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Identification of harmful drinking in subjects who have had their driving license suspended due to alcohol use: a retrospective Italian study

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Abstract. – OBJECTIVE: Early identification of Harmful Drinking (HD) is difficult, and underestimated. The aim of our retrospective study was to investigate the presence of HD in a population of subjects who had their driving license suspended due to driving under the influence of alcohol.

MATERIALS AND METHODS: We retrospectively recruited 979 subjects. During the first appointment (T0), clinical and laboratory characteristics of patients were evaluated, and the AUDIT questionnaire was administered. Two groups were then defined: Harmful Drinking (HD) and non-HD, and all subjects underwent a brief interview for 5-10 minutes before being assigned to a group.

RESULTS: 95.9% of our sample were identified as non-HD, whereas 4.1% of them were HD; twenty-one (2.1%) of the HD underwent a control appointment (T1), and 17 (1.7%) of them were diagnosed with alcohol use disorder (AUD); there was a statistically significant reduction in mean daily alcohol intake ($p<0.009$), and in the mean values of the blood markers of HD between T0 and T1 in HD.

CONCLUSIONS: The present study shows that 4.1%, and 1.7% of subjects presented a diagnosis of HD and AUD, respectively, and their entry in a protocol of drinking monitoring proved beneficial in reducing alcohol intake. Thus, the implementation of strict surveillance of subjects found driving under the influence of alcohol involving a network of professional figures (from police forces to specialists in alcohol addiction treatment) may help to detect and to treat subjects with HD and AUD, and to monitor their alcohol use over time.

Key Words:
Harmful drinking, Alcohol use disorder, Drinking and driving.

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Introduction

The International Statistical Classification of Diseases defines Harmful Drinking (HD) as "a pattern of psychoactive substance use that is causing damage to health. The damage may be physical (i.e., as in cases of liver disease due to alcohol misuse) or mental (i.e., episodes of depressive disorder secondary to heavy consumption of alcohol)"[1]. When HD is associated with symptoms in accordance with the Diagnostic and Statistical Manual of Mental Disorder (DSM-V), a diagnosis of Alcohol Use Disorder (AUD)[2] may be made.

Despite the availability of simple tools (laboratory tests and questionnaires) for the identification of HD in clinical out-patient and inpatient settings[1,3,4], early identification of HD is still fairly difficult to ascertain, and the majority of patients with HD are underestimated. Worldwide, the diagnosis of AUD is more clearly determined and ranges between 3% and 15%[1,4,5]. However, only 30% of patients affected by HD or AUD attending a medical setting are clearly diagnosed[1,4], and only 10% of patients with HD and AUD are treated in specific Centers for Alcohol Addiction (CAT)[1,4]. One of the main reasons for this underestimation is partially related to the fact that subjects with HD and AUD tend to be in denial, often not considering their drinking habit a problem that needs to be resolved, and rarely asking practitioners or specialists for help. In addition, in order to fill this gap, several studies[6-10] have investigated the use of alcohol in social contexts outside medical settings (i.e., workplaces or drivers involved in traffic accidents). However, early identification of HD in drivers who have had their driving license suspended since they have violated the legal limit of alcohol use has not been undertaken.

Thus, the primary outcome of our retrospective study is to investigate the presence of HD in a population of subjects who had their driving license suspended while driving under the influence of alcohol; the secondary outcome was to test the efficacy of a strict protocol of drinking monitoring to reduce alcohol intake.

Materials and Methods

Protocol of Drinking Monitoring After the Suspension of Driving Licenses in Italy

This protocol of drinking monitoring of subjects found driving under the influence of alcohol, with only slight inter-regional differences, is currently employed in Italy[11]. All subjects found to be positive (>0.5 g of alcohol per liter: Italian legal limit of blood alcohol concentration for driving)[11] for a random breath alcohol test performed by the police at road checkpoints are subject to an administrative penalty (payment of a fine) or a criminal penalty with the suspension of their driving license for a period ranging from a minimum of 3 months up to 2 years depending on the level of their electronic breath analyzer (alcohol test) assessing the blood alcohol quantity[11]. In order to have their driving license back, the Italian law obliges them to undergo blood exams to identify whether any alterations of the common markers of HD [gamma-glutamyltranspeptidase (GGT) (normal value: 5-55 UI/L); aspartate aminotransferase (AST) (normal value: 5-50 UI/L), alanine aminotransferase (ALT) (normal value: 5-59 UI/L), and mean cellular volume (MCV) (normal value: 88-99 fL), carbohydrate-deficient transferrin (CDT)] are present[4]. With the results of these blood examinations, after a maximum of 8 weeks from the suspension of their driving license, subjects attend an appointment at the Local Medical Commission of Driving Licenses (LMCDL). If the laboratory results are normal and the subjects do not demonstrate any suspicious signs or symptoms of HD, the LMCDL authorizes return of the driving license (which will be valid only at the end of the penalty period), and schedule a new control appointment with additional checks of the laboratory markers of HD after 3 months, 6 months, or 1 year. In the case of altered laboratory values and/or the presence of specific signs and symptoms of HD, a high value of the breath alcohol test (>1.5 g/l), in the case of younger subjects (<30 years old), and in the case of only the alteration of CDT, the LMCDL requires the subject to attend a medical appointment at a CAT within 4 weeks. Subjects have to make this appointment, attend it, and return to the LMCDL with a final certification in which confirms: a) the use of alcohol is occasional and HD is not an issue; b) the use of alcohol is occasional and sometimes the subject presents episodes of binge drinking (defined as: ≥5 units for men and ≥4 units for women in about 2 hours)[1]; c) the use of alcohol has the characteristics of HD. The LMCDL may then decide to authorize the return or not of the driving license for 3 or 6 months; in the case of a negative conclusion, the LMCDL suggests scheduling a blood test to control the markers of HD with a further appointment

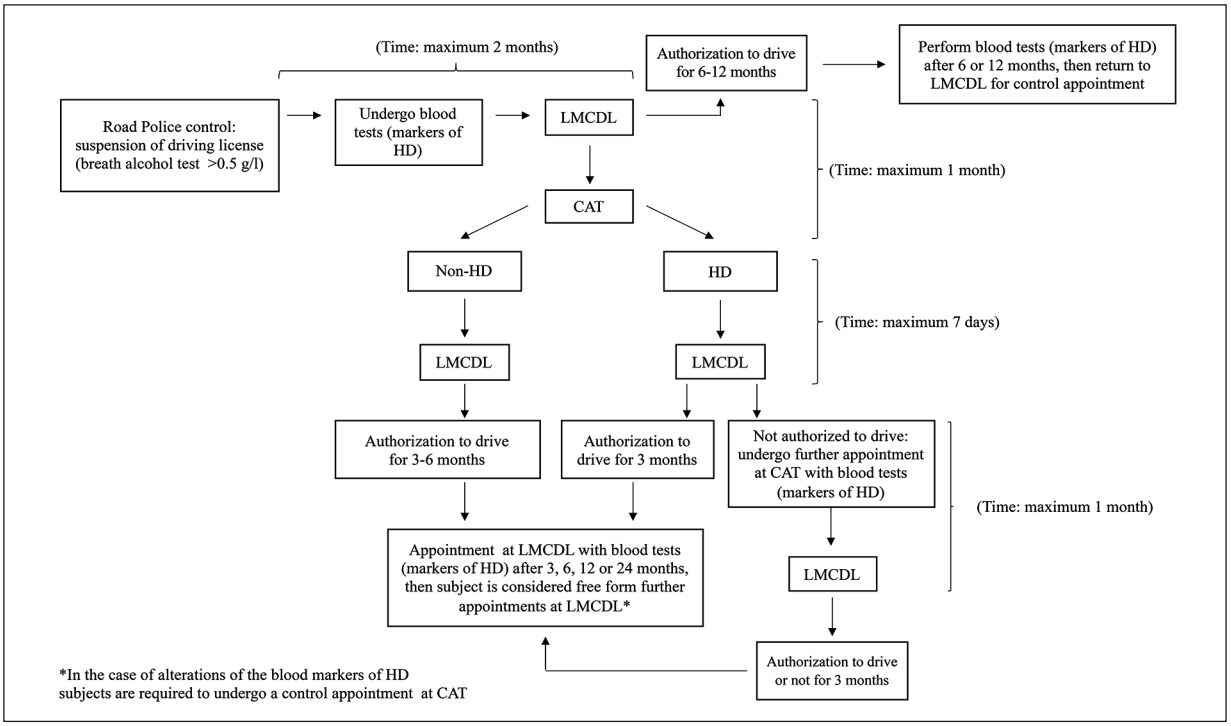

Figure 1. Example of the Italian monitoring protocol of drinking in a population of subjects whose driving license has been suspended as a result of driving under the influence of alcohol. HD: harmful drinking; LMCDL: Local Medical Commission of Driving Licenses; CAT: Centers for Alcohol Addiction.

at the CAT within 4 weeks (Figure 1). Once the subjects have attended the appointment, they return to the LMCDL, and the commission gives the subjects a final conclusive response with a program of future monitoring appointments (after 3, 6, 12 or 24 months) until they are given permission to suspend the protocol.

Retrospective Patient Recruitment

We retrospectively recruited 979 subjects, from 2005 to 2017, sent by the LMCDL for a medical appointment to the "G. Fontana" Centre for the Diagnosis and Treatment of Alcohol Addiction in Bologna, University of Bologna, or to the Department of Internal Medicine in Cento (Ferrara), University of Ferrara. All subjects attended the appointments as outpatients.

During the first appointment (T0), a physical examination was carried out to detect signs or symptoms of alcohol intoxication, alcohol withdrawal or HD; in addition, the amount of alcohol intake in the 4 weeks before suspension of the driving license, expressed in units of alcohol (1 unit = 10-12 g of pure alcohol which corresponds to 125 ml of wine, or 330 ml of beer, or 40 ml of spirits)[1] per day or per occasion, was recorded. In order to record the amount of alcohol intake, a quantity-frequency method to estimate the average of how many days per week subjects drank, and how much they typically consumed alcohol on a given drinking day was used[12]; in addition, due to its greater rapidity (about 10-15 minutes to administer) this method was the most suitable for our setting. Moreover, values of blood laboratory markers of HD, and the scores emerging from the administration of the Alcohol Use Disorder Identification Test (AUDIT)[13] were also recorded.

Considering the definition of HD as "a damage to health"[1], in order to characterize a patient affected by HD, besides signs and symptoms, the alterations of blood laboratory markers were recorded, while the AUDIT score was considered with extreme caution since some subjects may not declare the real amount of their alcohol intake. Namely, alterations of GGT, MCV, AST and ALT may reveal initial liver damage and malnutrition of subjects due to chronic alcohol use[4]. However, even though CDT is considered a common marker of alcohol misuse[4], it has a very short half-life[14,15], and it was not included to characterize subjects with HD. In addition, since ALT is not specific in identifying alcohol-related

liver damage[4] it was not included in the definition of subjects with HD either. Therefore, subjects with only alterations of ALT and AST/ALT <1 (typical of liver damage due to other etiologies than alcohol), and elevation of only CDT were classified as non-HD, whereas subjects with at least two (MCV and GGT) or three (MCV, GGT and AST) alterations of the more specific and sensitive laboratory markers of alcohol misuse were classified as HD.

Due to the difficulties in contacting almost 1,000 subjects seen over a very long period of time (12 years), informed consent was not obtained. In addition, taking into account that the present study is a retrospective analysis without sensitive data, approval of the Ethics Committee was not formally requested.

The Offered Intervention at the CAT

All subjects attended a brief session consisting of counseling for 5-10 minutes aimed at educating the subjects about problematic drinking, increasing motivation to change behavior, and reinforcing skills to address problematic drinking[16,17]. In particular, simple advice was given: a) do not drink before driving or during work; b) if you decide to drink, do it moderately (not more than 2 units of alcohol per day, and not more than 4 units per occasion for men; not more than 1 unit a day, and not more than 3 units per occasion for women)[18]; c) do not drink alcohol on an empty stomach, do not use alcohol during pregnancy, and do not use alcohol if you are following chronic pharmacological therapy. This advice was in accordance with the guidelines of the World Health Organization regarding the low risk drinking of alcohol intake (<40 g/day of alcohol for men, and >20 g/day of alcohol for women)[1]. If symptoms of alcohol withdrawal were identified in accordance with the CIWA-Ar score[19], oral pharmacological treatment with benzodiazepines or sodium oxybate to treat symptoms of alcohol withdrawal in combination with thiamine to prevent the onset of Wernicke encephalopathy was prescribed for 2 weeks[4,20]. At the end of the first appointment (T0), a final certification to be given to the LMCDL was issued. The LMCDL could then decide to authorize return of the driving license or to request to a second follow up appointment (T1) where subjects have to be tested again for the serological markers of HD, and where the doctor has to do a further evaluation of the clinical condition comparing old and new serological markers, re-recording the amount of alcohol intake, and re-administration of the AUDIT test in association with another brief counseling session. The subject must then return to the LMCDL with a second certification. The decision of the LMCDL to authorize return of the driving license is generally made in consideration of the result of the CAT certification, the general clinical characteristic of the patient, age, recurrence of the offence, and level of alcohol concentration at the time of the breath analyzer control. However, some of these sensitive data were collected only by the LMCDL, and not available for our analysis.

Statistical Analysis

Results are expressed as means ± standard deviation. Continuous (age, mean daily number of cigarettes, mean daily and occasional alcohol intake, mean AUDIT score, mean values of laboratory markers of HD) and categorical (gender, employment, smoking) variables between males and females, between non-HD and HD groups, and within the HD group between T0 and T1, were analyzed with Student's *t*-test and chi-square test, respectively. A p-value <0.05 was considered to be statistically significant. Data analyses were performed using the STATA 15.1 statistical software program.

Results

Demographic Data and Drinking Habits

The demographic data of our sample with differences between males and females are shown in Table I. No gender differences were found. Mean age was statistically significant higher in the HD group with respect to the non-HD group (42.5 ± 10.8 *vs.* 41.2 ± 11.8: p<0.0001). A considerable number of the whole sample (17%) were <30 years old, but none of them were in the HD group. The majority of our sample (67.4%) were smokers, and no statistically significant difference between subjects with HD and non-HD was shown (p = 0.307); however, a statistically significant higher mean number of cigarettes smoked in subjects with HD *vs.* those with non-HD (24.0 ± 11.6 *vs.* 19.6 ± 10.7: p<0.039) was found.

A total of 95.9% of our sample were subjects with daily or occasional alcohol intake with the characteristic of non-HD, whereas 4.1% of them (n = 40; 38 males, and 2 females) were subjects with HD. In addition, a statistically significant higher mean daily alcohol consumption was recorded in

Table I. Characteristics of the whole sample.

		Whole sample	Females	Males	p
Subjects	No. subjects (%)	979 (100)	66 (6.7)	913 (93.3)	
Age	Mean age (mean ± SD)	41.2 ± 11.8	42.5 ± 10.8	41.1 ± 11.9	0.3451
	No. subjects (%)				
	< 30 years	166 (17.0)	7 (10.6)	159 (17.4)	0.281
	30/39	324 (33.1)	21 (31.8)	303 (33.2)	
	40/49	251 (25.6)	17 (25.8)	234 (25.6)	
	50/59	154 (15.7)	16 (24.2)	138 (15.1)	
	> = 60	54 (8.6)	5 (7.6)	79 (8.7)	
Employment	Yes	922 (94.2)	56 (84.8)	866 (94.8)	0.001
	No	57 (5.8)	10 (15.2)	47 (5.2)	
Smoking	Yes	660 (67.4)	44 (66.7)	616 (64.5)	0.893
	No	319 (32.6)	22 (33.3)	297 (32.5)	
No. of cigarettes	Mean daily use (mean ± SD)	19.6 ± 10.7	20.5 ± 8.2	19.5 ± 10.8	0.5384
≥ 10 cigarettes per day	No. of subjects (%)	598 (61.1)	42 (63.6)	556 (60.9)	0.659
Units of alcohol (grams)	No. of subjects and mean daily use (mean ± SD)	359 3.0 ± 1.7	22 2.8 ± 2.0	337 3.0 ± 1.7	0.685
	No. of subjects and mean occasional use (mean ± SD)	441 2.3 ± 1.1	28 1.9 ± 0.8	413 2.3 ± 1.1	0.1066
Binge drinkers	No. of subjects (%)	20 (2.0)	0 (0) 20 (2.0)		
AUDIT score	No. of subjects (%)				
	< 8 points	844 (86.2)	56 (5.7)	788 (80.4)	0.486
	8-13 points	108 (11.0)	6 (0.6)	102 (10.4)	
	> 13 points	27 (2.7)	4 (0.4)	23 (2.3)	

subjects with HD *vs.* non-HD (4.0 ± 2.5 *vs.* 2.9 ± 1.6: $p<0.002$). Two percent of the whole sample were binge drinkers, mostly with non-HD. A statistically significant higher number of patients with an AUDIT score ≥8 points was found in subjects with HD *vs.* non-HD ($p<0.0001$); however, 50% of subjects with HD had a negative AUDIT score. Mean values of the laboratory markers of HD were statistically significantly higher in subjects with HD *vs.* non-HD (Table II).

At the end of the T0 appointment, 939 subjects (non-HD) returned to the LMCDL with a substantially positive certification which would guarantee them being allowed to drive for a period ranging from 6 to 12 months. Only those who presented CDT alterations were required to undergo a further control of CDT (not before 2-3 weeks) and if this proved normal then the LMCDL authorized return of their driving license with a monitoring protocol to undergo further blood markers and an appointment at the LMCDL after 3 months. Considering the very long period of recruitment (12 years), three different methods of analysis of the CDT were used, with three different cut-offs (Radio Immuno Assay-RIA: cut-off = 2.5%; Capillary Electrophoresis-CE: cut-off = 1.6%; High Performance Liquid Chromatography-HPLC: cut-off = 1.8%)[21-23], thus it was not possible to clearly ascertain the average value of CDT across subjects.

The remaining 40 subjects were diagnosed with HD. It is worth noting that 3 of them presented symptoms of moderate alcohol withdrawal which needed pharmacological treatment due to a CIWA-Ar score >10 points[19], and thus, at their consent, they were treated with sodium oxybate (50 mg/kg/day) for 2 weeks in association with thiamine (100 mg/day) for 4 weeks[20]. The remaining subjects who did not present any symptoms of alcohol withdrawal were advised to make an appointment with their general practitioners and to undergo abdominal ultrasonography in order to investigate whether any liver damage was present.

Follow-Up in Subjects With HD

Among subjects with HD (n = 40), only twenty-one of them (2.1% of the whole sample) (21/40) were required by the LMDCL to attend a further control appointment (T1) at the CAT, while for the remaining subjects (n = 19) the LMCDL decided to authorize return of the driving license for a very short period of time, suggesting they repeated the blood test for the markers of HD, and again attending an appointment at the LMCDL after 3 months.

Table II. Comparison between subjects with non-Harmful Drinking versus Harmful Drinking.

		Non Harmful Drinking	Harmful Drinking	*p*
Subjects	Total (%)	939 (95.9)	40 (4.1)	
	Male (%)	875 (89.3)	38 (4.2)	0.654
	Female (%)	64 (6.5)	2 (3.0)	
Age	Mean age (mean ± SD)	41.2 ± 11.8	50.5 ± 8.3	< 0.0001
	No. of subjects (%)			
	< 30 years	166 (17.0)	0 (0)	< 0.0001
	30/39	321 (32.7)	3 (0.9)	
	40/49	232 (23.6)	19 (7.6)	
	50/59	144 (14.7)	10 (6.5)	
	> = 60	46 (4.6)	8 (9.5)	
Employment	Yes	886 (88.4)	36 (3.9)	0.249
	No	53 (5.4)	4 (7.0)	
Smoking	Yes	636 (64.9)	24 (3.6)	0.307
	No	303 (30.9)	16 (5.0)	
Number of cigarettes	Mean daily use (mean ± SD)	19.6 ± 10.7	24.0 ± 11.6	0.039
		575 (61.1)	23 (57.5)	0.635
Units of alcohol (g)	No. of subjects and mean occasional use (mean ± SD)	332 2.9 ± 1.6	27 4.0 ± 2.5	0.002
	No. of subjects and mean daily use (mean ± SD)	433 2.3 ± 1.1	8 2.1 ± 1.5	0.7325
	Binge drinkers	19 (2.0)	1 (2.5)	0.835
AUDIT score	No. of subjects (%)			
	< 8 points	824 (87.8)	20 (50.0)	< 0.0001
	8-13 points	92 (9.8)	16 (40.0)	
	> 13 points	23 (2.4)	4 (10.0)	

During the T1 appointment, the three patients treated for symptoms of alcohol withdrawal who had concluded the pharmacological therapy with sodium oxybate (CIWA-Ar score was 0) did not present any side effects or craving for sodium oxybate and declared that they were completely abstinent from alcohol. The remaining 18 subjects stated that they had significantly reduced their alcohol intake. The improvement of the clinical condition of all 21 subjects was observed not only by a significant reduction of the blood markers of HD between T0 and T1 (Table III), but also by a statistically significant reduction of the reported units of alcohol per day (3.04 ± 3.08 *vs.* 0.90 ± 1.81: $p<0.009$). While a statistically significant reduction of MCV and AST between T0 and T1 was found, the reduction of GGT levels and the AUDIT score did not achieve statistical significance; however, an objective trend toward reduction of GGT and AUDIT score was observed. The three subjects who manifested symptoms of alcohol withdrawal presented a diagnosis of severe AUD following the criteria of DSM-V[2], while after a more accurate clinical investigation, 14 of the remaining 18 subjects presented a diagnosis of mild-moderate AUD. In consideration of this, in the final certifications to be given to the LMCDL, all these subjects were invited to follow a rehabilitation program for AUD at our CAT. The LMCDL confirmed what the CAT suggested

Table III. Difference between Appointment 0 and Appointment 1 in the AUDIT score, and laboratory markers of alcohol intake (mean daily and occasional) of the 21 subjects with Harmful Drinking who underwent the follow-up appointment (Appointment 1).

	Appointment 0 Mean ± Standard Deviation	Appointment 1 Mean ± Standard Deviation	*p*
AUDIT score	8.4 ± 5.2	5.5 ± 4.3	0.06
AST	79.3 ± 67.9	40.8 ± 22.1	0.02
GGT	256.7 ± 230.0	151.1 ± 197.9	0.1186
MCV	104.1 ± 4.4	99.0 ± 4.8	0.0009
Units of alcohol (g/day)	3.04 ± 3.08	0.90 ± 1.81	0.009

and authorized the return of their driving license for a very short period (3 months) only if they declared they would follow the program proposed by our CAT. Data of further follow up appointments were not recorded in this study.

Discussion

This is the first study investigating the presence of HD in a population of subjects who had their driving license suspended as a result of driving under the influence of alcohol above the legal limit. The study shows a high number of subjects driving a car when affected by HD, almost 50% of them presented a diagnosis of AUD, were older and heavy smokers. In addition, a monitoring protocol of HD (from the police checkpoint to the appointment at a CAT) seems to be an efficient measure to reduce heavy drinking.

Worldwide, the number of deaths due to HD remains high and the difficulties in early identification is well known[4]. HD is responsible for approximately 5.9% of all deaths worldwide (3.3 million deaths) and accounts for 5.1% of the global disease burden[1,3], it can lead to approximately 200 different diseases, including fourteen different types of cancer, and it can also have an addictive element[1,3]. In Italy, it has been estimated that among 35 million Italians that habitually drink alcohol, 700,000 of them (2%) present HD. In addition, as in the rest of Europe[4], a very limited number (<10%) of subjects with HD or AUD in Italy follow a rehabilitation program in a CAT[24]. In our sample, 4.1% of the subjects were affected by HD and, 1.7% presented a diagnosis of AUD. Namely, they presented a higher risk condition for the consequences of alcohol-related problems; thus, they may all need to be treated. However, it was not possible to draw any comparison with the general population since the subjects who tested negative at the police checkpoint were not recruited. On the other hand, our sample consisted of subjects driving over the legal limit of alcohol for Italian law, putting themselves and others at risk of accidents. Indeed, they also present with hazardous drinking which is defined as "a quantity or pattern of alcohol consumption that places individuals at risk for adverse health events"[18] giving the detection of HD a more important value.

Moreover, during the last two decades, the mean age of patients affected by HD or AUD has decreased, as indirectly shown by the age of first drink in Europe which is around 14-15 years[18]; however, in our study the prevalence of HD increased progressively with the age of the subjects. It is conceivable to assert that in a chronic condition, such as alcohol misuse, older subjects are more predisposed to develop HD or AUD. This is also demonstrated by the fact that almost 50% of subjects in the non-HD group were <50 years. In addition, the association of alcohol and cigarette smoking is frequently found in subjects with HD and/or AUD[25,26]. This data was showed in our HD group. In fact, although no differences were found in smoking habit, the number of cigarettes smoked per day was significantly higher in subjects with HD with respect to those without HD.

Furthermore, the AUDIT test is considered the most useful tool for detecting HD in all medical settings[27]. Taking into account that AUDIT is a self-administered questionnaire in which the participant can deny or minimize his/her alcohol habits, in our study we considered its scores with caution. In fact, 50% of our subjects affected by HD – clearly shown by the alteration of the blood markers – did not present a pathological score (<8 points). This may sound strange, but on the other hand, it reflects the fact that subjects tried to mask their habits of drinking alcohol during completion of the questionnaire. Therefore, the AUDIT questionnaire alone may not be considered an adequate tool for detection of HD; it needs to be combined with a clinical evaluation and the results of the blood markers of HD to acquire a prominent position in detecting the presence of HD.

As regards the laboratory markers, CDT was excluded in our analysis. However, while CDT is considered a marker of relapse (almost 50-60 grams of alcohol for at least 10 days)[4,14,15], in this specific context CDT does not represent a specific marker for identification of alcohol-related damage, for which a more complete examination with more specific markers of organ damage needs to be considered. Indeed, for the detection of HD, which was the main purpose of our study, CDT is of little use. In addition, CDT needs a very short period of time to normalize (10-12 days)[14,15], and taking into account that our subjects generally underwent the first control of markers of HD 3-4 weeks after the suspension of their driving license, they will have had time to stop drinking and normalize their blood levels of CDT, presenting a normal value at the time of their appointment at the LMCDL. On the contrary, needing a longer period of time to achieve normal values (2-3 weeks for GGT and AST, and 2-3 months for MCV)[4], the other parameters of HD were more

helpful. In fact, the 21 subjects with HD who attended the follow-up appointment (T1) declared they were abstinent or had reduced their alcohol intake, as confirmed by a statistically significant reduction of all the laboratory parameters of HD. On the other hand, it is worth noting that some patients may be missed from the diagnosis of HD; indeed, some of them may present very modest alterations of the laboratory markers of HD which normalize at the time of the appointment at the LMCDL, and are therefore not required to attend an appointment at a CAT.

Despite the moderate quality evidence of the efficacy of single brief advice and counseling session for HD[28], several studies have been published to test its efficacy. Since we have no data about the recidivism of our subjects, the absence of further follow-up appointments, and the absence of a control group, it was not possible to collect data about the efficacy of the brief counseling sessions in a medium or longer period both for non-HD and HD subjects. However, in subjects with HD a significant improvement of alcohol habits in the short-term period was detected, as demonstrated by the significant reduction of laboratory markers of HD. It is conceivable to assert that the brief counseling session may play a role. On the other hand, it is worth noting that subjects were extremely motivated to follow a specific program to reduce or quit alcohol intake, since this would have guaranteed the authorization from the LMCDL to drive again. Driving a car makes individuals independent, and in the majority of cases makes it possible to go to work without any assistance. To have your driving license back could be a strong motivation to abstain from alcohol, or to reduce it, particularly in those who have not developed physical symptoms of alcohol withdrawal in whom this clinical condition would be much more difficult.

Limitations

Our study presents some limits. First of all, the retrospective evaluation is "per se" a strong limit. Secondly, some additional data (i.e., breath alcohol test values, concomitant use of medications, illicit drugs) which would have more strongly characterized our population and our analysis were not recorded. Third, any data regarding recidivism of our subjects with non-HD were not collected, and this would have improved our awareness about the efficacy not only of any penal sanction, but also of the monitoring protocol and of the brief counseling session in limiting the risk of HD especially in the younger population. Fourth, subjects with HD reduced and improved their drinking habits; however, no control group was recruited, and a very low number of patients with HD limits the strength of our data.

Conclusions

In summary, since the 4% and 1.7% of our population with HD and/or AUD are highly at risk for the consequences of alcohol-related damage "per se" and for other conditions, and considering the difficulties in detecting HD and AUD in the general population, it is necessary to continue with and even increase the roadside check-points, and the subsequent monitoring protocol of drinking in subjects driving under the influence of alcohol and whose driving licenses have been suspended. Indeed, as already demonstrated both in the European Union[6,29], and in Anglo-Saxon countries[9,10], prevention policies have been efficient in reducing risk of traffic accidents and deaths associated with alcohol use. Thus, a monitoring program with the involvement of a network of several professional figures (policy makers, lawyers, police forces, experts in forensic medicine, and experts in the diagnosis and treatment of alcohol addiction) for the detection, and possibly treatment of subjects with HD and AUD in this context may be implemented. Controlled studies to investigate HD and AUD and the efficacy of a monitoring protocol of drinking in a population of subjects whose driving license has been suspended as a result of driving under the influence of alcohol are warranted.

Conflict of Interest
The Authors declare that they have no conflict of interests.

References

1) World Health Organization. Global Status Report on Alcohol and Health 2018.
2) American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fifth edition. Washington DC: American Psychiatric Publishing 2013.
3) GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the global burden of disease study 2016. Lancet 2018; 392: 1015-1035.

4) Carvalho AF, Heilig M, Perez A, Probst C, Rehm J. Alcohol use disorders. Lancet 2019; 394: 781-792.

5) Grant BF, Goldstein RB, Saha TD, Chou SP, Jung J, Zhang H, Hasin DS. Epidemiology of DSM-5 alcohol use disorder. JAMA Psychiatry 2015; 72: 757-766.

6) Allamani A, Voller F, Pepe P, Baccini M, Massini G, Cipriani F. Italy between drinking culture and control policies for alcoholic beverages. Substance Use Mis 2014; 49: 1646-1664.

7) Fell JC, Voas RB. The effectiveness of a 0.05 blood alcohol concentration (BAC) limit for driving in the United States. Addiction 2014; 109: 869-874.

8) Christophersen AS, MVTRland J, Stewart K, Gjerde H. International trends in alcohol and drug use among vehicle drivers. Forensic Sci Rev 2016; 28: 37-66.

9) Scherer M, Fell JC. Effectiveness of lowering the blood alcohol concentration (BAC) limit for driving from 0.10 to 0.08 grams per deciliter in the United States. Traffic Inj Prev 2019; 20: 1-8.

10) Rehm J, Manthey J, Lange S, Badaras R, Zurlyte I, Passmore J, StelemÐkas M. Alcohol control policy and changes in alcohol-related traffic harm. Addiction 2020; 115: 655-665.

11) Italian Minster of Justice. Law n. 125/2001, and Law n. 168/2002, 2002.

12) Poikolainen K, Podkletnova I, Alho H. Alcohol Accuracy of quantity-frequency and graduated frequency questionnaires in measuring alcohol intake: comparison with daily diary and commonly used laboratory markers. Alcohol Alcohol 2002; 37: 573-576.

13) Saunders JB, Aasland OG, Babor TF, de la Fuente JR, Grant M. Development of the Alcohol Use Disorders Identification Test (AUDIT): WHO Collaborative Project on Early Detection of Persons with Harmful Alcohol Consumption-II. Addiction 1993; 88: 791-804.

14) Stibler H. Carbohydrate-deficient transferrin in serum: a new marker of potentially harmful alcohol consumption reviewed. Clin Chem 1991; 37: 2029-2037.

15) Bortolotti F, Sorio D, Bertaso A, Tagliaro F. Analytical and diagnostic aspects of carbohydrate deficient transferrin (CDT): a critical review over years 2007-2017. J Pharm Biomed Anal 2018; 147: 2-12.

16) Fleming MF, Manwell LB, Barry KL, Adams W, Stauffacher EA. Brief physician advice for alcohol problems in older adults: a randomized community-based trial. J Fam Pract 1999; 48: 378-384.

17) Whitlock EP, Polen MR, Green CA, Orleans T, Klein J. Behavioral counseling interventions in primary care to reduce risky/harmful alcohol use by adults: summary of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2004; 140: 557-568.

18) World Health Organization (WHO). International Classification of Diseases (ICD) 11th Revision. The global standard for diagnostic health information 2018.

19) Sullivan JT, Sykora K, Schneiderman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). Br J Addict 1989; 84: 1353-1357.

20) Caputo F, Agabio R, Vignoli T, Patussi V, Fanucchi T, Cimarosti P, Testino G. Diagnosis and treatment of acute alcohol intoxication and alcohol withdrawal syndrome: position paper of the Italian Society on Alcohol. Intern Emerg Med 2019; 14: 143-160.

21) Viitala K, Lähdesmäki K, Niemelä O. Comparison of the axis % CDT TIA and the CDTect method as laboratory tests of alcohol abuse. Clin Chem 1998; 44; 1209-1215.

22) Bortolotti F, De Paoli G, Pascali JP, Trevisan MT, Floreani M. Analysis of carbohydrate-deficient transferrin: comparative evaluation of turbidimetric immunoassay, capillary zone electrophoresis, and HPLC. Clin Chem 2005; 51: 2368-2371.

23) Helander A, Wielders JP, Te Stroet R, Bergstrom JP. Comparison of HPLC and capillary electrophoresis for confirmatory testing of the alcohol misuse marker carbohydrate-deficient transferrin. Clin Chem 2005; 51: 1528-1532.

24) Italian Ministry of Health. Annual Report of the Ministry of Health to the Parliament about the interventions on alcohol related problems 2017.

25) Lasser K, Boyd JW, Woolhandler S, Himmelstein DU, McCormick D, Bor DH. Smoking and mental illness: a population-based prevalence study. JAMA 2000; 284: 2606-2610.

26) Falk DE, Yi HY, Hiller-Sturmhofel S. An epidemiologic analysis of co-occurring alcohol and tobacco use and disorders: findings from the National Epidemiologic Survey on Alcohol and Related Conditions. Alcohol Res Health 2006; 29: 100-110.

27) Knox J, Hasin DS, Larson FRR, Kranzler HR. Prevention, screening, and treatment for heavy drinking and alcohol use disorder. Lancet Psychiatry 2019; 6: 1054-1067.

28) Kaner EFS, Beyer FR, Muirhead C, Campbell F, Pienaar ED, Bertholet N, Cochrane Drugs and Alcohol Group. Effectiveness of brief alcohol interventions in primary care populations. Cochrane Database Syst Rev 2018, CD004148.

29) Novoa AM, Pérez K, Santamariña-Rubio E, Marí-Dell'Olmo M, Ferrando J, Peiró R, Tobias A, Zori P, Borrell C. Impact of the penalty points system on road traffic injuries in Spain: a time–series study. Am J Public Health 2010; 100: 2220-2227.