65

Anxious and depressive symptoms and health-related quality of life in a cohort of

people who recently attempted suicide: a network analysis

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Abstract

Background: Suicide is an international health concern with immeasurable impact from the perspective of human and social suffering. Prior suicide attempts, anxious and depressive symptoms, and relatively lower health-related quality of life (HRQoL) are among the most replicated risk factors for suicide. Our goal was to visualize the distribution of these features and their interconnections with use of a network analysis approach in individuals who recently attempted suicide.

Methods: Individuals with a recent suicide attempt were recruited from nine University Hospitals across Spain as part of the SURVIVE cohort study. Anxious and depressive symptoms, and perceived HRQoL were included in the network analysis. Network structures were estimated with the EBICglasso model. Centrality measures and bridge symptoms connecting communities were explored. Subnetworks comparing younger and older individuals, and women and men were analyzed.

Results: A total of 1,106 individuals with a recent suicide attempt were included. Depressed mood was the symptom with the greatest influence in the overall network, followed by anxiety symptoms such as feeling nervous, worrying, restless, and having difficulties to relax. Perceived general health was associated with increased suicidal ideation in the whole sample. Older people showed a specific connection between perceived general health and depressed mood.

Limitations: The cross-sectional design does not allow determination of established causality.

Conclusions: Depressed mood was the core network's symptom and, therefore, an important target in the management and prevention of suicide. HRQoL had more influence on the network of older populations, in which it should be a primary focus.

Keywords: Suicide; Anxiety; Depression; Health-related quality of life; Prevention; Network analysis

Highlights

- Identifying risk factors for suicide is crucial for developing prevention programs.
- Network analysis allows studying interrelations of symptoms in suicidal behaviors.
- Depressed mood is the core symptom in individuals who recently attempted suicide.

1. Introduction

Suicide is a significant public health concern with devastating effects on individuals and society. It is one of the leading causes of death worldwide, causing approximately 700,000 lives lost each year. One of the goals of the international community is to identify populations at risk of suicide and develop prevention strategies that target suicidal behavior (World Health Organization 2021). Individuals with a history of suicide attempt (SA) represent a highly vulnerable population given that a past SA is the most robust predictor of future suicide (Coppersmith et al., 2023; de la Torre-Luque et al., 2023; Suokas et al., 2001). SA occurs much more frequently than suicide death, with a lifetime prevalence ranging from 0.5% to 5% among adults globally, yet underreporting is common (Nock et al., 2008). Although no validated biomarkers have demonstrated utility in clinical practice (Manchia and Paribello, 2023), various risk factors, including neurobiological (Erlangsen et al., 2020; Miola et al., 2021), sociodemographic (Qin et al., 2003), and clinical factors (Baldessarini, 2020; O'Connor and Nock, 2014; Qin et al., 2003) have been identified, being psychiatric diagnoses major contributors to the risk of suicidal ideation, SA, and suicide death (Chesney et al., 2014; Nock et al., 2010; Salagre et al., 2021). Major depression is the most frequent psychiatric disorder associated to suicide, accounting for half to two thirds of all suicide deaths (Dong et al., 2019; Li et al., 2022; Ribeiro et al., 2018). Even isolated depressive symptoms have been reported to be associated with SAs (Wang et al., 2020). As a result, the U.S. Preventive Services Task Force suggests suicide risk assessment should always be conducted in the context of depression screening (LeFevre, 2014). Furthermore, anxiety has been significantly associated with an increased suicide, both when occurring in the context of major depression and when considered independently (Hawton et al., 2013; Stanley et al., 2018).

Suicide prevention strategies can be conceptually classified as direct interventions, which involve immediate and targeted actions for individuals at imminent risk, and indirect interventions, which focus on broader strategies targeting risk factors and promoting mental well-being in the population (Torok et al., 2020). Effective indirect interventions in suicide prevention include those targeting psychiatric conditions such as depression, anxiety, as well as those aimed at improving health-related quality of life (HRQoL) (Meerwijk et al., 2016). HRQoL encompasses physical, mental, and social aspects of well-being and functioning, serving as an important indicator of disease burden (Bullinger, 2002), with a bidirectional relationship with suicide. Thus, individuals with poorer HRQoL may be prone to suicidal behaviors, particularly among young people (Le et al., 2023). Furthermore, individuals who have attempted suicide generally exhibit significantly lower HRQoL compared to those who have not, beyond what could be accounted for by anxiety and depression symptoms (Fairweather-Schmidt et al., 2016), potentially perpetuating and exacerbating the

individual's vulnerability to suicidal behaviors. Other factors related to suicide are age and sex.
Generally, suicide is most common among men between the ages of 15 and 35 years (Knipe et al., 2022). While death by suicide is more prevalent among males, females have a higher prevalence of SAs, which is associated with a significant health-service utilization and higher public health cost.
Additionally, the risk of a SA becoming lethal increases with age (Miranda-Mendizabal et al., 2019).

Given the complex nature of suicide, involving various interacting factors (e.g., sociodemographic, psychiatric, and quality-of-life-related), understanding the interactions among these aspects is crucial for developing interventions that reduce the burden of suicide on individuals and society (Oliva and De Prisco, 2022). Network analysis is a statistical method that is based on the concept that the condition under investigation can be explained in part by the interaction of factors placed in a network (Borsboom, 2017). This analysis proved value in visualizing and understanding situations characterized by the involvement of multiple factors (Corponi et al., 2020; Scott et al., 2020), although limited by the impossibility of including all relevant factors to a given condition (Neal et al., 2022). It has been previously used in the field of suicide, with clinically useful and consistent results. Shiratori et al. examined reasons for suicide and found that depression and physical illness were among the most important reasons (Shiratori et al., 2014). Gijzen et al. focused on suicide ideation in adolescents with depression, identifying loneliness as the most important factor subserving suicidal ideation in this population (Gijzen et al., 2021). Schönfelder et al., 2021).

The aim of this study was to identify the interrelation among anxious and depressive symptoms that individuals who recently attempted suicide present after the attempt, and their connection to perceived HRQoL using a network analysis approach. Sub-analyses will also consider the impact of sex and age on the characteristics of SAs within the sample.

2. Methods

2 2.1. Participants

We analyzed baseline data from a national multisite cohort study conducted on individuals over 18 years old with a recent SA (within the last 10 days, as per the study protocol). Recruitment was done across nine University Hospitals across Spain, as part of the "The Suicide Prevention and Intervention Study" (SURVIVE) project (Pérez et al., 2020). Participants were fully informed about the objectives and procedures of the study prior to providing consent. SAs were self-reported, extracted from medical records or reports of emergency responders and law enforcement agencies, depending on the individual case. Intentionality and lethality of the SAs were recorded according to the Columbia Suicide Severity Rating Scale (C-SSRS). Further details on the study are available elsewhere (Pérez et al., 2020).

2.2 Variables assessment

2.2.1. Sociodemographic and clinical assessment

Sociodemographic variables included age, sex, working status (student, employed, unemployed, retired), and educational level (no education, elementary school, middle school, high-school, or higher).

Regarding clinical variables the Mini-International Neuropsychiatric Interview (MINI) (Sheehan et al., 1998) was used by a clinicians to assess the presence of current or lifetime psychiatric disorders among the participants. Among others, patients completed three scales we used for the network analysis: a) the General Anxiety Disorder Scale (GAD-7) (Spitzer et al., 2006) that assesses the self-reported worry and anxiety symptomatology of the past two weeks. Each item considers the frequency of the anxiety symptoms on a scale ranging from 0 (not at all) to 3 (nearly every day); b) the Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001) that evaluates the self-reported depressive symptom on a scale ranging from 0 (not at all) to 3 (nearly every day); and c) the EuroQoL-5D (Badia et al., 1999) that appraises the self-reported HRQoL organized in five dimensions. In addition, it also provides a visual analogue scale which corresponds to the current state of the overall subject's health, ranging from 0 (worst imaginable health state) to 100 (best imaginable health). Since anxious and depressive symptoms were comprehensively screened by PHQ-9 and GAD-7, the fifth item of the EuroQoL-5D ("anxiety/depression") was not included in our analyses.

2.3 Statistical Analyses

All analyses were conducted with RStudio, R version 4.1.2 (R Core Team, 2020).

2.3.1 Missing data

The R package "skimr" (Elin Waring, 2021) was used to inspect missing data. Missing data were imputed by using the R package "missRanger" (Mayer and Mayer, 2019). The parameter "num.trees" was set at 5,000, and the out-of-bag errors ranging from 0 (better performance) to 1 (worse performance) were calculated for each variable to measure accuracy, as in previous work (Fico et al., 2023).

2.3.2. Description of the sample and univariate analyses

Normal distribution was assessed for socio-demographic and clinical variables by adopting the Shapiro-Wilk normality test (Royston, 1982). In case of normal distribution, two-sample t-test was used to study age-related and sex-group differences. In case of not-normal distribution, the Mann-Whitney-Wilcoxon test was used instead. To compare categorical variables, the chi-squares test was employed. Significance was set at p<0.05 after adjusting p-values to Bonferroni correction for multiple comparisons.

2.3.3 Network Analysis

A network analysis was performed to explore the relationships between anxiety symptomatology (GAD-7), depressive symptomatology (PHQ-9), and HRQoL (EuroQoL-5D) in a sample of adults with a recent SA. To explore the role of age and sex on these relationships, the sample was divided according to the median-age and sex. Since data did not follow a normal distribution, a nonparanormal transformation of the data was applied before the network estimation (Epskamp et al., 2018). An optimal regularization parameter was selected to control for spurious connections in the network estimation criterion (EBIC) (Chen et al., 2008) to control for spurious connections in the network estimation. Network structures were estimated using Gaussian Markov random field (Costantini et al., 2015) with the EBICglasso model. A threshold was also used to remove edges not surviving p-value <0.05.

In the network, each node represents a variable and each edge the bidirectional and undirected correlation between a pair of nodes. Stronger correlations are represented by thicker and more saturated edges; blue and red edges indicate positive and negative partial correlations, respectively. Network centrality measures (Bringmann et al., 2019) of expected influence, betweenness, and closeness of different nodes were calculated (Epskamp et al., 2018; Epskamp and Fried, 2018). We defined the expected influence as the sum of all edges extending from a given node while maintaining

the sign of each edge (Robinaugh et al., 2016). Betweenness is the number of times a node lies within the shortest path between two other nodes (Brandes, 2001). Closeness is the inverse of the average shortest path length between two nodes, and measures how close a symptom is linked to other symptoms (Rubinov and Sporns, 2010). One- and two-steps bridge expected influence was used to explore the connectivity between specific communities in the network; it is defined as the sum of the value of all edges between a node and all nodes that are not in the same community (Jones et al., 2021).

The accuracy of edge weights was measured by the 95% confidence intervals (CIs) computing by bootstrapping (Efron, 1992). The stability of centrality indices was quantified using a casedropping bootstrap procedure, and the correlation stability coefficient (CS-coefficient) between centrality indices for the full sample was calculated. CS-coefficient represents the maximum proportion of cases that can be dropped, such that with 95% probability the correlation between the original centrality indices and centrality of networks based on subsets is 0.7.

To examine whether network structure changes considering age-difference and sex-groups, we separately assessed differences in network structure, global strength, and significant edges in both groups. Statistical significance was evaluated by a p-value <0.05.

The "bootnet" R package (Epskamp et al., 2018) and "qgraph" R package (Epskamp et al., 2012) were used to assess the network estimation and accuracy. Network comparison was conducted by "Network Comparison Test" R package (Van Borkulo et al., 2022).

3. Results

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3.1 Characteristics of the sample

A total of 1,106 individuals with recent SA were included in the analyses. Table 1 provides information about the socio-demographic and clinical characteristics of the whole sample. The mean total score of the PHQ-9 was 17.5 ± 6.2 , in line with moderate to severe depression (Kroenke et al., 2001); the mean GAD-7 total score was 12.4 ± 5.2 , in line with moderate severity of anxiety (Spitzer et al., 2006). The most prevalent psychiatric diagnoses were major depressive disorder (57.9%) and anxiety disorders (41.6%).

Socio-demographic and clinical differences based on age and sex are presented in Table S1 and S2 in the Supplementary material. Since the distribution of variables was not normal, the Mann-Whitney-Wilcoxon test was used.

3.2 Missing Data

Among the variables presenting missing data, all of them presented less than 2% of missing values. Errors estimated during the imputation of missing data were less than 10%.

3.3 Network structure of the total sample

3118 32 3319 The network estimated using all cases (n = 1,106) and including 13 variables is presented in Figure 1 and detailed in the weight matrix (Supplementary materials, Table S3). Information relative to the 34 3520 centrality measures is depicted in Figure 2. Specifically, the PHQ-9 item "Depressed mood" presented 36 37 38 39 40 39 40 3 40 3 41 42 4 3 42 5 42 6 47 27 consistently high centrality measures. The GAD-7 items "Feeling nervous", "Worrying", "Restless", and "Trouble relaxing" followed "Depressed mood" in terms of expected influence, but not in terms of betweenness and closeness. The GAD-7 items "Worrying" and "Restless", and the PHQ-9 items "Motor changes" and "Depressed mood", were the variables that better connected the different communities of the network as denoted by the one- and two-steps bridge expected influence (Figure 3). The HRQoL community was exclusively linked to other communities through the EuroQoL-5D item "General Health", specifically establishing a connection with the community related to 4928 50 depressive symptoms. This connection was characterized by a negative correlation, particularly in 5129 52 relation to the "Suicidal thoughts" item. Bootstrapping indicated good accuracy and stability with 5330 narrow confidence intervals for edge weights and stable centrality estimates for expected influence, 54 5531 while betweenness and bridge expected influence appeared unstable (CS (cor = 0.7) = 0.95) 56 5*7*32 (Supplementary materials, Figure S1, S2, S3).

3.4 Network comparisons

Networks comparing patients according to median age (41.5) did not differ in both network structure (p=0.69) or global strength (p=0.23). The network structures and individual edges differences are reported in Figure S4 in the Supplementary material. Mainly, the HRQoL community exhibited a correlation with the depressive symptom community only in older patients, while remaining separate in young patients. Specifically, the EuroQoL-5D item "General Health" showed a significant negative correlation with the PHQ-9 item "Depressed mood" (p=0.02). Networks comparing patients according to sex did not differ in both network structure (p=0.17) or global strength (p=0.63). The network structures and individual edges differences are reported in Figure S5 in the Supplementary material. The edge connecting the GAD-7 items "Feeling nervous" and "Restless" (p<0.001) was significantly greater in males.

4. Discussion

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The present study explored the interrelationship between self-reported anxious and depressive symptoms experienced by individuals with a recent SA and the interconnection with perceived HRQoL using a network analysis approach. The core symptom within the network was "Depressed mood", followed by anxious symptoms of "Feeling nervous", "Worrying", "Restless", and "Trouble relaxing". The foregoing depression- and anxiety-related symptoms are more important than others in maintaining the structure and properties of the network. Furthermore, the study reveals a negative correlation between perceived "General health" and "Suicidal thoughts," indicating that a decline in perceived general health is associated with an increase in suicidal ideation. Only among older individuals, a worse perceived "General health" is correlated with more severe "Depressed mood".

The first community observed in the network contains depressive symptoms as measured by PHQ-9. Among all factors in the network, "Depressed mood" exhibits the highest values of both betweenness and closeness, indicating its significant influence. The centrality of this node is consistent with findings from other studies that have adopted a network approach to study depressive and anxious symptoms in populations with major depression (Kaiser et al., 2021; Shen et al., 2022) or various psychiatric diagnosis (Beard et al., 2016). It is worth noting that our population was made of individuals with at least one SA, and that more than half of the analyzed sample had a lifetime diagnosis of major depression. From a neurobiological point of view, depression and suicidal behaviors share many aspects, such as an increase in markers of inflammation, alterations in serotonin systems, as well as changes in the functioning of the hypothalamic-pituitary-adrenal axis (Erjavec et al., 2021; Wisłowska-Stanek et al., 2021). Notably, in the network, the item "Suicidal thoughts" exhibits its strongest correlation with the item "Depressed mood", underscoring the crucial relationship between suicidal ideation and depression, as depression is the psychiatric disorder most associated with suicidal ideation (Ribeiro et al., 2018). To the best of our knowledge, this study represents the first report of this association in a sample of patients who were not primarily recruited based on their diagnosis but rather based on a previous SA. This highlights the importance of intervening in depressive mood to prevent suicidal ideation. Nevertheless, existing evidence reveals that a substantial proportion of individuals with depression reported not receiving adequate forms of assistance within the preceding year (Anmella et al., 2022; Gabilondo et al., 2011). These findings underscore the need to develop suicide prevention strategies that focus on depressed mood to target suicidal ideation a part from intervention focused on anxiety and impulse-control and substance use disorder (Nock et al., 2009; Nock et al., 2010). Such strategies should encompass both public health initiatives (McLaughlin, 2011; Roberto et al., 2023) and new interventions that leverage modern technologies, which are showing effective, albeit preliminary, results in the detection of suicide risk

(Anmella et al., 2023). In addition, our findings hold significance in terms of early interventions for individuals who have recently attempted suicide. Enhancing the post-suicide attempt treatment received by individuals is a key strategy for reducing suicides and suicide attempts. In fact, the immediate period following discharge from the hospital is particularly high-risk (Demesmaeker et al., 2022). Among patients who died by suicide, 15%-20% did so on the day of discharge, and 43% of those who died by suicide post-discharge did so within the first month (Shand et al., 2018). The persistence of depressive mood makes it one of the most important therapeutic targets for indirectly reducing the early risk of further attempts.

The other main community in our network is linked to anxiety symptomatology, with some GAD-7 items having a slightly lower importance than "Depressed mood" item. Anxiety disorders have been previously associated with SA (Nepon et al., 2010; Nock et al., 2009; Nock et al., 2010), and symptoms like "Feeling nervous", "Worrying", "Restless" and "Trouble relaxing" have been strongly correlated with both suicide planning and attempt (Heinz et al., 2020), or proposed as mediators of suicidal behavior (Kearns et al., 2022). Considering the importance of depressive and anxious domains in sustaining the overall symptomatology, the identification of nodes that act as bridges between these two dimensions becomes crucial. In our analysis, two items from the GAD-7 scale, namely "Worrying" and "Restless," along with two items from the PHQ-9, namely "Motor changes" and "Depressed mood", emerge as notable connectors between both communities. The bridging role of depressed mood (Beard et al., 2016; Cai et al., 2022), worry (Beard et al., 2016; Cai et al., 2022), and restlessness (Kaiser et al., 2021) has been previously documented in clinical and non-clinical populations, which is consistent with our findings in the current sample. It is noteworthy that all four items demonstrate a similar level of importance in connecting the two communities. Change in psychomotor function has been associated with the occurrence of SA (Rogers et al., 2016), and our study suggests that this association persists in the immediate aftermath of such events. Likewise, excessive worry may serve as a coping mechanism to mitigate or alleviate negative emotions (Schoenleber et al., 2014). However, it is important to acknowledge that our analysis did not incorporate the directionality of relationships between different nodes, rendering these speculations theoretical. Future investigations could thoroughly analyze the foregoing aspects by employing methodologies that consider the directionality of associations or by utilizing digital tools capable of capturing more precise measurements pertaining to the physical manifestations of these The final community within our network is associated with perceived HRQoL, and symptoms. among all the items, only "Suicidal thoughts" display a non-zero correlation with it. Specifically, "Suicidal thoughts" serves as a bridge between depressive symptomatology and perceived "General health". These two items are negatively correlated, a worsening in perceived general health is associated with increased suicidal ideation. Consistently, studies conducted on both selected population samples and randomly selected community populations found that poorer HRQoL was associated with higher increased likelihood of experiencing suicidal ideation (Fairweather-Schmidt et al., 2016; Farabaugh et al., 2012). Additionally, a case–control study revealed that the HRQoL of adults who attempted suicide was significantly lower than that of matched controls (Kumar and George, 2013). Moreover, the findings from a longitudinal epidemiological study indicated that baseline self-reported life dissatisfaction among adults was linked to a higher risk of suicide death over a 20-year follow-up period (Koivumaa-Honkanen et al., 2001). Consequently, interventions targeting the HRQoL, particularly in terms of general health, may have an impact on mitigating suicidal ideation.

Finally, we compared two different sub-networks based on age and sex and no statistically significant differences were found. Interestingly, the association between "Depressed mood" and "General health" appeared significant only in older people, further supporting the evidence that poor physical health is a risk factor for depression in this population (Maier et al., 2021), although the directionality of the association cannot be assumed from our model. Our results suggest that addressing general health should be one of the first targets to be considered in the management of depressive symptoms. Notably, it is worth considering the potential impact of loneliness within these contexts. Loneliness is known to be prevalent among older individuals (Domènech-Abella et al., 2017), and it has been linked to both poor physical health (Freak-Poli et al., 2021; Holt-Lunstad et al., 2015) depressive symptoms (Erzen and Çikrikci, 2018), poor clinical psychiatric outcomes (Oliva et al., 2022), reduced HRQoL (Park et al., 2020), and suicidality (McClelland et al., 2020). Therefore, addressing loneliness and fostering social connections may play a crucial role in improving general health, reducing depressive symptoms, and ultimately mitigating the risk of suicide in older individuals. Furthermore, although previous studies analyzing prevention outcomes in subgroups of patients in relation to their gender showed no differences between women and men (Krysinska et al., 2017), our analysis revealed that the association between "Feeling Nervous" and "Restless" appears to be stronger in men. Interventions for men should focus on the aspects of agitation and tension, given their higher risk of suicide death (Liotta et al., 2015).

The present work presents several strengths. First, it focuses on a large national sample of adults who have recently attempted suicide; second, our model is based on a population affected by different types of psychiatric disorders, and such heterogeneity may allow us to better observe the general aspects of suicide as a transdiagnostic entity (Oliva and De Prisco, 2022). However, several limitations must be considered to better interpret the data presented. First, although the interview was

conducted shortly after the SA, the two time points differed based on the needs of each patient to assume clinical stability needed to talk about the event. Delays in data collection may have weakened the relationship between current and past symptoms, resulting in generally small associations. Second, the specific symptoms analyzed and discussed in this paper are much more complex than those that can be captured by a 4-Likert scale, and for this reason the representation in our network necessarily represents a simplification. However, both the PHQ-9 and the GAD-7 scales have been widely used in a variety of clinical and non-clinical settings and have demonstrated good psychometric properties (Kroenke et al., 2001; Löwe et al., 2008). Third, it was not possible to control for the effects of current or past medications and their doses, as in most studies of this kind (De Prisco and Oliva, 2023; Ilzarbe and Vieta, 2023; Oliva et al., 2023). However, in emergency situations, the physician is often required to make certain decisions even without complete knowledge of the patient's medical and pharmacological history, so our model represents a situation very close to the real world. Fourth, the betweenness and bridge-expected influence centrality measures were somewhat unstable after bootstrapping the case-dropping subsets. However, the expected influence remained stable after bootstrapping. Fifth, the cross-sectional nature and lack of directionality in the connections do not allow us to understand any cause-and-effect relationships, an aspect that future studies should investigate further using cohorts and longitudinal designs (Vieta and Angst, 2021). Sixth, our analysis did not consider all possible mental health conditions that showed stronger relationships with the emergence of suicidal behaviour, such as PTSD, OCD and externalizing disorders (Batterham et al., 2018; Nock et al., 2009). Seventh, the HRQoL encompasses at the same time physical, mental, and social aspects of well-being and functioning, so it may not have captured the specific aspects of quality of life related to mental health. However, our specific aim was to capture the broad relationships between psychopathology and general health status. Eighth, it was not possible to account for the severity of SAs. Finally, it is critical to emphasize that identifying risk factors for suicide is a separate endeavor when compared to identifying factors that have predictive utility and are modifiable (McIntyre et al., 2021).

5. Conclusions

In a population of patients with at least one SA, depressed mood emerged as the core network's symptom, followed by anxiety symptoms such as feeling nervous, worrying, restless, and trouble in relaxing. Notably, depressed mood had the strongest correlation with suicidal ideation. These findings might give some guidance on the strategies to be implemented in the prevention of suicide. Addressing and preventing depressed mood might have a cascading effect on related dimensions such as anxiety and HRQoL. Perceived general health was directly linked to suicidal ideation. This highlights the importance of interventions targeting general health in suicide prevention efforts. Notably, in older population, a significant correlation was found between general health and depressed mood. Therefore, it becomes crucial to address both mental and physical health aspects to effectively reduce the risk of suicide.

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Conflict of interest

IG has received grants and served as consultant, advisor or CME speaker for the following identities: ADAMED, Angelini, Casen Recordati, Esteve, Ferrer, Gedeon Richter, Janssen Cilag, Lundbeck, Lundbeck-Otsuka, Luye, SEI Healthcare, Viatris outside the submitted work. She also receives royalties from Oxford University Press, Elsevier, Editorial Médica Panamericana.

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The rest of authors have no conflict of interest to declare.

Data Availability Statement

The data used in this study are not publicly available due to privacy and confidentiality restrictions. Access to the data can be requested through a formal data access process or collaboration with the SURVIVE group.

CRediT authorship contribution statement

Vincenzo Oliva: Visualization, Data curation, Conceptualization, Methodology, Formal analysis, Software, Writing - original draft. Natalia Roberto: Visualization, Data curation, Writing - original draft. Jorge Andreo-Jover: Writing - review & editing. Teresa Bobes: Writing - review & editing. Manuel Canal Rivero: Writing – review & editing. Anabel Cebriá: Writing – review & editing. Benedicto Crespo-Facorro: Writing - review & editing. Alejandro de la Torre-Luque: Writing review & editing. Marina Díaz-Marsá: Writing - review & editing. Matilde Elices: Writing review & editing. Verónica Fernández-Rodrigues: Writing - review & editing. Ana Gonzalez-Pinto: Writing - review & editing. Angela Palao Tarrero: Writing - review & editing. Iván Pérez-Diez: Writing – review & editing. Beatriz Rodríguez-Vega: Writing – review & editing. Miguel Ruiz-Veguilla: Writing - review & editing. Pilar A. Saiz: Writing - review & editing. Elisa Seijo-Zazo: Writing - review & editing. Alba Toll-Privat: Writing - review & editing. Roger S. McIntyre: Writing - review & editing. Eduard Vieta: Conceptualization, Supervision, Writing review & editing. Iria Grande: Visualization, Data curation, Conceptualization, Methodology, Supervision, Writing - review & editing. Víctor Pérez-Solà: Visualization, Data curation, Conceptualization, Methodology, Supervision, Writing – review & editing. The SURVIVE group: Data collection.

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62

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Table 1. Sociodemographic and clinical characteristics of the sample

Abbreviations: EuroQoL-5D – European Quality of Life-5 Dimension; GAD-7 - General Anxiety Disorder-7; PHQ-9 - Patient Health Questionnaire-9.

Figure 1: Graphical representation of the estimated network model. Blue nodes represent depressive symptoms measured with the PHQ-9 scale, green nodes represent anxiety symptoms measured with the GAD-7 scale, and pink nodes represent the health-related quality of life measured with the EuroQoL-5D scale. Blue links indicate positive effects and red links negative effects. The edge thickness represents the strength of the association between symptom nodes.

Abbreviations: EuroQoL-5D – European Quality of Life-5 Dimension; GAD7 - General Anxiety Disorder-7; PHQ9 - Patient Health Questionnaire-9.

Legend: ANH - Anhedonia; DEP - Depressed mood; SLE - Sleep problems; LOE - Lack of energy; APP - Appetite changes; GUI - Feeling guilty; CON - Difficulty in concentration; MOT - Motor changes; SUI - Suicidal thoughts; NER - Feeling nervous; SWO - Not able to stop worrying; WOR -Worrying; REL - Trouble relaxing; RES - Restless; IRR - Irritability; AFR - Feeling afraid; MOB -Mobility; CAR - Self-care; ACT - Usual activities; PAI - Pain/discomfort; HEA - General health.

Figure 2. Centrality Plots for EBICglasso network depicting the expected influence, betweenness and closeness of each node (variable).

Legend: ANH - Anhedonia; DEP - Depressed mood; SLE - Sleep problems; LOE - Lack of energy; APP - Appetite changes; GUI - Feeling guilty; CON - Difficulty in concentration; MOT - Motor changes; SUI - Suicidal thoughts; NER - Feeling nervous; SWO - Not able to stop worrying; WOR -Worrying; REL - Trouble relaxing; RES - Restless; IRR - Irritability; AFR - Feeling afraid; MOB -Mobility; CAR - Self-care; ACT - Usual activities; PAI - Pain/discomfort; HEA - General health.

Figure 3. Estimates of One-step and Two-step Expected Influence of the Network of the total sample.

Legend: ANH - Anhedonia; DEP - Depressed mood; SLE - Sleep problems; LOE - Lack of energy; APP - Appetite changes; GUI - Feeling guilty; CON - Difficulty in concentration; MOT - Motor changes; SUI - Suicidal thoughts; NER - Feeling nervous; SWO - Not able to stop worrying; WOR -Worrying; REL - Trouble relaxing; RES - Restless; IRR - Irritability; AFR - Feeling afraid; MOB -Mobility; CAR - Self-care; ACT - Usual activities; PAI - Pain/discomfort; HEA - General health. Click here to access/download;Figure (300 dpi and editable format);Figure1 - Netgraph.pdf







Click here to access/download:Figure (300 dpi and ± editable format);Figure 3 - Bridge.pdf



		N=1106		
		N/Mean (%/SD)		
Age		41.01 (15.7)		
Sex				
-	Female	776 (70.2)		
Educational level				
-	No education	45 (4.1)		
-	Elementary school	186 (16.8)		
-	Middle school	562 (51.0)		
-	High school or higher	311 (28.1)		
Working status				
-	Unemployed	324 (29.3)		
-	Employed	429 (38.8)		
-	Student	127 (11.5)		
-	Retired	226 (20.4)		
PHQ-9				
-	1 - Anhedonia	1.93 (1.1)		
-	2 - Depressed mood	2.20 (0.9)		
-	3 - Sleep problems	1.99 (1.1)		
-	4 - Lack of energy	2.23 (0.9)		
-	5 - Appetite changes	1.88 (1.1)		
-	6 - Feeling guilty	2.17 (1.0)		
-	7 - Difficulty in concentration	1.82 (1.1)		
-	8 - Motor changes	1.48 (1.1)		
-	9 - Suicidal thoughts	1.78 (1.1)		
-	Total	17.5 (6.2)		
GAD-7				
-	1 - Feeling nervous	1.96 (1.0)		
-	2 - Not able to stop worrying	1.91 (1.0)		
-	3 - Worrying	2.08 (1.0)		
-	4 - Trouble relaxing	2.09 (1.0)		
-	5 - Restless	1.41 (1.1)		
-	6 - Irritability	1.65 (1.1)		
-	7 - Feeling afraid	1.29 (1.2)		
-	Total	12.4 (5.2)		
Euro	oQoL-5D			
-	1 - Mobility	1.52 (0.9)		
-	2 - Self-care	1.50 (0.9)		
-	3 - Usual activities	2.18 (1.3)		
-	4 - Pain/discomfort	2.39 (1.2)		
-	General Health	46.4 (23.9)		
Psychiatric diagnosis				
-	Major depressive disorder	641 (57.9)		
-	Anxiety disorders	460 (41.6)		
-	Alcohol use disorder	176 (15.9)		
-	Substance use disorder	128 (11.6)		

Table 1. Sociodemographic and clinical characteristics of the sample

-	Post-traumatic stress disorder	122 (11.0)
-	Eating disorders	102 (9.2)
-	Obsessive compulsive disorder	53 (4.8)
-	Bipolar disorder I	34 (3.1)
-	Other psychotic disorders	26 (2.3)
-	Bipolar disorder II	15 (1.3)
-	Schizophrenia	13 (1.2)

Abbreviations: EuroQoL-5D – European Quality of Life-5 Dimension; GAD-7 - General Anxiety

Disorder-7; PHQ-9 - Patient Health Questionnaire-9.