

Effectiveness of the CAGE questionnaire, gamma-glutamyltransferase and mean corpuscular volume of red blood cells as markers for alcohol-related problems in the workplace

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Abstract

Objective: To evaluate the usefulness of gamma-glutamyltransferase (GGT) and mean corpuscular volume (MCV), as well as that of the CAGE questionnaire, in workplace screening for alcohol abuse/dependence.

Methods: A total of 183 male employees were submitted to structured interviews (Structured Clinical Interview for DSM-IV 2.0 and CAGE questionnaire). Blood samples were collected. Diagnostic accuracy and odds ratio were determined for the CAGE, GGT and MCV.

Results: The CAGE questionnaire presented the best sensitivity for alcohol dependence (91%; specificity, 87.8%) and for alcohol abuse (87.5%, specificity, 80.9%), which increased when the questionnaire was used in combination with GGT (sensitivity, 100% and 87.5%, respectively; specificity, 68% and 61.5, respectively). CAGE positive results and/or alterations in GGT were less likely to occur among employees not presenting alcohol abuse/dependence than among those presenting such abuse (OR for CAGE=13, $p<0.05$; OR for CAGE-GGT=11, $p<0.05$) or dependence (OR for CAGE=76, $p<0.01$; OR for GGT=5, $p<0.01$). Employees not presenting alcohol abuse/dependence were also several times more likely to present negative CAGE or GGT results.

Conclusions: The use short, simple questionnaires, combined with that of low-cost biochemical markers, such as GGT, can serve as an initial screening for alcohol-related problems, especially for employees in hazardous occupations. The data provided can serve to corroborate clinical findings.

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Keywords: Alcohol-related disorders; CAGE; Biological markers; Screening; Workplace

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1. Introduction

Alcohol abuse has been associated with low productivity, family distress and legal problems, all of which result in substantial costs to society (Harwood, 2000). According to the World Health Organization (WHO Report, 2002), alcohol consumption is the leading cause of increased numbers of disability adjusted life years (DALYs) in Brazil. In addition, as reported by the Social Welfare Administration (Odo et al., 2000), alcohol dependence is the third leading cause of overall absenteeism and the eighth leading cause of absenteeism due to illness.

To date, screening programs for alcohol-related problems in the workplace have been based on laboratory tests to detect alcohol consumption. However, these tests are not valid indicators of the social or behavioral problems caused by alcohol consumption (International Labour Office, 1996). Biological markers employed to indicate alcohol consumption have been included in mandatory periodic health checkups (Yano, Tagawa, Yamaoka, & Mori, 2001), fitness-for-job assessments (Arndt et al., 1998) and screening programs for alcohol-related problems. The major biological markers of alcohol consumption currently being used are gamma-glutamyltransferase (GGT), carbohydrate-deficient transferrin, and red blood cell volume, referred to as mean corpuscular volume (MCV) (Burge & Schneider, 1999; Litten & Allen, 1998; Sillanaukee, 1996). These two biological markers (GGT and MCV) are the only ones that are widely used (Bataille et al., 2003).

According to Aalto and Seppä (2005), 98% of primary care physicians in Finland (2.5% of them working in the field of occupational health care) reported using laboratory markers of alcohol consumption, such as GGT and MCV, for screening purposes. In the United States, Miller, Ornstein, Nietert, and Anton (2004) found that, in screening for alcohol abuse, MCV and GGT are used by, respectively, 54.2% and 35% of Practice Partner Research Network physicians. The authors also found that reluctance to order such tests was related to unfamiliarity with their use and interpretation.

Various studies have assessed the diagnostic accuracy of biochemical markers in determining the level and frequency of alcohol consumption (Anton, Lieber, & Tabakoff, 2002; Bataille et al., 2003; Glasinovic et al., 2001). Structured questionnaires such as the alcohol use disorders identification test (Hermansson, Knutsson, & Brandt, 2003) and CAGE questionnaire (Aertgeerts, Buntinx, Ansoms, & Fevery, 2001; Reynaud et al., 2000), as well as the criteria for alcohol abuse established in the DSM-III-R (Mundle, Ackermann, Munkes, Steinle, & Mann, 1999), and DSM-IV (Reynaud et al., 2000), have been also used.

In an analysis of six different clinical studies involving male subjects, Sillanaukee and Olsson (2001) observed that GGT presented a sensitivity of 59% and a specificity of 91% for identifying alcohol abuse. In another study (Reynaud et al., 2000), the sensitivity of MCV in the general population was found to be 24% for alcohol abuse and 63% for alcohol dependence, with a positive predictive value (PPV) of 83% and 93%, respectively. The authors found that the specificity of MCV for both conditions was 96%.

The performance of the CAGE questionnaire in screening patients with current alcohol abuse/dependence has been found to present a sensitivity of 21–94%, with a specificity of 77–97% (Aertgeerts et al., 2001; Fiellin, Reid, & O'Connor, 2000). In primary care settings or in the general population, the sensitivity of the CAGE questionnaire for dependence has been shown to be 82% and 75%, respectively, with a specificity greater than 90% (Cherpitel, 1998).

The debate surrounding the issue of whether biological markers are the most appropriate method of screening for alcohol abuse, achieving confirmation of suspicion of such abuse, monitoring abstinence and detecting relapses has yet to be resolved (Harasymiw & Bean, 2001). However, few studies have evaluated the diagnostic accuracy of using these tests in the workplace according to the diagnostic criteria for alcohol abuse/dependence.

The aim of this study was to evaluate the diagnostic accuracy and effectiveness of each biological marker and CAGE questionnaire in a sample of employees of a public university according to objective (DSM-IV) criteria for alcohol abuse/dependence.

2. Materials and methods

2.1. Sample

The initial study sample consisted of 183 male employees, randomly selected from among the 427 working in the Campus Administration sector of the University of São Paulo. The selection was made based on employee identification numbers: workers whose identification number ended in an even number were selected. Those who reported having been on medical leave ($n=8$) were excluded. Of the remaining 175 subjects invited to participate of the study, 3 refused to be interviewed, and 3 refused to have blood collected. Therefore, the final sample consisted of 169 subjects; all of whom gave written informed consent. This project was reviewed and approved by the Ethics Committee of the University of São Paulo School of Medicine Psychiatry Department. All participating subjects gave written informed consent prior to their inclusion in the study.

2.2. Measures

Subjects completed a sociodemographic questionnaire, as well as being submitted to a structured interview based on the DSM-IV criteria for alcohol abuse/dependence, known as the Structured Clinical Interview for DSM-IV (SCID 2.0), and completing the CAGE questionnaire (subjects responding affirmatively to two or more questions were classified as CAGE positive). A trained psychiatrist administered the questionnaires and conducted the interviews. Following the interview, blood samples were collected from the respondents.

2.3. Laboratory procedures

The clinical analysis laboratory of the University of São Paulo School of Pharmacy carried out the blood tests. A spectrophotometer (model U-3210; Hitachi, Tokyo, Japan) was used to determine the levels of liver enzymes. The GGT reference value at 37 °C was 7–45 U/L for males. A hematology analyzer (Cell-Dyn 1400; Abbott, Abbott Park, IL, USA) was used to determine blood cell size through electrical impedance, thereby allowing the calculation of the MCV. The reference value was 82–92 fL.

2.4. Statistical analysis

Univariate analyses were performed using the chi-square test and Fisher's exact test for categorical data. Age and numeric values for each biological marker are expressed as means and standard deviations. Differences between the groups were compared using the Student's *t*-test. Values of $P<0.05$ were considered statistically significant.

The diagnostic accuracy of the CAGE questionnaire and each biological marker, as well as of the GGT-CAGE, MCV-CAGE, GGT-MCV and GGT-MCV-CAGE combinations, was determined by calculating the sensitivity, specificity, predictive values and the receiver operating characteristic (ROC) curves

Table 1

Sociodemographic characteristics, gamma-glutamyltransferase and mean corpuscular volume values of the campus administration employees ($n=169$) classified as having no alcohol-related problems (NARP) or as presenting alcohol abuse (AA) or alcohol dependence (AD)

Sociodemographic characteristic	NARP $n=139$	AA $n=8$	AD $n=22$
Age (years \pm SD)*	45.4 \pm 9.3 n (%)	42.1 \pm 8.0 n (%)	47.4 \pm 8.5 n (%)
Family status			
Living with a spouse or steady partner	115 (82.7)	6 (75.0)	17 (77.3)
Living alone	24 (17.3)	2 (25.0)	5 (23.70)
Education			
≤ 8 years	110 (79.2)	4 (50.0)	21 (95.5)
> 8 years	29 (20.8)	4 [†] (50.0)	1 (4.5)
Occupation			
Maintenance	77 (55.4)	5 (62.5)	16 (72.7)
Other occupations	62 (44.6)	3 (37.5)	6 (27.3)
Clerical	23 (16.5)	0 (0.00)	2 (9.1)
Security	22 (15.8)	1 (12.50)	2 (9.1)
Driver	17 (12.3)	2 (25.0)	2 (9.1)
GGT (U/L \pm SD)*	48 \pm 63	120 \pm 73 [‡]	151 \pm 178 ^{††}
MCV (fL \pm SD)*	89 \pm 5	89 \pm 5	90 \pm 5

NARP: no alcohol-related problems group; AA: alcohol abuse group; AD: alcohol dependence group; SD: standard deviation; GGT: gamma-glutamyltransferase; MCV: mean corpuscular volume.

*Student's *t*-test.

[†] $p=0.02$.

[‡] $p=0.03$ vs. NARP.

^{††} $p=0.06$ vs. NARP.

according to laboratory reference values. In the tests involving the CAGE-GGT-MCV combination, a positive result was defined as an alteration or an elevation of at least one of the three, whereas the levels of both markers being below the cut-off point, together with CAGE negativity, was considered a negative result.

The ROC curves were constructed in order to provide a clear accuracy index for each test in which an area under the curve (AUC) >0.5 distinguished between the groups. A value of $P<0.05$ indicates that the AUC is significantly different from 0.5 (Zweig & Campbell, 1993). Odds ratios (ORs) were used to assess the relationships among the CAGE result, the biological markers and the groups. Statistical analyses were performed using the Statistical Package for Social Sciences, version 10.0 for Windows.

3. Results

According to the DSM-IV criteria, the prevalence of alcohol abuse/dependence for male Campus Administration employees during the year preceding the study was 4.7% ($n=8$) and 13% ($n=22$), respectively. Subjects were divided into three groups: the alcohol abuse (AA) group, the alcohol dependence (AD) group and the no alcohol-related problems (NARP) group ($n=129$, 82.3%).

Table 2

Sensitivity, specificity, predictive values and areas under the ROC curve of gamma-glutamyltransferase, mean corpuscular volume, CAGE and the combination of the three for identifying alcohol abuse and alcohol dependence

Diagnostic accuracy	GGT	MCV	CAGE	GGT+ CAGE	MCV+ CAGE	GGT+ MCV	GGT+MCV+ CAGE
	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)	% (95% CI)
Sensitivity							
AA	62.5 (26–90)	12.5 (1–53)	87.5 (47–99)	87.5 (47–99)	75.0 (36–95)	62.5 (26–90)	87.5 (47–99)
AD	63.6 (41–82)	45.5 (25–67)	90.9 (69–98)	100 (81–100)	95.5 (75–100)	72.7 (50–88)	100 (81–99)
Specificity							
AA	69.6 (62–76)	72.7 (65–79)	80.9 (74–86)	61.5 (53–69)	62.6 (55–70)	55.3 (47–63)	49.7 (42–58)
AD	72.8 (65–80)	76.2 (68–83)	87.8 (81–92)	68.0 (60–75)	70.1 (62–77)	58.5 (50–66)	55.1 (47–63)
PPV							
AA	9.3 (3.5–21)	2.2 (0.1–13)	18.4 (8–35)	10.1 (4.5–20)	9.0 (4–19)	6.5 (2–15)	8.0 (3.5–16)
AD	25.9 (15–40)	22.2 (12–37)	52.6 (36–69)	31.9 (21–44)	32.3 (21–45)	20.8 (13–32)	25.0 (17–36)
NPV							
AA	97.4 (92–99)	94.4 (88–97)	99.2 (95–100)	99.0 (94–100)	98.1 (92–100)	96.7 (90–99)	98.8 (92–100)
AD	93.0 (86–97)	90.3 (83–95)	98.5 (94–100)	100 (95–100)	99.0 (94–100)	93.5 (86–97)	100 (94–100)
AUC							
AA	78* (60–96)	66 (46–86)	43 (24–61)	74 [†] (59–89)	69 (51–87)	58 (38–78)	68 (52–84)
AD	90 [‡] (82–97)	68* (56–80)	61 (47–74)	84 [‡] (78–90)	83 [‡] (75–90)	65 (53–77)	77 [‡] (69–84)

GGT: gamma-glutamyltransferase; MCV: mean corpuscular volume; 95% CI: 95% confidence interval; AA: alcohol abuse group; AD: alcohol dependence group; AUC: area under the (receiver operating characteristic) curve; 95%.

[‡] $p < 0.001$.

* $p < 0.01$.

[†] $p = 0.02$.

The mean age was lowest in the AA group, although the differences between the groups were not significant. As shown in Table 1, 138 (77.5%) of the Campus Administration workers evaluated were married or cohabitating, whereas only 31 (23.5%) were living alone. The majority (80%) had less than 8 years of schooling, and 58% worked in the maintenance division. There was a significant association between the presence of alcohol abuse and having had more than 8 years of schooling ($n=4$, 11%). The majority (79.8%) had had less than 8 years of schooling, and 58% worked in the maintenance division.

The highest GGT values (Table 1) were seen in the AD group. Means for AA and AD groups were statistically different from those obtained for the NARP group. The MCV values were slightly higher in the AD group than in the other groups, although there were no differences between the AA group and the AD group.

The diagnostic accuracy of the CAGE questionnaire, GGT and MCV for alcohol abuse/dependence are presented in Table 2. The CAGE questionnaire, alone or in combination with GGT, MCV or both, presented the greatest sensitivity for alcohol abuse (87.5%). Regarding alcohol dependence, the sensitivity of the CAGE questionnaire was nearly 91%, compared with 100% for the combinations CAGE-GGT and CAGE-GGT-MCV. The probability of a positive result on the CAGE questionnaire expressing the presence of abuse was somewhat less than 20%, although it reached 50% for dependence. In contrast, the negative predictive value (NPV) for CAGE, GGT or MCV, alone or in combination, for not presenting alcohol abuse/dependence, was greater than 90%, reaching 99.2% for abuse (CAGE) and 100% for dependence (CAGE-GGT and CAGE-GGT-MCV).

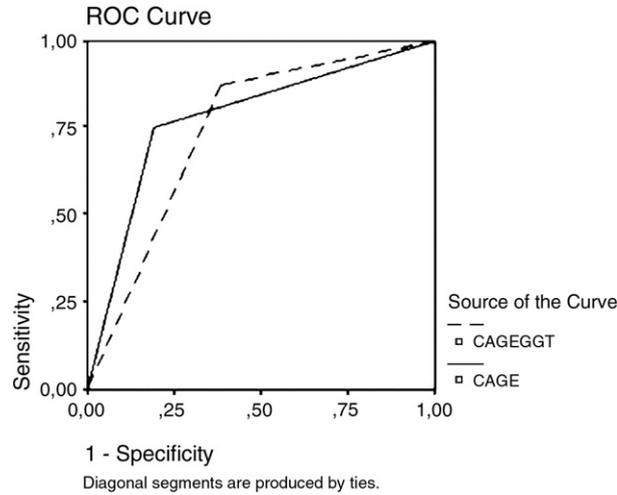


Fig. 1. Receiver operating characteristic curves for CAGE and the combination of CAGE-gamma-glutamyltransferase (GGT) in the alcohol abuse group.

In the ROC curve (Table 2), CAGE and the CAGE-GGT combination were statistically different from the null hypothesis of area for alcohol abuse (Fig. 1). The largest AUC with discriminative power was for the AD group and CAGE ($p < 0.001$). Results for CAGE and its use in conjunction with GGT, MCV and the GGT-MCV combination (Fig. 2) were above the null hypothesis of area for the AD group ($P < 0.05$).

The ORs for CAGE, GGT, MCV and the CAGE-GGT-MCV combination are summarized in Table 3. Employees in the AA group and in the AD group were thirteen times and seventy six times more likely to present positive CAGE results ($OR = 13, p < 0.05, OR = 76, p < 0.01$, respectively). The AD group was five times more likely to have alterations in GGT than were those in the NARP group ($OR = 5, p < 0.012$).

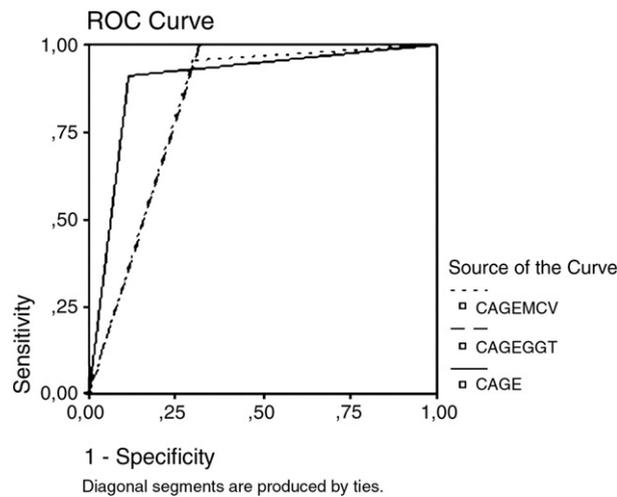


Fig. 2. Receiver operating characteristic curves for CAGE and the combination of CAGE-gamma-glutamyltransferase (GGT) and CAGE-mean corpuscular volume (MCV) in the alcohol dependence group.

Table 3

Statistical comparisons related to the use of CAGE, gamma-glutamyltransferase and mean corpuscular volume of the groups studied

Group	CAGE	GGT	MCV	CAGE+GGT	CAGE+MCV	CAGE+GGT+MCV
	OR (95%CI)					
AA	13 (3–89)*	4 (0.8–19)	0.4 (0.2–2)	11 (2–212)*	5 (1–36)	6 (1–130)
AD	76 (20–507) ‡	5 (2–12) ‡	2.6 (1–7)	–	49 (10–89)	–
NARP	0.01 (0.04–0.003) ‡	0.2 (0.2–0.4) ‡	0.5 (0.2–1)	0.01 (0.06–1300) ‡	0.04 (0.009–0.1)*	0.02 (0.001–0.1) ‡

GGT: gamma-glutamyltransferase; MCV: mean corpuscular volume; OR: odds ratio; 95% CI: 95% confidence interval; AA: alcohol abuse group; AD: alcohol dependence group; NARP: no alcohol-related problems group.

* $P < 0.05$.

‡ $P < 0.01$.

The chance that employees in the NARP group would produce positive CAGE results or CAGE positive results with some alteration in GGT, or positive results for one of the CAGE-biochemical marker combinations, was significantly lower than that of employees in the AA and AD groups.

4. Discussion

The objectives of this study were to determine the validity of GGT and MCV for alcohol-related problems in the workplace and to evaluate their effectiveness in prevention programs by examining the presence of these problems among male employees of the University of São Paulo Campus Administration sector, which is primarily a maintenance service for several common areas of the West Campus of the University. Since there are few female Campus Administration employees ($n = 11$), they were not included in the study.

The prevalence of alcohol dependence among the males working in the Campus Administration sector was 13%, lower than the 16% prevalence for males 35 years of age or older in Brazil as a whole (Carlini, Galduróz, Noto, & Nappo, 2002). The lower prevalence among Campus Administration employees might be an example of the ‘healthy worker’ effect, by which segments of the working population exhibit better health status than that seen in the general population. With regard to sociodemographic data, alcohol abuse was significantly associated with more than 8 years of study, while studies on the subject has seen the opposite (Crum, Bucholz, Helzer, & Anthony, 1992; Marques-Vidal et al., 2000). These data may reflect the difference in average years of study among Brazilians occupied with less than 40 years (7.5 years) and with more than 40 years (5.4 years) (IBGE, 2006).

No other statistical differences were found among the groups (NARP, AA and AD) in terms of sociodemographic characteristics. However, it is important to note that 19% of the professional drivers ($n = 21$) were found in the AA subgroup ($n = 2$) or AD subgroup ($n = 2$).

The selection of workers for hazardous occupations, as well as their sociodemographic characteristics and the prevalence of the disease are strongly related to the definition of preventive strategies for alcohol-related problems in the workplace. Henderson, Hutcheson, and Davies (1996) cited the following reasons to conduct workplace screenings for alcohol abuse: pre-employment evaluation, random testing, with-cause testing, routine testing and follow-up testing. However, suspecting an employee of alcohol abuse or dependence has some specific implications and obligations. Tests of high sensitivity and specificity are needed for such workplace screening testing.

Among the instruments employed in this study, the CAGE questionnaire was the most sensitive and specific, mirroring the findings reported in the review conducted by [Fiellin et al. \(2000\)](#) and producing striking results related to NPV (CAGE for AA, NPV=99.2%; CAGE for AD, NPV=98.5%). In order to properly interpret the results of the CAGE questionnaire, it should be borne in mind that the CAGE questionnaire is capable of detecting heavy or risk consumption of alcohol, which can account for the false-positive results obtained in the present study (CAGE for AA, PPV=18.4%; CAGE for AD, PPV=52.6%), as well as for those obtained in the study mentioned above. It is also of note that the CAGE questionnaire was designed to evaluate a retrospective period of four weeks. Therefore, the CAGE-negative results in the AA and in the AD group might indicate abstinence during this period.

[Aertgeerts et al. \(2001\)](#) found that the use of biochemical markers alone in screening for alcohol abuse/dependence in outpatient primary care produced unsatisfactory results. [Reynaud et al. \(2000\)](#) evaluated the combined use of GGT and MCV in outpatient centers for alcohol problems and in the specialized alcohol-dependency unit of a hospital and found that GGT, MCV and the GGT-MCV combination presented markedly greater sensitivity for dependence (90%), and that the specificity remained relatively high (PPV > 75%). However, in the present study, the PPV of GGT and MCV both was < 26% among the Campus Administration employees. This discrepancy could be related to differences in the study setting. Here, once again, it is important to note that the health status of employees in a workplace should, logically, be better than that of patients treated in a primary care facility or a specialized clinic. The prevalence of health problems in general and of disorders related to alcohol would be expected to be lower among the workers than among the patients, the latter group being more likely to present high rates of alcohol consumption.

The use of the CAGE questionnaire in combination with GGT, MCV or both allowed us to identify all individuals with alcohol dependence, but presented progressive worsening in specificity and in the likelihood of high levels of a positive result come from an individual with alcohol dependence (PPV < 32%).

Negative results for the CAGE, CAGE-GGT or CAGE-GGT-MCV in pre-employment screening tests might indicate a low probability of alcohol abuse/dependence (NPV = 100% for the CAGE and NPV = 99% to CAGE-GGT), whereas positive results might indicate a misidentification rate of 50% (CAGE for AD) or even 100% (MCV for AA). Positive results for the CAGE and GGT would not confirm or rule out the presence of alcohol abuse or dependence. Therefore, when these instruments are used in random testing, the results should be interpreted with caution. It is recommended, considering the OR observed, particularly in the selection of employees for hazardous occupations, the careful interpretation of the negative results obtained. We suggest an algorithm ([Fig. 3](#)) for the application of examinations, the interpretation of the results and the evaluation of the potential consequences of those results ([Fig. 3](#)). Nevertheless, the routing of employees to preventive programs at different levels should not be construed as a confirmation of diagnosis but rather as an indication of increased risk to the individual and to the company.

The use of such tests to confirm supervisor or manager suspicions in a with-cause or routine testing must be avoided. In view of the low specificity of the biological markers, it is likely that there are clinical conditions other than alcohol-related problems that could explain the false-positive results.

Some limitations of this study should be noted. Due to the sociodemographic characteristics of the Campus Administration, it was not possible to assess the accuracy of the instruments among female workers. The CAGE questionnaire has not been evaluated for its ability to detect patterns of heavy or risk consumption. In addition, medical conditions that can alter GGT and MCV results were not studied. In interpreting the results, however, the possibility of other conditions has been suggested. The cross-sectional design of this study did not allow the relationship between the changes in the results for each of

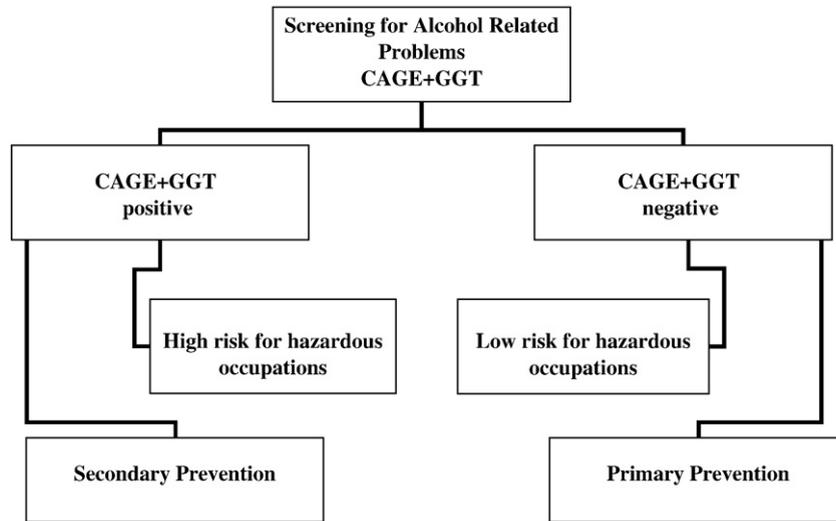


Fig. 3. Screening for alcohol-related problems algorithm in the workplace.

the instruments and the time of abstinence. Therefore, the application of the instruments in follow-up testing was not evaluated. Another important aspect is the fact that this study did not employ the carbohydrate-deficient transferrin marker, which has been shown to have, for males, a sensitivity of 65–79% and a specificity of 94% (Sillanaukee & Olsson, 2001). However, considering the cost of this test, it is important to remember that health checkups have become increasingly more expensive, representing increases of up to 70 US dollars per examinee (Yano et al., 2001).

The use short, simple questionnaires, combined with that of low-cost biochemical markers, such as GGT, can serve as an initial screening for alcohol-related problems, especially for employees in hazardous occupations. The data provided can serve to corroborate clinical findings.

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References

- Aalto, M., & Seppä, K. (2005). Use of laboratory markers and AUDIT questionnaire by primary care physicians to detect alcohol abuse by patients. *Alcohol and Alcoholism*, *40*, 520–523.
- Aertgeerts, B., Buntinx, F., Ansoms, S., & Fevery, J. (2001). Screening properties of questionnaires and laboratory tests for the detection of alcohol abuse or dependence in a general practice population. *British Journal of General Practice*, *51*, 206–217.
- Anton, R. F., Lieber, C., & Tabakoff, B. (2002). Carbohydrate-deficient transferrin and gamma-glutamyltransferase for the detection and monitoring of alcohol use: Results from a multisite study. *Alcoholism, Clinical and Experimental Research*, *26*, 1215–1222.
- Arndt, V., Brenner, V., Rothenbacher, D., Zschenderlein, B., Fraisse, E., & Fliedner, T. M. (1998). Elevated liver enzyme activity in construction workers: Prevalence and impact on early retirement and all-cause mortality. *International Archives of Occupational and Environmental Health*, *71*, 405–412.

- Bataille, V., Ruidavets, J. -B., Arveiler, D., Amouyel, P., Ducimetiere, P., Perret, B., et al. (2003). Joint use of clinical parameters, biological markers and CAGE questionnaire for the identification of heavy drinkers in a large population-based sample. *Alcohol and Alcoholism*, 38, 121–127.
- Burge, S. K., & Schneider, D. (1999). Alcohol-related problems: Recognition and intervention. *American Family Physician*, 59, 361–370.
- Carlini, E. A., Galduróz, J. C. F., Noto, A. R., & Nappo, A. S. (2002). I Levantamento domiciliar sobre o uso de drogas psicotrópicas no Brasil: Estudo envolvendo as 107 maiores cidades do País—2001. *CEBRID—Centro Brasileiro de Informações Sobre Drogas Psicotrópicas: UNIFESP—Universidade Federal de São Paulo, São Paulo*.
- Cherpitel, C. J. (1998). Performance of screening instruments for identifying alcohol dependence in the general population, compared with clinical populations. *Alcoholism, Clinical and Experimental Research*, 22(7), 1399–1404.
- Crum, R. M., Bucholz, K. K., Helzer, J. E., & Anthony, J. C. (1992). The risk of alcohol abuse and dependence in adulthood: The association with educational level. *American Journal of Epidemiology*, 135, 989–999.
- Fiellin, D. A., Reid, M. C., & O'Connor, P. G. (2000). Screening for alcohol problems in primary care. *Archives of Internal Medicine*, 160, 1977–1989.
- Glasinovic, J. C., Lobos, X., Scriveranti, M., Severin, M. C., Quiroga, T., & Moncada, C. (2001). Carbohydrate deficient transferrin, gammaglutamyl transferase and mean corpuscular volume in the evaluation of recent alcohol intake in excessive drinkers. *Revista Médica de Chile*, 129, 375–381.
- Harasymiw, J., & Bean, P. (2001). The combined use of the early detection of alcohol consumption (EDAC) test and carbohydrate-deficient transferrin to identify heavy drinking behaviour in males. *Alcohol and Alcoholism*, 36, 349–353.
- Harwood, H. (2000). Updating estimates of the economic costs of alcohol abuse in the United States: Estimates, update methods, and data. *Report prepared by The Lewin Group for the National Institute on Alcohol Abuse and Alcoholism, Rockville*.
- Henderson, M., Hutcheson, G., & Davies, J. (1996). Testing and screening. In: *Alcohol and the Workplace*. Copenhagen: WHO Regional Publications, European Series. Geneva 67, pp. 50–51.
- Hermansson, U., Knutsson, A., Brandt, L., Huss, A., Rönnerberg, S., & Helander, A. (2003). Screening for high-risk and elevated alcohol consumption in day and shift workers by use of the AUDIT and CDT. *Occupational Medicine*, 53, 518–526.
- IBGE—Instituto Brasileiro de Geografia e Estatística (2006). *Pesquisa nacional por amostra de domicílios*. www.ibge.gov.br.
- International Labour Office (1996). *Management of alcohol and drug-related issues in the workplace. Appendix V* (pp. 42). Geneva.
- Litten, R. Z., & Allen, J. P. (1998). Clinical application of biochemical markers of alcohol consumption. In J. P. Allen & F. Poldrugo (Eds.), *Use of carbohydrate deficient transferrin among general practitioners*. Geneva: International Council on Alcohol Addictions—ICAA publication Lausanne.
- Marques-Vidal, P., Arvelier, D., Evans, A., Montaye, M., Bingham, A., Ruidavets, J. B., McMaster, D., Haas, B., Amoyel, P., & Ducimetière, P. (2000). Patterns of alcohol consumption in middle-aged men from France and Northern Ireland. The PRIME Study. *European Journal of Clinical Nutrition*, 54(4), 321–328.
- Miller, P. M., Ornstein, S. M., Nietert, P. J., & Anton, R. F. (2004). Self-report and biomarker alcohol screening by primary care physicians: The need to translate research into guidelines and practice. *Alcohol and Alcoholism*, 39, 325–328.
- Mundle, G., Ackermann, K., Munkes, J., Steinle, D., & Mann, K. (1999). Influence of age, alcohol consumption and abstinence on the sensitivity of carbohydrate-deficient transferrin, gamma-glutamyltransferase and mean corpuscular volume. *Alcohol and Alcoholism*, 34, 760–766.
- Odo, S. A., Araújo, A. C., Santos, A. F., Toledo, F. C. P., Yonamine, M., Silva, A. O., & Leite, M. C. (2000). Indicações e limites das análises toxicológicas para substâncias psicoativas. *Revista de Psiquiatria Clínica*, 27, 50–56.
- Reynaud, M., Schellenberg, F., Loiseux-Meunier, M. -N., Scwan, R., Maradeix, B., Planche, F., et al. (2000). Objective diagnosis of alcohol abuse: Compared values of carbohydrate-deficient transferrin (CDT), gamma-glutamyltransferase (GGT), and mean corpuscular volume (MCV). *Alcoholism, Clinical and Experimental Research*, 24, 1414–1419.
- Sillanaukee, P. (1996). Laboratory markers of alcohol abuse. *Alcohol and Alcoholism*, 31, 613–616.
- Sillanaukee, P., & Olsson, U. (2001). Improved diagnostic classification of alcohol abusers by combining carbohydrate-deficient transferrin and gamma-glutamyltransferase. *Clinical Chemistry*, 47, 681–685.
- WHO REPORT (2002). *Reducing risks, promoting healthy life*. Geneva: WORLD HEALTH ORGANIZATION.
- Yano, E., Tagawa, K., Yamaoka, K., & Mori, M. (2001). Test validity of periodic liver function tests in a population of Japanese male bank employees. *Journal of Clinical Epidemiology*, 54, 945–951.
- Zweig, M. H., & Campbell, G. (1993). Receiver-operating characteristic (ROC) plots: A fundamental tool in clinical medicine. *Clinical Chemistry*, 39, 561–577.