Screening of alcohol use disorders in psychiatric outpatients: influence of gender, age, and psychiatric diagnosis

Cribaje de trastornos por consumo de alcohol en pacientes psiquiátricos ambulatorios: influencia de género, edad, y diagnóstico psiquiátrico

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Abstract

Alcohol use disorders (AUD) are 2 times higher among psychiatric patients than in the general population. The under-recognition of this dual diagnosis can entail several negative outcomes. Early assessment with a screening tool like the CAGE questionnaire could be an opportunity to improve patients' prognoses. The objective of this study is to assess AUD risk in an outpatient psychiatric sample with a modified CAGE, considering the influence of age, gender and clinical psychiatric diagnosis. An observational, multicentric, descriptive study was carried out. The 4-item CAGE scale, camouflaged in a healthy lifestyle questionnaire, was implemented, using a cut-off point of one. 559 outpatients were assessed. 54% were female and the average age was 50.07 years. 182 patients presented a CAGE score ≥1 (45.1% of men and 21.9% of women). Gender was the strongest predictor of a positive result in CAGE, as men were 3.03 times more likely to score ≥1 on the CAGE questionnaire (p < .001, 95% CI: 0.22-0.49). Patients with bipolar and personality disorders had the highest rates of CAGE scores ≥1 (45.2 and 44.9%, respectively), with a significant association between diagnosis and a positive score (p = .002). Patients above 60 years were 2.5 times less likely to score ≥1 on the CAGE (p = .017, 95% CI: 0.19-0.85). Specific screening questionnaires, like the CAGE scale, can be an easy and useful tool in the assessment of AUD risk in psychiatric outpatients. Male patients with a bipolar or personality disorder present a higher risk of AUD.

Keywords: Alcohol use disorder; CAGE; Screening; Dual pathology; Psychiatric outpatients.

Resumen

Los trastornos por uso de alcohol (TUA) son 2 veces más frecuentes en pacientes psiquiátricos que en la población general. El infradiagnóstico de patología dual puede tener diversas consecuencias negativas; una valoración precoz con herramientas de cribaje como la escala CAGE podría mejorar el pronóstico de estos pacientes. El objetivo de este estudio es valorar el riesgo de TUA en pacientes psiquiátricos ambulatorios con una CAGE modificada, considerando la influencia de edad, género, y diagnóstico psiquiátrico. Se realizó un estudio descriptivo observacional, multicéntrico. La escala CAGE de 4 ítems, camuflada en un cuestionario de vida saludable, se aplicó utilizando el punto de corte de 1. Se valoraron 559 pacientes. El 54% eran mujeres, y la edad media fue de 50,07 años. 182 pacientes presentaron una puntuación ≥1 (45,1% de los hombres y 21,9% de las mujeres). El género fue el predictor principal de un resultado positivo en la escala CAGE, siendo 3,03 veces más probable que los hombres obtengan una puntuación ≥1 (p < ,001, 95% IC: 0,22-0,49). El trastorno bipolar y los trastornos de personalidad presentaron las tasas más altas de puntuaciones ≥1 (45,2 y 44,9%, respectivamente) con una asociación significativa entre diagnóstico y un resultado positivo (p = ,002). Los pacientes de más de 60 años mostraron 2,5 veces menos probabilidades de obtener una puntuación positiva (p = ,017, 95% IC: 0,19-0,85). Cuestionarios específicos, como CAGE, pueden ser herramientas sencillas y útiles para valorar el riesgo de TUA en pacientes psiquiátricos ambulatorios. Los pacientes hombres con trastorno bipolar o de personalidad presentan un riesgo más elevado de TUA.

Palabras clave: Trastornos por uso de alcohol; CAGE; Cribaje; Patología dual; Pacientes psiquiátricos ambulatorios.

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According to a recent study (Rehm et al., 2015), the prevalence of alcohol dependence (AD) in the general population in Europe has been estimated to be around 3.4%. In the Spanish general population, although low rates of AD have been published (1.4% of men and 0.3% of women), rates of at risk alcohol consumption have been considered to be around 4-6% (Pulido et al., 2014). In primary care, higher rates of alcohol use disorder (AUD) and AD have been established (11.7 and 8.9%, respectively) (Miquel et al., 2016). AUD prevalence could probably have been underestimated in Spain due to cultural factors (Rehm, Rehm, Shield, Gmel, & Gual, 2013). Alcohol use disorders (AUD) are more frequent in psychiatric patients than in the general population, with a risk approximately 2 times higher among psychiatric patients (Mansell, Spiro, Lee, & Kazis, 2006; Regier et al., 1990). Dual diagnosis (DD) patients are described as those patients suffering from the co-existence of a psychiatric illness and a substance use disorder, such as AUD (Luoto, Koivukangas, Lassila, & Kampman, 2016; Morojele, Saban, & Seedat, 2012; San et al., 2016; Torrens, Mestre-Pintó, Montanari, Vicente, & Domingo-Salvany, 2017). Several negative outcomes associated with AUD have been described in psychiatric populations. AUD might exacerbate positive symptoms, interfere with treatment adherence, tolerance and response, and worsen the prognosis of psychiatric disorders (Dixon, Weiden, Haas, Sweeney, & Frances, 1992; Duke, Pantelis, & Barnes, 1994; Fowler, Carr, Carter, & Lewin, 1998; Lejoyeux et al., 2013; Noordsy et al., 1991; Sullivan, Fiellin, & O'Connor, 2005; Vorspan, Mehtelli, Dupuy, Bloch, & Lépine, 2015; Worthington et al., 1996). A lower quality of life, social complications, higher rates of violence and suicide, higher frequency and longer hospital admissions have also been described (Cantor-Graae, Nordström, & McNeil, 2001; Dervaux et al., 2006; Drake, Osher, & Wallach, 1989; Gerding, Labbate, Measom, Santos, & Arana, 1999; Hulse & Tait, 2002; Mueser et al., 2000; Mukamal, Kawachi, Miller, & Rimm, 2007; Soyka, 2000; Soyka, Albus, Immler, Kathmann, & Hippius, 2001; Suominen, Isometsä, Haukka, & Lönnqvist, 2004; Urbanoski, Cairney, Adlaf, & Rush, 2007). AUD are also associated with multiple medical conditions and psychiatric comorbidities, and imply negative consequences across physical and psychological outcomes (Bowman & Gerber, 2006; Mathalon, Pfefferbaum, Lim, Rosenbloom, & Sullivan, 2003). Therefore, an early identification of AUD can be useful to prevent several complications, as well as an intervention opportunity to propose an integrated treatment to DD patients.

Under-recognition of AUD in the general population, in clinical settings (Barrio et al., 2016; Ratta-Apha et al., 2014; Shaner et al., 1993; Weisner & Matzger, 2003), and in psychiatric populations (Pristach, Smith, & Perkins, 1993; Smith & Pristach, 1990) has been systematically reported. The literature supports the use of screening instruments to increase early recognition of AUD (Barnaby, Drummond, McCloud, Burns, & Omu, 2003; Fiellin, Reid, & O'Connor, 2000). The CAGE questionnaire is a brief, easily applied, and widely used screening questionnaire in the detection of AUD in the general population (Baltieri & Andrade, 2008; Curran, Gawley, Casey, Gill, & Crumlish, 2009) as well as in clinical (Berks & McCormick, 2008; Fiellin et al., 2000; Lejoyeux et al., 2012; Mitchell, Bird, Rizzo, Hussain, & Meader, 2014) and psychiatric samples (Castells & Furlanetto, 2005; Derks, Vink, Willemsen, van den Brink, & Boomsma, 2014; Etter & Etter, 2004; Kim, Shin, Kim, & Lee, 2016; Lejoyeux et al., 2014; Malet, Schwan, Boussiron, Aublet-Cuvelier, & Llorca, 2005; Oe at al., 2016; Tang et al., 2016). It has also been used to assess geriatric patients (Draper et al., 2015; León-Muñoz et al., 2015), and in gender studies (de Oliveira, Kerr-Correa, Lima, Bertolote, & Santos, 2014).

The CAGE scale consists of four questions on the use of alcohol (Ewing, 1984; Mayfield, McLeod, & Hall, 1974). The name derives from the first letter from the keywords included in each question:

1. Have you ever felt you should cut down on your drinking?
2. Have people annoyed you by criticizing your drinking?
3. Have you ever felt bad or guilty about your drinking?
4. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (eye-opener)?

This questionnaire seems to detect alcohol abuse and dependence more accurately than other screening tools (Fiellin et al., 2000; Hearne, Connolly, & Sheehan, 2002). An average sensitivity of 71% and specificity of 90% for clinical populations has been estimated (Dhalla & Kopec, 2007; Mitchell et al., 2014). It has been validated in several languages, including Spanish (Rodríguez-Martos, 1986). In order to make the interview less intimidating for the patient, modified or "camouflaged" questionnaires derived from the original CAGE have been also designed (Castells & Furlanetto, 2005) and used in general and clinical Spanish populations (Córdoba et al., 1998; Escobar, Espí, & Canteras, 1995; González García et al., 1997; Rodríguez-Martos, 1986; Rodríguez Fernández, Gómez Moraga, & García Rodríguez, 1997), but to date there is a lack of studies in psychiatric Spanish populations. The reliability of the CAGE scale to assess AUD has been validated in psychiatric outpatients, schizophrenic patients and anxiety or depressive disorders (Corradi-Webster, Laprega, & Furtado, 2005; Dervaux et al., 2006; Encrenaz, Kovess-Masféty, Sapinho, Chee, & Messiah, 2007; Rosenberg et al., 1998; Teitelbaum & Mullen, 2000). However, these few studies in mental health population have been focused on a single diagnostic category (Agabio, Marras, Gessa, & Carpiniello, 2007; Dervaux et al., 2006; Etter & Etter, 2004), have not performed comparative analyses between diagnostic

categories (Corradi-Webster et al., 2005; Ratta-Apha et al., 2014; Teitelbaum & Mullen, 2000) or have only included inpatients (Dervaux et al., 2006, Masur & Monteiro, 1983; Rosenberg et al., 1998).

Several authors have described differences in AUD prevalence according to gender in general and psychiatric populations (Cantor-Graae et al., 2001; Dervaux et al., 2006; Eberhard, Nordström, Höglund, & Ojehagen, 2009; Goldstein, Smith, Dawson, & Grant, 2015; Gual et al., 2016; Hasin, Stinson, Ogburn, & Grant, 2007; Keyes, Grant, & Hasin, 2008; Khan et al., 2013; McCreadie, 2002; Pulido et al., 2014; Rehm et al., 2015; Satre, Wolfe, Eisendrath, & Weisner, 2008). The frequency of AUD has also been related to age (Hasin et al., 2007), especially in psychiatric patients (Sheidow, McCart, Zajac, & Davis, 2012). However, the influence of age and gender on the prevalence of AUD, in relation to different psychiatric disorders, has not been thoroughly described.

The primary objective of the present study is to describe the prevalence of AUD in a large Spanish sample of psychiatric outpatients using the "camouflaged" CAGE questionnaire. As secondary objectives, the authors aim to investigate age and gender differences, as well as differences related to the psychiatric clinical diagnosis, according to the CAGE screening results.

Methods

Design and study population

An observational, multicentric, descriptive and transversal study was carried out. The sample was recruited in four different outpatient psychiatric clinics (Centre de Salut Mental Terrassa Rambla, Hospital Universitari Mutua Terrassa, Barcelona; Equipo de Salud Mental de Zafra, Servicio Extremeño de Salud, Badajoz; Equipo de Salud Mental de Llerena, Servicio Extremeño de Salud, Badajoz; Centre de Salut Mental Cornellà, Parc Sanitari Sant Joan de Deu, Barcelona). Patients were recruited using convenience sampling. Due to urban-rural clinical differences in psychiatry (Peen, Schoevers, Beekman, & Dekker, 2010), patients from both settings were included. Even though their exact role varies by region, psychiatric outpatient clinics are essential to mental health care access in Spain.

Inclusion criteria were: older than 18 years, being able to understand the study and provide reliable information, and agree to participate in the study. Patients who did not agree to participate or presented an intellectual disability were excluded. Participants provided written informed consent. This study was approved by the local ethic committees.

Data collection and study procedures

The inclusion period was from May 2015 to August 2015. A total of 559 patients were recruited and interviewed by trained interviewers. After providing informed consent, patients performed an in-person interview and written questionnaires. Sociodemographic data (age and gender) and the ICD-10 (International Statistical Classification of Diseases and Related Health Problems, 10th Revision, World Health Organization, 1992) diagnosis were obtained from medical records. Patients completed the 4-item CAGE questionnaire camouflaged in a healthy lifestyle questionnaire. This modified "camouflaged" CAGE includes 8 extra questions about exercise, diet, sleeping habits, smoking and use of other drugs (Annex). Each affirmative response in the original 4-item CAGE was scored as 1. A cut-off score ≥1 was used in the statistical analysis of the present study. Patients were classified according to the main psychiatric diagnostic categories: schizophrenia and other related psychotic disorders, bipolar disorders, depressive disorders, anxiety disorders, and personality disorders. In order to analyze the CAGE scores according to age, patients were also divided in four age subgroups (18-30 years, 31-45 years, 46-60 years, and above 60 years).

Data analysis

The prevalence of a comorbid AUD with another mental disorder in Spanish population has been found to be 23.43% (Autonell et al., 2007). Using this report to estimate the initial sample size at the 0.05 level of significance with a confidence level of 99% for testing the hypothesis, the power analysis showed that 466 individuals would be the minimum required sample.

For descriptive statistics, numbers and frequencies were used for qualitative variables, and means and standard deviations for the quantitative variables analysis. Chi square statistic was used to compare categorical and t Student test for quantitative variables. As the influence of gender could change across different age groups due to cultural differences and generation gap, a combined analysis of gender*age was performed, as well as a gender*psychiatric diagnoses, to assess influence on CAGE scores. A two-way between groups analysis of variance (ANOVA) was used to investigate the influence of gender and age, and gender and psychiatric diagnoses, on CAGE scores. The multivariate analysis was based on direct logistic regression. Statistical significance was set at $p < 0.05$. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) software for Windows (version 19).

Results

Description of the sample

The final sample consisted of 559 patients, 257 (46%) patients were male and 302 (54%) were female. The average age was 50.07±13.56 years, ranging between 18 and 85 years old. No significant association was found between age and gender (χ^2=0.30, p=0.96).

The most frequent diagnostic category was depressive disorders (42.8%), followed by psychotic disorders (23.8%) and anxiety disorders (17%). Personality disorders (8.8%) and bipolar disorders (7.6%) were the other diagnoses included in the sample. Statistically significant differences were found in the diagnostic distribution according to gender (χ^2=22.32, p<0.001, phi=–0.20) with depressive disorders being more common in women and psychotic disorders more common in men.

Mean CAGE scores

The mean CAGE score in the whole sample was 0.7±1.17, with men showing a statistically significant higher mean CAGE score (M=1.04, SD=1.34) than women (M=0.42, SD=0.91) (t=6.33, p<0.01, two-tailed). The magnitude of the mean difference (MD=0.63, 95% CI: 0.431-0.820) was moderate (eta squared=0.071). When each single item of the CAGE questionnaire was analyzed independently, men also showed a statistically higher percentage of positive responses than women in all of them. The size of the effect of gender was small to moderate according to the Cohen's criteria (Cohen, 1988) (Table 1).

Figure 1 illustrates the mean CAGE scores according to gender and age group. Mean scores in men were highest between 30 to 60 years, and decreased thereafter, while in women mean scores were highest in the group between 18-30 years and progressively decreased with age. A two-way between-groups analysis of variance (ANOVA) was conducted to explore the impact of sex and age on CAGE scores. Patients were divided in four age groups, as described previously. The interaction effect between sex and age group effect was not statistically significant, F(2,559)=0.59, p=0.62. There was a statistically significant main effect for age, F(2,559)=2.72, p=0.044, and for gender F(2, 559)=24.87, p<0.001. The effect size for age was small (partial eta squared=0.015), while the effect size for gender was small to moderate (partial eta squared=0.043). *Post-hoc* comparisons (Tukey HSD test) indicated that the mean score for the >60 year age group (M=0.47, SD=0.94) was significantly different from the 30-45 group (M=0.82, SD=1.3) (p=0.045). The 18-30 year age group (M=0.78, SD=1.01) and the 45-60 year age group (M=0.75, SD=1.2) did not differ significantly from either of the other groups.

An analysis of the influence of sex and diagnostic categories on the mean CAGE scores was performed using a two-way between-groups analysis of variance (ANOVA). Highest mean CAGE scores were found in the subgroup of patients with personality disorders in both genders. Thereafter, in women, bipolar and depressive disorders showed highest scores as compared with other diagnostic subgroups, while men with psychotic and bipolar disorders had highest scores (Figure 2). The interaction effect between sex and diagnostic group was not statistically significant, F(2,554)=2.13, p=0.75. There was a statistically significant main effect for diagnostic group, F(2,554)=5.29, p<0.001, and for gender F(2, 554)=33.82, p<0.001. The effect size for diagnosis was small to moderate (partial eta squared=0.037), while the effect size for gender was moderate (partial eta squared=0.059). *Post-hoc* comparisons using the Tukey HSD test indicated several differences between diagnostic groups (table 2).

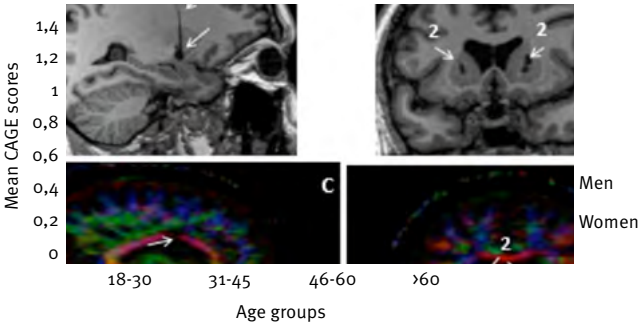

Figure 1. Mean CAGE scores in each age group according to gender

Table 1. *CAGE items results by gender*

	Men (n=257)	**Women** (n=302)	**Total** (n=559)	**Test**	***p***	**Size effect *phi***
CAGE 1: Have you ever felt you should **Cut down** on your drinking? (n, % "yes")	92 (35.8%)	32 (10.6%)	124 (22.2%)	χ^2 =49.64	‹0.001	0.30
CAGE 2: Have people **Annoyed** you by criticizing your drinking? (n, % "yes")	69 (26.8%)	47 (15.6%)	116 (20.8%)	χ^2 =10.08	0.002	0.14
CAGE 3: Have you ever felt bad or **Guilty** about your drinking? (n, % "yes")	73 (28.4%)	35 (11.6%)	108 (19.3%)	χ^2 =24.12	‹0.001	0.21
CAGE 4: Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover (**Eye-opener**)? (n, % "yes")	42 (16.3%)	11 (3.6%)	53 (9.5%)	χ^2 =24.63	‹0.001	0.22

Note. χ2: chi square test, t: T Student test for independent variables.

Table 2. *Influence of sex and diagnostic categories on the mean CAGE scores: Post-hoc comparisons (Tukey HSD test)*

Diagnostic group	Diagnostic group	Mean difference	p
Psychotic disorders	Bipolar disorders	0.01	1
	Depressive disorders	0.39*	0.011
	Anxiety disorders	0.51**	0.006
	Personality disorders	-0.16	0.904
Bipolar disorders	Psychotic disorders	-0.01	1
	Depressive disorders	0.38	0.24
	Anxiety disorders	0.50	0.10
	Personality disorders	-0.17	0.94
Depressive disorders	Psychotic disorders	-0.39*	0.011
	Bipolar disorders	-0.38	0.24
	Anxiety disorders	0.12	0.89
	Personality disorders	-0.55*	0.013
Anxiety disorders	Psychotic disorders	-0.51**	0.006
	Bipolar disorders	-0.50	0.10
	Depressive disorders	-0.12	0.89
	Personality disorders	-0.68**	0.005
Personality disorders	Psychotic disorders	0.16	0.90
	Bipolar disorders	0.17	0.94
	Depressive disorders	0.55*	0.013
	Anxiety disorders	0.68**	0.005

Note. *p<0.05, **p<0.01.

Positive results in CAGE screening

A CAGE score ≥1 was found in 182 patients (32.6% of the sample, 45.1% of men and 21.9% of women). A significant association between gender and a CAGE score ≥1 was noted (χ^2=33.22, p<0.01, phi=–0.248). The phi coefficient, using Cohen's criteria (Cohen, 1988), indicates a small to medium effect of gender on a positive result in the CAGE scale.

A significant association between diagnosis and a score ≥1 on the CAGE questionnaire was found (χ2=16.6, p=0.002). The effect size was moderate (Cramer´s V=0.17). The diagnostic groups where more patients scored ≥1 in the CAGE questionnaire were bipolar (45.2%) and personality disorders (44.9%), followed by psychotic disorders (39.4%). The anxiety disorder group had the lower percentage of patients with a positive CAGE score (Table 3).

Regarding the influence of age in a positive result in the CAGE scale, a Chi-square test for independence was conducted. As noted in Table 2, the group under 30 years showed the highest percentage of patients scoring ≥1 (44.9%), while the group over 60 showed the lowest percentage (24.8%). These results did not reach statistical significance (p=0.068).

A logistic regression was performed to assess the likelihood of a positive result (cut-off ≥1) in the CAGE questionnaire. The model contained three independent variables (sex, age group, and diagnostic category). The full model containing all predictors was statistically significant (χ2=53.34, p<0.001), and hence was able to identify patients presenting an AUD. The model explained between 9.2% (Cox and Snell R square) and 12.8% (Nagelkerke R squared) of the variance in a positive CAGE score and correctly classified 68.8% of cases. All the independent variables made a statistically significant contribution to the model. The strongest predictor of a positive screening was gender, with an odds ratio of 0.33. Women were 3.03 times less likely to have a CAGE score above one as compared to men (p<0.001, 95% CI: 0.22-0.49). The second strongest predictor was related to age, as the group over 60 years presented

Table 3. *CAGE scores according to diagnostic categories and age groups (n, %)*

Diagnoses	CAGE<1	CAGE≥1	*Test*	*p*
Psychotic disorders	80 (60.6%)	52 (39.4%)		
Bipolar disorders	23 (54.8%)	19 (45.2%)		
Depressive disorders	172 (72.6%)	65 (27.4%)		
Anxiety disorders	73 (77.7%)	21 (22.3%)		
Personality disorders	27 (55.1%)	22 (44.9%)		
Total*	375 (67.7%)	179 (32.3%)	χ^2 =16.64	0.002
Age				
18-30	27 (55.1%)	22 (44.9%)		
31-45	101 (66.0 %)	52 (34.0%)		
46-60	152 (66.7%)	76 (33.3%)		
>60	97 (75.2%)	32 (24.8%)		
Total	377 (67.4%)	182 (32.6%)	χ^2 =7.13	0.068

Note. χ^2: chi square test. *Diagnostic data was missing for 5 patients.

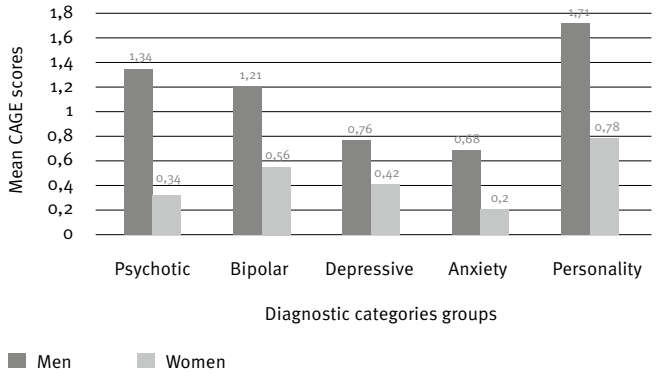

Figure 2. Mean CAGE scores in each diagnostic group according to gender

an odds ratio of 0.4. Therefore, older patients were 2.5 times less likely to have a CAGE score above one (p=0.017, 95% CI: 0.19-0.85). The last predictor was the diagnostic category, with an odds ratio of 0.48 for the anxiety disorder group (p=0.021, 95% CI: 0.26-0.89), a result indicating that patients suffering from anxiety disorders were 2.08 times less likely to have a positive score on the CAGE scale, after controlling for all the other factors in the model. The other diagnostic categories, separately assessed, had no significant association with a positive score in the CAGE scale.

Discussion

This is the first study to evaluate the prevalence of AUD using the CAGE questionnaire in a Spanish psychiatric population. In addition, to our knowledge, this study also provides the first data about the influence of age, gender and psychiatric diagnostic categories in this assessment.

The aim of this study was to assess the prevalence of AUD in a sample of Spanish psychiatric outpatients using the CAGE scale. In any diagnostic test, cut-off value is an important issue as it affects test sensitivity and specificity. The overall sensitivity and specificity of the CAGE questionnaire has been estimated to be 71% and 90% respectively for clinical populations (Dhalla & Kopec, 2007; Mitchell et al., 2014). In schizophrenic patients, a cut-off score of 1 or more shows a 91% sensitivity and an 83% specificity (Dervaux et al., 2006), varying to 82% and 94% respectively, when using a cut-off point of 2. In another sample of psychiatric outpatients (Corradi-Webster et al., 2005), a cut-off point of 1 rendered a 100% sensitivity and a 73% specificity, while a cut-off point of 2 showed a 53% sensitivity and 87% specificity. Hence, in psychiatric samples, a cut-off point of 1 seems to provide high sensitivity while maintaining sufficient specificity. Furthermore, although a CAGE cut-off value of 2 (two or more affirmative answers) has been used in several studies (Berks & McCormick, 2008; Castells & Furlanetto, 2005; Fiellin et al., 2000; Hearne et al., 2002; Mayfield et al., 1974; Paz Filho et al., 2001), several published results suggest that the best cut-off value for the CAGE questionnaire among psychiatric outpatients is 1 (Agabio et al., 2007; Bradley, Bush, McDonell, Malone, & Fihn, 1998; McGarry & Cyr, 2005; Ogborne, 2000). In relation to age and gender, it has also been established that the cut-off point for case definition should be one positive response, as this value may improve sensitivity for women or elderly people (Bradley et al., 1998; Cherpitel, 1995; Jones, Lindsey, Yount, Soltys, & Farani-Enayat, 1993). Therefore, in this study, a cut-off of 1 was used.

Our finding of positive screening of AUD in 32.6% in psychiatric outpatients, as defined by a CAGE score ≥1, is similar to that found in other studies, albeit with smaller samples. Sample sizes of 56 patients (Agabio et al., 2007), 71 (Teitelbaum & Mullen, 2000), 114 (Masur & Monteiro, 1983; Dervaux et al., 2006), 127 (Corradi-Webster et al., 2005), 151 (Etter & Etter 2004), 165 (Ratta-Apha et al., 2014), 247 (Rosenberg et al., 1998), and 366 patients (Mayfield et al., 1974) have so far been published.

Regarding gender differences, our results were consistent with several published reports and epidemiologic surveys describing higher rates of AUD in men than in women both in the general population (Goldstein et al., 2015; Hasin et al., 2007; Keyes et al., 2008; Khan et al., 2013; Rehm et al., 2015) and in psychiatric samples (Cantor-Graae et al., 2001; Dervaux et al., 2006; Eberhard et al., 2009; McCreadie, 2002; Satre et al., 2008). Gender differences were also noted in the pattern of positive answers obtained in the CAGE test (Table 1). Men more frequently provided a positive answer to CAGE1 and CAGE3 questions (35.8% and 28.4%, respectively), while positive answers in women were more related to guilt and self-reproach feelings (CAGE2 and CAGE3) (15.6% and 11.6%, respectively). In both genders, the question with lower percentages of positive answers was CAGE4 (16.3% in men and 3.6% in women). These results could point out to a different sensitivity of the CAGE questions to detect AUD in men and women.

In the general population, the frequency of AUD has been inversely related to age (Hasin et al., 2007), as patients over 65 years seem to have lower rates of alcohol consumption and AUD, as compared to those aged 50-64 (Gum, King-Kallimanis, & Kohn, 2009; Moore et al., 2005; Moos, Schutte, Brennan, & Moos, 2009; Wu & Blazer, 2014). In agreement with these results a negative association between a positive screening in the CAGE and being older than 60 years was found in the present study. AUD have also been reported to be higher in younger subjects from the general population (Glass, Grant, Yoon, & Bucholz, 2015; Grant et al., 2015; Rehm et al., 2015). There are very few studies assessing the influence of age in AUD screening in psychiatric samples. Younger age has been associated with substance use disorders, but not with AUD in a sample of psychiatric severely ill inpatients (Mueser et al., 2000). Rates of AUD and drug use disorder could be even higher in the emerging adulthood with mental health disorders, as evidenced

in a study performed in patients aged from 18 to 25 years (Sheidow et al., 2012). In our sample, younger patients did not present higher rates of positive CAGE screening as compared to the other age groups in the whole sample. When our sample was divided by gender (Figure 1), women did present a higher positive screening in the age group between 18-30 years, while men presented higher positive rates in the middle age groups (31-60 years). These results could suggest a different risk of alcohol consumption according to gender in psychiatric populations.

As to our knowledge, this is the first study to assess AUD screening in different diagnostic categories from a large sample of psychiatric outpatients using the CAGE questionnaire. So far, most of the studies performed in psychiatric facilities have focused on a single disorder or diagnostic category, i.e., outpatients with schizophrenia or schizoaffective disorder (Dervaux et al., 2006; Etter & Etter, 2004), or mood disorders (Agabio et al., 2007), while other studies have not informed about the psychiatric diagnoses (Corradi-Webster et al., 2005; Masur & Monteiro, 1983; Ratta-Apha et al., 2014; Rosenberg et al., 1998; Teitelbaum & Mullen, 2000). Regarding the clinical setting, patients have been recruited at hospitalization facilities (Masur & Monteiro, 1983; Mayfield et al., 1974; Rosenberg et al., 1998), both inpatient and outpatient units (Dervaux et al., 2006; Teitelbaum & Mullen, 2000) or from community services (Agabio et al., 2007; Etter & Etter, 2004; Ratta-Apha et al., 2014). A selection bias, especially in inpatient settings, can overestimate AUD due to Berkson's fallacy, because of the higher probability of receiving specialized treatment (Soyka, 2000; Etter & Etter, 2004). None of the studies developed in general psychiatric community facilities have performed a comparison between diagnostic categories.

AUD seems to coexist with several psychiatric diseases, mainly affective disorders, anxiety disorders, and personality disorders (Anthenelli, 2012; Grant et al., 2004a, 2004b, 2015; Hasin & Grant, 2015; Kessler et al., 1997; Klimkiewicz, Klimkiewicz, Jakubczyk, Kieres-Salomoński, & Wojnar, 2015; Mellos, Liappas, & Paparrigopoulos, 2010; Rosenberg et al., 1998). Different hypothesis have been proposed to explain the comorbidity between psychiatric conditions and AUD: self-medication, alleviation of dysphoria, psychosocial risk factors, genetic predisposition, or shared neurobiological vulnerability (Buckley, 2006; Mueser, Drake, & Wallach, 1998). Patients suffering from severe mental illnesses, as bipolar disorders, schizophrenia, or some personality disorders, could be especially prone to present dysphoria and negative affects, as well as to exhibit multiple risk factors (Mueser et al., 1998). In our study, patients with bipolar disorders (45.2%) or personality disorders (44.9%) showed the highest rates of a CAGE score ≥1, followed by psychotic disorders (39.4%). These prevalence rates are in line with those reported in the literature. The presence of AUD in patients with a bipolar disorder has been estimated to be around 45% in several studies (Cardoso et al., 2008; Farren, Hill, & Weiss, 2012; Kessler et al., 1997), which is similar to our reported rate. In the study from Agabio et al. (2007), 30.4% of the outpatients with an affective disorder showed a CAGE score ≥1. In their study, no differences were found in the frequency of AUD between unipolar and bipolar spectrum, although this analysis was performed using the diagnostic criteria from the Structured Clinical Interview for DSM-IV, Axis I Disorders, not the CAGE questionnaire. Other authors have reported prevalence rates from 10 to 60% of lifetime AUD in unipolar depressed patients (Klimkiewicz et al., 2015; Satre et al., 2008; Sullivan et al., 2005; Worthington et al., 1996). In agreement with our results, a prevalence of AUD between 16.4 to 30% has been reported in patients with a diagnosis of personality disorder (Echeburúa, de Medina, & Aizpiri, 2005; Grant et al., 2004a; Klimkiewicz et al., 2015; Mellos et al., 2010).

Regarding AUD in patients with schizophrenia and related disorders, a prevalence rate between 29 to 60% has been consistently reported (Dervaux et al., 2006; Cantor-Graae et al., 2001; McCreadie, 2002; Soyka, 2000). Similar CAGE scores as the presented in our study have been published in a sample of outpatients with schizophrenia and schizoaffective disorders, with CAGE score ≥1 in 37.7% of the patients (Etter & Etter, 2004). In our sample, patients with an anxiety disorder had a lower percentage of a positive CAGE score (22.3%) than other diagnostic groups. AUD has been described in 7 to 18% of patients with anxiety disorders (Klimkiewicz et al., 2015; Vorspan et al., 2015). A recent metaanalysis has confirmed the association between AUD and anxiety disorders, with an OR of 1.636 for any anxiety disorder and alcohol abuse, and an OR of 2.53 for alcohol dependence (Lai, Cleary, Sitharthan, & Hunt, 2015). Other authors have found non-significant or no associations between AUD and specific anxiety disorders (Grant et al., 2004b; Hasin & Kilcoyne, 2012; Goldstein et al., 2015; Grant et al., 2015). These discrepant results could be explained by the high clinical heterogeneity in this subgroup of patients, possibly leading to distinct comorbidity with AUD.

Gender differences in positive AUD screening were also observed when our sample was split by diagnosis (Figure 2). Personality disorders had the highest positive rates for both genders. Afterwards, men showed high positive rates in the subgroup with psychotic disorders followed by bipolar disorder, while in women, the second diagnostic group with more prevalent positive results for the CAGE screening was the bipolar disorder, followed by psychotic disorders. This gender difference, according to psychiatric diagnosis, strengthens the need of gender specific approaches when screening and treating AUD in psychiatric patients.

In the present study, the strongest predictor of a positive screening for AUD using the CAGE scale was gender, followed by age, and psychiatric diagnoses. Therefore, presenting a male gender and being younger than 60 years

were predictors of a positive result. Patients diagnosed with an anxiety disorder were more likely to obtain a negative score in the CAGE scale as compared to the other diagnostic groups. Other authors also described male gender, younger age, and antisocial personality disorder, among others, as predictive of substance use disorders in psychiatric patients (Mueser et al., 2000).

This study has several limitations. Firstly, AUD were not assessed with structured interviews to confirm the results provided by the CAGE questionnaire. The cross-sectional design prevents analysis of causal relationships between AUD, psychiatric conditions, and other risk factors. Sociodemographic data, as well as substance use disorders and medical conditions, which could act as confounding factors, were not registered. The use of a cut-off point of 1 in the CAGE questionnaire provides a higher sensitivity but a lower specificity, therefore some patients classified by our screening as presenting a high risk for an AUD could be false positives, overestimating the frequency of AUD risk in our sample. As for the strengths of our study, a large sample of outpatients, from a broad age range and different diagnostic categories, was included. Moreover, 54% of our patients were female, often under-represented in studies. For all these reasons, our sample might provide a more realistic perspective of AUD in this population.

In summary, the high rates of AUD seen in psychiatric outpatients, and the difficulty to accurately assess these patients, supports the use of specific screening instruments, like the CAGE questionnaire. Special attention should be provided to patients presenting risk factors for an AUD, as male gender, age under 60 years old, as well as the presence of bipolar, personality, and psychotic disorders. Further research may examine the relationship between AUD and comorbid psychiatric disorders, together with the influence of other medical, social, and demographic factors.

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Disclosures

The authors do not report any conflict of interest associated with the present study.

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Annex

CAGE questionnaire camouflaged adapted for Spanish patients (translated to English)

1. Do you think you eat too many sweets?
2. Have you ever been offered a joint or a cocaine dose?
3. Have people annoyed you by criticizing your drinking?
4. Have you ever thought about doing some exercise weekly?
5. Do you consider you sleep enough hours to feel fit during the day?
6. Have you ever felt you should cut down on your drinking?
7. Have you ever considered seriously quitting smoking?
8. Have you ever been told you should eat more fruits and vegetables?
9. Have you ever felt bad or guilty about your drinking?
10. Have you ever been told you should smoke less?
11. Have you ever had a drink first thing in the morning to steady your nerves or to get rid of a hangover?
12. Have you ever thought about switching your habit of taking sleeping pills to relaxation techniques?