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The Use of Carbohydrate-Deficient Transferrin in Occupational Setting: A Systematic Review

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Abstract

Background: Alcohol consumption is prohibited in some categories of workers due to its temporary and long-term effects. The purpose of this study is to review and evaluate the use of carbohydrate-deficient transferrin (CDT) as a biomarker to screen alcohol consumption in workers.

Methods: A systematic review was performed, searching three databases, PubMed, Scopus and Isi Web of Knowledge, up to December 2021, screening for studies that used CDT as a biomarker in workers. A quality assessment was performed on the included studies.

Results: Seven studies met the inclusion criteria, accounting for more than 3200 workers from five different countries; in the samples observed, a positive percentage of CDT was found in the single studies between 7 and 24%. The large interval could be due to the differences in populations in the included studies; furthermore, not all workers are prohibited from drinking on the job. Four out of the seven studies also included questionnaires on alcohol consumption assessment. Finally, included articles were stratified by occupational hazards and by industrial sector. Interestingly, different methods of analysis and different cut-offs were used by the different authors.

Conclusions: The use of CDT as a biomarker of alcohol consumption has high specificity. However, further studies are needed to be able to strongly validate the use of CDT for screening purposes in the working population to detect alcohol abuse.

Keywords: CDT;Occupational health; Alcohol consumption; Biomarker

Background

The harmful use of alcohol is one of the leading risk factors for population health worldwide, among health targets of Sustainable Development Goals there is "strengthen the prevention and treatment of substance abuse, including narcotic drug abuse and harmful use of alcohol" [1].

Total alcohol per capita consumption in the world's population over 15 years of age rose from 5.5 liters of pure alcohol in 2005 to 6.4 liters in 2010 and was still at the level of 6.4 liters in 2016. The highest levels of per capita alcohol consumption are observed in countries of the WHO European Region. Globally an estimated 237 million men and 46 million women have alcohol use disorders, with the highest prevalence of alcohol use disorders among men and women in the European Region (14.8% and 3.5%) [1].

Prevalence of heavy episodic drinking (HED) (defined as 60 or more grams of pure alcohol on at least one occasion at least once per month) has decreased globally from 22.6% in 2000 to 18.2% in 2016 among the total population, but remains high among drinkers. In Europe the alcohol per capita consumption (APC) (15+ years) in litres of pure alcohol in 2016 was 9.8 (this data should be constant till 2025), the HED prevalence 26.4 [1].

Globally an estimated 0.9 million injury deaths were attributable to alcohol, including around 370000 deaths due to road injuries, 150000 due to self-harm and around 90000 due to interpersonal violence. Of the road traffic injuries, 187000 alcohol-attributable deaths were among people other than drivers [1].

In-depth questioning and physical examination, the work-up in such cases includes carrying out relevant laboratory blood tests: GGT, AST, ALT, MCV and CDT (carbohydrate-deficient transferrin). One thing that all these indirect, more or less sensitive and specific, alcohol markers have in common is that they cover only a limited period of time and may be affected by other factors, such as severe hepatobiliary disease, metabolic disorders, genetic variants and medications [2].

Thus, the choice a biomarker should be performed carefully, taking into account both the query (recent alcohol intake, risky alcohol behavior or abstinence) and the summons procedure (point in time at which the date of sample collection is announced) [3].

In assessing fitness to drive in cases where there is a question of alcohol problems, laboratory testing– usually determination of the relevant alcohol-related parameters CDT, GGT, AST, ALT and MCV in the blood – provides an important piece of the puzzle in the assessment of alcohol consumption or improving/disproving self-reported abstinence.

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If someone is declared unfit to drive because of alcohol problems (abuse, dependence), the traffic medicine guidelines in Switzerland require long-term complete abstinence from alcohol (for at least 6 months, and possibly for 12 months). To check that the person has not been drinking, tests for the indirect alcohol markers are done about every 6-8 weeks; the blood samples are usually taken by the general practitioner [4]. CDT has been shown to be specific and sensitive, but results are only above the upper limit of normal after the consumption of more than 60 g alcohol daily for more than two weeks, so it often does not detect short periods of high intake [5]. In addition, the CDT concentration does not rise in a certain group of people who drink alcohol regularly (false negative result in non-responders) [6]. The use of different methods for CDT assays (immunochemistry/ HPLC) also gives rise to discussion because of different sensitivities, specificities, and references ranges.

Carbohydrate-deficient transferrin (CDT) was first proposed as a marker of alcohol abuse in the late 1970s [7]. The percent of CDT has been evaluated extensively as a marker of alcohol use and abuse [7,8] and has been observed to have high sensitivity and specificity in distinguishing chronic, hazardous drinking subjects from abstainers or very light social drinkers [9,10].

As a limit to the usefulness of CDT as a biomarker, a CDT increase might be due to nonalcoholic causes (e.g. viral cirrhosis, hepatocellular carcinoma) [11] although they are not as frequent and high CDT levels can be attributed to genetic transferrin polymorphism and rare congenital disorders of glycosylation (CDG) [12].

Its use was later widely investigated and improved, especially by the use of capillary electrophoresis methods [13] and CDT is at present described as the most specific marker of chronic alcohol abuse [4,13].

A Meta-Analysis [14] on the relationship between Alcohol Consumption and Sickness Absence indicate that risky, high-risk drinking and HED may increase the risk of absenteeism; Melvin et al suggest implementation of population-based strategies that may address the burdens of alcohol-related Sickness Absence. For the authors additionally, economic evaluations of alcohol policies should incorporate their impacts on Sickness Absence.

Several studies have argued that workplaces should develop methods for identifying and counteracting alcohol related problems at an early stage of misuse [15-19]. Early identification of elevated and risky levels of alcohol consumption may reduce alcohol consumption and absenteeism [20,21].

In selected groups of problem drinkers, CDT is a highly specific alcohol marker [22-24], but also in an unselected population [25], CDT was found to have a better discriminatory power than GGT for identifying lower levels of alcohol consumption [26].

This review represents an attempt to provide an updated overview of the current state of knowledge on the use of CDT as a biomarker, noting its strengths and weaknesses.

Methods

The study involved a systematic review process that was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Statement criteria (PRISMA) [27]. The review was not registered and a protocol was not prepared. Principal scientific databases namely PubMed, Scopus and ISI Web of Knowledge were searched to identify studies addressing the use of Carbohydrate Deficient Transferrin to identify the intake of Alcohol in workers, published up to December 20th, 2021. We used two search lines that included the terms "Carbohydrate Deficient Transferrin" to assess the specific laboratory methodology used to detect the alcohol intake, and the terms "biomarker*", "blood", "occupational", "job", "work" to identify the outcome. The two lines were combined with the operator "OR".

All of the titles and abstracts that were retrieved by the computerized search were independently reviewed by two of the authors who made a selection of the papers that are relevant for the review purposes, in accordance with the inclusion criteria. These referred to original, human peer-reviewed articles, including descriptive epidemiological-occupational surveys, medical reports, case series, cohort and case-control studies published in English, and reporting toxicological examination on workers about alcohol intake. To be included in the review, studies had to describe biomonitoring of human samples to analyze CDT to detect the alcohol consumption in workers. No limits regarding the alcohol intake were adopted, and no restrictions were imposed on the geographical areas of investigation, patient origin, analytical or statistical methods used. Exclusion criteria the article type (reviews, case reports, conference papers, studies on analytical methods), publications that did not focus on alcohol intake in an occupational population, or published in languages other than English.

The preliminary search identified a total of 2074 articles: 552 in Pubmed, 969 in Scopus and 553 in ISI Web of Knowledge databases, respectively. 703 duplicates were removed from the total number of papers. Two authors independently excluded 1322, as they did not meet the inclusion criteria based on the title and abstract analyses. From the 49 selected works a total of 7 papers remained for review. All of the full texts of the articles that were considered suitable for review were obtained and subjected to a critical evaluation. Overall, our search retrieved a total of 7 articles for review (Figure 1).

Each eligible study was critically reviewed by three investigators and the principal characteristics were extracted in order to determine the demographic and occupational characteristics of cases, disease features, and workplace information. The Newcastle Ottawa Scale [28] was used to assess the methodological quality of the included studies.

The results of the eligible studies are described in the following sections and then organized into tables summarizing information concerning case identification, periods of investigations, geographical areas of origin, type of study, working activities of studied population, number of workers involved in the study, alcohol markers used, study outcome and reference (Table 1).

Results

The preliminary search identified a total of 2074 articles: 552 in Pubmed, 969 in Scopus and 553 in ISI Web of Knowledge databases, respectively; 703 duplicates were removed from the total number of papers. Two authors independently excluded 1322 papers, as they did not meet the inclusion criteria. From the remaining 49 selected works, 7 papers were selected after full text critical evaluation (Figure 1).

We extracted from studies the following data: case identification, periods of investigations, geographical areas, study design, occupational sector, population characteristics, main biomarker for alcohol use assessment, analytical method for CDT measurement, screening tool for alcohol use other than CDT, study outcome, prevalence of workers with CDT values higher than cut-off, references (author, year, journal name) (Table 1).

Furthermore, for each study we extracted data on analytical methodology used for CDT measurement with specific cut off values

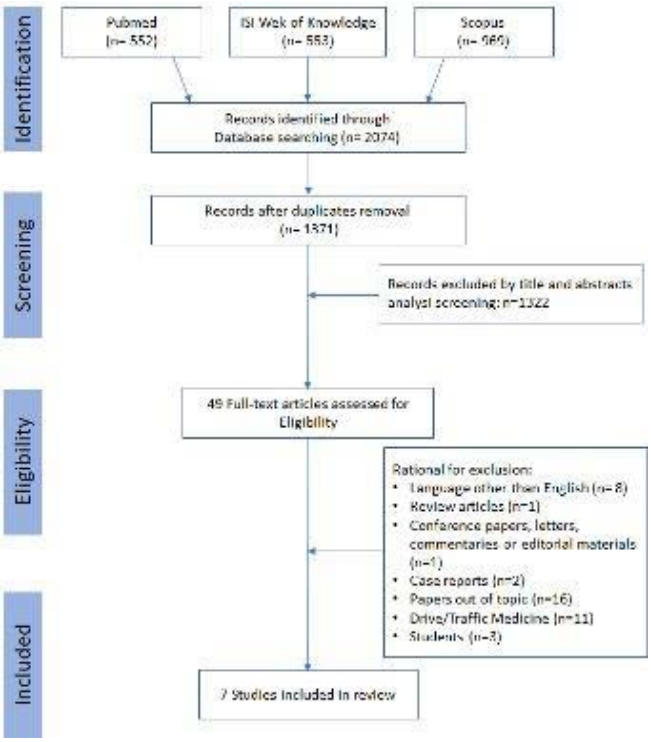

Figure 1: Process of Articles for Review.

Table 1: Characteristics of included studies, including details on the population, alcohol markers used and study outcome.

Study period	Country	Type of Study	Working Activities Investigated	Numbers of Workers (Male-Females)	Markers	Study outcome	References
Jannuary 2010-jan 2012	Spain	cross-sectional survey	agriculture 296, Construction 47, Services 42	385 (287 males, 98 females) migrant workers during a routine health examination	CDT (immunoturbidimetric assay)	Identify workers with a hazardous drinking problem by means of a self-reported questionnaire (Alcohol Use Disorders Identification Test-AUDIT) and a biomarker (carbohydrate-deficient transferrin-CDT) and to ascertain asso- ciated risk factors.	Perez-Carceles, 2014 J Occup Health
February 1997 and January 2000	Sweden	Cross sectional study	Trasport sector	990 (677 male, 313 females):	CDT (radioimmunoassay)	In routine health examinations, study if there is any difference between permanent day and shift workers	Hermansson, 2003
				399 daytime (57% men)	GGT		Occup Medic
				294 two-shift (55% men)			
				30% three shift (96% men)			
16 months	Sweden	cross-sectional study	Transport sector	570 (358 male, 63%) (2121 women, 37%):	CDT (RIA)	The purpose of this study was to compare the	Hermansson, 2000
				Nonmanualworkers 361	GGT	performances of AUDIT, CDT, and y-glutamyltransferase (GGT) in a routine health examination (Alcohol Screening) in the workplace.	Alcohol Clin Exp Res
				Manual workers 209			
-	Russia	cross-sectional study	Welders exposed to Manganese	137 male welders	B-Mn	To study interaction between manganese exposure and alcohol	Ellingsen, 2014
			turners/fitters	137 male turners/fitters	U-Mn		Neurotoxicol Teratol
					B-Pb		
					B-Hg		
					U-Hg		
					CDT (capillary electrophoresis)		

January 2018 to December 2018	Italy	Cross-sectional	Office workers Unemployed	157+157 controls	CDT (capillary Electrophoresis) AST ALT GGT MCV	How work status predict alcohol consumption	De Sio, 2020
-		Cross-sectional	workers (employed at several divisions in production and office)	175 male	CDT (flow cytometry) MCV EtG-EtS GGT ALT AST	To explore the suitability of the direct urinary biomarkers ethyl glucuronide (EtG) and ethyl sulphate (EtS) to assess moderate but regular alcohol consumption	Kilo, 2016, Int Arch Occup Environ Health
-			Predominantly unemployed, visited at employment agencies and occupational health units	509 (80% men)	CDT (high performance liquid chromatography) GGT MCV EtG PEth	Comparing test results for a set of alcohol biomarkers commonly used to indicate recent drinking (acute biomarkers) or regular consumption (chronic biomarkers) in blood samples received for routine measurements from employment-related health controls	Naumann, 2020, Alcohol and Alcoholism

Table 2: Frequency of positive CDT with stratification by gender, occupation and risks.

Study	Sample	% CDT+	% male	% female	Occupazione	Rischi occupazionali
Hermansson et al. 2000	570 (358 male)	18.4	8.9	9.9	Transportation Manual workers Non-Manual Workers	
Hermansson et al. 2003	990 (677 male)	11	11.5	9.9	Transportation	Shift workers
Perez et al. 2014	385 (287 male)	11.2	15.7	8.2	Farmers Construction workers	
Elligsen et al. 2014	137+137 (137 male)	11.6 6.6	11.6 6.6	-		Welders Turners-fitters
Kilo et al. 2016	175 (male)	13.1	13.1	-	Production sector Office workers	
De Sio et al. 2020	157 (office worker)	7	-	-	Office workers	
Neumann J et al. 2020	509 (80% male)	24	-	-	Employment agencies	

for identifying workers with hazardous alcohol behaviour (Table 2).

For each study, a quality assessment was performed using the NOS. All included study was at least satisfactory in quality (≥6).

Hermansson et al in two studies from 2000 and 2003 used CDT and GGT as markers to study alcohol consumption in transport shift workers in the Swedish population [29,30]. The 2000 work carried out on a sample of 570 workers (358 man and 212 female) resulted in 18.4% of positive results (9.9% female and 8.9% men - although this difference in the study was not significant); no significant differences were found in the comparison between manual and non-manual workers. In the work of 2003 against a large sample of workers (990 of which 677 badly) 11% of workers tested positive including 9.9% of Female and 11.5% of males with a lower incidence of the phenomenon at under 35 years of age and in workers assigned to two-shift work (to the detriment of three shift work and Daytime work). An interesting fact is that 80% of the positive subjects had a length of service of at least one year and 65% of at least 5 years. In both of Hermansson's [29,30] works the recruitment of workers was carried out on a voluntary basis and this appears as a weakness in the study, thus creating an important selection bias deriving from the fact that since the study was aimed at a sample of workers any identification of alcohol-related problems could trigger work problems of various types and degrees. The working populations investigated are interesting for the type of work performed, in fact both shift work and transport are activities of particular interest for the Occupational Physician; however, it would have been interesting to have also the data of the tasks and the stratification of the samples by task; the authors differentiate in the work of 2003 [30] the type of shift carried out (1-2-3 shifts per day) being able to theoretically constitute the shifting process at the basis of which there could be a lifestyle that could affect eating habits and drinking; at the basis of this aspect of shift work there was the idea that night shift work could be characterized by a greater tendency to drink alcohol, which was however not supported by the data that emerged from the research. In the work of 2000 [29], a 16-month screening was then conducted and it was observed that holidays can affect the outcome of the screening by detecting an increase in the use of alcohol (binge drinkers) in the vicinity of the same. The use of the double investigation tool and therefore of the CDT and the audit was very critical, something frequently found in the Health Surveillance protocols of the Occupational Physician. The results of the two tests were found to be inconsistent, resulting in a very low convergence of results between the two tests of 7.6%. The authors

note that a possible explanation supporting this difference between the two tests (the questionnaire and the serological) is that while the first investigates the last year, the second covers only the last few weeks. Despite the differences between AUDIT and CDT, the authors conclude in the 2000 paper [29] stating that CDT and AUDIT must be complementary instruments for alcohol screening. Another important point to note in the two studies is that the examinations were envisaged as screening and therefore this is profoundly different from checks made to verify the possible existence of problems related to alcohol and which may impact on suitability for work; while this latter aspect has an important impact on the AUDIT (possibility of insincere answers when assessing job suitability) it has less impact on the CDT, but even in the latter case, since there were two voluntary screening campaigns from the jobs understands whether the tests carried out and reported in the study were those of workers who, once they entered the study, did not miss any calls and therefore if workers who did not respect the follow-up schedules were expected to leave the study; this last aspect appears important because if the workers were not excluded (with the previous tests carried out) they were given the possibility, during periods of greater alcohol intake, not to undergo the CDT measurement, thus distorting the real percentages of positives found. Perez et al. [31], out of a sample of 385 migrant workers (74.5 man) from Spain conducted a study on the use of CDT and audits to identify subjects at risk. The survey is based on voluntary adherence to alcohol screening, 53.8% was found to be abstemious, 32.5% was classified as not at risk and 13.8% classified as at risk (CDT or AUDIT positive); of the latter 11.2% were positive for CDT and 8.6% positive for AUDIT; in this work a significant correlation was found between CDT and AUDIT even though this correlation was found in only 20 out of 53 cases (both tests positive); interesting is the stratification by professions where it is noted that work in agriculture found 14.2% of the subjects examined at risk of alcohol, 17.4% of positives in the construction sector and 7% in services; male gender and living stably in the country (for more than 85 months) have also been correlated with being classified at risk of alcohol; the office sector was the one with the lowest number of cases at risk of alcohol; however, there are no data on CDT positivity alone due to work activity. In this study, voluntary adherence to the study does not appear to be a critical point of the study, in fact the selection of the sample was carried out randomly and the adhesion was 100% of the selected, this procedure effectively canceled the bias of selection that is generally created in voluntary membership. The sample used, however, creates numerous critical points in the analysis of the data, in fact they are migrant workers largely of the Muslims faith, many of whom then entered Spain irregularly, and many had practical jobs and were afraid of losing their work (and therefore the authenticity of the answers to the questions was doubtful); the sample is stratified by activity (agriculture, industry and service sector respectively 82, 15.3 and 2.8% men and women 2, 35.7 and 62.2%). Elligsen et al. [32] in a study on manganese exposure of welders (137 male) also screened for alcohol consumption by examining CDT; the sample comes from shipyards and industry that manufactures heavy machinery. The welders compared to the control population (turners / fitters) reported much higher alcohol consumption data in the interview; however the CDT values are comparable. The CDT was found to be higher than the limit values in 11.7% of welders and in 6.6% of turners / fillers; in this study, CDT was used to see how the use of alcohol affects the neurotoxic effects of manganese. The study was also conducted in this case on a voluntary basis but subjects with a known history of alcohol abuse were excluded, both of these aspects appear to be a limitation having in fact modified the original sample and somehow excluded the subjects who would most be were interesting in order to study the phenomenon of alcohol abuse in the workplace, however this exclusion was made necessary by the fact that the primary outcome of the study was not to analyze the problem of alcohol in the workplace but instead to study the effects of the Mn on exposed workers. The study also conducted an interview on alcohol use which was found to underestimate alcohol consumption in relation to CDT data (as also found in the study by Searles [33]), moreover CDT is significantly correlated with finger tapping (outcome of neurobehavioral test) while the questions on alcohol consumption are not associated, this data demonstrates once again how anamnestic data on alcohol, more importantly in the workplace, underestimate the alcohol intake. An important limitation of the study is that the study of alcohol intake is not the primary outcome of the study and therefore more detailed data on CDT positives are lacking (such as stratification by professional activity) but in any case it is noted that CDT is a tool useful for investigating work environments to verify how alcohol can influence other occupational exposures, in fact the authors conclude by stating that the measurement of sCDT should be considered used in future epidemiological studies of neurotoxicity in Mn exposed populations. In the work of Kilo et al [34] the authors used a questionnaire on alcohol consumption habits and biomarkers such as ethylglucuronide and CDT; as a strength in the selection of the sample there is that of having selected a working population that had no known exposures to substances that could affect liver function; the workers and controls were taken from the chemical sector both in the production sector and in the office sector. 13.1% of the workers resulted with values exceeding the CDT limit; this figure of 13.1% must be contextualized to the fact that the workers covered by the study have no restrictions on the use of alcohol. From the study conducted, it emerges that a very delicate part of the investigation is always characterized by the interview on alcohol habits which, as also highlighted by Popham and Schmidt [35], in addition to being unreliable, is also a sensitive issue in assessments of work environments. Another slightly critical aspect is that in the same study the authors, having used two different laboratories, used two different CDT analysis methods (nephelometry and capillary electophoresis) with different cut-off values (respectively 2.6 and 1.3%) and subsequently have used for the comparison the z-score transformation. In this study, too, detailed data on the positivity of worker-related CDT is lacking. De Sio et al. [36] conducted a study on Office Workers on a sample of 157 workers and as many controls (non-workers) using, among other markers, that of the CDT; analysis of the data reveals a difference in CDT between office workers (7.0%) and unemployed (13.4%) even if this difference is not significant ($p = 0.06$), the study appears weak due to the small number of subjects on the type of analysis that was conducted (matching procedure using Propencity score). The selection of the sample appears critical under different aspects, in the first instance they are workers who come to a medical evaluation to obtain licenses, licenses to shoot and therefore in the event of a positive outcome for alcohol they would be withdrawn or not confirmed these licenses, this could involve the fact that the subjects come to visit after abstention from alcohol use (knowing that the same will be evaluated); the workers chosen for the study also do not carry out work activities for which an alcohol intake control is required.

Neumann et al. [37] conducted a study on 509 workers, comparing acute and chronic alcohol consumption biomarkers. The workers were selected during medical visits at employment agencies and from occupational health units, the subjects regularly underwent evaluation concerning drinking risk and were predominantly unemployed. Overall, positive CDT values were highlighted in 24% of the cases (126 samples) analyzed with high performance liquid chromatography (cut off were set at values ≥ 2.0%).

Comparing the data on the frequency of cases of positive CDT highlighted significant differences in the populations observed in the different studies (Table 2).

An interesting aspect that emerged from the analysis of the literature is that although 6 works have been selected globally, the methods of analysis used by the different authors are different and that with the same methods, depending on the calibrations used for the instruments, we also have different cut-offs (Table 3).

Discussion

This review represents an attempt to provide an updated overview of the current state of knowledge on the use of CDT as a biomarker, noting its strengths and weaknesses in screening workers for the verification of alcohol consumption.

CDT is the only FDA approved marker test for the identification of hazardous drinking [38]. There are many articles in the literature, but little research has focused on the usefulness of this biomarker as a screening indicator in occupational health care populations.

The analysis of the literature reveals an interesting aspect in the field of occupational medicine and that is that there is still a shortage of jobs where CDT is used as an examination for monitoring the use of alcohol or its correlation to occupational injuries [39] , on the contrary there are more jobs where CDT is used as a mass screening tool and therefore outside the interventions of the occupational physician. This lack of data in the specific occupational medicine literature is probably caused by the fact that the detection of positivity in tracing tests for the use of alcohol in the workplace is the cause most of the time of sanctions on the worker that they may have - in some cases - even consequences on job stability. Due to this aspect that affects the working population, a selection bias that is generated in the recruitment of workers in screening campaigns must also probably be attributed. In fact, it should be noted that where screening is voluntary, it allows all workers, aware of breaking the rules on the use of alcoholic beverages, not to undergo tests and therefore to generate an underestimation of the observed event. Still on the nature of the risk of being identified as workers at risk of drinking alcoholic beverages - with all the sanctioning consequences of the case - the not always consistent association between positive CDT and positive questionnaires must be attributed. The latter in fact, being based on the outing of the worker who finds himself having to "confess" his problem related to alcohol, appear as strongly weakened tools when used in the workplace and even more so when they must be filled in by name and not with respect for anonymity. In this regard, perhaps it is possible to say that if in screening checks the audit and CDT can be considered complementary tools, in occupational medicine and if used as nominal tools in the workplace, questionnaires run the risk of being not very representative of the picture. of reality. To confirm the complex picture found in the use of medical history tools on alcohol intake in working populations, there is also Elligsen [32] who notes that the retrospective self-assessment of alcohol consumption underestimates real consumption, in particular for those with high consumption [33].

In the use of these different screening tools (questionnaires and biomarkers), the discrepancy of results appears extremely critical in occupational medicine, placing the occupational physician in the face of important case management issues in the face of discordant results; in fact, in these cases, while respecting the necessary clinical observation over time to better understand the case, the occupational physician has the task of suspending from work individuals who may be at risk for safety reasons for the worker himself and third parties. The non-concordance of the tests (CDT and AUDIT) was also highlighted by the present analysis of the literature in the study by Hermansson et al. [30], showing that the majority of workers are not open about their alcohol consumption and voluntarily underestimate it [40]. The need for a systematic review on CDT as a marker in occupational health arises from the knowledge that questionnaires as a measuring tool in workers present many difficulties; objective biomarkers, such as CDT, should therefore be studied and routinely used.

The main limitations of the studies reviewed are the recruitment of workers on a voluntary basis [29, 30], this clearly creates a selection bias by excluding (as mentioned they avoid screening) the subjects with greater problems.

Conclusions

The CDT is found, also in line with the data collected in this review, a useful tool for investigation in the workplace and for the analysis of conditions related to the use of alcohol in the workplace but also to verify how alcohol may influence other occupational exposures, such as chemical agents that affect liver function or whose hepatic metabolism can cause activation or inactivation of metabolites with harmful effects on the health of workers.

The topic dealt with is of great importance in the Italian and European context. In fact, the Italian legislation (which transposes European Directives) requires the Occupational Physician to verify the absence of alcohol addiction conditions for some professions. In this regard, it should be specified that the CDT examination is a simple biomarker that can at most identify a risk situation and that the diagnosis of alcohol dependence is based on clinical and non-laboratory criteria.

Ultimately, it is clear that further studies are needed to be able to strongly validate the use of CDT in the working population as a screening test and therefore as an operational tool for detecting conditions at risk of alcohol dependence in the working population.

Table 3: CDT analysis and cut-offs.

	CDT Methodology	Cut-off
Hermansson et al. 2000	RIA	<20 U/l for men
		<27 U/l for women
Hermansson et al. 2003	RIA	<20 U/l for men
		<27 U/l for women
Perez et al. 2014	Immunoturbidimetric assay	2.60%
Elligsen et al. 2014	capillary electrophoresis	1.70%
Kilo et al. 2016	nephelometry	2.60%
	capillary electrophoresis	1.30%
De Sio et al. 2020	capillary electrophoresis	1.60%
Neumann J et al. 2020	high performance liquid chromatography	≥ 2.0%

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