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RESEARCH ARTICLE

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A network study to differentiate suicide attempt risk profiles in male and female patients with major depressive disorder

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Abstract

Suicide attempts are a possible consequence of Major Depressive Disorder (MDD), although their prevalence varies across different epidemiological studies. Suicide attempt is a significant predictor of death by suicide, highlighting its importance in understanding and preventing tragic outcomes. Researchers are increasingly recognizing the need to study the differences between males and females, as several distinctions emerge in terms of the characteristics, types and motivations of suicide attempts. These differences emphasize the importance of considering gender-specific factors in the study of suicide attempts and developing tailored prevention strategies. We conducted a network analysis to represent and investigate which among multiple neurocognitive, psychosocial, demographic and affective variables may prove to be a reliable predictor for identifying the 'suicide attempt risk' (SAR) in a sample of 81 adults who met DSM-5 criteria for MDD. Network analysis resulted in differences

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between males and females regarding the variables that were going to interact and predict the SAR; in particular, for males, there is a stronger link toward psychosocial aspects, while for females, the neurocognitive domain is more relevant in its mnestic subcomponents. Network analysis allowed us to describe otherwise less obvious differences in the risk profiles of males and females that attempted to take their own lives. Different neurocognitive and psychosocial variables and different interactions between them predict the probability of suicide attempt unique to male and female patients.

KEYWORDS
major depressive disorder, network analysis, sex differences, suicide attempt, suicide risk

1 | INTRODUCTION

Suicidal behaviour is a worldwide phenomenon: the World Health Organization (Anon, n.d.) has estimated that approximately 703,000 individuals worldwide take their own lives annually. Over the past 5 years, this grim total has reached over 3 million people. Furthermore, for each of these individuals, there are approximately 20 others who attempt suicide. In Italy, an average of 4,000 deaths by suicide occur each year, 78.8% of which are men, according to the Istituto Superiore di Sanità—ISS (EpiCentro, n.d.). Suicide, therefore, must be considered a topic of major interest for public mental health, where identifying possible risk and protection factors is of fundamental importance (Costanza et al., 2020; Odone et al., 2018).

Indeed, research is increasingly trying to identify clinical and epidemiological markers (Dong et al., 2019) of suicidal behaviour to promote targeted strategies for mental health (Baldessarini et al., 2019; Darvishi et al., 2015; Orpana et al., 2019; Turecki & Brent, 2016) focused on risk assessment and prevention. Among the risk factors, attempted suicide is a highly significant marker and people who killed themselves had likely attempted suicide before (Gvion & Levi-Belz, 2018). This assumption seems to be supported by other studies, indicating that the rate of death by suicide is 100 times higher in people who attempt suicide, in at least one occasion, than in the general population. In addition, non-fatal suicide attempts and/or repeated attempts are among the strongest predictors of 'taking one's own life' (Bachmann, 2018; Kokkevi et al., 2012; Pawlak et al., 2018; Sher, 2019; Walsh et al., 2017) with the risk remaining high for many years after the attempt was made. When considering retrospectively diagnosed MDD, however, recent data suggest that knowledge of the cause of death may lead to a possible bias presuming that death occurred in the presence of MDD (Bryan, 2021; de Beurs, 2022). These data highlight that preventive strategies could benefit from the thorough analysis of predictors of suicidal behaviour (Gvion & Levi-Belz, 2018; Isometsä, 2014; Moreno et al., 2021). Moreover, if we want to use these predictors efficiently, we should gain a thorough knowledge of how factors, such as the age and sex of the individual may drive the overall risk.

Key Practitioner Message

- Males and females show opposite pattern of variables that predict suicide attempt.
- Network analysis allows to overcome the limitations of traditional statistics.
- To better understand psychopathology, new methods should be explored.
- Treatment choices must consider which variables drive the network in the two sexes.

Epidemiologic statistics confirm that people who attempt suicide suffer mainly from Major Depressive Disorder (MDD) (56–87%) (Pawlak et al., 2018) and that about half of them before committing suicide had contacted health services in the last weeks of their life (Pawlak et al., 2013; Yoshimasu et al., 2008). A multitude of studies have found risk factors for suicide ideation or suicide attempt among patients with comorbidities such as MDD, dysthymia, anxiety disorders, bipolar disorder and schizophrenia (Bolton et al., 2010; Eikelenboom et al., 2018; Moitra et al., 2021) independently from the pathologies involved (Baldessarini et al., 2019). However, many of these studies just focused on suicide ideation, suicidal behaviour or their combination (May, 2016), and making these designs reductive because they do not allow the disentanglement of other risk factors.

Additionally, psychosocial adjustment represents a critical aspect to consider. Psychosocial functioning, indeed, regards many specific aspects of our daily routine defining the dimension of a person's quality of life (Grendas et al., 2019). Psychosocial duties involve several domains like work, money management, social relationships, time for leisure, personal autonomy and cognitive efficacy.

From the literature emerges that job termination, poverty and work-related stressors (Baldessarini et al., 2019; Han et al., 2016) play a crucial role in suicide, while aspects related to loneliness, lack of social support and severe difficulties in fulfilling daily tasks are strongly related to attempting suicide (Dennis et al., 2009; Kleiman & Liu, 2013; Sokero et al., 2003). Moreover, several studies examined the contribution of different factors to the risk of suicide attempts within the interpersonal context, where interpersonal and communication difficulties were found to be strongly related to suicide attempt risk (SAR) (Gvion & Levi-Belz, 2018).

Another important element of SAR appears to be sex (Dalca et al., 2013; Denneson et al., 2020; Gvion & Levi-Belz, 2018; Miranda-Mendizabal et al., 2019): female patients display a significantly higher rate of SAR than male patients, while the latter had a higher rate of mortality from suicide. Men tend to apply high-lethal methods more frequently than women, which may partially explain the difference between attempts and actual deaths. However, available information on the risk for suicide completion in females is limited and often extrapolated from studies conducted in males (Dalca et al., 2013). Some exceptions though exist. Oquendo et al. (2007) analysed whether risk factors of suicide may differ between males and females diagnosed with MDD. Factors increasing the risk of future suicidal behaviour for females were the presence of previous suicide attempts, suicidal ideation, the lethality of past attempts (people with high-lethality attempts tend to report greater suicidal intent and more previous attempts), hostility, subjective depressive symptoms, fewer reasons for living, comorbidity with borderline personality disorder and smoking. In males, the risk of future suicidal acts increased with a family history of suicides, past use of substances, smoking, comorbidity with borderline personality disorder and early parental separation. The precipitating factors seem to have different influences regarding not only sex but also cognitive factors, social aspects and negative life events and contexts (Delgado-Gomez et al., 2012; Pawlak et al., 2018). But overall, it is likely that the sex of the patient drives and characterizes different risk profiles and vulnerabilities. Several reviews indicate that multilevel interventions are the best choice for suicide prevention (Zalar et al., 2018).

Traditional analyses for the prediction of suicide attempts have limited accuracy and just scale risk detection for the vast variety of factors involved (Walsh et al., 2017). But accurate suicide attempt prediction requires a more complex approach if we truly want to understand the most relevant elements, how they are connected and what factors are driving the overall predisposition. Furthermore, risk needs to be detected early to put preventive measures into place promptly. Currently, identified risk factors lack the capacity to distinguish individual trajectories. Thus, if we want to be able to detect the distinct clinical pathways of individuals that are at risk of attempting suicide, then a paradigm shift is essential. The firmly established traditional approach linking just one or a few factors to SAR-related phenotypes has led to limited understanding of the complex underlying dynamics, which has hampered progress in the development of efficient prevention. Therefore, we propose to use network science and dynamic system theory which, through the graphical and numerical mapping of the interactions between the variables studied, with suicide attempts, will make it possible to provide a 'snapshot' of their interdependence, making it possible to identify those nodes (variables) that more than others explain the variance (presence or absence) of suicide attempt in male and female patients.

We believe that network analysis is a contemporary statistics approach that can effectively address the complexity of this topic (McNally, 2016). Indeed, it can explore the reciprocal interactions of variables involved in suicidal behaviours and identify the most critical factors predicting the predisposition to attempt suicide. In this way, the predictors can be measured, monitored and modified thanks to targeted preventive strategies. In the literature, a study that explored the phenomenon of suicide with network analysis (de Beurs et al., 2019) found that perceived burdensomeness, internal entrapment (i.e., the emotional pain caused by one's thoughts), depressive symptoms and history of suicide ideation, best explained suicide ideation, allowing to identify four larger clusters: mental wellbeing, interpersonal needs, personality and suicide-related factors.

Here, we introduce sex as a risk factor and hypothesize that risk factors (comorbidity, severity of depression, psychosocial impairment, low cognitive functions, etc.) interact differently in male and female patients and that SAR is driven by different components according to the sex of the patient.

Network analysis will help to determine if one domain or function is more important than others, if changes in one domain, factor or symptom lead to changes in other ones, and what factor (variable) is driving the network. In sum, network analysis will not only indicate which domains and factors mostly predict the presence or absence of suicide attempts and are central to clinically high-risk patients but will have important implications for clinical practice motivating differential and personalized prevention strategies based on sex linked SAR profiles.

The main aim of this study was to identify sex-specific patterns predicting suicidal behaviour in a sample of patients with Major Depressive Disorder, by exploiting the network analysis approach to allow future algorithms to optimize prediction and prevention of suicidal risk. Our long-term objective is to provide insights into which variables can be targeted by specific treatments to prevent individuals with major depression from committing or persisting in suicidal behaviours.

2 | METHOD

2.1 | Participants

The sample included 81 adults (mean age: 53.7 years, SD: 10; 55 women, 26 men) diagnosed with MDD, according to DSM-5 criteria. The sample was recruited at the Psychiatric Clinic 'Villa dei Gerani' (Catania, Italy). The study was approved by the Ethical Committee of the 'Azienda Sanitaria Provinciale 3 (ASP3)' of Catania, with 'Villa dei Gerani Clinic' as the clinical coordinator of the study (approval date of the extended study 24 July 2012). The study met the ethical administrative requirements under Italian legislation in force when the study's administrative process started (03.06.2012) according to CM 6 02.09.2002, GU 214 12.09.2002 and D 29.03.2008 of the Italian Medicine Agency (Agenzia Italiana del Farmaco, AIFA) and

GU 76 31.03.2008, Art 10 (Procedures for Observational Studies). This study was conducted in accordance with the Declaration of Helsinki.

2.2 | Procedures and measures

Tests and questionnaires administered to subjects by a psychologist during their first visit to the centre are listed below. They are divided into three main domains.

- Neurocognitive domain

Montreal Cognitive Assessment—MoCA (Santangelo et al., 2015), for assessing overall cognitive functioning.

Frontal Assessment Battery—FAB (Iavarone et al., 2004), for executive functions.

Digit Span Forward and Digit Span Backward (Monaco et al., 2013), for assessing auditory-verbal short-term memory and working memory.

Rey Auditory Verbal Learning Test—RAVLT (immediate and deferred recall) (Ricci et al., 2022), for the ability to learn non-semantically structured material and verbal long-term memory.

Vocabulary subtest of *WAIS IV* (Benson et al., 2010), for word knowledge and verbal concept formation.

Phonetic Verbal Fluency—FAS (Costa et al., 2014), for verbal cognitive flexibility.

- Psychosocial domain

Functioning Assessment Short Test—FAST (Rosa et al., 2007), for the assessment of *Autonomy* in daily tasks, *Occupational functioning*, *Cognitive functioning*, *Financial issues*, *Interpersonal relationships* and *Leisure Time*. The higher the score in the subscales, the more serious the difficulties, so *FAST* measures disability.

- Affective domain

The *Hamilton Depression Rating Scale* (*HDRS*) (Hamilton, 1960) and the *Beck Depression Inventory-II* (*BDI-II*) (Beck et al., 1961, 1988) were used for assessing the degree of severity of depressive symptomatology.

Information was collected concerning the patients' history, including the number of previous depressive episodes, the number of attempts in which they tried to take their own lives and how long the current Depressive Episode lasted. Suicide attempt (SA) refers to the number of episodes of attempted suicide before and up to the assessment performed at the psychiatric hospital 'Villa dei Gerani' where the data presented in this study were collected. This variable, therefore, refers to retrospective data.

In order to enhance the comparison between the two groups, males and females, we approached the variable SA differently. Instead of treating it as a continuous variable, which would involve documenting the precise count of suicide attempts by each patient in the analysed dataset, we categorized it as a dichotomous variable—specifically, the presence or absence of suicide attempts. This decision allowed us to first address the issue of patients potentially having made unrecognized and/or unreported suicide attempts, and second, it enabled us to employ mixed statistical models for network computation.

As a result, we were able to focus our analysis exclusively on determining which variables interacted and to what extent, depending only on the presence or absence of a suicide attempt. Importantly, this approach also avoided introducing differences in the 'severity' of patients who had made multiple attempts.

Furthermore, it's noteworthy that within the female group, a subset of patients had made more than one suicide attempt, with a maximum of three attempts. However, since these individuals constituted a minority within their group, we chose to minimize their influence on the analysis.

The network models, described in the following paragraphs, make it possible to identify which variables predict the variance of the variables with which they have connections. This allowed us to assess whether the presence/absence of suicide attempts is predicted differently between the two sexes and, specifically, what other variables should be considered in the prediction. The concept was to construct, without explicit risk indicators (either genetic or psychological), probability through predictability. If, therefore, the presence of suicide attempts is linked to a certain network configuration, this configuration, if reoccurring, is indicative of a risk profile that indicates a greater chance of carrying out a new suicide attempt. This higher probability can be considered risk. Thus, 'Suicide Attempt Risk Profile' indicates the probability that an individual will attempt a new suicide, if the network variables interact producing a risk profile, accompanied by a specific degree of predictability.

We also added the variable 'presence/absence of comorbidity' (made dichotomous to amalgamate the comorbidity factor without having to diversify avoiding small groups that could have interfered with the generation of network models), the number of 'previous depressive episodes' and 'duration of current depressive episode'. The last two measures were treated as ordinal in the analysis. Other variables taken into consideration were *Age* and *Years of education*, which from the literature constitute factors that can positively or negatively affect depression as they are linked to the individual's resilience (Kim et al., 2021; Roudsari et al., 2018; Versteeg & Kappe, 2021).

2.3 | Statistical analysis

2.3.1 | Descriptive and inferential statistics

The data were initially analysed qualitatively to obtain general demographic information about the sample through the estimates of mean, standard deviations and percentages. The corrected scores (by age and schooling) of individual tests were treated as variables in the statistical and network analysis. Traditional independent *t* tests, parametric or non-parametric unidirectional analysis of variance (ANOVA) was performed to determine the difference among groups (males and females) for continuous variables. The Chi-squared test was used for dichotomous variables. Normal distribution was established by the Shapiro–Wilk test ($p > 0.05$ for normal intake). In addition, the homogeneity of variances within each group was established by Levene's test for equal variation ($p > 0.05$ for the assumption of equal variance), and when violated, Welch's correction for unequal variances was applied.

Mixed model and regression analyses were used to understand which variables were better predictors than others in estimating the presence or absence of 'suicide attempt' in the full sample and after partitioning by sex. Because of the dichotomy of 'suicide attempt', logistic regression analysis was conducted to further explore the predictive value of psychosocial, neurocognitive and affective performances (dependent variables). Predictive effects were considered significant at the .05 level and are presented as odds ratios (OR) with 95% interval. All analyses were conducted using SPSS version 26.0 (SPSS Inc., Chicago, IL, United States) and *R* software (Version 4.0.3/2020-10-10). The code used in R for part of the statistical analysis and all of the network analysis is reported in the supporting information.

2.3.2 | Network analysis

We analysed the data and programmed the networks with *R* software (Version 4.0.3/2020-10-10).

We estimated the network models for the three groups (*Entire sample*, *Males* and *Females*) and compared the network structure visually and by comparing differences in edge significance and explained variance of variables. We estimated the network models with the *mgm* package (Haslbeck & Waldorp, 2020). These networks are mixed graphical models (MGMs), which model relationships according to the distributional assumption of the respective variables: continuous, categorical and ordinal.

All the relationships represented in our model are pairwise interactions ($k = 2$, interactions). In addition, the resulting network consists of the estimates of the relationships between the variables taken two by two, and these relationships are controlled for by all other variables. This means that the absence of a relationship between two variables indicates that those two variables are conditionally independent given all the other variables.

We used regularization, for selecting the tuning parameter and limiting the Lq-penalization of estimating false positives, and *k-folds cross validation* (tenfolds) as reported by Jung and Jianhua (2015). With this method, we have one data set, which we divide randomly into 10 parts. We used nine of those parts for training and reserved one tenth for testing. We repeated this procedure 10 times, each time reserving a different tenth for testing. Further technical details about MGMs can be found elsewhere (Haslbeck & Waldorp, 2020).

The *qgraph* package was used for the visualization of network models (Epskamp et al., 2012). The network layout was determined with the Fruchterman–Reingold algorithm to transform the network into a system of massive particles (Fruchterman & Reingold, 1991).

Nodes are interpreted as particles and edges as the pushes they give each other. The algorithm attempts to minimize the used energy of the physical system. Fruchterman and Reingold's (1991) algorithm adds 'uniform vertex distribution' compared to earlier versions. To make the various networks compatible with each other, the layout of the full sample was used and reproduced in that of the two subgroups. In addition, to better understand the relationships between variables, individual layouts of the two subgroups were also considered.

The predictability of each node in the network was also calculated (i.e., *nodewise predictability*). This measure represents how much variance of the variable is explained by all the other variables with which it has connections (Haslbeck & Waldorp, 2018). High values of predictability indicate that most of the variance of that variable can be predicted by the variables with which it has direct connections. For continuous variables, the proportion of explained variance (i.e., R2) was chosen as the measure of predictability: a value of 0 means that the node is not predicted by all neighbouring nodes in the network, while a value of 1 means that the node can be perfectly predicted by its neighbouring nodes. For categorical variables, on the other hand, accuracy/correct classification ('CC') is specified as predictability along with normalized accuracy ('nCC') and model intercept (marginal) accuracy ('CCmarg'). Combining these three measures allows us to visualize the decomposition of total accuracy into 'intercept' and 'contribution of other variables'.

We then explored differences in the centrality of variables between the three networks; two main measures of centrality were analysed (Bringmann et al., 2019). The strength of centrality consists of the number of connections of a node. If a symptom has many connections in a certain psychopathological system, it can be considered a risk factor for the development of a variety of other symptoms. In weighted networks, as in this study, links connecting nodes are no longer treated as binary interactions but are weighted in proportion to the strength of the correlations. Betweenness is a parameter measuring how much a node is involved in the shortest path between two nodes and determines which nodes are most likely to connect other nodes to each other and, therefore, which are most likely to facilitate connections in the network. Through this measure, it is possible to identify the most important domains by studying the connectivity between a patient's problems and symptoms.

For example, from our research analysing parental distress between mothers and fathers in children with cancer, although in the scales used both parents had a peak in anxiety scores, the betweenness allowed us to understand that in the fathers, anxiety, compared to the mothers, had a secondary influence in the symptomatologic picture (although it was the highest score in the questionnaire). It was not the best symptom on which to intervene as it was instead the depressive symptomatology (variable with the highest betweenness) that redistributed the most information in the network (Scarponi et al., 2023).

The algorithm for calculating 'shortest paths' is that of Dijkstra (1959) implemented in R and repurposed by Opsahl et al. (2010).

In interpreting these indices, bootstrap tests were performed to analyse their stability (bootstrapped strength centrality and bootstrapped betweenness) and make sure that central nodes were also among all the subsamples of the data and whether the centrality of a node remained stable in 95% of the bootstrapped subsamples.

Lastly, a cluster holding algorithm was computed to explore the differences in connectivity structure among the three groups from an additional perspective. Clusters of nodes represent more connected subnetworks in a larger network. The cluster identifies a group of nodes that can be affected more rapidly when a node that is part of it changes its state. The *walktrap* algorithm was used that provides a measure of similarities between vertices based on random walks across the network connections (*igraph* package) (Csardi & Nepusz, 2005), which can capture the community/cluster structure in the graph (Pons & Latapy, 2005). The number of clusters identified equals the number of latent factors in each dataset.

3 | RESULTS

3.1 | Descriptive and inferential results

Descriptive analyses are reported for demographic data in the table below (Table 1). Regarding the presence/absence of comorbidities, 33 patients (40.7%) had at least one comorbidity, while 48 (59.3%) had none. In addition, out of 33, 11 subjects had more than one comorbidity. Individual disorders divided by sex are in Table 1. In the male sample, of 26 subjects, half had at least one comorbidity (50%); in the female sample, of 55 subjects, 20 had at least one comorbidity (40%).

Preliminary descriptive analysis showed that most of the continuous variables were not normally distributed. Only age, HDRS, BDI-II, REY_I and REY_D were. This can be explained by the size and the composition of the sample, as psychiatric patients often display high symptomatic variability.

Regarding homogeneity of variance, Levene's test showed significance for 'suicide attempts' ($p = 0.008$) and for 'occupational' ($p = 0.027$). Welch's correction remained significant only for 'suicide attempts'.

These two data combined clearly show how there are strong differences between the variances in the two groups (males and females) in the 'suicide attempts' variable. For further confirmation, the Chi-squared test (Fisher's exact test) was performed for this variable (being dichotomous and dealing with small samples), which was also found to be significant ($p = 0.038$).

In contrast, Chi-squared for 'comorbidity' and 'suicide attempts' was not significant ($p = 0.326$).

Nonparametric ANOVAs performed controlling for the variable 'sex' were not significant except for the variables 'cognitive' ($p = 0.039$) and 'interpersonal' ($p = 0.042$). However, when the groups were divided by 'suicide attempts', the only significance was found for 'HDRS' ($p = 0.035$). People who have tried to commit an act of suicide have an average score (HDRS: 24.89) higher than those who have never had episodes (HDRS: 22.02).

Because of the differences between the two groups, the point-biserial correlations between the dichotomous variable 'suicide attempt', 'comorbidity' and all other continuous variables were performed separately. The numerical results are shown below in Table 2.

To understand what variables were most predictive of suicide attempt, a logistic regression analysis was performed to express the probability of the occurrence of an event (in this case presence or absence of suicide attempts).

Keeping all other predictor variables constant, the odds of 'suicide attempt' occurring increased by 3.5% (95% CI [1.18, 11.4]) for a one-unit increase in sex, until an increase of 11% if the confidence level is included. In the dataset, '0' is equivalent to male and '1' to female. Also, holding all other predictor variables constant, the odds of 'suicide attempt' occurring increased by 2.16% (95% CI [0.78, 6.24]) for a one-unit increase in 'comorbidity', by 1.08% (95% CI [0.99, 1.21]) for 'cognitive' and by 1.09% (95% CI [0.97, 1.24]) for 'occupational'. Finally, to test the accuracy of the model, a ROC curve was constructed by plotting the true positive rate (TPR) against the false positive rate (FPR). The resulting AUC parameter (area under the curve) is 0.684. A logistic regression model was also conducted by splitting the dataset according to the two sexes, but none of the variables were significant; therefore, data are not reported.

3.2 | Network analysis results

The network analysis conducted on the whole sample (Figure 1, left side) showed that in patients with MDD, there is a separation between the neurocognitive and psychosocial domains (Platania et al., 2023). The latter also includes the two nodes assessing depression: HDRS (Node 7) and BDI-II (Node 8). The demographic variables 'age' (Node 1) and 'years of education' (Node 2), the 'number of previous episodes' (Node 4) and the 'current episode duration' (Node 5) and the 'presence and absence of comorbidity' (Node 6) are all part of the network where the neurocognitive domain is located.

This division is even more pronounced when analysing clusters within the network. The *walktrap* algorithm used reports the presence of three distinct clusters (Figure 1, right side). The first, dark blue, includes all psychosocial, depressive and 'suicide attempts' variables. The second, in green, includes all neurocognitive variables other than memory, comorbidity (treated dichotomously, i.e., absence or presence of comorbidity) and duration of current episode. Finally, a third cluster became evident, in orange, which we named the 'memory cluster'. It includes all neurocognitive memory nodes (Node 11: SPAN_FW, Node 12: SPAN_BW, Node 13: REY_I and Node 14: REY_D) and the number of previous depressive episodes (Node 4).

The network was also well interconnected: density index = 0.277 and number of edges = 64. This suggests that there is suboptimal stability because change in a single node leads to changes that easily spread to the rest of the network (Cramer et al., 2016).

TABLE 1 Demographic and clinical characteristics of the overall sample and of the two subgroups 'males' and 'females'.

	All sample		Males		Females	
Demographics	**Sample**	**Percentage**	**Sample**	**Percentage**	**Sample**	**Percentage**
Sample size	81	100	26	32.1	55	67.9
Mean age	53.2 ± 9.7	\	52.1 ± 9.1	\	53.7 ± 10.1	
Years of education						
Primary school	9	11.1	1	3.8	8	14.5
Secondary school	39	48.1	11	42.3	28	50.9
High school	24	29.6	11	42.3	13	23.6
University and more	9	11.1	3	11.5	6	10.9
Suicide attempt						
Absence	43	53.1	18	69.2	25	45.5
Presence	38	46.9	8	30.8	30	54.5
Comorbility						
Presence	33	40.7	13	50.0	20	36.4
Absence	48	59.3	13	50.0	35	63.6
Previous depressive episodes						
No episodes	11	7.6	4	4.6	7	12.5
1/2 episodes	57	39.6	39	44.8	18	32.1
3/4 episodes	64	45.2	38	43.7	26	46.4
5/5+ episodes	11	7.6	6	6.9	5	8.9
Current episode duration						
<15 days	4	4.9	3	11.5	1	1.8
15 days to 1 month	14	17.3	4	15.4	10	18.2
>1–6 months	44	54.3	11	42.3	33	60.0
7–12 months	12	14.8	6	23.1	6	10.9
>12 months	7	8.6	2	7.7	5	9.1
Single comorbidity						
Social phobia/generalized anxiety	12	36.4	4	30.8	8	40.0
Alcohol abuse	5	15.2	2	15.4	3	15.0
Panic attacks/agoraphobia	3	9.1	1	7.7	2	10.0
Eating disorders/somatoforms	1	3.0	0	0.0	1	5.0
Psycho-affective disorder	1	3.0	0	0.0	1	5.0
More than one comorbidity						
Alcohol abuse + DOC	1	3.0	1	7.7	0	0.0
Alcohol abuse + social phobia	4	12.1	2	15.4	2	10.0
Social phobia + panic attacks	5	15.2	3	23.1	2	10.0
Social phobia + eating disorder	1	3.0	0	0.0	1	5.0
Total	33	100.0	13	100.0	20	100.0

Note: Type and number of comorbidities are also reported.

As for the centrality analysis in Figure 2, when considering 'betweenness', the two nodes with the highest values and thus being the main conduit of information passing within the network are MoCA (Node 9) (1.00) and cognitive (Node 18) (0.55).

In this network nodes assessing depression (BDI-II and HDRS), the presence of comorbidities and suicide attempt nodes do not have a great influence on the network independently. Also, demographic variables such as age, years of education and characteristics of depressive episodes (Nodes 4 and 5) do not have a major effect.

Regarding predictability in the whole sample, our variable of interest, suicide attempts (Node 3) had a percentage of variance explained by the other variables with which it has connections equal to 55,3% (CC = 0.553).

TABLE 2 Point-biserial correlations between ‘suicide attempts’, ‘comorbidity’ and all the other continuous variables in males and females.

	Males	Females	Males	Females
Point-biserial correlations	**Suicide attempt**		**Comorbidity**	
Age	−0.105	−0.139	−0.382	−0.012
Years of education	−0.060	−0.095	0.235	−0.093
HDRS	0.206	0.182	0.026	0.024
BDI	−0.065	0.043	−0.010	−0.029
MoCA	−0.049	0.298	0.008	0.423
FAB	0.074	0.122	−0.169	0.050
SPAN_FW	−0.282	0.235	−0.002	0.342
SPAN_BW	−0.242	0.365	−0.430	0.363
REY_I	−0.115	0.146	0.129	0.089
REY_D	−0.028	0.042	−0.340	0.075
Vocabulary	0.059	0.040	−0.441	0.084
Fluency (FAS)	0.136	0.142	−0.312	0.186
Autonomy	0.067	0.121	−0.190	−0.065
Cognitive	0.171	−0.233	0.387	−0.144
Financial	−0.010	0.132	−0.181	0.284
Interpersonal	0.286	−0.012	0.173	0.136
Occupational	0.096	0.185	0.116	−0.031
Leisure	0.355	0.011	0.078	−0.027

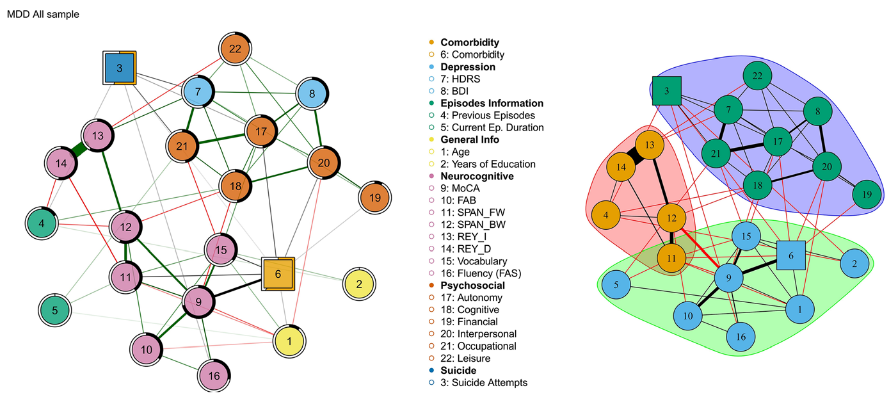

FIGURE 1 Network and clusters obtained by analysing the entire population of patients with MDD. Left side—square nodes: categorical variables; round nodes: continuous variables; lines between nodes: partial correlations between variables (thicker the edge, greater the correlation value); green edges: positive correlations; red edges: negative correlations; black-coloured edges: partial correlations between dichotomous and continuous variables. Around each node, the predictability value was represented by a ring; the blacker the ring, the more predictable the variable by all connected nodes. For dichotomous variables, orange was used. Right side—representation of the clusters identified through the walktrap algorithm. Black edges: intra-cluster connections; red edges: inter-cluster connections.

The situation in predicting the variable ‘suicide attempts’ changes when the two sexes were analysed separately.

3.2.1 | Males network profile

The top part of Figure 3 shows the network for only the group of male patients with major depression. The separation between the two macro-domains (neurocognitive and psychosocial) is more pronounced due to the reduced number of connections (38 edges) and, therefore, the lower density of the network (edge density = 0.164). Some nodes have no connections or very weak ones (Node 1, age, and Node 2, years of education) and cluster analysis led to the division of the graph into multiple clusters occasionally composed of only two variables. The important finding is that the variable ‘suicide attempt’ (Node 3) is more predicted now than in the entire sample: other

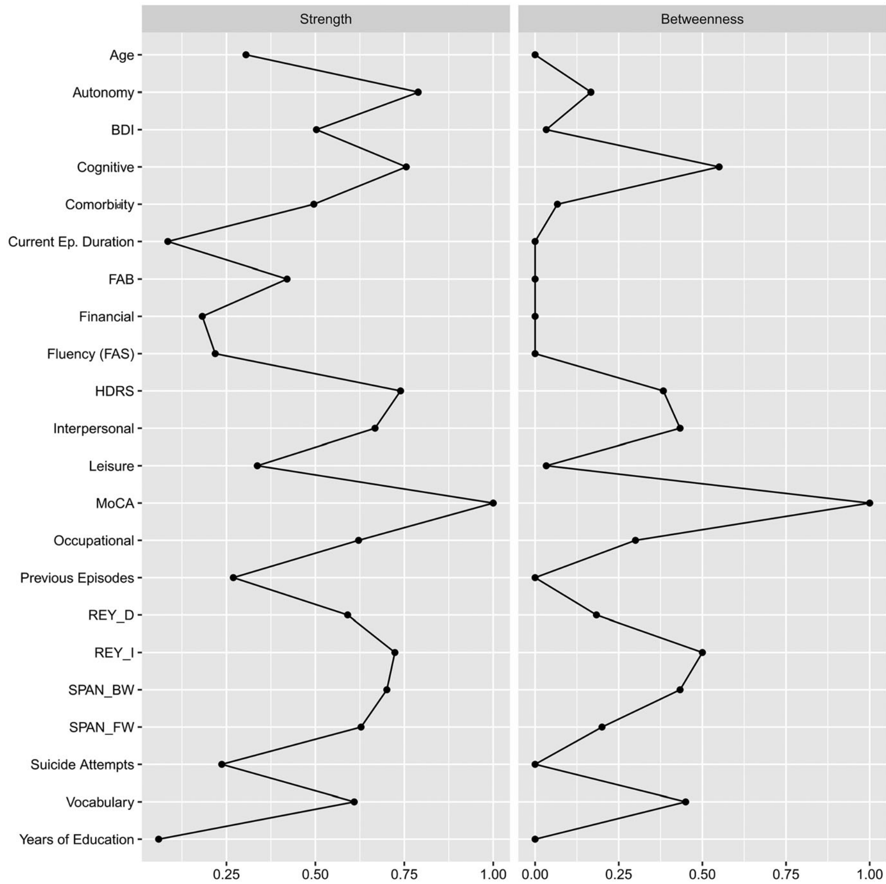

FIGURE 2 Centrality analysis (strength and betweenness) for the network of the whole sample of patients with major depression. Variables were entered in alphabetical order.

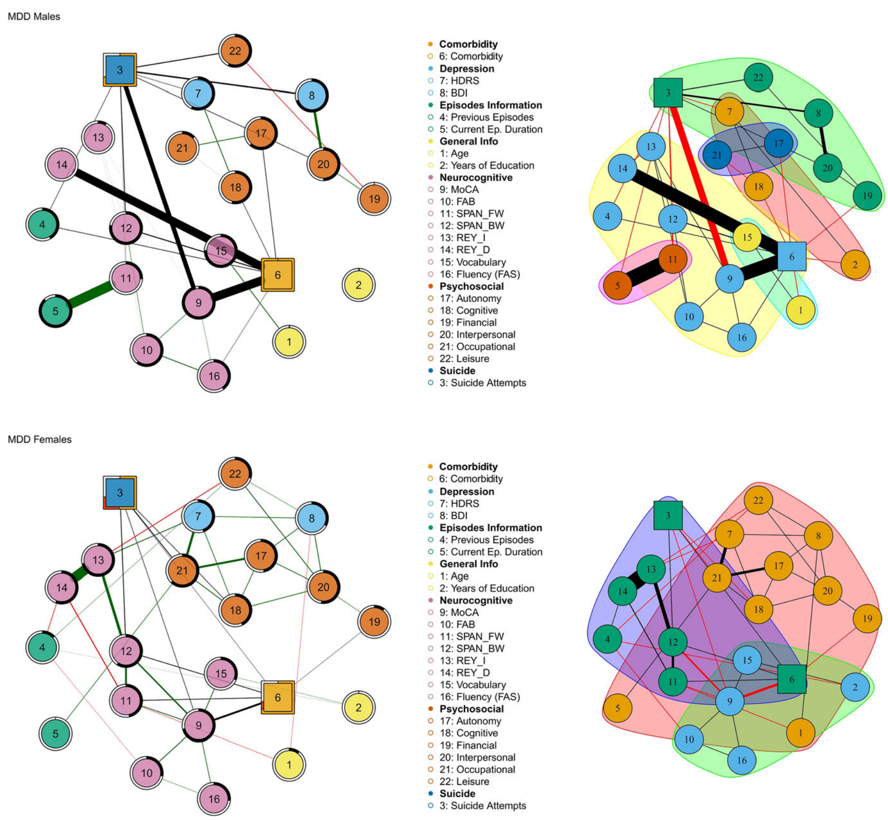

FIGURE 3 Network and clusters obtained by analysing the two sexes separately. The upper half represents the male population; the lower half represents the female population. See Figure 1's caption for graphical legend. In addition, the red part of the ring in dichotomous variables is the additional accuracy achieved by all remaining variables.

variables explain 68% (CC = 0.68) of its variance. Second, although there are still some connections with the neurocognitive cluster (Nodes 11 and 9), most of the correlations are with psychosocial variables and the depressive scales (more with the Beck scale than the Hamilton). Furthermore, the psychosocial variables that are clustered together with suicide attempts (Figure 2, upper right part) are ‘financial’, ‘interpersonal’ and ‘leisure’. The presence or absence of comorbidity in male patients does significantly affect the prediction of a suicide attempt directly although it has a strong hub role in the network along with Node 3 (Figure 4, blue line, Number 6 on the *x* axis).

3.2.2 | Female network profile

The bottom part of Figure 3 shows the network of female patients with MDD. The network more closely reflects the pattern and relationships present in the entire population.

The network is denser and more connected than that of the male population (number of edges = 42; density factor = 0.181). There are no particularly strong connections, and some variables do not contribute to the formation of the graph because they have no connections.

The variable of interest indicating the presence or absence of ‘suicide attempts’ (Node 3) achieves the highest predictivity value (compared to males and the overall population) with a percentage of the variance explained of 70.6% (CC = 0.706), which is rather high.

In addition, the variables that allow this degree of predictivity are completely different from the male population. Looking at the cluster analysis (Figure 3, bottom right part), we observe the same three clusters characteristic of the population as a whole but with some changes. First, the psychosocial cluster (in orange), including the depression scales, has now incorporated the variables ‘age’ (Node 1) and ‘current episode duration’ (Node 5). Second, the neurocognitive cluster (in green) has shrunk to make more room for what we have called the ‘memory cluster’. This cluster now also includes ‘suicide attempts’ and ‘comorbidities’ (Nodes 3 and 6). However, Node 3 also continues to have connections with psychosocial variables, particularly Node 21 (occupational) Node 18 (cognitive) and Node 6 (comorbidity).

The index of ‘betweenness’ shown in Figure 4 (magenta line) shows first that depressive nodes, although remaining with values below 0.4, have a higher centrality than in males. Moreover, the ‘exchange station’ of information in the network, in addition to the ‘MoCA’ node, is represented by the memory-related nodes.

From Figure 4, which compares the analysis of ‘betweenness centrality’ among the three groups, the profiles of males and females are very different from each other in terms of the nodes that have the function of redistributing information.

The highest peaks for males (blue line) are the ‘suicide attempt’ and ‘comorbidity’ nodes while for females (magenta line) the peaks belonging to the neurocognitive domain (MoCA, SPAN-FW/BW, REY-I/D and vocabulary) have more prominence. The nodes that have the most reverberation within the network are precisely the ones best suited to which to direct treatment because the possible benefits/changes are also ‘felt’ by the other nodes with which there are connections.

4 | DISCUSSION

The purpose of our study was to explore the different profiles of suicidal risk in male and female patients suffering from Major Depressive Disorder, providing additional information to optimize treatment and develop preventive targeted strategies. To address this challenge, traditional statistical analyses were completed using the network analysis approach.

First of all, our thesis on the existence of important sex differences in suicide attempts was confirmed, as male and female patients differed significantly and thus support a widely documented phenomenon (Denneson et al., 2020). In more detail, being female increases the odds of suicide attempts, up by 11%. Moreover, having a comorbidity didn't associate with higher suicide attempts, at least, as far as the analyses performed with the described sample are concerned. This last result, seemingly in contrast with the studies mentioned above, can be explained by two limitations of our study design: the relatively small size of the sample and the consideration of comorbidities in a presence/absence perspective only. This hypothesis is further confirmed by another finding of our study: the sole presence of another pathology associated with depression increases the risk of suicide

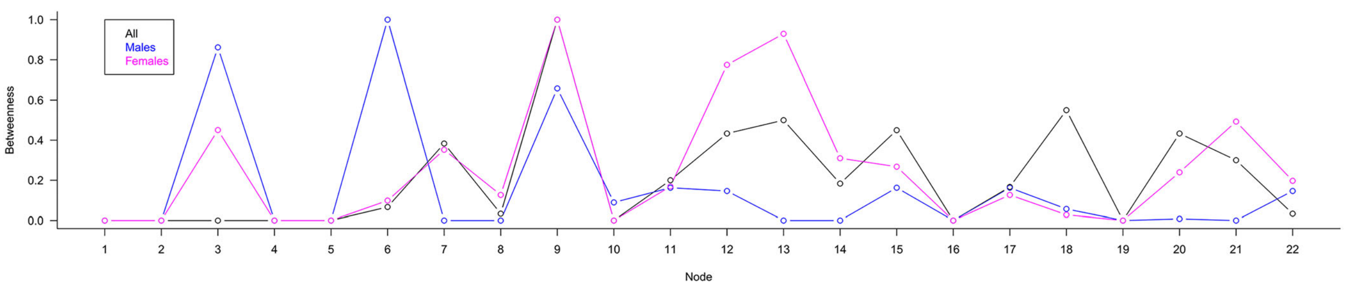

FIGURE 4 Betweenness measures for the three groups (full sample in black, males in blue and females in magenta). The higher the peak of the single variable, the greater the role of that node as a hub in the network.

attempts by 2.16%. Therefore, we can hypothesize that, in this case, the absence of a significant difference in suicide attempts based on comorbidities could be explained by methodological limitations.

Second, suicide attempts are significantly related to the levels of depression: who tried to commit suicide shows higher levels at the Hamilton Depression Rating Scale, and this is observed in both sexes. Focusing on diagnostic protocols, it is interesting to note that HDRS seems to correlate better (Table 2) with the presence of 'suicide attempts' when compared to the BDI-II. This finding can be explained in various ways: several studies demonstrate that HDRS seems to be a psychometric tool more sensitive for MDD, while BDI-II is a more efficient assessment tool for bipolar depression (Carneiro et al., 2015; Guerrera et al., 2023; Hunt et al., 2003; Platania et al., 2023; Rush et al., 1986). This is due to both the different markers of the pathologies and the uneven subjective experience felt by patients, differently represented by the tests (Platania et al., 2020). In fact, the patient's subjective experience of his or her symptoms, which he or she recounts or reports depending on the test or questionnaire used, may also vary depending on the type of questions or the way they are written. Moreover, HDRS is a clinician-rated tool, while BDI-II is a self-report measure. Thus, due to their structure, the tools have different characteristics: the BDI-II score consists of two almost equally represented domains (cognitive and somatic-affective), whereas the HDRS has an under-representation of somatic symptoms, giving instead more emphasis to insomnia, anxiety and other symptoms.

Finally, traditional inferential analysis outlines different profiles of psychosocial impairment for males and females who attempted suicide. Indeed, males who attempted suicide display difficulties in the management of their free time and of their social relationships, while females experience troubles at work and in their ability to perform daily tasks independently. This representation has been extended using network analysis, which provided more in-depth information than the traditional analyses mentioned previously.

In more detail, the network of male patients displays a high level of predictability of suicide attempts, equal to 68%, explained mainly by psychosocial and depressive variables. Note that, in this case, the BDI-II seems to better represent the symptoms of male subjects, showing that although the Hamilton Scale (HDRS) is a more in-depth interview, males are more likely to describe their distress in a self-administered questionnaire. This leads us to hypothesize that it is possible to structure not only a sex-specific preventive treatment for suicide attempts but also a sex-specific diagnostic protocol. Economic difficulties, social isolation and impairment in the management of their free time are the most critical risk factors for males trying to commit suicide, while comorbidities have a connection with many other variables involved in SAR but not in a direct way. Therefore, a targeted intervention for males should promote interpersonal openness to depressive feelings, social support and behavioural activation.

The network of females, instead, displays the highest level of predictability of suicide attempts: 70%. Female patients were characterized by a higher impact of neurocognitive variables in predicting suicide attempts, particularly for those regarding the mnemonic realm, represented by short-term, long-term and working memory related assessment (SPAN-FW, SPAN-BW, REY-I and REY-D). Moreover, different aspects of psychosocial functioning have an important impact on the network, especially the ones related to personal independence (occupational, financial and autonomy). Furthermore, comorbidities are directly connected to suicide attempts. Consequently, here, intervention should focus on supporting the autonomy of female patients with specific training, not only referring to the daily management of external tasks but also focussing on the personal perception of psychic efficiency. Job counselling and treatment of comorbidities should be considered priorities, as well.

4.1 | Limitations

This study has some limitations: first, the numerosity of the entire sample and the fact that the two samples analysed (males and females) are not of equal numbers (though this reflects the general prevalence of major depression in the population). This may lead to a critical interpretation of the results even though the bootstraps of the centrality analyses of the network models were stable (as reported in Section 3). Second, to fully understand and predict SAR, there is a need for further investigations of the impact of other variables such as anxiety, sleep, quality of life, individual's degree of autonomy, resilience and the specific typologies of comorbidities, here treated as dichotomous variables (presence/absence).

5 | CONCLUSION

To conclude, network analysis has allowed us to overcome the limitations of traditional inferential analysis and to describe a more detailed risk profile for SAR in male and female patients. As such, network analysis represents a promising methodology for the creation of targeted diagnostic, treatment and preventive strategies, contributing to enrich the clinical tools available (Castellano et al., 2020). Given that suicide is a major global problem, there is a need for deeper knowledge and the development of efficient prevention methods (Zalar et al., 2018).

The results from this study confirm and expand those of the literature:

1. Network analysis allowed for a richer analysis of the relationships between variables predicting SAR in males and females when simple regression analyses did not yield significant results. The networks showed different interaction patterns in the two sexes that need to be considered when developing individual intervention programmes.
2. Having a history of suicide attempts can increase SAR and can lead to trying to take one's own life. Our analysis shows that people with more attempts have higher scores on depressive scales than those with fewer attempts. In addition, in the global sample and particularly in the network of males, having a history of past depressive episodes predicts SAR compared to females, where the

'suicide attempt' node has no direct connection with that node (4: number of previous episodes).

3. Having one or more comorbidities is a risk factor in attempting suicide in both sexes. It also is a direct predictor for SAR in the overall population but particularly in females because it helps explain part of the variance in the 'suicide attempt' node and is recognized as being part of the 'memory cluster'.

   In males, on the other hand, comorbidity was not a direct predictor of SAR but, by going to influence both neurocognitive and psychosocial variables (it has a very high betweenness centrality), it acts on it indirectly.

Consequently, the need exists to provide individual treatments considering the entire internal and external context in which an individual lives. Enacting suicide attempts exposes the person to repeating such behaviour. Therefore, quick, targeted but at the same time complex interventions that affect as many variables as possible are not only necessary but constitute a responsible choice for specialists.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

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