. *Accid Anal Prev* 2009; 41(3):453-61.
18. Izadi N, Malek M, Aminian O, Saraei M. Medical risk factors of diabetes mellitus among professional drivers. *J Diabetes Metab Disord* 2013; 12(1):23.
19. Graveling AJ, Frier BM. Driving and diabetes: problems, licensing restrictions and recommendations for safe driving. *Clin Diabetes Endocrinol* 2015; 1(1):8.
20. Roth GA, Forouzanfar MH, Moran AE, Barber R, Nguyen G, Feigin VL, et al. Demographic and epidemiologic drivers of global cardiovascular mortality. *N Engl J Med* 2015; 372(14):1333-41.
21. Li G, Brady JE, Chen Q. Drug use and fatal motor vehicle crashes: a case-control study. *Accid Anal Prev* 2013; 60:205-10.
22. Kartchner HM, Nirula R. Acute medical impairment among elderly patients involved in motor vehicle collisions. *Injury* 2015; 46(15):208-9.
23. Leproust S, Lagarde E, Salmi LR. Systematic screening for unsafe driving due to medical conditions: Still debatable. *BMC Public Health* 2008; 8(1):27.
24. A Glance Guide. To the current medical standards of fitness to drive. Swansea: Drivers Medical Group DVLA; 2010.
25. Beirness DJ, Beasley EE. Alcohol and drug use among drivers: British Columbia Roadside Survey 2008. Canada: Transportation Association of Canada; 2009.

26. Hanna R. Contribution of medical conditions to passenger vehicle crashes. Washington, D.C: National Highway Traffic Safety Administration; 2009.
27. Kibayashi K, Shimada R, Nakao KI. Fatal traffic accidents and forensic medicine. *IATSS Res* 2014; 38(1):71-6.
28. Cross JM, McGwin G Jr, Rubin GS, Ball KK, West SK, Roenker DL, et al. Visual and medical risk factors for motor vehicle collision involvement among older drivers. *Br J Ophthalmol* 2009; 93(3):400-4.
29. Lagarde E, Chastang JF, Lafont S, Coeuret-Pellicier M, Chiron M. Pain and pain treatment were associated with traffic accident involvement in a cohort of middle-aged workers. *J Clin Epidemiol* 2005; 58(5):524-31.
30. Engeland A, Skurtveit S, Mørland J. Risk of road traffic accidents associated with the prescription of drugs: a registry-based cohort study. *Ann Epidemiol* 2007; 17(8):597-602.
31. Khanjani N, Mousavi M, Dehghanian A, Jahani Y, Souri H. The role of drug and alcohol use and the risk of motor vehicle crashes in Shiraz, Iran 2014: a case-crossover study. *Traffic Inj Prev* 2017; 17:1-4.
32. World Health Organization. Alcohol in the European Union: consumption, harm and policy approaches: Final report, Copenhagen 27 March 2012. Geneva: World Health Organization; 2012.
33. Roerecke M, Rehm J. Alcohol use disorders and mortality: a systematic review and meta-analysis. *Addiction* 2013; 108(9):1562-78.
34. Schulze H, Schumacher M, Urmeew R, Alvarez J, Bernhoft IM, de Gier HD, et al. Driving under the influence of drugs, alcohol and medicines in europe-findings from the DRUID project. Luxembourg: European Monitoring Centre for Drugs and Drug Addiction; 2012.
35. Taylor B, Irving H, Kanteres F, Room R, Borges G, Cherpitel C, et al. The more you drink, the harder you fall: a systematic review and meta-analysis of how acute alcohol consumption and injury or collision risk increase together. *Drug Alcohol Depend* 2010; 110(1-2):108-16.
36. Vaca FE, Li K, Hingson R, Simons-Morton BG. Transitions in riding with an alcohol/drug-impaired driver from adolescence to emerging adulthood in the United States. *J Stud Alcohol Drugs* 2016; 77(1):77-85.
37. Hetland A, Carr DB. Medications and impaired driving. *Ann Pharmacother* 2014; 48(4):494-506.
38. Mailis-Gagnon A, Lakha SF, Furlan A, Nicholson K, Yegneswaran B, Sabatowski R. Systematic review of the quality and generalizability of studies on the effects of opioids on driving and cognitive/psychomotor performance. *Clin J Pain* 2012; 28(6):542-55.
39. LeRoy AA, Morse ML. Multiple medications and vehicle crashes: analysis of databases. *Sci Eng Med* 2008; 5:810-58.
40. Suriyawongpaisal P, Plitapolkarnpim A, Tawonwanchai A. Application of 0.05 per cent legal blood alcohol limits to traffic injury control in Bangkok. *J Med Assoc Thai* 2002; 85(4):496-501.
41. Åberg L. Drinking and driving: intentions, attitudes, and social norms of Swedish male drivers. *Accid Anal Preve* 1993; 25(3):289-96.
42. Owsley C, Ball K, McGwin G Jr, Sloane ME, Roenker DL, White MF, et al. Visual processing impairment and risk of motor vehicle crash among older adults. *JAMA* 1998; 279(14):1083-8.
43. Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation: analysis and implications. *Arch Intern Med* 1995; 155(5):469-73.
44. Classen S, Crizzle AM, Winter SM, Silver W, Eisenschenk S. Evidence-based review on epilepsy and driving. *Epilepsy Behav* 2012; 23(2):103-12.