Needs of Female Outpatients with Alcohol Use Disorder: Data from an Italian Study

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Running title: Needs of women with AUD

Abstract

Aims: Alcohol use disorder (AUD) is a common mental disorder characterized by sex-gender differences (SGDs). The present study was aimed at evaluating attitudes displayed by Italian AUD treatment services towards investigating the presence of SGDs in their patients and implementing gender-specific treatments for female AUD patients.

Methods: Potential SGDs were initially investigated in a sample of AUD outpatients, subsequently followed by a national survey on the adoption of specific interventions for female AUD outpatients.

Results: The presence of SGDs was confirmed in a sample of 525 (332 men; 193 women) AUD outpatients, including a higher prevalence of anxiety and mood disorders, and episodes of violence and trauma among female AUD outpatients compared to males. Despite the presence of these SGDs, only less than 20% of a total of 217 Italian AUD treatment services reported the implementation of specific strategies for female AUD outpatients. The majority of services (94%) reported investigating episodes of violence and/or trauma, largely resorting to specific procedures only when these issues were detected.

Conclusions: Our findings confirm the presence of SGDs among AUD outpatients, including a higher prevalence of anxiety and mood disorders and episodes of violence and trauma among females compared to males. However, only a small number of services has adopted a gender medicine approach in AUD treatment. These results underline the urgency of investigating the specific needs of female, male, and non-binary AUD patients in order to personalize and enhance the effectiveness and appeal of AUD treatment.

Short Summary

Women with alcohol use disorder (AUD) may display specific needs (e.g., possibility to receive psychiatric treatment in the same AUD service; implementation of specific plans for patients

reporting episodes of trauma and violence). Nevertheless, less than 20% of our sample of Italian services reported applying specific strategies for female AUD outpatients.

Keywords: alcohol use disorder, sex/gender differences, women, violence, trauma, treatment services.

Abbreviations: APA, American Psychiatric Association; AUD, Alcohol Use Disorder; CI, Confidence Intervals; IQR, InterQuartile Ranges; OR, Odds Ratios; PTSD, post-traumatic stress disorder; SGDs, sex-gender differences; SUD, Substance Use Disorder

Introduction

Alcohol Use Disorder (AUD) is a highly prevalent mental disorder (APA, 2022) characterized by a strong desire to consume alcohol, inability to control alcohol intake, and consequent episodes of excessive alcohol consumption associated with higher risks of developing devasting consequences such as acute intoxication, injury, violence, cancers, hypertension, suicide, and mortality (MacKillop et al., 2022). Worldwide, lifetime prevalence of AUD is approximately 8.6% of the general population (Glantz et al., 2020) with a large variability between countries. Among high income countries, the highest and lowest values have been estimated in Australia (22.7% of general population) and Italy (1.3%), respectively (Glantz et al., 2020). A recent national report has recently confirmed the prevalence of AUD in Italy as being lower than the European average (Scafato et al., 2023).

Numerous studies have highlighted the existence of relevant differences between men and women in the onset, progression, and clinical manifestation of several psychiatric diseases, as well as in response to treatments and associated adverse events (Mauvais-Jarvis et al., 2020). As these differences may include both biological (sex differences) and social–cultural–economic differences (gender differences), with sex and gender also interacting, use of the denomination "sex-gender differences (SGDs)" has been recommended to include both terms and relative interactions (Madsen et al., 2017).

AUD is no exception when it comes to presenting SGDs (Agabio et al., 2017; McCaul et al., 2019; McCrady et al., 2020; White, 2020). As an example, AUD is historically more prevalent in men than in women, with worldwide values estimated as corresponding to approximately 20.5% and 7.8% of male and female populations, respectively (Glantz et al., 2020). However, over the last few years, this SGD has narrowed, particularly among the younger populations (Slade et al., 2016). Furthermore, it is well-known that following ingestion of equivalent amounts of alcohol, women achieve higher blood alcohol levels than men, displaying a higher vulnerability to alcohol-related medical consequences (McCaul et al., 2019). These SGDs are mainly due to the smaller volume of distribution caused by their lower body water content and higher body fat percentage, and lower first-pass

metabolism of alcohol resulting from a lower activity of the enzyme alcohol dehydrogenase, ADH compared to men (McCaul et al., 2019). Some studies have also reported a phenomenon known as telescoping effect (Tower et al., 2023) characterized by earlier onset of AUD in men than women, with no difference in the average age of accessing services, suggesting a faster progression of AUD in women that may lead them to seek specialized services earlier than men.

Despite these SGDs in AUD, the potential influence of both sex and gender in the efficacy and safety of medications approved for the treatment of AUD has been understudied, both clinically and preclinically (McCrady et al., 2020). Indeed, particular attention should be paid to several SGDs which may require personalized medical treatment in men and women with AUD. For instance, it has been observed that, compared to men with AUD, women with AUD more frequently suffer from anxiety and depression (McCrady et al., 2020; White, 2020; Lespine et al., 2022). Furthermore, women with AUD report episodes of trauma and violence more frequently than men with AUD (McCrady et al., 2020; Guinle and Sinha, 2020). The relationship between trauma and violence on the one hand, and alcohol use on the other, is bidirectional, as having been exposed to violence, particularly in childhood and adolescence, increases the risk of developing AUD (Guinle and Sinha, 2020), and alcohol use and intoxication increase the risk of episodes of physical and sexual violence, particularly among women (Lemke et al., 2008; Devries et al., 2014). These SGDs suggest the need for a gender approach to be adopted in providing personalized treatment for men and women with AUD (Fonseca et al., 2021), as provided for in recent Italian legislation (Law 3/2018, GU n.25, 31.01.2018; Decree-Law 13.06.2019).

Despite the presence of these SGDs, we hypothesized that it was unlikely that all Italian services had adopted a gender-specific approach in the treatment of AUD outpatients. Accordingly, we aimed to evaluate attitudes displayed by Italian AUD treatment services towards investigating the presence of SGDs in their patients and implementing gender-specific treatments for female AUD patients. To achieve these aims, we first investigated potential SGDs in a sample of Italian AUD outpatients, and

subsequently conducted a national survey by mailing a questionnaire on specific interventions for female AUD patients to all Italian AUD treatment services.

Materials and Methods

Evaluation of potential SGDs in a sample of AUD outpatients

Two AUD outpatient treatment services located in the Emilia Romagna region, namely Lugo and Rimini, were selected. Briefly, as for all other public AUD treatment services in Italy, access to these services is mainly voluntary, although may also be recommended by other services; the treatment dispensed includes free medical, pharmacological, and socio-rehabilitative therapies and psychological/psychotherapeutic support through a multi-professional approach provided by physicians, psychologists, nurses, social workers, and educators.

Medical records of AUD outpatients receiving treatment at these two services from January 1, 2019 to December 31, 2019 were evaluated. Inclusion criteria were: 18 years or older and a primary diagnosis of mental and behavioral disorder due to alcohol use (meeting ICD-10 criteria - diagnosis group F10.0 – F10.9). Presence of other comorbid disorders, cognitive deficits, or linguistic-cultural limitations were not viewed as criteria for exclusion. Data of included patients were collected from computerized medical records compiled by physicians involved in the treatment of AUD patients. Physicians were interviewed if data were found to be missing. The Ethics Committee of the Local Health Authority of Romagna approved the study (January 24, 2020; n. 2599).

The following data were collected:

- *Socio-demographic data*: gender, age, marital status, level of education, professional status, living situation, cohabitation, and citizenship;
- *Clinical-anamnestic data*: age at start of problematic drinking (i.e., consuming more than 40 and 60 g/day, for women and men, respectively, according to the World Health Organization risk levels, see MacKillop et al., 2022 for a detailed description), age at first entry to an AUD service, latency time (i.e., time between age at start of problematic drinking and first entry to an AUD service), any

previous AUD treatment (e.g., pharmacological, psychological/psychotherapeutic, socio-rehabilitative or self-help group interventions) external to the actual service, family history of AUD (i.e., 1st and 2nd degree relatives), lifetime and current history of substance use disorders from substances other than alcohol (e.g., tobacco, heroin, cocaine) or other behavioral disorders (e.g., gambling), comorbid psychiatric disorders and type of disorder (e.g., personality disorders, psychotic spectrum disorders, anxiety disorders, mood disorders), and experience of trauma and/or violence.

When information on episodes of trauma and violence was not available from medical records, physicians involved in the treatment of AUD patients were interviewed. In detail, we asked whether their outpatient had been exposed to traumatic experiences, defining trauma as an unexpected and sudden event that (i) the subject experienced as destabilizing and devastating, and which exceeded the person's ability to respond, (ii) left the subject in a condition of helplessness and unable to face/manage a shocking and uncontrollable experience, (iii) overwhelmed the individual's normal defenses making him/her incapable of reacting and leading to the raising of pathological defenses. We then asked whether the outpatient had been subjected to experiences of violence defined as intentional use of physical force or power by a person or people resulting in physical injury or psychological harm. We explained that violent behavior, despite causing physical and psychological injury and harm, may not necessarily generate trauma in the victim if they actively and developmentally faced up to the event experienced, activating personal and relational resources to re-elaborate it and/or therapeutic paths and restorative experiences. At the same time, we also indicated that even apparently non-violent behaviors, such as denigratory and oppressive attitudes, and developmental experiences of neglect or inconsistency, might generate trauma if subjectively experienced as uncontrollable, destabilizing, and devastating.

Attitudes of Italian AUD treatment services toward consideration of gender differences and episodes of violence

All Italian services involved in the treatment of AUD and Substance Use Disorder (SUD) were listed and detailed information including email address, telephone number, and name of the person in

charge was collected. We contacted each service to explain the aims of our study, requesting their availability to take part in the study, and explaining that participation consisted in filling a five-question questionnaire focused on AUD treatment and that answers would be anonymized. In addition to questions relating to the treatment of women with AUD, the questionnaire also included questions on non-binary AUD patients. The questionnaire was e-mailed to services that had agreed to take part, asking them to fill in and return the questionnaire (see Table 1). Briefly, questions were aimed at investigating whether services:

i) collect information relating to patient's sexual orientation and/or gender identity

ii) adopt strategies for non-binary patients

iii) adopt strategies for women

iv) investigate current and/or past episodes of physical/psychological violence and/or trauma

v) adopt strategies in the presence of violence/trauma.

Services were given the opportunity to further elucidate their answer or justify answers provided. With regard to answers provided to the last question, two authors, experts in the treatment of individuals with AUD subjected to episodes of violence and/or trauma (MCS, LR), evaluated all additional comments and commented on their appropriateness. In detail, strategies structured and focused on violence (e.g., protocols, guidelines, protected structures, other antiviolence procedures) were deemed appropriate, whilst strategies which failed to focus specifically on episodes of violence and trauma such as, for instance, group psychotherapy sessions, were deemed inappropriate.

Statistical analysis

The Shapiro-Wilk test was used to assess the normal distribution of variables. Data are provided as medians and interquartile ranges (IQR) for continuous variables, and numbers and percentages for dichotomous variables. Continuous and dichotomous variables were compared using the Wilcoxon rank sum test and the χ^2 test, respectively. Clinical-anamnestic data were considered as dependent variables for linear and logistic models. Their results are expressed as Odds Ratios (OR) and 95%

Confidence Intervals (95% CI). The effect of potential confounding effects of socio-demographic variables was studied with adjusted models. The software used for analysis were STATA (version 16), and RStudio (version 4.2.3). Statistical significance was set at $p<0.05$.

Results

SGDs among AUD patients referring to treatment services.

Table 2 shows the socio-demographic characteristics of our sample of 525 patients, with a male/female ratio of 1.7:1. Compared to men, women displayed higher levels of education, were more frequently married, more frequently unemployed and lived in shared accommodation with their partner, children, or others, and were not Italian.

As shown in **Table 3**, compared to men, women had a shorter latency time and, more frequently than men, suffered from anxiety and mood disorders, and reported episodes of violence and trauma. Among participants who reported episodes of violence and trauma, no difference was observed between Italians and non-Italian women and men (episodes of violence: 52 Italian women and 15 non-Italian women; 43 Italian men and 6 non-Italian men; p=0.24714; traumatic episodes: 23 Italian women and 8 non-Italian women; 9 Italian men and 3 non-Italian men; p=0.73744; data not shown). Taking potential socio-demographic confounders into account (see **Table 4**), women and men did not show significant independent differences in median age at start of problematic drinking, previous treatment or AUD, familiarity with AUD, or lifetime and recent use of psychoactive substances.

Attitudes displayed by Italian AUD treatment services toward consideration of potential SGDs and episodes of violence

Between June and December 2023, 855 AUD and/or SUD treatment services in Italy were listed and contacted by e-mail (see Figure 1); if no response was received, we phoned the services directly. We excluded 144 services as they were no longer operational, thus obtaining a final list comprising 711 services, of which 514 (72.3%) answered our phone call, and 217 (42.2% of responders) filled in and returned the questionnaire by email.

Out of the 217 services that took part in our study (see Figure 1) (*i*) 84.8% confirmed they routinely collected information on sexual orientation and/or gender identity during the first observation and diagnostic phase of treatment, (*ii*) 6.9% and (iii) 18.9% reported adopting specific initiatives for non-binary patients and women, respectively, (iv) 94.0% affirmed specifically investigating current and/or past episodes of physical/psychological violence and/or trauma, and (*v*) 71.6% of those affirming investigation of episodes of violence and/or trauma confirmed they routinely adopt specific procedures on detection of violence and/or trauma.

Some services provided additional information. In detail,

1) to the first answer focused on *Patient's sexual orientation and/or gender identity,* several services added that this was not mentioned unless patients referred to the matter spontaneously, with others raising the issue at later stages of AUD treatment;
2) to the second answer focused on *Initiatives for non-binary patients,* no services added further information on initiatives taken for non-binary people; some stated the use of toilets with no gender indication, although this was not an initiative implemented specifically for non-binary people;
3) regarding the third answer, *Initiatives for women*, some services reported the presence of female health operators amongst their members of staff or an all-female team of health operators. Some referred to specific group activities accessible solely by female AUD patients. One service mentioned a project devoted to AUD women, which included collaboration with a mental health center and pediatric and gynecology wards. Another center described the progressive activation of a series of projects specifically devoted to women, in collaboration with other services for the prevention and treatment of sexually transmitted diseases and unplanned pregnancies, and for women reporting episodes of violence. Another service reported the organization of initiatives aimed at increasing awareness on this topic. Finally, one service reported implementing a project aimed at preventing AUD in women;

4) with regard to the fourth question *Questions on episodes of violence and/or trauma*, numerous services confirmed how these episodes were investigated during the unstructured anamnestic survey. Several services admitted that questions were not asked routinely, although relevant information on these issues was collected when spontaneously provided by patients. Other services reported the use of structured or semi-structured interviews such as the Addiction Severity Index (which also investigates past and recent psychological, physical and sexual violence; McLellan et al., 1980), Adverse Childhood Experiences (Felitti et al., 1998), Adult Attachment Interview (George et al., 1985), and Addictive Behavior Questionnaire (Caretti et al., 2018). Finally, some services stated how during physical examination, signs pointing to recent episodes of physical violence were investigated;
5) on answering the fifth question on *Specific procedures in case of violence or trauma,* ninety-nine services added further details of strategies adopted. Of these, 54.5% (54 out of 99) were deemed to be appropriate for use in dealing with victims of violence, whilst 36.4% (36 out of 99) were inappropriate, and 9.1% (9 out of 99) unclear. With regard to appropriate strategies, the majority of services reported using specific protocols developed by antiviolence centers, protected structures, refugee centers and/or other antiviolence procedures. Some services did not describe specific protocols but mentioned taking appropriate action for the situation at hand. Two services mentioned an intervention devoted to the families of women reporting episodes of violence. Another service described a protocol in which forensic physicians help other health operators to manage the clinical case, referring those affected to antiviolence centers or emergency departments. The most frequently reported inappropriate strategies comprised individual and group psychotherapies.

Discussion

The results obtained confirmed several of the SGDs already reported by previous studies (e.g., White, 2020; Lespine et al., 2022). In detail, in our sample, compared to males, female AUD outpatients

displayed higher educational levels, were more frequently married, lacking permanent employment, and did not live alone, thus confirming data from a recent Italian national survey (Italian Ministry of Health, 2020) and a regional study (Agabio et al., 2021). We also observed a telescoping effect among female AUD patients as, compared to males, they referred a significantly lower latency time to treatment. Previous studies observed a similar phenomenon, although the finding has been criticized by other studies that detected no evidence of this phenomenon in the general population, weaker evidence among younger individuals, or only partially supportive evidence of SGDs in AUD latency (Towers et al., 2023). We also confirmed a higher prevalence of anxiety and depression in female compared to male AUD outpatients (McCrady et al., 2020; White, 2020; Lespine et al., 2022). These results suggest that female AUD outpatients may require medical treatment earlier than males, as well as additional psychiatric treatment for comorbid anxiety and depression. To personalize and modulate therapeutic interventions, employment and housing stability, essential aspects in recovery from AUD and SUD, should also be investigated (Cano et al., 2017).

One of the major challenges is linked to increasing the rate of individuals with AUD seeking and receiving medical treatment. Despite the documented efficacy of available treatments, less than 10% of individuals with AUD receive formal treatment, with lower rates of women compared to men (McCrady et al., 2020). It has been hypothesized that this difference may be associated with the failure of AUD services to match women's needs (Venegas et al., 2021). To better match these needs, AUD services would need to provide childcare, prenatal care, treatment for co-occurring mental disorders (e.g., anxiety and depression), and supplemental social services, possibly in the context of women-only programs (McCrady et al., 2020).

Our study revealed a male: female ratio (1.7:1) that failed to overlap fully with estimations provided in a recent national survey (3.3:1; Italian Ministry of Health, 2020). Our male: female ratio seemed to better resemble that of people accessing hospital emergency departments for alcohol related issues (2.3:1; Italian Ministry of Health, 2020). This finding may suggest the existence of lower barriers to treatment for women with AUD in services selected for our study compared to other services. Indeed,

the services selected for the purpose of this study, which adopted a multidisciplinary approach involving physicians, psychologists, nurses, social workers, and educators, many of which females, may have proved more appealing to female AUD patients. The main barriers for women seeking AUD treatment include multiple factors, such as lack of social support, stigma, parental role, and tendency to refer to primary care (McCaul et al., 2019; McCrady et al., 2020; Lespine et al., 2022); this hypothesis should therefore be investigated in-depth to provide additional input with regard to strategies aimed at reducing barriers and facilitating access to AUD treatment for Italian women.

Our study also revealed a higher frequency of non-Italians in the sample of female compared to male AUD outpatients. This finding may be due to the high presence of largely female immigrants from Eastern European countries, where AUD is highly prevalent (Gualdi-Russo et al., 2009). This SGD should also be taken into consideration for the purpose of personalizing and modulating therapeutic interventions, for instance, inclusion of a cultural mediator on the team of health operators of AUD treatment services.

A higher prevalence of traumatic episodes and violence in female AUD outpatients compared to males was also confirmed (Guinle and Sinha, 2020). Specifically, compared to men, episodes of violence and trauma were four- and two-fold higher among women, respectively. This SGD is of particular importance for health operators involved in the treatment of AUD, since having experienced trauma or violence during childhood or adolescence increases the risk of developing both AUD (Guinle and Sinha, 2020) and post-traumatic stress disorder (PTSD), a mental disorder more frequently manifested in women (10-12%) than men (5-6%; Singh and Wendt, 2024). On the other hand, use of alcohol as a coping mechanism to deal with stressful, negative events or post-traumatic symptoms is more frequent among women (Peltier et al., 2019), with alcohol intoxication representing a risk factor for exposure to sexual violence. All these factors merge to create a vicious circle between episodes of trauma and violence and AUD. Previous studies investigated how episodes of violence and trauma impact treatment outcomes of people with SUD (Pirard et al., 2005; Di Nicola et al., 2024). For instance, a recent Italian study observed a direct relationship between childhood

trauma and risk of suicide attempts among people with SUD, mostly constituted by women (Di Nicola et al., 2024). Accordingly, specific treatments should be provided to people with AUD or SUD who refer episodes of violence (Schumm et al., 2018), with our findings suggesting that female AUD outpatients may experience a greater need for these treatments than AUD males.

Almost all (94%) services that took part in our survey investigated the presence of episodes of violence and trauma, of which 67% referred recourse to specific procedures when exposure to violence and/or trauma was detected. However, some procedures were not deemed fit for purpose. Accordingly, our results suggest that not all Italian services adopt the most suitable approach in the treatment of AUD outpatients who report episodes of violence or trauma.

Finally, as hypothesized, the results of our study reveal how less than 20% of the sample of Italian services investigated have effectively implemented specific strategies for women with AUD. These strategies include the presence of female health operators, group activities devoted exclusively to female AUD outpatients, collaboration with mental health centers and pediatric and gynecology wards, projects aimed at preventing and treating sexually transmitted diseases and unplanned pregnancies, projects tailored for women who report episodes of violence, and projects aimed at increasing awareness of alcohol-related consequences and preventing AUD in women. Nevertheless, the vast majority failed to implement gender-specific strategies for women with AUD.

Globally, these findings suggest that despite the presence of SGDs, outpatients with AUD are frequently not treated using a gender-specific approach (Fonseca et al., 2021). Treatment of AUD continues to be based on the results obtained by clinical studies performed prevalently on male AUD patients, according to an androcentric model. In 2018, in Italy, a national law stated the need to adopt a gender medicine approach throughout the National Health Service and provided a plan aimed at disseminating gender medicine across the entire nation (Law 3/2018, GU n.25, 31.01.2018; Decree-Law 13.06.2019). Nevertheless, few studies have investigated potential SGDs in Italian AUD outpatients or in people affected by excessive alcohol use (Agabio et al. 2017, 2021; Allamani et al., 2000; Guerrini et al., 2006; Mancinelli et al., 2013; Pavarin et al., 2017; Picci et al., 2012; Shield et

al., 2013; Stroffolini et al., 2018). To date no studies have specifically investigated the needs of women with AUD who refer episodes of violence and/or trauma and the implementation by AUD treatment services of gender-specific strategies for women with AUD.

Conclusions

Our findings confirm the presence of SGDs among Italian AUD outpatients and suggest the presence of specific needs in women with AUD, including the possibility of obtaining referrals for additional psychiatric treatment in the center in which AUD treatment is provided, presence of a cultural mediator, and implementation of specific plans for patients who report episodes of trauma and violence. Unfortunately, less than 20% of the sample of Italian services studied reported the implementation of specific strategies in the treatment of female AUD outpatients. Globally, our results underline the need for further studies aimed at identifying the specific needs of female AUD outpatients and evaluating the most appropriate treatment strategies. The results obtained in our study may help to persuade Italian policy makers to facilitate implementation of strategies with the aim of improving the appeal, quality and effectiveness of treatment for AUD patients according to the specific needs of women, men, and non-binary patients.

Limitations of the Study

The study featured a series of limitations. As data were collected from medical records, we indirectly evaluated potential SGDs and may have inadvertently limited data to biological differences rather than gender issues such as identifying as a man or woman regardless of biological sex or being non-binary. These aspects were generally not discernible from medical records, and physician interviews failed to provide additional data, thus suggesting the need to focus specifically on the complex issues of gender and sexual orientation, which represent elements of discrimination and risk factors for AUD (Allen and Mowbray, 2016; Gonzales et al., 2016). In addition, the heterogeneity in assessing traumatic exposure among services may limit the generalizability of our findings to other countries

or settings. A further limitation was represented by the limited sample size of AUD patients and period considered (1 year).

Author Contributions

Conceptualization: Teo Vignoli, Caterina Staccioli, Liana Fattore, Roberta Agabio; Data curation: Maristella Salaris, Samantha Sanchini, Elisa Martino, Lorena Rigoli, Francesco Salis, Liana Fattore, Roberta Agabio; Formal analysis and investigation: Maristella Salaris, Samantha Sanchini, Elisa Martino, Lorena Rigoli, Francesco Salis; Writing - original draft preparation: Liana Fattore, Roberta Agabio; Writing - Review and editing: Teo Vignoli, Caterina Staccioli, Fabio Caputo, Liana Fattore, Roberta Agabio; Resources: Teo Vignoli and Caterina Staccioli; Supervision: Teo Vignoli, Caterina Staccioli, Fabio Caputo, Liana Fattore and Roberta Agabio.

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Conflicts of Interest

The authors declare no conflict of interest.

Ethical Approval

The study was approved by the Ethics Committee of the Local Health Authority of Romagna, Italy (January 24, 2020; n. 2599).

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Data Availability

The data analyzed during the current study are available from the corresponding author on reasonable request.

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Table 1. Questionnaire administered to the services for AUD treatment

	Questions	Possible answers
1	Do you collect information relating to sexual orientation and/or gender identity of the patient during the observational and diagnostic phase?	- No - Only if the patient spontaneously decides to talk about it - Yes
2	Do you adopt specific initiatives for non-binary people with alcohol use disorder (e.g., dedicated consulting rooms, toilets without indication of gender, etc.)?	- No - Yes (in this case, briefly describe them)
3	Do you adopt specific initiatives for women with alcohol use disorder (e.g., dedicated consulting rooms, dedicated female staff, etc.)?	- No - Yes (in this case, briefly describe them)
4	Do you investigate into present and/or previous episodes of physical and/or psychological trauma and/or violence during the observational and diagnostic phase?	- No - Only if the patient spontaneously decides to talk about it - Yes (in this case, briefly describe how)
5	If present and/or previous episodes or trauma and/or violence are reported, do you adopt specific strategies?	- No - Yes (in this case, briefly describe them)

Legend: AUD: alcohol use disorder

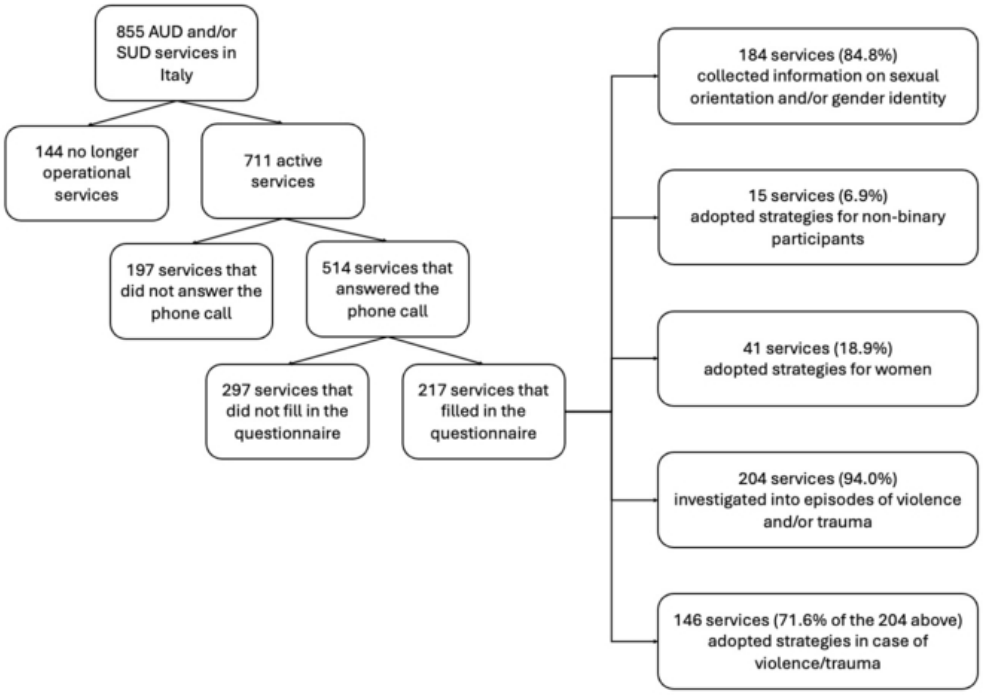

Figure 1. Flow-chart diagram of the enrollment phase and answers provided by the centers that filled in the questionnaire
Legend: AUD: alcohol use disorder; SUD: substance use disorder

56x43mm (300 x 300 DPI)

Table 2. Socio-demographic characteristics of an Italian sample of AUD outpatients

	Men	Women	p
n (%)	332 (63.2)	193 (36.8)	
Age			
Median (IQR)	51.1 (14.1)	51.6 (10.5)	0.429
≤ 39 years n (%)	58 (17.5)	20 (10.4)	0.116
40-49 years n (%)	91 (27.4)	65 (33.7)	
50-59 years n (%)	125 (37.7)	76 (39.4)	
≥ 60 years n (%)	58 (17.5)	32 (16.6)	
Education			
Low (none, elementary certification, middle school certification) n (%)	234 (70.5)	95 (49.2)	**0.000**
Higher (secondary school diploma, degree) n (%)	98 (29.5)	98 (50.8)	
Marital status			
Single n (%)	140 (42.2)	61 (31.6)	**0.016**
Married, separated, divorced, widowed n (%)	192 (57.8)	132 (68.4)	
Employment			
Permanent n (%)	151 (45.5)	60 (31.1)	**0.001**
Unemployed n (%)	181 (54.5)	133 (68.9)	
Housing			
Permanent residence (private home) n (%)	286 (86.1)	177 (91.7)	0.057
Transient residence (homeless, community, dormitory) n (%)	46 (13.9)	16 (8.3)	
Domestic situation			
Living alone n (%)	106 (31.9)	42 (21.8)	**0.013**
Cohabiting (partner and/or children, family of origin, friends, colleagues, others) n (%)	226 (68.1)	151 (78.2)	
Citizenship			
Italian n (%)	298 (89.8)	152 (78.8)	**0.001**
Not Italian n (%)	34 (10.2)	41 (21.2)	

Legend: AUD: alcohol use disorder; IQR: interquartile ranges.

Table 3. Clinical-anamnestic data of our sample of AUD outpatients: Wilcoxon rank sum test and χ^2 test

	Males	Females	p-value#
Age at start of problematic drinking (in years; median and IQR)	30 (17)	35 (15.5)	**0.000**
Latency time (in years; median and IQR)	12.4 (9.4)	9.6 (7.8)	**0.048**
At least one previous AUD treatment n (%)	166 (50.0)	95 (49.2)	0.864
Familiarity with AUD (1st and 2nd degree relatives) n (%)	36 (10.8)	35 (18.1)	**0.018**
Lifetime use of psychoactive substances n (%)	109 (32.8)	36 (18.7)	**0.000**
Recent use of psychoactive substances n (%)	99 (29.8)	32 (16.6)	**0.003**
Psychiatric comorbidity n (%)	166 (50.0)	140 (72.5)	**<0.000**
Psychotic disorder n (%)	29 (8.7)	14 (7.3)	0.551
Personality disorder n (%)	60 (18.1)	44 (22.8)	0.190
Anxiety disorders n (%)	73 (22.0)	80 (41.5)	**<0.000**
Mood disorders n (%)	84 (25.3)	96 (49.7)	**<0.000**
Traumatic experiences n (%)	49 (14.8)	67 (34.7)	**<0.000**
Violent experiences n (%)	12 (3.6)	31 (16.1)	**<0.000**

Legend: AUD: alcohol use disorder; IQR: interquartile ranges; # p-value deriving from Wilcoxon rank sum test (continuous variables), and χ^2 test (dichotomous variables).

Table 4. Regression models according to sex of clinical-anamnestic data of our sample of AUD outpatients

	OR (95% CI) for male sex – unadjusted	p-value unadjusted	OR (95% CI) for male sex – adjusted*	p-value adjusted*
Age at start of problematic drinking	0.02 (0.00 – 0.48)	**0.018**	0.25 (0.01 – 4.54)	0.349
Latency time	6.87 (0.74 – 64.19)	0.093	17.48 (1.60 – 190.87)	**0.020**
At least one previous AUD treatment	0.74 (0.40 – 1.32)	0.306	0.57 (0.28 – 1.10)	0.098
Familiarity with AUD (1st and 2nd degree relatives)	0.60 (0.28 – 1.29)	0.191	0.46 (0.19 – 1.09)	0.079
Lifetime use of psychoactive substances	2.03 (1.09 – 3.85)	**0.027**	1.52 (0.74 – 3.16)	0.252
Recent use of psychoactive substances	1.90 (0.96 – 3.93)	0.071	1.90 (0.87 – 4.32)	0.113
Psychiatric comorbidity	0.28 (0.14 – 0.53)	**0.000**	0.23 (0.10 – 0.47)	**0.000**
Psychotic disorder	0.86 (0.29 – 2.72)	0.796	0.70 (0.19 – 2.62)	0.589
Personality disorder	0.76 (0.38 – 1.54)	0.434	0.58 (0.25 – 1.33)	0.198
Anxiety disorders	0.33 (0.18 – 0.60)	**0.000**	0.36 (0.18 – 0.69)	**0.002**
Mood disorders	0.32 (0.18 – 0.58)	**0.000**	0.35 (0.18 – 0.68)	**0.002**
Traumatic experiences	0.31 (0.16 – 0.59)	**0.000**	0.19 (0.08 – 0.42)	**<0.000**
Violent experiences	0.17 (0.05 – 0.46)	**0.001**	0.11 (0.03 – 0.36)	**0.001**

Legend: AUD: alcohol use disorder; 95% CI: 95% confidence interval; OR: odds ratio; *adjusted for variables displayed by Table 2.

Reply to Alcohol and Alcoholism Editorial Office

Dear Sirs,
Please find Figure 1 uploaded as a high-resolution image.
We have cited Table 2 at the beginning of the Results (please find manuscript R2 with track changes and clean).
Best regards,
Roberta Agabio

Needs of Female Outpatients with Alcohol Use Disorder: Data from an Italian Study

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Running title: Needs of women with AUD

Abstract

Aims: Alcohol use disorder (AUD) is a common mental disorder characterized by sex-gender differences (SGDs). The present study was aimed at evaluating attitudes displayed by Italian AUD treatment services towards investigating the presence of SGDs in their patients and implementing gender-specific treatments for female AUD patients.

Methods: Potential SGDs were initially investigated in a sample of AUD outpatients, subsequently followed by a national survey on the adoption of specific interventions for female AUD outpatients.

Results: The presence of SGDs was confirmed in a sample of 525 (332 men; 193 women) AUD outpatients, including a higher prevalence of anxiety and mood disorders, and episodes of violence and trauma among female AUD outpatients compared to males. Despite the presence of these SGDs, only less than 20% of a total of 217 Italian AUD treatment services reported the implementation of specific strategies for female AUD outpatients. The majority of services (94%) reported investigating episodes of violence and/or trauma, largely resorting to specific procedures only when these issues were detected.

Conclusions: Our findings confirm the presence of SGDs among AUD outpatients, including a higher prevalence of anxiety and mood disorders and episodes of violence and trauma among females compared to males. However, only a small number of services has adopted a gender medicine approach in AUD treatment. These results underline the urgency of investigating the specific needs of female, male, and non-binary AUD patients in order to personalize and enhance the effectiveness and appeal of AUD treatment.

Short Summary

Women with alcohol use disorder (AUD) may display specific needs (e.g., possibility to receive psychiatric treatment in the same AUD service; implementation of specific plans for patients

reporting episodes of trauma and violence). Nevertheless, less than 20% of our sample of Italian services reported applying specific strategies for female AUD outpatients.

Keywords: alcohol use disorder, sex/gender differences, women, violence, trauma, treatment services.

Abbreviations: APA, American Psychiatric Association; AUD, Alcohol Use Disorder; CI, Confidence Intervals; IQR, InterQuartile Ranges; OR, Odds Ratios; PTSD, post-traumatic stress disorder; SGDs, sex-gender differences; SUD, Substance Use Disorder

Introduction

Alcohol Use Disorder (AUD) is a highly prevalent mental disorder (APA, 2022) characterized by a strong desire to consume alcohol, inability to control alcohol intake, and consequent episodes of excessive alcohol consumption associated with higher risks of developing devasting consequences such as acute intoxication, injury, violence, cancers, hypertension, suicide, and mortality (MacKillop et al., 2022). Worldwide, lifetime prevalence of AUD is approximately 8.6% of the general population (Glantz et al., 2020) with a large variability between countries. Among high income countries, the highest and lowest values have been estimated in Australia (22.7% of general population) and Italy (1.3%), respectively (Glantz et al., 2020). A recent national report has recently confirmed the prevalence of AUD in Italy as being lower than the European average (Scafato et al., 2023).

Numerous studies have highlighted the existence of relevant differences between men and women in the onset, progression, and clinical manifestation of several psychiatric diseases, as well as in response to treatments and associated adverse events (Mauvais-Jarvis et al., 2020). As these differences may include both biological (sex differences) and social–cultural–economic differences (gender differences), with sex and gender also interacting, use of the denomination "sex-gender differences (SGDs)" has been recommended to include both terms and relative interactions (Madsen et al., 2017).

AUD is no exception when it comes to presenting SGDs (Agabio et al., 2017; McCaul et al., 2019; McCrady et al., 2020; White, 2020). As an example, AUD is historically more prevalent in men than in women, with worldwide values estimated as corresponding to approximately 20.5% and 7.8% of male and female populations, respectively (Glantz et al., 2020). However, over the last few years, this SGD has narrowed, particularly among the younger populations (Slade et al., 2016). Furthermore, it is well-known that following ingestion of equivalent amounts of alcohol, women achieve higher blood alcohol levels than men, displaying a higher vulnerability to alcohol-related medical consequences (McCaul et al., 2019). These SGDs are mainly due to the smaller volume of distribution caused by their lower body water content and higher body fat percentage, and lower first-pass

metabolism of alcohol resulting from a lower activity of the enzyme alcohol dehydrogenase, ADH compared to men (McCaul et al., 2019). Some studies have also reported a phenomenon known as telescoping effect (Tower et al., 2023) characterized by earlier onset of AUD in men than women, with no difference in the average age of accessing services, suggesting a faster progression of AUD in women that may lead them to seek specialized services earlier than men.

Despite these SGDs in AUD, the potential influence of both sex and gender in the efficacy and safety of medications approved for the treatment of AUD has been understudied, both clinically and preclinically (McCrady et al., 2020). Indeed, particular attention should be paid to several SGDs which may require personalized medical treatment in men and women with AUD. For instance, it has been observed that, compared to men with AUD, women with AUD more frequently suffer from anxiety and depression (McCrady et al., 2020; White, 2020; Lespine et al., 2022). Furthermore, women with AUD report episodes of trauma and violence more frequently than men with AUD (McCrady et al., 2020; Guinle and Sinha, 2020). The relationship between trauma and violence on the one hand, and alcohol use on the other, is bidirectional, as having been exposed to violence, particularly in childhood and adolescence, increases the risk of developing AUD (Guinle and Sinha, 2020), and alcohol use and intoxication increase the risk of episodes of physical and sexual violence, particularly among women (Lemke et al., 2008; Devries et al., 2014). These SGDs suggest the need for a gender approach to be adopted in providing personalized treatment for men and women with AUD (Fonseca et al., 2021), as provided for in recent Italian legislation (Law 3/2018, GU n.25, 31.01.2018; Decree-Law 13.06.2019).

Despite the presence of these SGDs, we hypothesized that it was unlikely that all Italian services had adopted a gender-specific approach in the treatment of AUD outpatients. Accordingly, we aimed to evaluate attitudes displayed by Italian AUD treatment services towards investigating the presence of SGDs in their patients and implementing gender-specific treatments for female AUD patients. To achieve these aims, we first investigated potential SGDs in a sample of Italian AUD outpatients, and

subsequently conducted a national survey by mailing a questionnaire on specific interventions for female AUD patients to all Italian AUD treatment services.

Materials and Methods

Evaluation of potential SGDs in a sample of AUD outpatients

Two AUD outpatient treatment services located in the Emilia Romagna region, namely Lugo and Rimini, were selected. Briefly, as for all other public AUD treatment services in Italy, access to these services is mainly voluntary, although may also be recommended by other services; the treatment dispensed includes free medical, pharmacological, and socio-rehabilitative therapies and psychological/psychotherapeutic support through a multi-professional approach provided by physicians, psychologists, nurses, social workers, and educators.

Medical records of AUD outpatients receiving treatment at these two services from January 1, 2019 to December 31, 2019 were evaluated. Inclusion criteria were: 18 years or older and a primary diagnosis of mental and behavioral disorder due to alcohol use (meeting ICD-10 criteria - diagnosis group F10.0 – F10.9). Presence of other comorbid disorders, cognitive deficits, or linguistic-cultural limitations were not viewed as criteria for exclusion. Data of included patients were collected from computerized medical records compiled by physicians involved in the treatment of AUD patients. Physicians were interviewed if data were found to be missing. The Ethics Committee of the Local Health Authority of Romagna approved the study (January 24, 2020; n. 2599).

The following data were collected:

- *Socio-demographic data*: gender, age, marital status, level of education, professional status, living situation, cohabitation, and citizenship;
- *Clinical-anamnestic data*: age at start of problematic drinking (i.e., consuming more than 40 and 60 g/day, for women and men, respectively, according to the World Health Organization risk levels, see MacKillop et al., 2022 for a detailed description), age at first entry to an AUD service, latency time (i.e., time between age at start of problematic drinking and first entry to an AUD service), any

previous AUD treatment (e.g., pharmacological, psychological/psychotherapeutic, socio-rehabilitative or self-help group interventions) external to the actual service, family history of AUD (i.e., 1st and 2nd degree relatives), lifetime and current history of substance use disorders from substances other than alcohol (e.g., tobacco, heroin, cocaine) or other behavioral disorders (e.g., gambling), comorbid psychiatric disorders and type of disorder (e.g., personality disorders, psychotic spectrum disorders, anxiety disorders, mood disorders), and experience of trauma and/or violence.

When information on episodes of trauma and violence was not available from medical records, physicians involved in the treatment of AUD patients were interviewed. In detail, we asked whether their outpatient had been exposed to traumatic experiences, defining trauma as an unexpected and sudden event that (i) the subject experienced as destabilizing and devastating, and which exceeded the person's ability to respond, (ii) left the subject in a condition of helplessness and unable to face/manage a shocking and uncontrollable experience, (iii) overwhelmed the individual's normal defenses making him/her incapable of reacting and leading to the raising of pathological defenses. We then asked whether the outpatient had been subjected to experiences of violence defined as intentional use of physical force or power by a person or people resulting in physical injury or psychological harm. We explained that violent behavior, despite causing physical and psychological injury and harm, may not necessarily generate trauma in the victim if they actively and developmentally faced up to the event experienced, activating personal and relational resources to re-elaborate it and/or therapeutic paths and restorative experiences. At the same time, we also indicated that even apparently non-violent behaviors, such as denigratory and oppressive attitudes, and developmental experiences of neglect or inconsistency, might generate trauma if subjectively experienced as uncontrollable, destabilizing, and devastating.

Attitudes of Italian AUD treatment services toward consideration of gender differences and episodes of violence

All Italian services involved in the treatment of AUD and Substance Use Disorder (SUD) were listed and detailed information including email address, telephone number, and name of the person in

charge was collected. We contacted each service to explain the aims of our study, requesting their availability to take part in the study, and explaining that participation consisted in filling a five-question questionnaire focused on AUD treatment and that answers would be anonymized. In addition to questions relating to the treatment of women with AUD, the questionnaire also included questions on non-binary AUD patients. The questionnaire was e-mailed to services that had agreed to take part, asking them to fill in and return the questionnaire (see Table 1). Briefly, questions were aimed at investigating whether services:

i) collect information relating to patient's sexual orientation and/or gender identity

ii) adopt strategies for non-binary patients

iii) adopt strategies for women

iv) investigate current and/or past episodes of physical/psychological violence and/or trauma

v) adopt strategies in the presence of violence/trauma.

Services were given the opportunity to further elucidate their answer or justify answers provided. With regard to answers provided to the last question, two authors, experts in the treatment of individuals with AUD subjected to episodes of violence and/or trauma (MCS, LR), evaluated all additional comments and commented on their appropriateness. In detail, strategies structured and focused on violence (e.g., protocols, guidelines, protected structures, other antiviolence procedures) were deemed appropriate, whilst strategies which failed to focus specifically on episodes of violence and trauma such as, for instance, group psychotherapy sessions, were deemed inappropriate.

Statistical analysis

The Shapiro-Wilk test was used to assess the normal distribution of variables. Data are provided as medians and interquartile ranges (IQR) for continuous variables, and numbers and percentages for dichotomous variables. Continuous and dichotomous variables were compared using the Wilcoxon rank sum test and the χ^2 test, respectively. Clinical-anamnestic data were considered as dependent variables for linear and logistic models. Their results are expressed as Odds Ratios (OR) and 95%

Confidence Intervals (95% CI). The effect of potential confounding effects of socio-demographic variables was studied with adjusted models. The software used for analysis were STATA (version 16), and RStudio (version 4.2.3). Statistical significance was set at $p<0.05$.

Results

SGDs among AUD patients referring to treatment services.

Table 2 shows the socio-demographic characteristics of our sample of 525 patients, with a male/female ratio of 1.7:1. Compared to men, women displayed higher levels of education, were more frequently married, more frequently unemployed and lived in shared accommodation with their partner, children, or others, and were not Italian.

As shown in **Table 3**, compared to men, women had a shorter latency time and, more frequently than men, suffered from anxiety and mood disorders, and reported episodes of violence and trauma. Among participants who reported episodes of violence and trauma, no difference was observed between Italians and non-Italian women and men (episodes of violence: 52 Italian women and 15 non-Italian women; 43 Italian men and 6 non-Italian men; p=0.24714; traumatic episodes: 23 Italian women and 8 non-Italian women; 9 Italian men and 3 non-Italian men; p=0.73744; data not shown). Taking potential socio-demographic confounders into account (see **Table 4**), women and men did not show significant independent differences in median age at start of problematic drinking, previous treatment or AUD, familiarity with AUD, or lifetime and recent use of psychoactive substances.

Attitudes displayed by Italian AUD treatment services toward consideration of potential SGDs and episodes of violence

Between June and December 2023, 855 AUD and/or SUD treatment services in Italy were listed and contacted by e-mail (see Figure 1); if no response was received, we phoned the services directly. We excluded 144 services as they were no longer operational, thus obtaining a final list comprising 711 services, of which 514 (72.3%) answered our phone call, and 217 (42.2% of responders) filled in and returned the questionnaire by email.

Out of the 217 services that took part in our study (see Figure 1) (*i*) 84.8% confirmed they routinely collected information on sexual orientation and/or gender identity during the first observation and diagnostic phase of treatment, (*ii*) 6.9% and (iii) 18.9% reported adopting specific initiatives for non-binary patients and women, respectively, (iv) 94.0% affirmed specifically investigating current and/or past episodes of physical/psychological violence and/or trauma, and (*v*) 71.6% of those affirming investigation of episodes of violence and/or trauma confirmed they routinely adopt specific procedures on detection of violence and/or trauma.

Some services provided additional information. In detail,

1) to the first answer focused on *Patient's sexual orientation and/or gender identity,* several services added that this was not mentioned unless patients referred to the matter spontaneously, with others raising the issue at later stages of AUD treatment;
2) to the second answer focused on *Initiatives for non-binary patients,* no services added further information on initiatives taken for non-binary people; some stated the use of toilets with no gender indication, although this was not an initiative implemented specifically for non-binary people;
3) regarding the third answer, *Initiatives for women*, some services reported the presence of female health operators amongst their members of staff or an all-female team of health operators. Some referred to specific group activities accessible solely by female AUD patients. One service mentioned a project devoted to AUD women, which included collaboration with a mental health center and pediatric and gynecology wards. Another center described the progressive activation of a series of projects specifically devoted to women, in collaboration with other services for the prevention and treatment of sexually transmitted diseases and unplanned pregnancies, and for women reporting episodes of violence. Another service reported the organization of initiatives aimed at increasing awareness on this topic. Finally, one service reported implementing a project aimed at preventing AUD in women;

4) with regard to the fourth question *Questions on episodes of violence and/or trauma*, numerous services confirmed how these episodes were investigated during the unstructured anamnestic survey. Several services admitted that questions were not asked routinely, although relevant information on these issues was collected when spontaneously provided by patients. Other services reported the use of structured or semi-structured interviews such as the Addiction Severity Index (which also investigates past and recent psychological, physical and sexual violence; McLellan et al., 1980), Adverse Childhood Experiences (Felitti et al., 1998), Adult Attachment Interview (George et al., 1985), and Addictive Behavior Questionnaire (Caretti et al., 2018). Finally, some services stated how during physical examination, signs pointing to recent episodes of physical violence were investigated;
5) on answering the fifth question on *Specific procedures in case of violence or trauma,* ninety-nine services added further details of strategies adopted. Of these, 54.5% (54 out of 99) were deemed to be appropriate for use in dealing with victims of violence, whilst 36.4% (36 out of 99) were inappropriate, and 9.1% (9 out of 99) unclear. With regard to appropriate strategies, the majority of services reported using specific protocols developed by antiviolence centers, protected structures, refugee centers and/or other antiviolence procedures. Some services did not describe specific protocols but mentioned taking appropriate action for the situation at hand. Two services mentioned an intervention devoted to the families of women reporting episodes of violence. Another service described a protocol in which forensic physicians help other health operators to manage the clinical case, referring those affected to antiviolence centers or emergency departments. The most frequently reported inappropriate strategies comprised individual and group psychotherapies.

Discussion

The results obtained confirmed several of the SGDs already reported by previous studies (e.g., White, 2020; Lespine et al., 2022). In detail, in our sample, compared to males, female AUD outpatients

displayed higher educational levels, were more frequently married, lacking permanent employment, and did not live alone, thus confirming data from a recent Italian national survey (Italian Ministry of Health, 2020) and a regional study (Agabio et al., 2021). We also observed a telescoping effect among female AUD patients as, compared to males, they referred a significantly lower latency time to treatment. Previous studies observed a similar phenomenon, although the finding has been criticized by other studies that detected no evidence of this phenomenon in the general population, weaker evidence among younger individuals, or only partially supportive evidence of SGDs in AUD latency (Towers et al., 2023). We also confirmed a higher prevalence of anxiety and depression in female compared to male AUD outpatients (McCrady et al., 2020; White, 2020; Lespine et al., 2022). These results suggest that female AUD outpatients may require medical treatment earlier than males, as well as additional psychiatric treatment for comorbid anxiety and depression. To personalize and modulate therapeutic interventions, employment and housing stability, essential aspects in recovery from AUD and SUD, should also be investigated (Cano et al., 2017).

One of the major challenges is linked to increasing the rate of individuals with AUD seeking and receiving medical treatment. Despite the documented efficacy of available treatments, less than 10% of individuals with AUD receive formal treatment, with lower rates of women compared to men (McCrady et al., 2020). It has been hypothesized that this difference may be associated with the failure of AUD services to match women's needs (Venegas et al., 2021). To better match these needs, AUD services would need to provide childcare, prenatal care, treatment for co-occurring mental disorders (e.g., anxiety and depression), and supplemental social services, possibly in the context of women-only programs (McCrady et al., 2020).

Our study revealed a male: female ratio (1.7:1) that failed to overlap fully with estimations provided in a recent national survey (3.3:1; Italian Ministry of Health, 2020). Our male: female ratio seemed to better resemble that of people accessing hospital emergency departments for alcohol related issues (2.3:1; Italian Ministry of Health, 2020). This finding may suggest the existence of lower barriers to treatment for women with AUD in services selected for our study compared to other services. Indeed,

the services selected for the purpose of this study, which adopted a multidisciplinary approach involving physicians, psychologists, nurses, social workers, and educators, many of which females, may have proved more appealing to female AUD patients. The main barriers for women seeking AUD treatment include multiple factors, such as lack of social support, stigma, parental role, and tendency to refer to primary care (McCaul et al., 2019; McCrady et al., 2020; Lespine et al., 2022); this hypothesis should therefore be investigated in-depth to provide additional input with regard to strategies aimed at reducing barriers and facilitating access to AUD treatment for Italian women.

Our study also revealed a higher frequency of non-Italians in the sample of female compared to male AUD outpatients. This finding may be due to the high presence of largely female immigrants from Eastern European countries, where AUD is highly prevalent (Gualdi-Russo et al., 2009). This SGD should also be taken into consideration for the purpose of personalizing and modulating therapeutic interventions, for instance, inclusion of a cultural mediator on the team of health operators of AUD treatment services.

A higher prevalence of traumatic episodes and violence in female AUD outpatients compared to males was also confirmed (Guinle and Sinha, 2020). Specifically, compared to men, episodes of violence and trauma were four- and two-fold higher among women, respectively. This SGD is of particular importance for health operators involved in the treatment of AUD, since having experienced trauma or violence during childhood or adolescence increases the risk of developing both AUD (Guinle and Sinha, 2020) and post-traumatic stress disorder (PTSD), a mental disorder more frequently manifested in women (10-12%) than men (5-6%; Singh and Wendt, 2024). On the other hand, use of alcohol as a coping mechanism to deal with stressful, negative events or post-traumatic symptoms is more frequent among women (Peltier et al., 2019), with alcohol intoxication representing a risk factor for exposure to sexual violence. All these factors merge to create a vicious circle between episodes of trauma and violence and AUD. Previous studies investigated how episodes of violence and trauma impact treatment outcomes of people with SUD (Pirard et al., 2005; Di Nicola et al., 2024). For instance, a recent Italian study observed a direct relationship between childhood

trauma and risk of suicide attempts among people with SUD, mostly constituted by women (Di Nicola et al., 2024). Accordingly, specific treatments should be provided to people with AUD or SUD who refer episodes of violence (Schumm et al., 2018), with our findings suggesting that female AUD outpatients may experience a greater need for these treatments than AUD males.

Almost all (94%) services that took part in our survey investigated the presence of episodes of violence and trauma, of which 67% referred recourse to specific procedures when exposure to violence and/or trauma was detected. However, some procedures were not deemed fit for purpose. Accordingly, our results suggest that not all Italian services adopt the most suitable approach in the treatment of AUD outpatients who report episodes of violence or trauma.

Finally, as hypothesized, the results of our study reveal how less than 20% of the sample of Italian services investigated have effectively implemented specific strategies for women with AUD. These strategies include the presence of female health operators, group activities devoted exclusively to female AUD outpatients, collaboration with mental health centers and pediatric and gynecology wards, projects aimed at preventing and treating sexually transmitted diseases and unplanned pregnancies, projects tailored for women who report episodes of violence, and projects aimed at increasing awareness of alcohol-related consequences and preventing AUD in women. Nevertheless, the vast majority failed to implement gender-specific strategies for women with AUD.

Globally, these findings suggest that despite the presence of SGDs, outpatients with AUD are frequently not treated using a gender-specific approach (Fonseca et al., 2021). Treatment of AUD continues to be based on the results obtained by clinical studies performed prevalently on male AUD patients, according to an androcentric model. In 2018, in Italy, a national law stated the need to adopt a gender medicine approach throughout the National Health Service and provided a plan aimed at disseminating gender medicine across the entire nation (Law 3/2018, GU n.25, 31.01.2018; Decree-Law 13.06.2019). Nevertheless, few studies have investigated potential SGDs in Italian AUD outpatients or in people affected by excessive alcohol use (Agabio et al. 2017, 2021; Allamani et al., 2000; Guerrini et al., 2006; Mancinelli et al., 2013; Pavarin et al., 2017; Picci et al., 2012; Shield et

al., 2013; Stroffolini et al., 2018). To date no studies have specifically investigated the needs of women with AUD who refer episodes of violence and/or trauma and the implementation by AUD treatment services of gender-specific strategies for women with AUD.

Conclusions

Our findings confirm the presence of SGDs among Italian AUD outpatients and suggest the presence of specific needs in women with AUD, including the possibility of obtaining referrals for additional psychiatric treatment in the center in which AUD treatment is provided, presence of a cultural mediator, and implementation of specific plans for patients who report episodes of trauma and violence. Unfortunately, less than 20% of the sample of Italian services studied reported the implementation of specific strategies in the treatment of female AUD outpatients. Globally, our results underline the need for further studies aimed at identifying the specific needs of female AUD outpatients and evaluating the most appropriate treatment strategies. The results obtained in our study may help to persuade Italian policy makers to facilitate implementation of strategies with the aim of improving the appeal, quality and effectiveness of treatment for AUD patients according to the specific needs of women, men, and non-binary patients.

Limitations of the Study

The study featured a series of limitations. As data were collected from medical records, we indirectly evaluated potential SGDs and may have inadvertently limited data to biological differences rather than gender issues such as identifying as a man or woman regardless of biological sex or being non-binary. These aspects were generally not discernible from medical records, and physician interviews failed to provide additional data, thus suggesting the need to focus specifically on the complex issues of gender and sexual orientation, which represent elements of discrimination and risk factors for AUD (Allen and Mowbray, 2016; Gonzales et al., 2016). In addition, the heterogeneity in assessing traumatic exposure among services may limit the generalizability of our findings to other countries

or settings. A further limitation was represented by the limited sample size of AUD patients and period considered (1 year).

Author Contributions

Conceptualization: Teo Vignoli, Caterina Staccioli, Liana Fattore, Roberta Agabio; Data curation: Maristella Salaris, Samantha Sanchini, Elisa Martino, Lorena Rigoli, Francesco Salis, Liana Fattore, Roberta Agabio; Formal analysis and investigation: Maristella Salaris, Samantha Sanchini, Elisa Martino, Lorena Rigoli, Francesco Salis; Writing - original draft preparation: Liana Fattore, Roberta Agabio; Writing - Review and editing: Teo Vignoli, Caterina Staccioli, Fabio Caputo, Liana Fattore, Roberta Agabio; Resources: Teo Vignoli and Caterina Staccioli; Supervision: Teo Vignoli, Caterina Staccioli, Fabio Caputo, Liana Fattore and Roberta Agabio.

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Conflicts of Interest

The authors declare no conflict of interest.

Ethical Approval

The study was approved by the Ethics Committee of the Local Health Authority of Romagna, Italy (January 24, 2020; n. 2599).

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Data Availability

The data analyzed during the current study are available from the corresponding author on reasonable request.

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